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VII. Türkiye *in vitro* Diagnostic (IVD) Symposia: Inflammation 27-29 April 2022 Izmir

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İÇİNDEKİLER

INVITATION

Dear Colleagues,

We invite you to the 7th Turkey in vitro Diagnostics (IVD) Symposium with the theme of "INFLAMMATION", which we will traditionally hold online between April 27-29, 2022, as the Izmir Branch of the Turkish Biochemical Society.

While many factors such as trauma, stress, infectious agents, smoking, alcohol use, autoimmune diseases, and radiation exposure trigger the inflammatory process, conditions such as excessive weight, sedentary life, unhealthy diet can also cause inflammation. Inflammation is one of the self-protection reactions of the organism and is at the forefront of the common working areas of all health-related disciplines.

Details on “Inflammation” in this symposium; we aim to review the clinic together from the foundations, to increase the quality of knowledge and experience of our young colleagues who participate, and to evaluate the latest information and data together with speakers who are competent in their fields, as in previous years.

Dear colleagues, the symposium was attended by research assistants, experts and faculty members from "all disciplines" who conduct scientific studies on "symposium topics", university undergraduate and graduate students in the field of health, and scientists interested in the subject, stakeholders engaged in production and importation related to the subject. We are waiting for our industrialists and companies.

All oral and poster papers that will be accepted to the symposium scientific program as a result of the evaluations of the scientific advisory board will be published in the special supplement of the Turkish Journal of Biochemistry indexed within the scope of SCI-Expanded, and it will be possible to publish the full texts of the selected oral papers in the same journal.

"Research Awards" will be given to the studies to be selected by the referee committee from the oral or poster papers presented at the symposium.

You can follow all the developments regarding the VII.Turkey in vitro Diagnostics Symposium on our page www.ivd2022.org.

We invite you to the symposium with our sincere love and respect.

Prof. Dr. Dogan YUCEL
Chairman of the Board
Honorary President of the Symposium

Prof. Dr. Hilal KOCDOR
Head of TBD Izmir Branch
Symposium Chair

DAVET

Değerli Meslektaşlarımız,

Sizleri, Türk Biyokimya Derneği İzmir Şubesi olarak gelenekselleştirdiğimiz, 27-29 Nisan 2022 tarihleri arasında çevrimiçi olarak gerçekleştireceğimiz "İNFLAMASYON" temalı VII. Türkiye *in vitro* Diyagnostik (IVD) Sempozyumu'na davet ediyoruz.

Travma, stres, enfeksiyon etkenleri, sigara, alkol kullanımı, otoimmün hastalıklar, radyasyon maruziyeti gibi pek çok etken inflamatuar süreci tetiklerken, aşırı kilo, hareketsiz yaşam, sağlıksız beslenme gibi durumlar da inflamasyona yol açabilir. İnflamasyon, organizmanın kendini koruma reaksiyonlarından biridir ve sağlıkla ilgili tüm disiplinlerin ortak çalışma alanlarının başında yer alır.

Bu sempozyumda "İnflamasyon"la ilgili ayrıntıları; temelden kliniğe beraberce gözden geçirmeyi, katılım yapan genç meslektaşlarımızın bilgi ve deneyim kalitesini yükseltmeyi, geçtiğimiz yıllarda olduğu gibi en yeni bilgi ve verileri, alanında yetkin konuşmacılarla birlikte değerlendirmeyi amaçlıyoruz.

Değerli meslektaşlarım, sempozyuma, "sempozyum konu başlıkları" ile ilgili bilimsel çalışmalar yapan "tüm disiplinlerden" araştırma görevlisi, uzman ve öğretim üyesi meslektaşlarımızı, sağlık alanındaki üniversite lisans, lisansüstü öğrencilerimizi ve konuya ilgi duyan bilim insanlarını, konu ile ilgili üretim ve ithalat yapan paydaş sanayici ve firmalarımızı bekliyoruz.

Sempozyum bilimsel programına, bilimsel danışma kurulunun değerlendirmeleri sonucunda kabul edilecek tüm sözel ve poster bildiriler, SCI-Expanded kapsamında indekslenen Turkish Journal of Biochemistry dergisinin özel ekinde yayımlanacak, yine aynı dergide seçili sözel bildirilerin tam metinlerinin yayınlanması imkânı olacaktır.

Sempozyumda sunulan sözlü ya da poster bildirilerinden hakem kurulu tarafından seçilecek olan çalışmalara "Araştırma Ödülleri" verilecektir.

"İNFLAMASYON" temalı VII. Türkiye *in vitro* Diyagnostik Sempozyumu ile ilgili tüm gelişmeleri web sayfamızdan (www.ivd2022.org.) takip edebilirsiniz.

Sizleri en içten sevgi ve saygılarımızla sempozyuma davet ediyoruz.

Prof. Dr. Doğan YÜCEL
TBD Yönetim Kurulu Başkanı
Sempozyum Onursal Başkanı

Prof. Dr. Hilal KOÇDOR
TBD İzmir Şubesi YK. Başkanı
Sempozyum Başkanı

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The symposium was supported by TUBITAK 2223-B Domestic Scientific Event Organization Support Program.

"Sempozyum, TÜBİTAK 2223-B Yurt İçi Bilimsel Etkinlik Düzenleme Desteği Programınca desteklenmiştir. "

SCIENTIFIC PROGRAM

27 Nisan 2022, Çarşamba

10:00 - 10:30	**AÇILIŞ VE AÇILIŞ KONUŞMALARI** Hilal KOÇDOR – Sempozyum Başkanı, TBD İzmir Şb.. YK Başk. Doğan YÜCEL – TBD Genel Başkanı
10:30 - 11:00	**1. OTURUM: AÇILIŞ KONFERANSI** **Oturum Başkanı:** Nur OLGUN
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11:40 - 12:10	"İnflamasyon Biyokimyası, Mediyatörler ve Mekanizmaları"- Eser Yıldırım SÖZMEN
12:10 - 12:40	"İnflamasyon ve İmmünite" - Haluk Barbaros ORAL
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13:30 - 15:00	**3. OTURUM: TANI – BİYOBELİRTEÇLER VE TESTLER-I** **Oturum Başkanları:** Semra DEMOKAN, Mehmet ŞENES
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14:00 - 14:30	"Sepsis Tanısında Kullanılan Biyobelirteçler" - Necati GÖKMEN
14:30 - 15:00	"Hiper-inflamasyon (COVID-19) Tanısında Kullanılan Biyobelirteçler" - Tanıl KOCAGÖZ
15:00 - 15:10	ARA
15:10 - 16:50	**4. OTURUM: TANI – BİYOBELİRTEÇLER VE TESTLER-II** **Oturum Başkanları:** Oya İTİL, Ferhan SAĞIN
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15:50 - 16:20	"İnflamasyonda Klinik Moleküler Görüntüleme"- Oğuz DİCLE
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SS9: "Kurkuminin Anaplastik Tiroid Kanserinde Antimetastatik Potansiyeli ve Docetaxel ile Kombine Etkinliği"- Mehmet Ali KOÇDOR, Yağmur KAYA, Arzu YILDIRIM, Hilal KOÇDOR

18:30 - 18:45	ARA
18:45 – 20:15	**SÖZLÜ SUNUM OTURUMU- 2** **Hakemler:** Gülşen AKALIN ÇİFTÇİ, Sinem Ezgi TURUNÇ, Ebru SEZER

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SS11: "Sentezlenen Nanogümüş ile Temizlik Sektöründe Farklı Ürün Gruplarının Geliştirilmesi"- Hande UÇAK MERDOL, Cansu YILDIZ, Aylin RAZLIKLI, Ceyda HEMEN

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SS13: "PPARγ Aktivasyonunun Hipertansif Sıçanların Beyinsapında Çeşitli Yolaklara Etkisi"- Nazlıcan ŞEREN, Ima DOVINOVA, Miroslav BARANCIK, Güliz ARMAGAN

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28 Nisan 2022, Perşembe

10:00 - 12:00	**5. OTURUM: HASTALIKLAR BAZINDA İNFLAMASYON-I** **Oturum Başkanları:** Fatoş ÖNEN, Aylin SEPİCİ DİNÇEL
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10:30 - 11:00	"İnflamasyonun İlaç Metabolizması Üzerine Etkileri ve Farmakogenetik Faktörler" - Melih BABAOĞLU
11:00 - 11:30	"Metabolik Sendrom, Obezite ve İnflamasyon" - Koray ATİLA
11:30 - 12:00	"Hareket ve İnflamasyon" - Bilge KARA
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14:30 - 14:40	ARA
14:40 - 16:10	**7. OTURUM: HASTALIKLAR BAZINDA İNFLAMASYON-III** **Oturum Başkanları:** Nuh Zafer CANTÜRK, Mehmet Ali KOÇDOR
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15:10 - 15:40	"Travma ve İnflamasyon"- Anıl Murat ÖZTÜRK
15:40 - 16:10	"İnflamasyon ve Ozon Terapi"- Hamit Selim KARABEKİR
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SS25: "Güçlü Probiyotikler Semaforin Yolu Üzerinden Nöroinflamasyonu ve Bağırsak-Beyin Eksenindeki Ferroptozi Azaltır"- Fatih KAR, Ceyhan HACIOĞLU, Ezgi KAR, Dilek BURUKOĞLU DÖNMEZ, Güngör KANBAK

SS26: "Favipiravir Kullanan ve Kullanmayan COVID-19 Hastalarda INR, PT, aPTT Testlerinin Değerlendirilmesi"- Mehmet Ali GÜL, Nezahat KURT, Alpaslan ÖZTÜRK, Mustafa ÇAPRAZ

SS27: "İdiyopatik Granülamatöz Lobüler Mastit Hastalığının Karşılaştırmalı Proteomik Analizi: Hastalığın Teşhisi için Olası Biyobelirteçlerin Araştırılması" Merve Gülsen Bal ALBAYRAK, Turgay ŞİMŞEK, Murat KASAP, Nuh Zafer CANTÜRK, Gürler AKPINAR

17:50-18:05	ARA
18:05 - 19:35	**SÖZLÜ SUNUM OTURUMU- 4** **Hakemler:** Ahmet ALACACIOĞLU, Tarık SALMAN, Meriç ŞENDURAN

SS28: "Biyotransformasyon ve Ekstraksiyon Yöntemlerinin Etkisiyle Propolisin THP-1 Hücre Hattı Üzerindeki İnflamatuvar Etkisi"- Burak DURMAZ, Latife Merve OKTAY, Hikmet MEMMEDOV, Nur Selvi GÜNEL, Hatice KALKAN YILDIRIM, Eser YILDIRIM SÖZMEN

SS29: "Toll-Etkileşimli Proteinin Hepatoselüler Karsinom Hücre Hatlarının İnflamasyon Durumuna Etkisi"- Ayşe Banu DEMİR

SS30: Yaşlı Hastalarda Kırılganlık ile İnflamatuar Belirteçlerin İlişkisinin Değerlendirilmesi"- Fatma Sena DOST, Mehmet Selman ÖNTAN, Ahmet Turan IŞIK

SS31: "Kilo Veren Obez Hastalarda Yanıt Biyobelirteçlerinin Ölçülmesinin Önemi"- Özlem DEMİRELCE, Parvana MİKAİLOVA, Meltem KİLERCİK, Mustafa SERTESER

SS32: "Adölesanlarda Biniciliğin Kor Kasları Üzerindeki Etkilerinin İncelenmesi"- Pınar KUYULU, Bilge KARA

SS33: "Kronik Bel Ağrılı Hastalarda C-Reaktif Protein ile Bel Ağrısı ve Bel Ağrısı Kaynaklı Fiziksel Yetersizlik ve Özürlülük Düzeyi Arasındaki İlişki"- Veli NEHİR, Sema SAVCI

SS34: "Nöroblastomda İmmün ve Inflamatuar Cevapta Heterojenite"- Tekincan AKTAŞ, Deniz KIZMAZOĞLU, Safiye AKTAŞ, Efe SERİNAN, Emre ÇEÇEN, Dilek İNCE, Zekiye ALTUN, Nur OLGUN

SS35: "Ankilozan Spondilitli Hastalarda Hastalık Aktivite Skorları ile Diyafragma Fonksiyonu Arasındaki İlişki: Pilot Çalışma"- Uğur VEREP, Elanur ÇİÇEK, Tuba DEMİRCİ YILDIRIM, Fatoş ÖNEN, Seher ÖZYÜREK

SS36: "Hipofizin İnflamasyona Yanıtı;Boş Sella Sendromu"- Başak KOÇDOR, Zeynep Zehra GÜMÜŞ

SCIENTIFIC PROGRAM

29 Nisan 2022, Cuma

09:00-11:00	**8. OTURUM: HASTALIKLAR BAZINDA İNFLAMASYON-IV** **Oturum Başkanları:** Hale AKBAYLAR, Meltem TAŞBAKAN
09:00-09:30	"İnflamasyon ve Transplantasyon"- Tarkan ÜNEK
09:30-10:00	"İnflamasyon ve Barsak Hastalıkları"- Müjde SOYTÜRK
10:00-10:30	"İnflamasyon ve Mikrobiyota"- Nur ARSLAN
10:30-11:00	"Diyabetik Ayak"- Şevki ÇETİNKALP
11:00-11:15	ARA
11:15-12:45	**9. OTURUM: TEDAVİDE ANTİ-İNFLAMATUVAR YAKLAŞIMLAR** **Oturum Başkanları:** Aysun PABUÇCUOĞLU, Hülya YAZICI
11:15-11:45	"Anti-inflamatuvar Tedavide Yeni Yaklaşımlar (Nanoteknoloji Uygulamaları)"- Özgen ÖZER
11:45-12:15	"Bitkisel Antiinflamatuarlar"- Erdem YEŞİLADA
12:15-12:45	"İnflamasyonda Akupunktur ve Mezoterapi Tedavileri"- Nüket KARABEKİR
13:15-13:30	ARA
13:30-15:00	**10. OTURUM: in vitro DİYAGNOSTİK: İNOVATİF ÖRNEKLER** **Oturum Başkanları:** Füsun ÖZMEN, Oytun PORTAKAL
13:30-14:00	"Hızlı Test Kitlerinin Gelişim ve Üretimi Hikayesi" - Kağan Etka YÖRÜK (Vitrosens Biotechnology)
14:00-14:30	"Point-of-Care Testleri" - Ilgın ÖZTÜRK, Kartal YAĞLIDERE (TURKLAB Medical Devices)
14:30-15:00	IVD Sanayiinde Bir Analizin Üretiminde Bir Lotta 100 L Üretimden 40 Ton Üretime Geçmede 'Bir Ölçek Büyütme Hikayesi" - Salih UCA (Archem Diagnostics)
15:00-15:10	ARA
15:10-16:40	**11. OTURUM: İNFLAMASYON TANISINDA in vitro DİYAGNOSTİK VE GELECEK PANELİ** **Oturum Başkanları:** Diler ASLAN, Doğan YÜCEL
15:10-15:40	"İnflamasyon Belirteci Olarak Sitokinlerden Klinik Yararlanım" - Sedef YENİCE
15:40-16:10	"İnflamasyon Tanısında IVD ve Geleceğin Biyokimyası" - Nuray ULUSU
16:10-16:40	"İnflamasyonda IVD Tıbbi Cihazlar: Günümüz ve Gelecek" - Muhittin SERDAR
16:40-17:30	**KAPANIŞ VE ÖDÜL TÖRENİ**

Poster Bildiri Programı

PS1:"GECİKMİŞ KAS AĞRISINDA NÖRODİNAMİK MOBİLİZASYON TEKNİĞİNİN İNFLAMASYON BİYOBELİRTEÇLERİ İLE AĞRI, BASINÇ AĞRI EŞİĞİ, NORMAL EKLEM HAREKETİ, KAS KUVVETİ VE FONKSİYONEL DURUM ÜZERİNE ETKİSİNİN ARAŞTIRILMASI" Rabia ŞEMSİ, Uğur SÖZLÜ, Selda BAŞAR, Aylin SEPİCİ DİNÇEL

PS2:"YOĞUN BAKIM HASTALARINDA COVID-19 MORTALİTESİNİ ÖNGÖRMEDE FİBRİNOJEN/ALBUMİN VE D-DİMER/ALBUMİN ORANLARI" Şükran BIÇAKCI, Medine ALPDEMİR, Fatih SERİN, Mehmet ŞENES

PS3: "BNP TESTİ İÇİN BİYOTİN İNTERFERANSININ DEĞERLENDİRİLMESİ" Murat AKŞİT, İnanç KARAKOYUN, Ahmet Erkin BOZDEMİR, Banu İŞBİLEN BAŞOK, Ayfer ÇOLAK

PS4: "DİYET İNFLAMATUVAR İNDEKS, FİZİKSEL AKTİVİTE, SERUM LİPİDLERİ VE ABDOMİNAL OBEZİTE İLİŞKİSİ" Nuriye KAHIR, Ceren GEZER

PS5: "İNFLAMATUVAR BAĞIRSAK HASTALIKLARINDA BİYOMARKER OLARAK SERUM ALBÜMİN/GLOBÜLİN ORANI" Parvana MİKAİLOVA, Özlem DEMİRELCE, Meltem KİLERCİK, Mustafa SERTESER

PS6: "TOL L-BENZERİ RESEPTÖR 7 VE 8 POLİMORFİZMLERİNİN COVID-19 ŞİDDETİ İLE İLİŞKİSİ" Gökhan BAĞCI, Oğuz GÜNDOĞDU, Ayşe Nur PEKTAŞ, Binnur BAĞCI, Onur AVCI, Sinan GÜRSOY, Kenan KAYGUSUZ, Nazif ELALDI

PS7: "ROMATİZMAL HASTALIKLAR VE İNFLAMASYON" Ayşenur YALÇINTAŞ KANBUR

PS8: "AKCİĞER KANSERINDE SARI KANTARON'UN (HYPERICUM PERFORATUM) IN-VIVO ETKISININ ARAŞTIRILMASI" Efe Özgür SERİNAN, Safiye AKTAŞ, Aylin EROL, Özde Elif GÖKBAYRAK, Zekiye ALTUN

PS9: "ANKİLOZAN SPONDİLİT HASTALARINDA SPİNAL MOBİLİTENİN DEĞERLENDİRİLMESİNDE OTUR-UZAN TESTİ" Yasemin ACAR, Nursen İLÇİN, İsmail SARI

PS10: "U937 MONOSİT HÜCRELERİNDEN KİMYASAL UYARIMLA FARKLILAŞTIRILAN M1 VE M2 POLARİZE MAKROFAJ HÜCRELERİNİN SİTOKİN PROFİLLERİNİN BELİRLENMESİ" Fatih HUNÇ, Gökhan DURUKSU, Meltem ÖZLEN DİLLİOĞLUGİL

PS11: "BETAİN DOZA BAĞIMLI OLARAK HEPG2 HÜCRELERİ ÜZERINDE ANTİ-İNFLAMATUAR VE ANTİ-PROLİFERATİF ETKİ SERGİLER" Fatih KAR, Meliha KOLDEMİR GÜNDÜZ, Güllü KAYMAK

PS12: "METİLTİYAZOL TÜREVLERİNİN ANTİİNFLAMATUAR AKTİVİTELERİNİN DEĞERLENDİRİLMESİ" Dilek ERDAŞ, Halide Edip TEMEL, Gülşen Akalın ÇİFTÇİ, Leyla YURTTAŞ, Asaf Evrim EVREN

PS13: "MULTIPLE MYELOMDA INFLAMASYON BELİRTEÇLERİNİN PROGNOSTİK FAKTÖRLERLE İLİŞKİSİNİN DEĞERLENDİRİLMESİ" Nuran Ahü BAYSAL, Çiğdem SÖNMEZ, Fevzi ALTUNTAŞ

PS14: " İZOLE TROMBOSİTOPENİ İLE SEYREDEN COVID-19 OLGUSU" Ahmet YURTTAS, Hazel Öztürk BELİN, Ahmet URSAVAŞ, Bedrettin ORHAN, Halis AKALIN

PS15: " COVID-19 TANISI İÇİN APTASENSÖR GELİŞTİRİLMESİ" Nursima UÇAR, Duygu HARMANCI, Simge BALABAN HANOĞLU, Ezgi MAN, Figen ZİHNİOĞLU, Serap EVRAN, Candan ÇİÇEK, Rüçhan SERTÖZ, Bilgin ARDA, Tuncay GÖKSEL, Kutsal TURHAN, Suna TİMUR

PS16: " TÜRKİYE'NİN FARKLI BÖLGELERİNDEN ELDE EDİLEN *PISTACIA VERA* İÇ KABUĞU EKTRESİNİN, İNVAZİV MEME KANSERİ HÜCRE HATLARINDAKİ OKSİDATİF STRES VE PROLİFERASYON ÜZERİNDEKİ ETKİSİNİN KARŞILAŞTIRILMASI" İpek GÜRKEBABÇI, Başak KOÇDOR, Halil ATEŞ, Hilal KOÇDOR

INVITED SPEAKERS ABSTRACTS [DAVETLİ KONUŞMACI ÖZETLERİ]

IS-01
SURGERY AND INFLAMMATION: SURGICAL INFLAMMATION

Prof. Dr. Iskender SAYEK
Hacettepe University Faculty of Medicine, General Surgery
Retired Faculty Member

The aim of inflammation is both to eliminate the cause of cell injury and the necrotic cells and tissues resulting from cell injury. Following this, the repair process begins. Surgical intervention is an important inflammation triggering stimulus. Surgical inflammation is defined as an inflammatory response that develops after surgery or trauma. Surgical inflammation overlapping with each other consists of three phases: neural, immune and endocrine phases.

There are multiple factors that affect the severity of inflammation. The extent of the surgery and the severity of the trauma are important factors. The three components of the inflammatory response are hormonal, metabolic, and immunological. A balanced inflammatory response protects the organism against infection, whereas an excessive immune response leads to organ damage. Here, especially the exaggerated secretion and unbalanced release of cytokines cause the development of systemic inflammatory response syndrome (SIRS). An important effect in the development of this process is endothelial cell activation. Accumulation of neutrophils and platelets at the injury site and expression of inflammatory cytokines and/or adhesion molecules lead to endothelial activation. Endothelial destruction and disruption of the function and integrity of the endothelium result in increased permeability, which leads to sepsis and organ damage.

Healing and tissue repair improve with the control of the inflammatory response. Recently, lipoxins, resolvins, protectines, and vasoinhibins have emerged as signaling molecules that regulate many cell functions, and the evidence highlights their role in resolving the inflammatory response. Their roles and effects in the future will be clarified by scientific studies.

IS-02
PATHOPHYSIOLOGY OF INFLAMMATION

Prof. Dr. Sevket RUACAN
Koç University, Faculty of Medicine, Department of Medical Pathology, Istanbul, Turkey

Inflammation is defined as a defense mechanism developed by the organism through the process of evolution against injurious agents. Two principal elements have been identified in the inflammatory process: 1. Cells; 2. Vascular changes. Early observations on inflammation were made by Ehrlich who identified polymorphonuclear leucocytes; Cohnheim and von Recklinghausen who recognized vascular changes and cell migration and Metchnikoff who described phagocytic macrophages. Ehrlich and Metchnikoff were awarded by the Nobel prize in 1908 for their contributions to the field. Inflammation can be initiated external agents like bacteria, viruses, fungi, parasites or foreign bodies or molecules. Injured or dead tissue elements may also start inflammation. Genetically based hypersensitivity reactions leading to autoimmune diseases or abnormal reactions of the inflammatory system leading to autoinflammatory syndromes have been recognized. Behçet's disease and Familial Mediterranean Fever are classified in this group.

Studies have shown that early manifestations of inflammation are enlargement and increase in permeability of vessels initiated by signals from local cells. Following this inflammatory cell in the circulation pass through the vessel wall into tissues by novel mechanisms. These cells activate other cells to migrate, proliferate and destroy injurious agents by secreting many molecules. Eventually the injurious agent is removed and inflammation ends.

Recent studies have demonstrated cellular and molecular mechanisms of binding and transmigration of inflammatory cells from the circulation to the tissues and their functions. These studies revealed receptor and sensor systems inside the cells which react to inflammatory signals (inflammasome).

Finally, a new function of neutrophils has been elucidated. In response to inflammation these cells release molecules outside the cells. This process is called neutrophil extracellular traps or NET's and is believed to be related to numerous diseases.

IS-03
BIOCHEMISTRY OF INFLAMMATION; ITS MEDIATORS AND ACTIVITIES

Prof. Dr. Eser Yıldırım SOZMEN
Ege University, Faculty of Medicine, Department of Medical Biochemistry, Izmir, Turkey

Inflammation is a process which aims to protect the host against bacteria, viruses, and infections; it is executed by immune and non-immune cells. Acute inflammatory response is mainly driven by mast cells which release histamine, bradykinin, TNF and IL-1 subsequently resulting in vasodilation by nitric oxide and vascular leakage of leucocytes and activation of complement and clotting system. The foreign agent undergoes phagocytosis and is rendered harmless by increased concentration oxygen radical and nitric oxide. However, various factors such as aging, obesity, stress, environmental factors lead to low-grade "sterile" induction of inflammation, and it's defined as chronic systemic inflammation (CSI). Pathogen-associated molecular patterns (PAMPs) and/or Damage-associated molecular patterns (DAMPs) activate inflammatory response by binding to Pattern Recognition Receptors (mannose binding receptor, scavenger receptor, Toll-like receptor, G-protein receptor etc). While

binding with mannose (C-type lectine) receptor and scavenger receptor directly activate phagocytosis which covers lysosomal activation and reactive oxygen radical production, Toll-like receptor activation leads to activation of AP-1 and Nuclear factor kappa B then these molecules increase gene expressions of proinflammatory mediators (NLRP-3, e-selectin, TNF, IL-6, IL-1, MCP-1 etc). G protein-mediated activation results in an increase in IFN alpha/beta. TNF, IL-1beta and IFN-gamma enhance apoptosis by inducing different mediators. On the other hand, classically activated macrophages also release many cytokines, adhesion molecules, growth factors, and matrix metalloproteinases. The main distinction of SCI from acute inflammatory response is that CSI involve the immune attack and activated macrophages. Altogether these effects might lead to tissue damage and result in chronic inflammatory diseases.

IS-04
INFLAMMATION AND IMMUNITY

Prof. Dr. H. Barbaros ORAL
Uludağ University, Faculty of Medicine, Department of Immunology, Bursa, Turkey

Inflammation is not a singular phenomenon, but rather a combination of a wide variety of immune responses to a particular stimulus (such as pathogens, tissue damage). It is a challenge where the immune system uses every weapon in its arsenal. The inflammation process begins with the recognition of pathogens, tissue damage and foreign substances to the host by the cells of the innate immune system through pattern-recognizing receptors (PRR). In this process, the activation of NF-kB, which is involved in the transcription of inflammatory mediators and surface molecules, and the activation of the inflammasome complex through NLRs, which are NOD-like receptors, play an important role. As a result, various proinflammatory cytokines and chemokines are produced and released to perform the effector functions of inflammation. Blood-borne neutrophils and monocytes migrate to the scene by extravasation with the activation of endothelium and the effect of chemokines. Meanwhile, these cells are accompanied by a protein-rich fluid called exudate, resulting in edema. Mast cells and tissue-resident macrophages promote this migration by acting rapidly on vessels, including vasodilation and increased vascular permeability, by releasing vasoactive molecules such as histamine, leukotrienes, and prostaglandins. Neutrophils release toxic compounds such as ROS, RNS, and various proteases, which have the potential to harm both the pathogen and the host. At this stage, macrophages and dendritic cells are processed so that antigens are taken and presented to T cells. The innate immune response and the character of the resulting inflammation are factors that determine which direction the adaptive immune response will polarize. Depending on the type of pathogen and other factors, the resulting Th population may evolve into a proinflammatory (Th1), anti-inflammatory (Th2), or regulatory (Treg) phenotype. Resolution of inflammation is accomplished by promoting the conversion of leukotrienes produced by neutrophils, macrophages, and other cells into lipoxins, which initiates the cessation of inflammation. Meanwhile, increased Fas ligand, resolvins and protectins lead to apoptosis of neutrophils. Macrophages phagocytised apoptotic neutrophils and cellular debris within the tissue involved.

IS-05
CLASSIC AND NEW BIOMARKERS OF INFLAMMATION

Prof. Dr. Z. Günnur DIKMEN
Hacettepe University, Faculty of Medicine, Department of Medical Biochemistry, Ankara, Turkey

In response to inflammation, infection, tissue injury and travma; a complex acute phase response develops in the body. Cytokines such as IL-6, IL-1, TNF-α, IFN-γ and TGF-β are released by macrophages and monocytes, leading to the production or suppression of acute phase proteins by the liver. Substances that increase during inflammation are termed positive acute phase reactants and the ones decrease are termed negative acute phase reactants.C-reactive protein (CRP) is a positive acute phase reactant which plays an active role in the inflammatory process. CRP is produced as a homopentameric protein which can irreversibly dissociate at sites of inflammation and infection into five separate monomers. CRP levels increase by at least 25% during inflammatory disorders; the increase occurs within 24 to 48 hr, and the level may be 2000 times normal. CRP has a half-life of 6-8 hr, can quickly return to within the normal range if the right treatment is given. CRP correlates well with the erythrocyte sedimentation rate, however not always directly. RBCs are negatively charged cells and ESR can increase due to the presence of positively charged proteins such as fibrinogen and immunoglobulins which increase during inflammation.
Fibrinogen is a soluble glycoprotein synthesized in the liver and act as a is a positive acute phase mediator of inflammation. Fibrinogen acts on different cell types through cell-specific integrin and non-integrin receptors to induce specific inflammatory functions. Under physiological conditions, plasma concentrations of fibrinogen range from 200 -400mg/dL, and fibrinogen has a half-life of approximately 4 days. However, in pathological conditions, such as injury, infection or inflammation, the blood concentration of fibrinogen increases up to 20 fold which is related to the risk for thrombosis and atherosclerosis.
Procalcitonin (PCT) is as an early marker of sepsis and can be used as a guide to the management of antibiotic therapy. PCT is produced by monocytes and hepatocytes after exposure to bacterial endotoxin, PCT levels within 2–4hr rise sharply, reach a plateau within 6–8hr. PCT assays determine if the systemic inflammatory reaction is due to bacteremia with a specificity of 79%. Serum PCT levels appear to correlate with the severity of the microbial attack and rapidly decrease after appropriate antibiotic treatment. In contrast to CRP, local bacterial infections, severe viral infections are not associated with increased PCT. In sepsis, PCT increase is observed 24-28 hr before CRP. Albumin is a negative acute phase protein. Inflammation reduces albumin concentration by decreasing its synthesis, hence inflammatory factors such as TNF and Interleukin-1 also suppress albumin synthesis and increase catabolic rate which cause hypoalbuminemia. Inflammation also cause the blood vessels to become leaky and cause extravasation of albumin into the tissues that results in oedema formation and decrease the plasma albumin concentration. Hypoalbuminemia is

associated with increased length of hospital stay and complications.
Prealbumin (Transthyretin) is another negative phase protein frequently used in the assessment of patient's nutritional status, hence inflammation influence it more strongly. Prealbumin concentration correlate with the severity of the inflammation. Prealbumin levels are inversely correlated with markers of inflammation. Increase in prealbumin is usually observed following decline in CRP and other inflammatory markers.
Novel inflammatory markers such as neutrophil to lymphocyte ratio, albumin to fibrinogen ratio, CRP to albumin ratio have emerged as useful biomarkers to predict systemic inflammation. Kynurenin pathway related with tryptophan catabolism is significantly upregulated in response to inflammation, and elevated levels of KP metabolites (quinolinic acid, kynurenic acid, xanthurenic acid) serve as sensitive markers of chronic systemic inflammation.

IS-06
BIOMARKERS USED IN THE DIAGNOSIS OF SEPSIS

Prof. Dr. Necati GOKMEN
Dokuz Eylül University, Faculty of Medicine, Department of Anesthesiology and Reanimation, Izmir, Turkey

Sepsis is a clinical syndrome that includes physiological, biological, and biochemical abnormalities due to the dysregulation of the host's response to infection. Sepsis and the resulting inflammatory response can lead to multiple organ dysfunction syndromes (MODS) and death. Some biomarkers have been used to help diagnose sepsis disease and determine disease severity and prognosis. Unfortunately, a biomarker with sufficient sensitivity and specificity, which makes or excludes a definitive diagnosis, has not been determined yet.
For sepsis, Liquid Phase Pattern Recognition Molecules (PRMs), cytokines and chemokines, complement system, Damage Associated Molecular Patterns (DAMPs), cell membrane receptors, micro RNAs (miRNA), non-coding RNAs (ncRNA), cell proteins, several biomarkers have been identified, such as metabolites and soluble receptors. Classical biomarkers such as C-Reactive Protein (CRP), Interleukin-6 (IL-6), and Procalcitonin (PCT) are the best known. However, the need to identify good combinations remains.

IS-07
RADIOLOGICAL IMAGING OF INFLAMMATION

Prof. Dr. Oguz DICLE
Dokuz Eylül University, Faculty of Medicine, Department of Radiology, Izmir, Turkey

Radiology has imaging methods that are specific and non-specific to inflammation. The cellular and fluid changes revealed by the inflammatory process produce direct or indirect findings to imaging methods, and these findings are used in the differential diagnosis. Especially in magnetic resonance imaging, perfusion changes, imaging of the inflamed vessel wall and changes in inflammatory bowel disease, and inflammation imaging with hyperpolarized contrast agents are frequently used methods with the sequences developed in recent years. It also contributes to the sensitive diagnosis of inflammation with diffusion-weighted imaging. In this presentation study, information about the details of the subject will be shared with examples.

IS-8
THE ROLE OF NUCLEAR MEDICINE IN CLINICAL MOLECULAR IMAGING OF INFLAMMATION

Prof. Dr. Zehra OZCAN
Ege University, Faculty of Medicine, Department of Nuclear Medicine, Izmir, Turkey

Current developments in biotechnology and widespread use of imaging modalities significantly improved diagnosis and management of inflammatory conditions. These methods both provide accurate localisation and helps defining the severity and extent of disease in addition to prognostication or monitoring therapeutic efficiency. Nuclear Medicine (NM), owing to its nature as a physiologic based modality has a great potential to detect inflammation related alterations early in the beginning before the morphologic changes occur. Therefore, molecular NM modalities lead to positive findings at an earlier period than the radiologic methods based on the morphologic tissue changes despite their high sensitivity and resolution. Two main modalities in NM, SPECT (single photon emission tomography) and PET (positron emission tomography) can be used for in-vivo identification of inflammation with different radiopharmaceuticals. Molecular imaging is generated through a variety of radiopharmaceutical agents targeting different cellular subtypes in the dynamic course of inflammation. F-18 FDG (fluoro-2-deoxy-D-glucose) PET imaging which reflects the increase glucose metabolism in inflammation has been the most common method in acute and chronic inflammatory conditions. Other agents in clinical use include radiolabelled chemokine receptors (Ga-68 pentaxifor, Cu-64 DOTA_FC131) and fibroblast activating proteins (Ga-68 FAPI and derives). These agents targeting different metabolic pathways or cellular receptors in inflammation are labelled with positron emitters and used for in-vivo molecular imaging with PET. Mostly in musculoskeletal or cardiovascular inflammations, if there is a septic involvement, radiolabelled leucocyte scintigraphy and SPECT is the method of choice for the specific assessment of infection. Currently hybrid technologies such as SPECT/CT or PET/CT providing anatomic and functional information together definitely improved diagnostic accuracy. It is suggested that the advances in imaging techniques and development of novel molecular biomarkers in imaging will enhance the value of NM and molecular imaging in inflammation.

IS-09
EFFECTS OF INFLAMMATION ON DRUG METABOLISM AND PHARMACOGENETIC FACTORS

Prof. Dr. Melih O. BABAOGLU
Hacettepe University, Faculty of Medicine, Department of Medical Pharmacology, Ankara, Turkey

Variability in drug metabolism and elimination can cause altered drug response and toxicity in human. The sources of variability

may be both genetic and non-genetic factors, such as diseases. Cytochrome P450 (CYP) enzymes play the most prominent role in the hepatic and extra-hepatic metabolism of drugs and their activities are also regulated by genetic and non-genetic mechanisms. The major CYP enzymes involved in drug metabolism are CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6 and CYP3A4.

Inflammation and chronic inflammatory diseases are characterized by elevated levels of pro-inflammatory cytokines and have been identified as important non-genetic factors that can regulate activities of drug-metabolizing enzymes. For example, some of our previous studies demonstrated that activities of CYP2C9 and CYP2C19 were suppressed by about 2 to 2.5 folds in patients with auto-immune disorders characterized by systemic inflammation. Such inhibitory effects have been associated with down-regulation of CYP activity or expression due to increased systemic cytokine levels in the patients.

The pro-inflammatory cytokines IL-6, IFN-gamma, TNF-alpha, IL-1-beta are commonly recognized as important mediators that can change CYP expression and activity. Individual cytokines and inflammatory diseases may affect the regulation of CYP enzymes through distinct biochemical pathways.

Pharmacogenetics is the field of research that studies how genetic variations may affect the drug response among individuals. Both inflammation and genetic variability on drug-metabolizing enzymes may interact to alter drug response and may cause a mismatch between the predicted drug response and the actual phenotype, which is called pheno-conversion. Integration of the knowledge on inflammatory status of the diseases and the identification of pharmacogenetic factors for individual patients may support implementation of personalized medicine.

IS-10
METABOLIC SYNDROME, OBESITY AND INFLAMMATION

Prof. Dr. Koray ATILA
Dokuz Eylül University, Faculty of Medicine, Department of General Surgery, Izmir, Turkey

Obesity is recognized as a serious public health problem, as it increases the risks of multiple diseases, such as diabetes, heart disease, high blood pressure, and some cancers. Metabolic syndrome consists of several metabolic abnormalities, including intraabdominal obesity, hyperglycemia, and hypertension. Inflammation is a natural part of the immune system and is the body's natural defensive response to many harmful, foreign and destructive effects. However, when inflammation develops against its tissues, chronic inflammation develops. Obesity causes low-grade chronic inflammation. Adipose tissue is one of the most important endocrine organ and it releases many inflammatory mediators such as Interleukin-1, Interleukin-6, Tumor Necrosis Factor-α, C-Reactive Protein and adipokines like adiponectine. Obese people have higher circulating concentrations of many inflammatory markers than lean people, and these are believed to play a role in causing insulin resistance and metabolic syndrome

IS-11
MOVEMENT AND INFLAMMATION

Prof. Dr. Bilge KARA
Dokuz Eylül University, Faculty of Physical Therapy and Rehabilitation, Department of Neurological Physiotherapy-Rehabilitation, Izmir, Turkey

The concept of movement includes physical activity and exercise. Physical activity is any bodily movement that increases energy expenditure above resting levels. Exercise is part of physical activity and is a planned and structured behaviour, Anti-inflammatory effects of exercise have focused on three possible mechanisms: the reduction in visceral fat mass; increased production and release of anti-inflammatory cytokines from contracting skeletal muscle and reduced expression of Toll-like receptors (TLRs) on monocytes and macrophages.

Studies have demonstrated that chronic inflammation may increase the risk of disability and mortality even in people who do not have clinical disease. Regular exercise protects against diseases associated with chronic low-grade systemic inflammation. Exercise induced changes in inflammation can be divided into acute effects and long-term effects. The pro-inflammatory cytokines (TNF-α, IL-1β, and IL-6) are released after physical activity of sufficient intensity, followed by the release of anti-inflammatory or regulatory cytokines. During exercise, IL-6 is the first detectable cytokine released from the contracting skeletal muscle cells into the blood. Muscle-derived IL-6 increases with exercise. The duration of exercise is the single most important factor that determines the magnitude of the systemic IL-6 response. Acute exercise bout initiates a complex, time dependent cascade of inflammatory events, which depends largely on the mode, intensity, duration of the exercise bout. Regular physical exercise training may be considered a long-lasting anti-inflammatory therapy, after the acute inflammatory actions are resolved. The long-term effects of exercise on reducing inflammation are thought to be mainly mediated by reductions in the size of adipose tissue.

IS-12
INFLAMMATION AND CANCER

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Tumors are not the lonely "creatures ". A malignant tumor exerts effects on the organism just as the organism's physiology exerts effects on the tumor. Inflammation predisposes to the development of cancer and promotes all stages of tumorigenesis, because recent studies on the mechanisms of pro-tumorigenic inflammatory pathways in cancer have revealed that the pathways evolved to mediate immunity to infection and promote tissue homeostasis. The polarized inflammation can play different roles during tumor initiation, growth, and progression. The inflammatory cells, particularly macrophages, have a paradoxal "dual effect" in tumor microenvironment with distinct timing through the prior to or after initiation of tumorigenesis or might become evident only at the later stages of tumorigenesis. Cancer cells as well as surrounding stromal and inflammatory

cells, organize in well-orchestrated interactions to form inflammatory tumor microenvironment(tme). Cells within the tme are highly functionally plastic, continuously changing their phenotypic and functional characteristics. Hence, a heigtened understanding of tumor-host crosstalk is gradually evident which follows that cancer is “not one disease”. It is a multi-faceted complex-constructed biology showing problematic effects on organism’s physiology, metabolism and immunity. This stochastic behavior of tumor cells challenges the development of effective anti-cancer treatment strategies and clinical trials, for studies do not catch the constant situation of all other confounding factors (‘ceteris paribus’). Other problems which present multiple scientific and logistical challenges for the development of cancer preventive agents targeting inflammation can be listed as: 1)who are the subjects at greatest risk?(cohort selection), 2)appropriate agent selection(target identification), 3)what are the best end-points?, 4)how to incorporate the temporal changes during carcinogenesis and inflammation into clinical trials that are relatively short?, 5)tumor heterogeneity: cancer is not one disease even ın the same target organ, cohort heterogeneity(pharmocogenetics,genetic-environmental changes and different stages of carcinogenesis), 6)heterogeneity of the inflammatory response(in different cancers, during carcinogenesis, different cohorts), and 7) incomplete understanding of molecular pathogenesis, including inflammatory response.

The best example of using inflammation as an anti-cancer therapeutic opportunity comes from study of cancer risk among long-term users of aspirin and nsaids. Much data indicates that use of these drugs reduces colon cancer risk by 40-50%. As the several cornerstone rules of engagement governing molecular and cellular mechanisms of tumor-promoting inflammation are constantly discovered, further development of anti-cancer therapies can be gradually distilled.

IS-13
INFLAMMATORY RESPONSE IN WOUND HEALING AND TISSUE REPAIR

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Inflammation, which is the second phase of wound healing, can be defined as the immune response of the organism against tissue damage. Considering that most of the injuries that occur on the skin in the evolutionary process are contaminated wounds, inflammation comes into play as a defense mechanism to prevent infection. This process, in which many cell types such as platelets, neutrophils, macrophages, mast cells, lymphocytes, keratinocytes, and dendritic cells play an active and synergistic role, provides debridement of the wound area before the repair phase begins, while forming a defense mechanism against infectious agents, and also acts as a secondary causes tissue destruction. The effects of vasoactive amines, plasma proteases, arachidonic acid metabolites, free radicals and cytokines secreted from inflammatory cells cause clinical symptoms such as edema, temperature increase and pain in the wound area. Chemotactic inflammatory mediators secreted from the cells also ensure that cell types such as fibroblasts and keratinocytes are brought to the environment, which will enable the wound to be repaired, that is, to proceed to the proliferation stage. With the effect of growth factors secreted from many cell types in the environment, neovascularization, collagen synthesis (granulation tissue formation), matrix formation and thus wound repair occur.

Fetal wound healing involves little inflammation, scarless regeneration, and complete restoration of dermal structures. It is known that some tissues such as oral mucosa heal with minimal inflammation and minimal scarring in adults. The inflammation process lasts for 1-3 days in a normal wound healing, the prolongation of this process appears as a "chronic wound" in the clinic. So why is there such a phase in wound healing? The answer to this question is hidden in the evolutionary process. Injuries that occurred in primitive times were animal bites, falls, and contaminated injuries in the form of injuries with stones and branches. It was not possible to clean these wounds in a hygienic environment and to protect them from infection with the help of antibiotics. In this case, the organism had to remove dead cells, infectious agents and foreign bodies formed in the wound area with its own mechanisms. Inflammation was necessary at this stage. However, nowadays, more controlled healing of the wound can be achieved. The fact that the inflammation process is particularly long and intense, delaying the repair process has paved the way for many studies to take this process under control.

IS-14
TRAUMA AND INFLAMMATION

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Trauma is the most common cause of death in individuals under the age of 45. Deaths after major trauma can occur in three separate periods. In the first period, deaths occur within seconds at the scene depending on the severity of the trauma and cannot be prevented.

Deaths in the second period usually occur in the first 24 hours in emergency departments due to hypovolemia, hypoxia or head trauma. Deaths in the third period are due to inflammation-related complications that occur in patients after trauma. Post-traumatic cell destruction products and mediators released by the body activate the innate immune system and cause the release of pro- and anti-inflammatory cytokines. In the seriously injured patient there is a high risk of developing immunological dysfunction and subsequently sepsis or the systemic inflammatory response syndrome (SIRS). This can lead to multi organ dysfunction syndrome (MODS) with a high possibility of death. The early and late MODS (biphasic inflammatory response) model was first described by the Moores, depending on the severity of the initial injury after trauma and the extent of the shock that occurred. Defined by Land in 2003, the damage-associated molecular model (DAMP) are molecules within cells that are a component of the innate immune response released from damaged or dying cells and they lead to a sepsis-like sterile hyperinflammation and life-threatening SIRS, often associated with MODS. Compensatory anti-inflammatory response syndrome (CARS), which is defined as the deactivation of the immune system against the pro-inflammatory response, may develop after the early systemic hyperinflammatory response induced by DAMP after severe trauma and resulting in

posttraumatic immunosuppression. The innate immune system has the most prominent role in organ failure after trauma. It is important to understand of the inflammatory response to trauma, immune dysregulation and reduced immunity after injury to manage the patients treatments.

IS-15
ROLE OF OSONE THERAPY AND PROLOTHERAPY ON INFLAMMATION

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Examining the role of ozone therapy and prolotherapy, which are complementary medicine applications as current treatment approaches in inflammation is extremely important in the clinic. Ozone (O3) is a gaseous nonradical molecule consisting of three oxygen atoms and is a colorless, pungent odorous molecule that is more unstable than oxygen. The basic logic of ozone therapy, which is one of the regenerative, in other words, regenerative medicine methods, is the development of living tissues that will replace and repair diseased tissues. Ozone therapy is a treatment method that uses the two powerful "antioxidant" and "anti-inflammatory" potentials of the human body and strengthens the body against diseases by causing an alarm reaction in the whole body. As a result of this "antioxidant" and "anti-inflammatory" response created by repeated ozone therapy sessions, the body's immune cells produce molecules called cytokines. This provides very successful results in the application of medical ozone, especially to patients with weak and impaired immune systems. Ozone rapidly transforms into molecular oxygen and oxygen radicals in biological environments, creating moderate oxidative stress in the body. Thus, ozone is perceived as an oxidative threat in the body. This results in the stimulation of enzymes working in antioxidant defense systems. It is possible to see these positive effects of ozone if it is used in appropriate doses. While at high concentrations it is toxic to cells, at low concentrations the expected ROS and hydrogen peroxide response may not be sufficient and the desired therapeutic effect may not be seen. The therapeutic concentration of ozone in the studies was determined as 10-80 µg/ml. At the same time, there is an increase in both oxygenase-1 enzyme activity with ozone application and it has been shown that this enzyme has antioxidant, antiapoptotic and anti-inflammatory effects. The higher the oxidative stress, that is, the free radical rate, the faster the disease and aging. Oxidative stress has been proven to be reduced in people receiving ozone therapy. Oxidative stress has been proven to be reduced in people receiving ozone therapy. This effect occurs by the elimination of the effect of free radicals as a result of the increase in antioxidant substances in our body. The aim of Prolotherapy, the other traditional medicine method, is to improve health promotion, improve functional capacity and reduce pain. After a careful history and physical examination, cases treated with conventional medical treatment may benefit from it. Conventional treatments for acute and chronic inflammation include rest, ice/heat, professional or home physical therapy and/or exercise program, behavioral changes, and non-steroidal anti-inflammatory drugs. Prolotherapy is an injection treatment and the injected solution consists of natural sugar or salt water. The body perceives this solution as harmful and sends cells to the injection site that initiate the natural healing process. In this way, the damaged joint or muscle tissue is provided to repair and renew itself. By nature, prolotherapy; by injecting a cell-renewing solution into the places where the ligaments (ligaments and tendons) around the joint where the pain is attached to the bones and into the adjacent joint space, the body's natural healing mechanisms are stimulated, thus strengthening the damaged structures around the joint, improving joint functions and reducing pain. In prolotherapy injections, a local inflammation occurs in the area where the given solution is applied, which triggers the release of growth factors and collagen formation. The first stage of healing is the inflammation stage. Namely, prolotherapy injections; it mimics the natural tissue healing process by stimulating the three phases of tissue healing, namely inflammation, proliferation and tissue regeneration.
It focuses on human needs, as the aim of medicine is to keep the individual in a state of complete emotional and physical well-being. In this respect, ozone therapy and prolotherapy, which are traditional medicine methods, are among the treatment options to meet this need with their effective role in the inflammatory and anti-inflammatory process. Scientific data on these treatment modalities should be supported by further clinical and experimental studies.
Key words: Ozone therapy, inflammation, prolotherapy, complementary medicine

IS-16
INFLAMMATION AND TRANSPLANTATION

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Oxidative stress is a major and recurrent cause of inflammation in organ transplantation. The ischemia-reperfusion injury that occurs during organ transplantations causes emergence of free oxygen radicals and pathological nitrogen species. This situaition increases oxidative stress. Reducing oxidative stress leads to increased consumption of endogenous antioxidants. Depending on the degree of oxidative stress, various degrees of damage may occur in the transplanted organ, and as a result, the function of the graft may be impaired. The decrease in adenosine triphosphate (ATP) level formed during ischemia leads to acidification in the intracellular and extracellular environment. This results in accumulation of sodium and calcium in the intracellular environment. Calcium ion accumulation leads to activation of calcium-dependent proteases, which initiates irreversible cell membrane damage that causes necrosis, apoptosis, and autophagic mechanisms. Especially increase in superoxide radicals and proinflammatory factors, decrease in nitric oxide production and activation of hypoxanthine-xanthine oxidase system in the liver increase hepatocellular damage by increasing oxidative stress. While ischemia creates serious tissue damage, reperfusion of the organ can lead to more severe damage. The increase in oxygen levels with reperfusion may contribute to the increase of reactive oxygen species. It has been shown that the key cells that initiate ischemia-reperfusion injury in the liver are Kuppfer cells, and the main mediators are reactive

oxygen species and reactive nitrogen species. Reactive oxygen species include hydrogen peroxide (H_2O_2), superoxide anion and hydroxyl radicals. The most biologically relevant reactive nitrogen species is nitric oxide (NO). Activation of Kuppfer cells together with reactive oxygen species causes formation of tumor necrosis factor-alpha (TNF-alpha) and interleukin-1 (IL-1). DNA damage and endothelial dysfunction may also occur during ischemia-reperfusion injury.

There is no proven treatment to prevent ischemia-reperfusion injury during reperfusion, other than ischemic preconditioning. During reperfusion, Kuppfer cells stimulate the secretion of CD4+ T lymphocytes; proinflammatory cytokines such as TNF-alpha and IL-1 are activated. Anti-inflammatory cytokines such as IL-4 and IL-10 also work to reduce ischemia-reperfusion injury. Meanwhile, there is a decrease in the levels of many antioxidants. In the late phase of reperfusion, reactive oxygen species and proinflammatory mediators can activate sinusoidal endothelial and CD4+ T cells, and they attract neutrophils to the injury site. Intercellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecules (VCAM-1) secreted by endothelial cells increase neutrophil infiltration.

Activation of innate immune responses is observed during ischemia-reperfusion injury. As a result, reactive oxygen products from damaged cells and damage associated molecular patterns (DAMP) such as high mobility group box-1 (HMGB-1) and heat shock proteins (HSPs) emerge. These are recognized by Toll-like receptors (TLRs). Activation of signal transduction proteins and transcription factors by TLRs results in the production and release of inflammatory cytokines and chemokines that enhance dendritic cell maturation.

N-acetyl cysteine is beneficial in many stages in reducing ischemia-reperfusion injury. In addition, to reduce inflammation in the graft; ant ischemic interventions, therapies targeting TLRs and Nuclear factor KappaB, therapies that reduce inflammatory cytokines and adhesion molecules, complement inhibition and antiapoptotic strategies can be used.

Transplanted tissues can be rejected as hyperacute, acute and chronic. The most important mechanism in the prevention of rejections is immunosuppression treatments that prevent the activation and functions of T cells.

IS-17
INFLAMATION AND MICROBIOTA

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The gut microbiome is a complex ecosystem in the host body. It lives in balance with its host.The peaceful coexistence of trillions of microorganisms in the human body is called symbiosis. Symbiosis is necessary for the host to live a healthy life. The intestinal barrier is a complex formation that separates the external environment from the sterile body environment. The structure and function of the intestinal barrier and the role of healthy microbiota in the protection of the intestinal barrier, as well as its effect on the local and systemic immune system, are important for understanding the relationship between inflammation and microbiota. Dysbiosis is defined as; the disruption of the intestinal microbial ecosystem; the decrease in diversity of microbiota; the decline of some species; and the dominance of others. Dysbiosis leads to effects such as disruption of the energy balance in the body and triggering inflammation, which are associated with many diseases in humans. It has been shown that there are mechanistic relationships between intestinal dysbiosis and inflammation-induced obesity, atherosclerosis, autoimmune diseases and neurological disorders. The integrity of the intestinal barrier, diversities in microbial species, and the presence of metabolites such as short-chain fatty acids, trimethylamine oxide and indole derivatives of tryptophan are significant in the pathogenesis of all these diseases.

Keywords: İntestinal microbiota, immun system, short chain fatty acids, mucus layer, atherosclerosis, arthritis

IS-18
DIABETIC FOOT

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Foot wound is one of the most important complications that determines morbidity and mortality in individuals with diabetes, including both microvascular and macrovascular pathogenesis. At the same time, it creates a situation that negatively affects the quality of life, body image, role performance, social-economic structure of the family and society, and life of the diabetic. About 15% of diabetics experience foot ulcers at some point in their lives. 20% of hospitalizations of diabetics are due to foot problems. 40-60% of lower extremity amputations performed for non-traumatic reasons are due to diabetes. It is the complication that causes the most hospital stay. More than 0.9% of patients undergoing diabetic amputation die while in hospital. It is a cause of job loss, disability and psychosocial trauma. Unfortunately, diabetes-related amputation occurs every 30 seconds in the world. In fact, it is easier to prevent the development of diabetic foot than to treat it; but unfortunately, education and practices are insufficient in this respect. However, the foot of every diabetic patient is a candidate to become a diabetic foot.

The first aim is to heal the diabetic foot wound of the patient as soon as possible and to protect the patient from amputation as much as possible. However, in advanced cases, amputation is inevitable. As it can be understood, education, treatment and protection of the healed foot of the patient with diabetic foot lesion are the work of a multidisciplinary team. It is not possible for all treatment to be undertaken by a physician. For this reason, it is necessary to establish a diabetic foot council and team. Diabetologist or internal medicine specialist trained in diabetes, diabetes education nurse, dietitian, infectious diseases specialist, orthopedist, dermatologist, vascular surgery specialist,
plastic surgeon, podiatrist, orthosis/prosthesis specialist, physiotherapist, psychiatrist and social services specialist should be included.

Tissue hypoxia resulting from hyperviscous blood due to hyperglycemia, decreases in erythrocyte flexibility, and difficulties in separating oxygen from glycosylated hemoglobin makes wound healing difficult. In addition, while the immune dysfunction caused by hyperglycemia creates susceptibility to infection in the wound, the decrease in tissue growth factors

(VEGF, TGF-ß, IGF-1, FGF), skin collagen accumulation and myofibroblasts causes delay or worsening of wound closure. This situation suggests the use and development of multiple treatment options. Our known and commonly used treatment options are:

- Glucose regulation (fasting blood glucose 80-130 mg/dL, postprandial blood glucose < 180 mg/dL, A1c < 7.5)
- Choosing the right agents for glucose regulation (metformin, GLP-1, DPP4i, insulin)
- Debridement
- Correct dressing selection
- Insoles and special shoes
- Antibiotherapy
- Vascular intervention
- Foot care and offloading
- Wound care products
- Hyperbaric oxygen therapy
- Vacuum
- Tissue transplants (flab, graft)
- Amputation
- Orthosis/prosthesis

IS-19
NEW APPROACHES TO ANTI-INFLAMMATORY THERAPY (NANOTECHNOLOGY APPLICATIONS)

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Currently, the therapeutic strategies used in anti-inflammatory therapy may not be sufficient to achieve an optimal pharmacological activity. Drug limitations can be summarized as non-specific biodistribution, low bioavailability and/or short half-life, or the need for high doses for expected effect and severe side effects.
To avoid some of these limitations, nanotechnology applications in treatment have come to the fore. With nanocarriers that are biologically compatible, allow controlled drug release, have the appropriate shape, size and surface charge, and are loaded with active at the appropriate concentration, it is aimed to target the disease site, to reduce toxicity and side effects without damaging the surrounding cells and tissues.
Steroid-based treatments have an important place in the treatment of inflammatory diseases or diseases with an inflammatory basis. Corticosteroids are a class of steroid hormones with a wide spectrum, especially glucocorticoids such as hydrocortisone and its derivatives, prednisolone, dexamethasone are frequently used. Nano-formulations have been prepared due to serious side effects that limit their use. For example, liposome formulations of triamcinolone and its derivatives, which are used as anti-inflammatory and immunosuppressive, have been prepared and their anti-inflammatory effect has been increased due to increased localization and absorption.
Phospholipids constitute the basic structure of the most widely used liposomes in nanotechnology applications. They are spherical vesicles formed by one or more biological membrane-like lipid bilayers with an aqueous phase between them and can be easily produced artificially. Drugs such as pegylated prednisolone liposomes, cyclosporine liposomes, glutathione pegylated liposomes, methyl prednisolone liposomes have stood out with their features such as high stability, high loading capacity and activation in the inflamed area.
Nanoparticles, are solid colloidal particles with sizes ranging from 10-1000 nm, prepared with polymers of natural or synthetic nature, that release dissolved, trapped, or adsorbed active substance in a controlled manner. In recent years, studies have been carried out on the delivery of active substances with solubility and stability problems or on the biotherapeutic large-molecule substances such as nucleic acids, peptides, and proteins in nanoparticle drug carrier systems. For this purpose, lipid nanoparticles, which have a low probability of acute and chronic toxicity due to the lipids they contain, and rapid degradation or stability problems due to their solid structure, have been frequently used.
However, while there are many liposome formulations both on the market and in clinical research, there are few nanoparticular systems whose clinical studies have been completed due to reasons such as biocompatibility, nanotoxicity, and scale-up costs. In the future, it is necessary to solve and optimize the difficulties for the safe, biocompatible, and reproducible production of these systems with the appropriate amount of biodistribution by designing industrial standard scale-up processes.

IS-20
HERBALS WITH ANTI-INFLAMMATORY EFFECT

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Scientific evidence has revealed that oxidation and inflammation are the main triggering factors inducing a wide range of diseases in the body. A range of anti-inflammatory agents exist to help control inflammatory reactions; however, they often have side effects and may sometimes not be sufficiently effective. On the other hand, several phytochemicals in herbals, particularly those with phenolic structure, have been clinically proven to exert anti-inflammatory activity without severe health risks. Among these, curcuminoids from turmeric rhizomes, gingerols from ginger rhizomes, and salicin from willow barks are examples of phenolic anti-inflammatory herbals. Moreover, several triterpenes, including boswellic acids from Boswellia oleoresin, and asiatiacosides and madecassosides from Centella leaves, were also reported to possess anti-inflammatory activity. In addition, lipid type components, i.e. galactolipids from rosehips and gamma-linolenic acid from Borage oil or Evening primrose oil; iridoid type components, i.e. harpagosides from devils claw roots, and oleuropein in olive leaves and bromelain enzyme from pineapple stems are recognized with significant anti-inflammatory activity. In this presentation, scientific evidence on the clinical efficiency of herbal anti-inflammatory drugs will be briefly discussed.

IS-21
ACUPUNCTURE TREATMENT AND MESOTHERAPY APPLICATIONS IN INFLAMMATION

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One of the goals of complementary medicine is to improve the quality of life. These applications range from nutritional support to acupuncture; ozone has a wide range of applications, from mesotherapy to mesotherapy. Acupuncture treatment provides an effect by stimulating the secretion of many pharmacologically effective substances in the organism through special disposable steel needles. Although inflammation is normally a pathological event, it is the body's first response to tissue damage and injury. The higher the rate of free radicals after tissue damage, the faster the disease and aging. The effect against free oxygen radicals has been proven with acupuncture treatment. This effect occurs by the elimination of the effect of free radicals as a result of the increase in antioxidant substances in our body. It is effective on endorphins, serotonin, PG, GABA and immunity.
It has current use for pain control and anti-inflammatory effect. The balancing, anti-inflammatory and antidepressant effects of acupuncture have also been accepted by WHO, and it stimulates the body's healing mechanisms and causes side effects in the patient. With this method, which does not cause any adverse effects, it is ensured that patients are protected from the side effects of long-term drug use. The effects of acupuncture are pain-reducing, relaxing, providing homeostasis, raising the immune system, and also psychological, restorative and regenerative effects. As it causes some biochemical-cellular changes, our body's immune system becomes active and healing is achieved with the "self-healing power". During the treatment, the needles are left at short intervals for about 20-30 minutes. The patient can be stimulated by needle movement. At the end of the treatment, the needles are removed. When we insert the needle into the acupuncture point, the nerve (receptor) is stimulated. This stimulus reaches the spinal cord through the nerve and then to the necessary centers in the brain. In both body and auricular acupuncture, the points have electrically low skin resistance and high skin conductivity. In summary, acupuncture treatment increases the leukocyte count. It helps the patient cope with stress. Strengthens organs and regulates body balance. Reduces toxic accumulation. It helps in mental balance. It reduces nausea and vomiting. Provides analgesic effect. It corrects sleep disorders. In conclusion, the use of acupuncture as an adjunct therapy to conventional medical therapy for many chronic inflammatory diseases and autoimmune problems appears acceptable, and its evidence based applicability should be validated by multiple comparative case-control studies.
Mesotherapy, another traditional medicine method, is a form of treatment applied by intradermal injection of herbal or pharmacological drugs using special fine needles. After the diagnosis of the disease is made, it is carried out in the form of intradermal administration of the drug mixture selected for the structure of the pathology, in small doses, with the help of special needles and using a special technique. With mesotherapy agents, the local microcirculation in the damaged tissue is stimulated, by affecting the inhibitory mechanisms at the dermal level, the reactions in the "visceral medullercerebral" pathway at the lateral medullary level are affected, the immune system-related cells in the dermis are affected, the given agents are delivered to deeper tissues with the help of interstitial tissue, resulting in higher concentrations in the target tissues. has been theorized to occur. After the application, the drug reaches the capillary vessel ends in the dermis layer of the skin and acts rapidly.
With this method, a well-chosen low-dose drug provides a well-tolerated efficacy with minimal risk. In the mesodermic theory, inflammation is suppressed by affecting the cells related to the immune system in the dermis; It is reported that the perception of pain is prevented by the central effect, the anti-inflammatory cell aggregation against the inflammatory effect of the needle is activated, and the microcirculation is regulated by the effect of the drugs used. The most important advantages of this minimally invasive procedure are treatment with small drug doses with ample dilution rates and protection from systemic side effects of drugs. Mesotherapy has a very wide application purpose and area, including medical mesotherapy and cosmetic mesotherapy. Various factors such as the person's health status, age, physical characteristics, need status are the conditions that change the content to be injected with the microinjection application.
Key words: Inflammation, Acupuncture, Mesotherapy

IS-22
CLINICAL UTILITY OF CYTOKINES AS INFLAMMATION BIOMARKERS

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Cytokines, including interleukins, interferons, tumor necrosis factors, and chemokines, have a variety of pro-inflammatory and anti-inflammatory effects in the body through different biochemical pathways and interactions. These critical mediators, which monitor and regulate immune and inflammatory responses through complex networks, serve as biomarkers for many diseases. Stimuli, actions, interactions, and downstream effects of cytokines have been studied more extensively in recent years, and clinical research has also sought to incorporate cytokines into causal patterns to aid diagnosis and treatment.
Of a large number of known cytokines, the determination of only a few (in particular IL -6, IL -8, TNF-α) in body fluids is of importance for routine diagnostics. Such determinations aim to detect the extent of undesirable, excessive inflammatory responses. Because of the pleiotropy and redundancy of the cytokine network, there is no disease for which cytokines represent a disease-specific marker. Rather, cytokines are important in assessing the activity of a particular disease because a shift in cytokine stage may correlate with the extent of disease-specific damage. This is true for systemic diseases associated with activation of the adaptive or innate immune system, e.g., chronic heart failure or SIRS, as markedly elevated cytokine plasma concentrations are measurable in these circumstances. For the same reason, some cytokines are used to assess the prognosis of the disease and to estimate the success of therapy. The results in neonatal sepsis also show that the determination of cytokines in plasma/serum can be used for the early diagnosis of certain complications. Thus, neonatal sepsis can be predicted with high clinical sensitivity and specificity within the first hours

after birth based on the increase of IL -6 or IL -8. With conventional acute phase proteins such as CRP, this is only possible after 24-48 hours. This presentation will provide an overview of the current diagnostic and prognostic indications for the determination of cytokines.

IS-23
IN VITRO DIAGNOSTICS TESTING AND FUTURE BIOCHEMISTRY IN THE DIAGNOSIS OF INFLAMMATION

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The study of biochemistry concepts, chemical processes and in vitro diagnostic devices and its related methods are changing very rapidly in the current century. Biochemical diagnostic, measurement of parameter, verification is very important for the evolving laboratory industry to solve current health problems with new perspectives. Technology and clinical laboratory tests are expeditiously, purposefully evolving. The scientific inquiry has many new routes today and all scientific research areas are trying to find new hypotheses, expectations, theories, formulations, suppositions, assumptions using artificial intelligence, technology of electronic, electric, chemical engineering methodologies for a better, healthy and long life. The scientists are working on to develop multifunctional wireless micro scale miniature robots for diagnostic testing. The recent developments in biotechnology have supported many technologies and complex systems for analysis of complex biological systems in health and disease. Biotechnology and in vitro
diagnostic testing and other technologies are tightly coupled and developing parallel in multiple ways to basic biochemical and molecular biological research for better diagnosis of inflammation.
The metabolic reprogramming, metabolic shifts of the immune system are characterized by significant changes in the acute and chronic inflammation triggered via various types of immunomodulators. However, the number and type of the immunomodulators are increasing everyday due to needs of novel technologies, endocrine disruptors, xenobiotics, mutations in the cells, viruses and bacteria. In this panel, I will talk about new technological developments on in vitro diagnostic tests used to show immunometabolic changes.

ORAL PRESENTATION FULL TEXT [SÖZLÜ SUNUM TAM METİNLERİ]

OP11: DEVELOPMENT OF DIFFERENT PRODUCT GROUPS IN THE CLEANING INDUSTRY WITH SYNTHESIZED NANOSILVER

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ABSTRACT

Objective: Thanks to the rapid progress of science and technology, the functional properties of the raw materials in the formulations are considered as innovation at the beginning, but today it is a necessity. Silver, with its unique chemical and biological properties, has been used in many studies in the past, such as the disinfection of drinking water1, the prevention of eye infections, and the treatment of cholera and epilepsy in the 17th century. In addition, it has been observed that viruses can bind to -SH structures in proteins and inhibit these structures, thus preventing the reproduction of such micro- organisms.

Materials-Method: Nano-sized colloidal silvers were synthesized using the "Turkevich" reduction method using trisodium citrate (C6H5O7Na3). Citrate was used both as a reducing agent and as a coating agent in the reaction. During the study, the synthesis of colloidal nanosilver, characterization studies and the creation of a liquid laundry detergent and disinfectant product selected from the cleaning product range will be carried out with the synthesized colloidal nanosilver.

Results: The synthesized colloidal nanosilver structures were characterized by ICP-MS, UV-VIS Spectroscopy and SEM analysis. According to the results of the ICP-MS analysis, the synthesized colloidal nanosilver concentration was found to be 159.08 mg/L. According to the UV-VIS analysis result, the absorbance value was 0.9317, while the wavelength was around 448 nm. The SEM images taken showed that the synthesized particle was 40-50 nm in size.

Conclusion: Colloidal nanosilver has been used successfully in 2 different product groups. After preparing liquid laundry detergent and disinfectant product groups containing peroxide, pH, viscosity, stability, microbial product analysis and SEM analyzes were performed. The SEM images taken showed that the colloidal nanosilver in the 2 products was 35-45 nm in size. The 3-month stability results of the product were evaluated as appropriate. In addition, it has been proven by accredited tests that the disinfectant product has antiviral activity.

Keywords: Colloidal particle; Nanosilver; Turkevich method; Laundry detergent; Disenfectant.

ÖZET

Amaç: Bilim ve teknolojinin hızla ilerlemesi sayesinde formülasyonlarda yer alan hammaddelerin fonksiyonel özellikleri başlangıçta yenilik olarak görülse de günümüzde bir zorunluluk haline gelmiştir. Eşsiz kimyasal ve biyolojik özelliklere sahip gümüş, 17. yüzyılda içme sularının dezenfekte edilmesi [1], göz enfeksiyonlarının önlenmesi, kolera ve epilepsi tedavisi gibi geçmişte birçok çalışmada kullanılmıştır. Ayrıca virüslerin proteinlerdeki -SH yapılarına bağlanarak bu yapıları inhibe ederek bu tür mikroorganizmaların çoğalmasını engellediği gözlemlenmiştir.

Materyal-Metod: Nano boyutlu koloidal gümüşler, trisodyum sitrat (C6H5O7Na3) kullanılarak "Turkevich" indirgeme yöntemi kullanılarak sentezlendi. Reaksiyonda hem indirgeyici ajan hem de kaplama ajanı olarak sitrat kullanılmıştır. Çalışma sırasında kolloidal nanogümüşün sentezi, karakterizasyon çalışmaları ve sentezlenen kolloidal nanogümüş ile temizlik ürünleri yelpazesinden seçilen sıvı çamaşır deterjanı ve dezenfektan ürününün oluşturulması gerçekleştirilecektir.

Bulgular: Sentezlenen koloidal nanogümüş yapılar ICP-MS, UV-VIS Spektroskopisi ve SEM analizi ile karakterize edildi. ICP-MS analizi sonuçlarına göre sentezlenen kolloidal nanogümüş konsantrasyonu 159,08 mg/L olarak bulunmuştur. UV-VIS analiz sonucuna göre absorbans değeri 0,9317, dalga boyu ise 448 nm civarındaydı. Alınan SEM görüntüleri sentezlenen parçacığın 40-50 nm boyutunda olduğunu gösterdi.

Sonuç: Kolloidal nanogümüş 2 farklı ürün grubunda başarıyla kullanılmaktadır. Peroksit içeren sıvı çamaşır deterjanı ve dezenfektan ürün grupları hazırlandıktan sonra pH, viskozite, stabilite, mikrobiyal ürün analizleri ve SEM analizleri yapılmıştır. Alınan SEM görüntüleri 2 üründeki koloidal nano gümüşün 35-45 nm boyutunda olduğunu gösterdi. Ürünün 3 aylık stabilite sonuçları uygun olarak değerlendirilmiştir. Ayrıca dezenfektan ürünün antiviral aktiviteye sahip olduğu akredite testlerle kanıtlanmıştır.

Anahtar Kelimeler: Koloidal parçacık; nanogümüş; Turkevich yöntemi; Çamaşır deterjanı; dezenfektan.

INTRODUCTION

Nowadays, many products are diversified by being produced with different raw materials thanks to the rapid progress of science and technology. This situation, which was considered as an innovation in the beginning, emerges as a necessity in today's conditions.

The cleaning and cosmetics sector is one of the sectors that has advanced itself significantly in terms of formula development and product creation. Innovative and functional products with more than one feature at the same time (antibacterial soaps, surface cleaners with polishing feature, moisturizing and healing creams, etc.) are available in the market. It is vital that different raw materials can carry their unique properties into a single final product and that these raw materials can be used together in order for such products to be available on the market.

Silver (Ag), which we can consider as one of these raw materials, was used in the preservation of drinking water many years ago [6], in the prevention of eye infections that may occur in newborn babies, and in the treatment of cholera and epilepsy in the 17th century, thanks to its unique chemical and biological properties. It has been evaluated as a multi-purpose medical product [7]. In today's scientific studies, it has been observed that silver binds to -SH structures in the proteins in the structure of various living

things and viruses and inhibits these structures, thus preventing the reproduction of such micro- organisms [8].

In noble metals, absorption in the visible region (~ 400-750 nm in wavelength) is observed due to the electron mean free path depending on decreasing in size. An oscillation is occurred from a free electron of a surface of a particle to another particle that is called 'the surface plasmon absorption'. The bright and shining color in metallic particles is observed because of this feature and the discrepancy of color is shown depending on their size shape and chemical environment [9,10,25]. There are many methods for synthesis of silver nanoparticle. In a study done in 2020, T. Liu et al used glycerol in their synthesis method. Silver ions are reduced successfully by glycerol which have free radicals. Small silver nanoparticles were obtained thanks to glycerol in this study [2].

In 2005, 2012 and 2018, researchers synthesied silver nanoparticle by poly-ol method at two different study. They used polyetilen glycol as a reducing agent in their studies [1,3,17,19]. In another study conducted in 2018, starch was used as a reducing agent and silver nanoparticle was synthesized [5].

A study in which sodium citrate was used as both a reducing and coating agent. Silver nanoparticles were successfully obtained after synthesis in the presence of temperature [4,23,24]. The reaction was showed in eq. 1

$$4Ag^{0}+C_6H_5O_7Na_3+2H_2O \xrightarrow[\text{reflux}]{\text{1 h}} 4Ag0 + C_6H_5O_7H_3 + 3Na^{+} + O_2$$

Eq. (1)

In our study, the antibacterial effects of silver were transferred to various products in the cleaning and cosmetics sector [20-22]. In the study, Turkevich method was used to synthesize silver nanoparticles to be used in different final products. Different product trials (hand gel, hand cream, environmental and surface disinfectants, surface cleaner, etc.) were successfully completed by performing characterization studies. In this way, it is aimed to bring silver resources to the cleaning and cosmetics sector by preparing them with domestic capital and local knowledge.

MATERIALS-METHOD:

Silver nitrate (AgNO3, 99%, Alfa Aesar) and trisodium citrate (Sigma Aldrich) were used for synthesis of silver nanoparticles. The solutions were prepared with pure water which is deionized with filtration and resin system. 5-15% Anoinic surfactants (BASF), < 5% nonionic surfactants (BASF,PCC), soap (ILMOR), polycarboxylates (Viking Cleaning and Cosmetic Co.), enzymes (Novozymes), perfumes (Hexyl Cinnamal) (Firmenich)and preservatives(methylchloroisothiazolinone,methylisothiazolinone) (THOR) were used to produce laundry detergent which contains silver nanoparticles. Hydrogen peroxide solution (50%, Koray Kimya) was used to produce disinfecting agent with silver nanoparticles. Optical and surface characterization techniques were used for synthesized silver nanoparticles and laundry detergent with silver nanoparticles. The absorption spectra were recorded at UV-Vis Spectrophotometer (Thermo Scientific, Genesys 10S). Functional groups on silver nanoparticles were determined by utilizing ATR method with Fourier Transform-Infrared Spectroscopy (FT-IR,Bruker Alpha Platinum ATR). Inductively Coupled Plasma Mass Spectrometer (ICP-MS, Agilent 7900) was used to find out the concentration of silver nanoparticles. Scanning Electron Microscopy (SEM) analysis was performed (Thermo Scientific Apreo S) operating at 7.5-10.0 kV.

Synthesis of Citrate Capped Silver Nanoparticles

In this study, Turkevich method was modified to obtain silver nanoparticles. $AgNO_3$ as silver precursor and trisodium citrate as reducing and capping agent were used to utilize silver nanoparticles effectively. AgNO3 solution were prepared and heated at 100 °C. After boiling was observed, 1% of Trisodium citrate solution was added to the AgNO3 solution which is colorless and clear. After adding the citrate solution, the color of solution turned to yellow, brown and then greenish and reddish gray. The heater was turned off and stirer was continued until it cooled down [14-16,23].

Development of Products

Silver nanoparticles were performed on laundry detergent [21] and disinfecting agent with hydrogen peroxide by optimizations on the formulations.

RESULTS

The characterization studies of the synthesized silver nanoparticles were completed using different microscopic and spectroscopic methods.

Thermo Scientific, Genesys 10S, UV-Vis Spectrophotometer was used for absorption spectra. Functional groups on silver nanoparticles were determined using ATR method with Fourier Transform-Infrared Spectroscopy (FT-IR, Bruker Alpha Platinum ATR). The concentration of silver nanoparticles was determined using Inductively Coupled Plasma Mass Spectrometry (ICP-MS, Agilent 7900). Scanning Electron Microscopy (SEM) analysis (Thermo Scientific Apreo S) was performed by operating at 7.5-10.0 kV and the surface morphology was examined.

The concentration of silver nanoparticles was performed as 159.08 mg/L by ICP-MS instrument. The FT-IR characterization of citrate capped silver nanoparticles and trisodium citrate were shown in Figure 1 and Table 1 ATR method was used for pelleted utilized silver nanoparticles. The peaks at 1399-1585 cm-1 (COO- functional groups), 3445 cm-1 (–OH groups) corresponded to trisodium citrate in Figure 1. In addition, some peaks belong to silver nanoparticles was observed some similarities with the peaks of trisodium citrate. This case was a kind of proof that trisodium citrate is coating the silver nanoparticles.

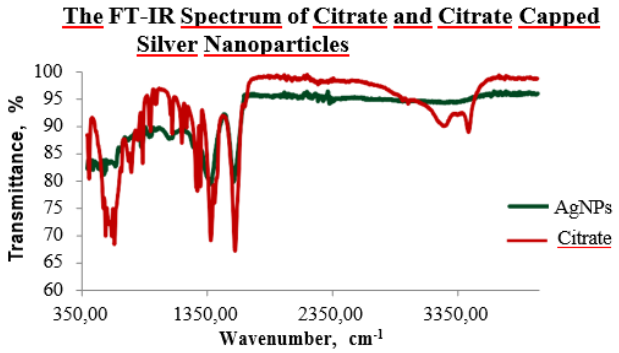

Figure 1. FT-IR spectrum with ATR method obtained from pelleted silver nanoparticles and trisodium citrate.

Table 1. Schematic of FT-IR analysis for silver nanoparticles

Functional Groups	Wavenumber (cm^{-1})
COO^-	1585 cm^{-1} ,1399 cm^{-1}
OH^-	3455 cm^{-1}

V-Vis spectroscopy is one of the most significant characterization techniques for metalic nanoparticles [9]. Unique SPR band is observed in spectrum because of absorption of silver nanoparticles. Their specific absorptions are generally around 400-500 nm. This characteristic property is depended on size distribution of silver nanoparticles. In Figure 2., utilized silver nanoparticles of UV-Vis spectrum was demonstrated and only one peak was observed for silver nanoparticles as 448 nm in wavelength.

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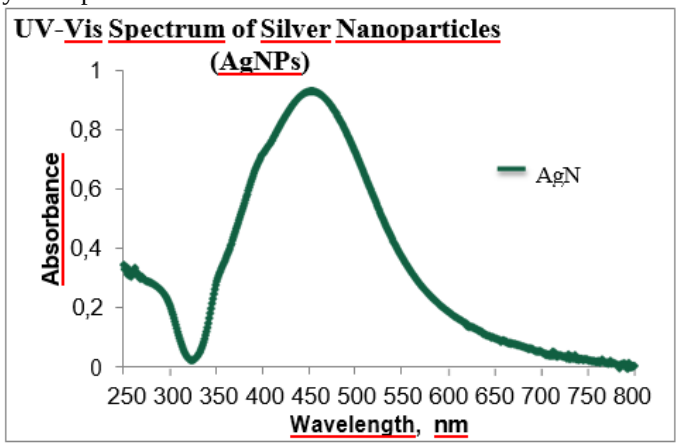

Figure 2. UV-Vis spectrum of silver nanoparticles.

SEM images of the utilized silver nanoparticles was demonstrated in Figure 3. The shape of silver nanoparticles was spherical shape and the size distribution of AgNPs were observed around 40-50 nm.

As seen in Figure 4 and 5, aggromelation of silver nanoparticles was not observed in the products. The shapes of silver nanoparticles in products were spherical shape and the size distribution of AgNPs were observed around 35-45 nm. The reason of decreases on size is surfactants which were in products [11,13,18,22].

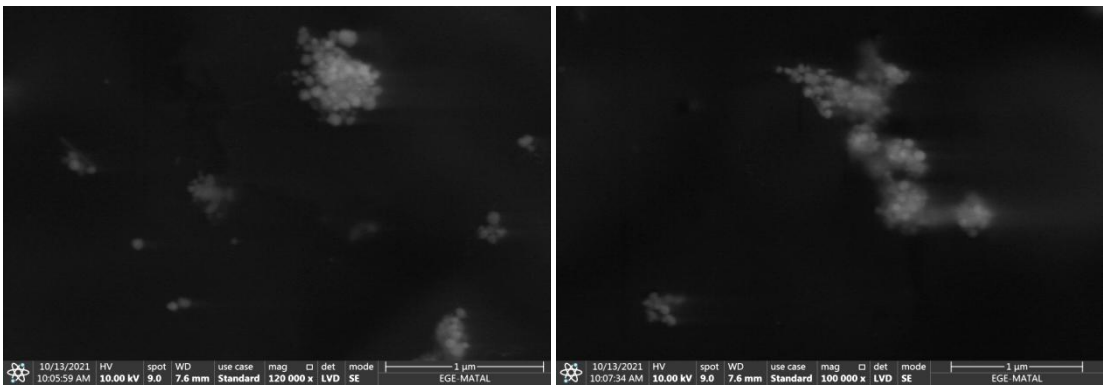

Figure 3. SEM images of silver nanoparticles.

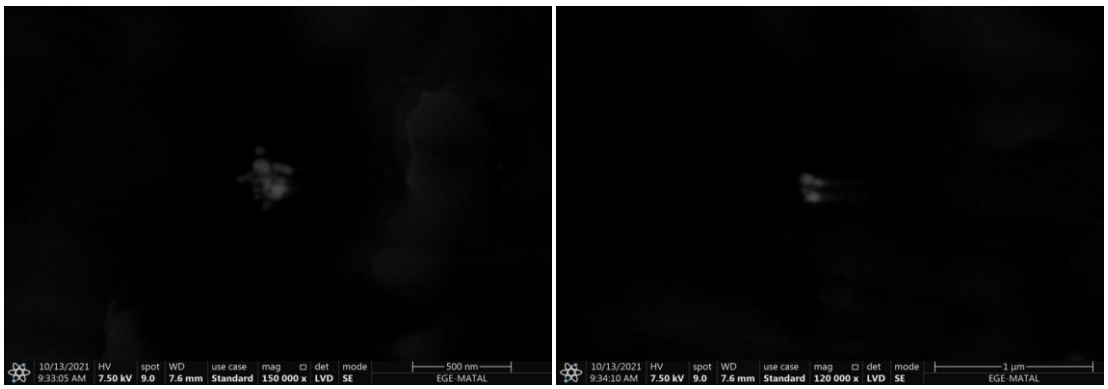

Figure 4. SEM images of laundry detergent with silver nanoparticles.

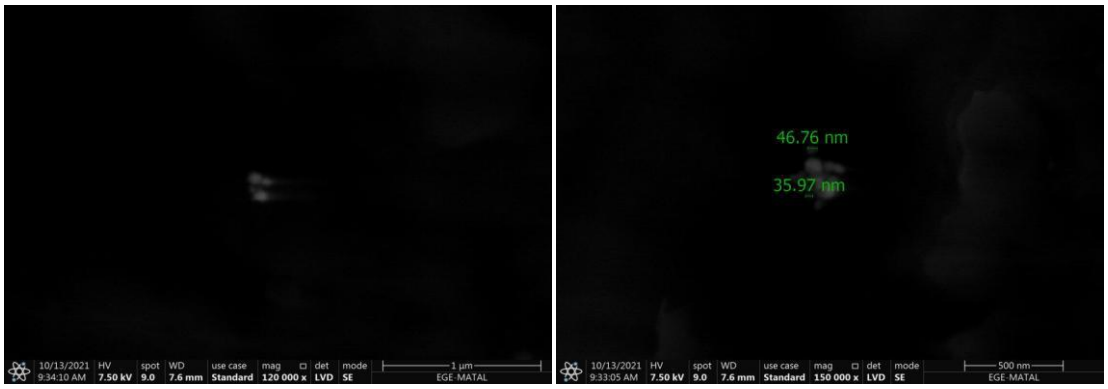

Figure 5. SEM images of disinfectant product with silver nanoparticles.

Microbial images of liquid laundry detergent with colloidal nanosilver are given in Figure 6. According to the results examined, as can be seen in the image symbolized by c, the colloidal nanosilver content acted as a preservative and no microbial growth was found.

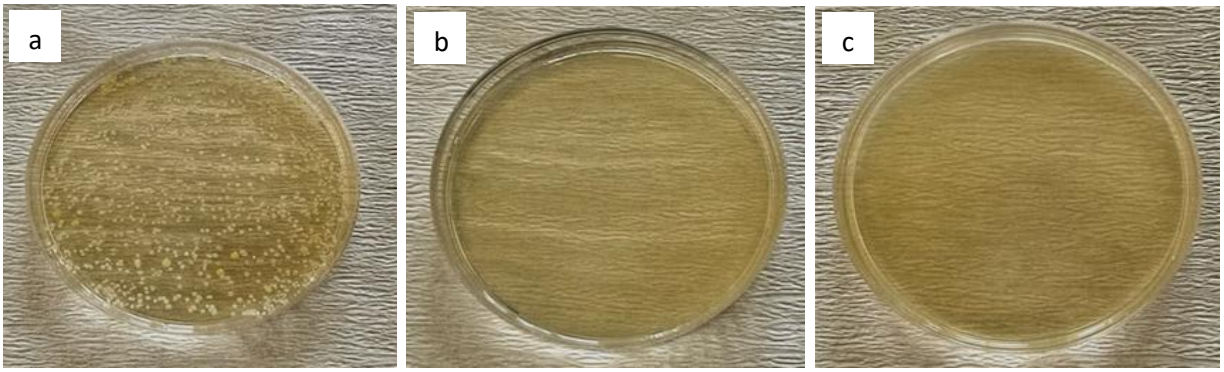

Figure 6. Microbial activity of laundry detergent with silver nanoparticles. a) The control group without preservative and collidal nanosilver, b) The product containing preservative c) The product containing collidal nanosilver without preservative.

It has been tested on experimental organisms of Poliovirus Type 1, Adenovirus Type 5, Murine Norovirus S99 Berlin, Vaccinia Virus ATCC VR-1508 according to TS 14476+A2 standard.

The disinfectant product with silver nanoparticles has been proven to be 99.99% virucidal activity on all tested organisms as shown in Table 2.

Table 2. Virucidal activity of disinfectant product with silver nanoparticles.

Virus name	Useage area	Reference virus titer	Disinfectant virus titer		Rate of decrease in virus titer	
			clean	unclean	clean	unclean
Poliovirus Type 1, LSc-2ab	public and personal space	5.5	1.5	1.5	4.0(log)	4.0(log)
Adenovirus Type 5, Strain adenoid 75, ATCC VR-5	public and personal space	5.5	1.5	1.5	4.0(log)	4.0(log)
Murine Norovirus, Strain S99 Berlin	public and personal space	6.0	2.0	2.0	4.0(log)	4.0(log)
Vaccinia Virus Strain Ankara (MVA) ATCC VR-1508	public and personal space	6.0	2.0	2.0	4.0(log)	4.0(log)

DISCUSSION

Within the scope of the study, colloidal nanosilver was successfully synthesized and adapted to the final products. According to the results of the ICP-MS analysis, the synthesized colloidal nanosilver concentration was found to be 159.08 mg/L. According to the UV-VIS analysis result, the absorbance value was 0.9317, while the wavelength was around 448 nm. The SEM images taken showed that the synthesized

particle was 40-50 nm in size.

For the peroxide containing disinfectant product containing colloidal nanosilver, pH, viscosity, stability, microbial activity and SEM analyzes were performed. The SEM images taken showed that the colloidal nanosilver in the product was 35-45 nm in size. The 3- month stability results on the product were evaluated as appropriate. In addition, the antiviral activity of the product has also been proven by the tests carried out.

A new formulation has been adapted to colloidal nanosilver liquid laundry detergent product. In the SEM images of the liquid laundry detergent, the presence of particles was proven and it was observed that aggregation was prevented due to the surfactants in it [11]. When we look at the microbial images, growth was observed in the control group, while growth was not observed in the other test groups. Colloidal nanosilver has been proven to inhibit the growth of bacteria in a preservative-free environment.

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OP18: INVESTIGATION OF THE ANTIMETASTATIC POTENTIAL OF *THYMBRA SPICATA* IN HUMAN BREAST ADENOCARCINOMA CELLS COMBINED WITH STANDART CHEMOTHERAPY

[*THYMBRA SPICATA*'NIN İNSAN MEME ADENOKARSİNOMA HÜCRELERİNDE ANTİMESTATİK POTANSİYELİNİN STANDART KEMOTERAPİ İLE KOMBİNE ETKİNLİĞİNİN ARAŞTIRILMASI]

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ABSTRACT

Objectives: *Thymbra* types in Turkish public medicine, antioxidant, antiseptic, antitussif, degassing, it is widely used due to antiinflammatory and antimicrobial activities. This study aims to determine the effects of the hexane plant prepared from the *Thymbra spicata* (*TS*) on human breast adenocarcinoma cell lines (MDA MB-231, BT-474), combined with the chemotherapeutic drug Paclitaxel (PAC) used in the clinic, and the effects of cyotoxic, antioxidant and metastatic process.

Materials-Methods: IC_{50} and IC_{25} concentrations of *TS* and PAC in MDA MB 231 and BT-474 cells were determined by MTT method. These two concentrations were compared with the control in the treatment groups. Cell motility as an indicator of metastatic potential evaluated by in vitro wound healing method. Free oxygen radicals were analyzed with Total Oxidant Level (TOS), Total Anti-Oxidant Level (TAS) kits. Colony formation potential was evaluated by Soft Agar Colony Formation Analysis (Spheroid Model).

Result: The combined group was most effective on total antioxidant levels. Compared to the control group, each of the treatment groups showed a statistically significant antioxidant effect; It was observed that all treatment and combination groups decreased the oxidative level, with the highest rate of PAC. The total antioxidant level in BT-474 was statistically significantly higher in all treatment groups compared to the control group. In both cell lines, *TS* groups were found to be effective in inhibiting migration and reducing tumorigenesis capacity.

Discussion: It has been observed in vitro that *TS* inhibits cell migration and invasion and reduces the capacity of tumorigenesis. We think that the effect of *TS* alone or in combination with standard chemotherapeutics should be tested in in vivo studies in future studies.

Keywords: *T. spicata*, invasion, metastasis, tumorigenesis, breast cancer

ÖZET

Giriş: Thymbra türleri Türk halk hekimliğinde, antioksidan, antiseptik, antitussif, gaz giderici, antienflamatuar ve antimikrobiyal aktiviteleri nedeniyle yaygın olarak kullanılmaktadır. Bu çalışma, *Thymbra spicata* (*TS*) dan hazırlanan hekzan ekstaktının insan meme adenokarsinom hücre hatlarında (MDA MB-231, BT-474), klinikte kullanılan kemoterapötik ilaç Paklitaksel (PAC) ile kombine olarak sitotoksik, antioksidan ve metastatik sürece etkilerini belirlemeyi amaçlamıştır.

Materyal-Metod: MDA MB-231 ve BT-474 hücrelerinde *TS* ve PAC ait IC_{50} ve IC_{25} konsantrasyonları, MTT yöntemi ile belirlendi. Bu iki konsantrasyon, tedavi gruplarında kontrol ile karşılaştırıldı. Metastatik potansiyelin bir göstergesi olarak hücre motilitesi in vitro yara iyileşme yöntemi ile değerlendirildi. Serbest oksijen radikalleri Total Oksidan Seviyesi (TOS), Total Anti Oksidan Seviyesi (TAS) kitleri ile analiz edildi. Soft Agar Koloni Oluşum Analizi (Sferoid Model) ile koloni oluşturma potansiyeli değerlendirilmiştir.

Sonuç: MDA MB-231'de Kombine Grup, total antioksidan düzeylerinde en etkili görüldü. Kontrol grubuna göre tedavi gruplarının her birinin anlamlı istatistiksel antioksidan etki gösterdiği; Oksidatif düzeyi, PAC in en yüksek oranda olmak üzere tüm tedavi ve kombin gruplarının azalttığı gözlendi. BT-474'de total anti oksidan seviyesini tüm tedavi gruplarında kontrol grubuna göre istatiksel olarak anlamlı derecede yüksektir. Her iki hücre hattında da *TS* grupları migrasyonu engellemede ve tümöregenez kapasitesini azaltmada etkili bulunmuştur.

Tartışma: *TS*'nin hücre migrasyon ve invazyonunu inhibe ettiği ve tümörigenez kapasitesini azalttığı in vitro olarak gözlenmiştir. Bundan sonraki çalışmalarda *TS*'nin tek başına ve standart kemoterapötiklerle kombine etkisinin in vivo araştırmalarda test edilmesi gerektiğini düşünüyoruz.

Anahtar Kelimeler: *T. spicata*, invazyon, metastaz, tümörigenez

INTRODUCTION

Breast cancer (BC) is the major and most common diagnosed cancer in women, which accounts for 30% of new female cancer cases and also the second cause of death in women worldwide. In 2022, regardless of gender, breast cancer was the second most frequently diagnosed cancer worldwide, with a frequency adding up to 11.9% [1]. Approximately one million breast cancer cases are diagnosed annually worldwide. It is assumed that one in eight women in the world will develop breast cancer [2]. Despite of new treatment options immunotherapy, antibody-drug conjugates, PARP inhibitors and chemotherapeutic regimes, hormonal therapies, surgery and radiation therapy, known as old methods, only one third of breast cancer patients are successfully treated [3]. Resistance to drug treatment, side-effects and cost are major limitations of current treatment strategies [4, 6]. Phytochemicals have exhibited their potential to be a part or substituent of cancer drugs, at the same time reduced the cost and the avoided adverse side effects. This situation led to the increase of bioactive phytochemicals focused studies to reduce chemothearapy related side effects and increase chemotherapy effectiveness. Moreover, different phytochemicals may play ameliorative role at different or multiple stages during cancer development [7]. Paclitaxel(PAC) is a taxane that stabilizes

microtubules. It inhibits their depolymerization to free tubulin and induces apoptosis. Although PAC is effective in the treatment of head and neck, breast, lung and ovarian cancer, its use is limited by myelotoxicity, neurotoxicity and poor solubility [8, 9].*Thymbra spicata* (*TS*) is a plant used especially in the Middle East, it grows in the Central and Southern Anatolian regions of Turkey. *TS* is a thyme-like plant and a member of the Lamiaceae family, which is called "Zahter" in Turkey [10,11]. *TS*; it is used among the folk in the treatment of asthma, colic, bronchitis. It is also used in the food industry as a flavoring and preservative in Turkey. Previous studies have proven the antibacterial, antimicrobial, and antifungal effects of *TS* [12, 14, 15, 16]. Breast cancers are heterogenous, showing variable morphologic and biological features and thus different response to treatment. Estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) assessment is routine in breast cancer in the diagnosis process. They are prognostic markers and important predictive factors for hormonal and anti-HER2-targeted therapy. Approximately 75% of breast cancer expreses ER/PR and 15% of breast cancers overexpress HER2. Triple-negative breast cancer (TNBC) is a molecularly diverse breast cancer subtype currently defined by what it lacks. With ER/PR and the absence of HER2 protein overexpression or *HER2* gene amplification. TNBC accounts for 15% of all breast cancers [17, 18]. Although treatment options are increasing in TNBC and HER2+ breast cancer the prognosis is still poorer for these types. Chemotherapy is the main treatment in HER2 group, despite the increase in the number of anti-HER2 drugs and TNBC. For this reason, many researchers are working on these two types of breast cancer to reduce chemothearapy related side effects and increase chemotherapy effectiveness. In our study, we targeted these two breast cancer types and selected the TNBC-specific MDA-MB-231 and the HER2+ feature BT-474 cell line.

The aim of this study was to determine the effects of hexane extract prepared from *Thymbra spicata* on the cytotoxic, antioxidant and metastatic process in human breast adenocarcinoma cell lines (MDA-MB-231, BT-474) in combination with the chemotherapeutic drug PAC.

MATERIALS AND METHODS

Cell Culture

MDA-MB-231, BT-474 cell lines were purchased from the American Type Culture Collection (ATCC). DMEM and RPMI 1640 (Gibco) supplemented with 10% fetal bovine serum and 1% penicilin/streptomycin, 1% amphotericin b. Cell lines were kept in a CO_2 incubator at 5% CO_2.

Cell Viability Assay

MDA-MB-231 and BT-474 cell lines were cultured and grown, then seeded in 96-well plates (10.000 cells/well). Cells were seeded in a 96-well plate and incubated overnight before treatment with the respective inhibitors. Cell viability was assessed using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. After incubation with dimethylsulfoxide was added to dissolve the water-insoluble purple precipitate. Absorbance of the resulting solution in individual wells was measured at 595 nm and IC_{50}, IC_{25} doses were determined and in other assays these doses were used, they were named as PAC50, PAC25, *TS*50, *TS*25.

Wound Healing Assay

MDA-MB-231 and BT-474 cells were seeded onto 6-well plate to create a confluent monolayer. The cell monolayer was scraped to create a straight a scratch was made using a 200 µl pipette tip through the middle of the plate. Tip and then incubated with indicated treatment. Wound closure was monitored at certain hourly intervals.

Oxidative Stress Index

Total Oxidant Status (TOS) and Total Antioxidant Status (TAS) were determined in both cell lines. Assay Diagnostics for serum TOS and TAS measurements (Turkey) commercial kits were used, and measurements were made according to the method recommended by the company.

Soft-Agar Colony Formation Assay

Cells are planted in flasks. Cells are incubated at 37°C in an incubator containing 5% CO_2. Previously determined IC_{50}, IC_{25} doses were also used in this assay. After treatment, the cells are incubated at 37°C in a 5% CO_2 incubator and after incubation, the medium is poured, culture flasks were washed with PBS. Cells are removed by adding trypsin to each flask. Collected cells were centrifuged at 1500 rpm. The supernatant is discarded. The pellet is suspended by adding medium on it. Then the bottom layer and the top layer are prepared. Bottom layer: Agarose is weighed, soluble in sterile distilled water. 2.5 ml is added to each well of a 6-well plate. Top layer: Agarose is weighed and dissolved in sterile distilled water. It is boiled in the microwave. The cell suspension is suspended with agarose and added to the bottom layer. Treatment groups are given at the doses determined on it. On 3rd and 7th day, images are taken with a phase-contrast microscope, and cell counts are made.

Statistical Analysis

Data were evaluated statistically with the licensed SPSS program. The conformity of the variables to the normal distribution (Kolmogorov-Smirnov/Shapiro-Wilk tests) was examined. Descriptive statistics: the mean ± standard deviation values of the variables were given. ANOVA was used to compare the groups. Significance was evaluated with the Holm-Sidak test, and p-Value <0.05 was considered statistically significant.

RESULTS

IC_{50} and IC_{25} doses were determined by MTT analysis in human breast cancer cell lines (MDA-MB-231 and BT-474). Proceed to other experimental stages with the determined doses. IC_{50} values were found as MDA MB-231 PAC IC_{50}: 60 nM, BT-474 IC_{50}: 6 nM, MDA MB-231 *TS* IC_{50}: 141 µg/mL, BT-474 *TS* IC_{50}: 220 µg/mL.

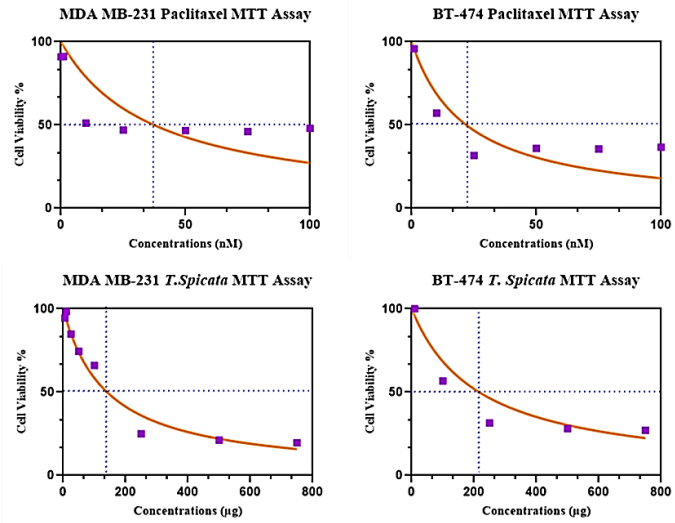

Figure 1. Cell Viability Assay (MTT), in MDA MB-231 and BT-474 cell lines, Paclitaxel and *T. spicata* 72-hour IC_{50} concentrations determined.

Cell migration was first analyzed by the Wound Healing Assay. In the MDA-MB-231 cell line, the *TS*50 Group significantly inhibited migration at the end of the 24th hour compared to both doses of the standard chemotherapeutic group PAC (Figure 2A, B). In BT-474 cell line, the Combined and *TS*50 Group were statistically significantly more successful in inhibiting migration compared to both doses of PAC (Figure 2C, D).

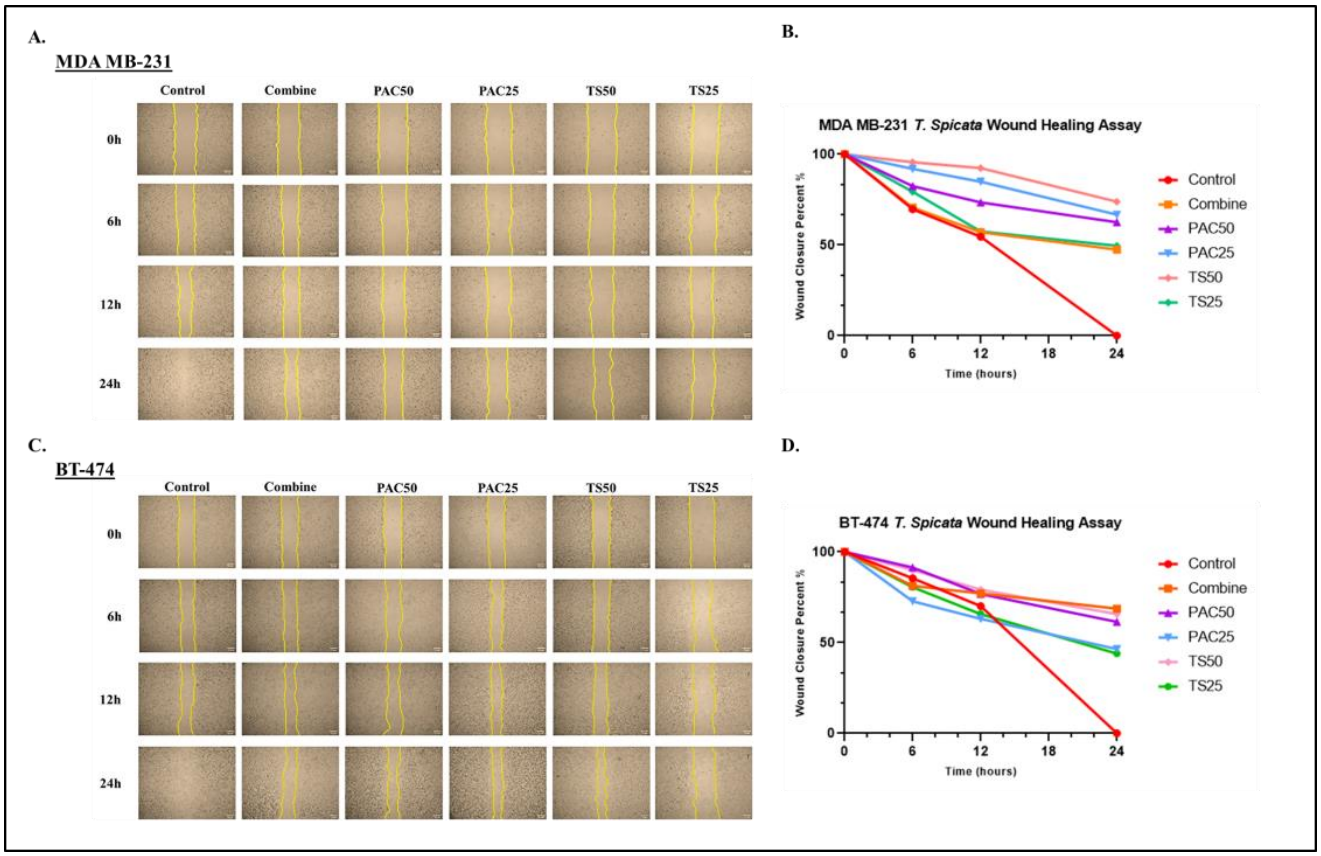

Figure 2. Wound Healing Assay to determine cell migration. Wound Healing Assays were performed at 0, 6,12 and 24 h. Wound Healing images on the MDA-MB-231 cell line, B. Wound Closure Percentage calculated based on the data shown in A, C. Wound Healing images on the BT-474 cell line, D. Wound Closure Percentage calculated based on the data shown in.

Free oxygen radicals were determined by measuring total antioxidant and total oxidant levels. Total antioxidant level of *TS*50 Group in MDA-MB-231 cell line was significantly higher than all groups. There was no statistically significant difference between the total antioxidant levels of the other groups. TOS of the Combined Group is statistically significantly higher than *TS*50 (Figure 3).

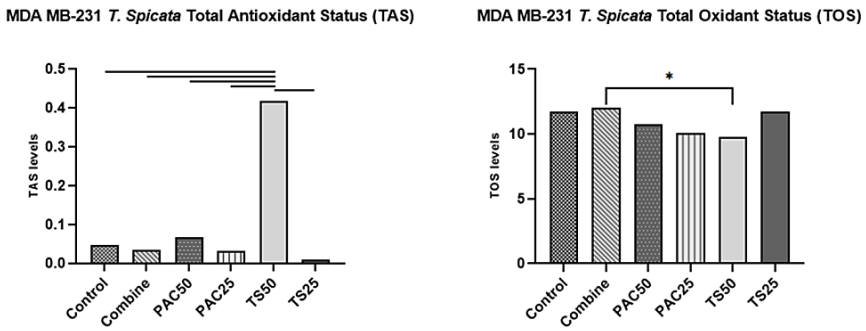

Figure 2. MDA-MB-231 Total Antioxidant Status (TAS), Total Oxidant Status (TOS).
The lines between the groups show statistical significance ($p<0.05$).

Total antioxidant level in BT-474 cell line was statistically significantly higher in the Control Group compared to the other groups. The total antioxidant level of the groups containing *TS* was significantly higher than the groups with standard chemotherapeutic groups. Considering the combined group, it was observed that *TS* increased the antioxidant properties of PAC. The oxidation level of the PAC50 Group was statistically significantly higher than the control and *TS*25 Groups (Figure 4).

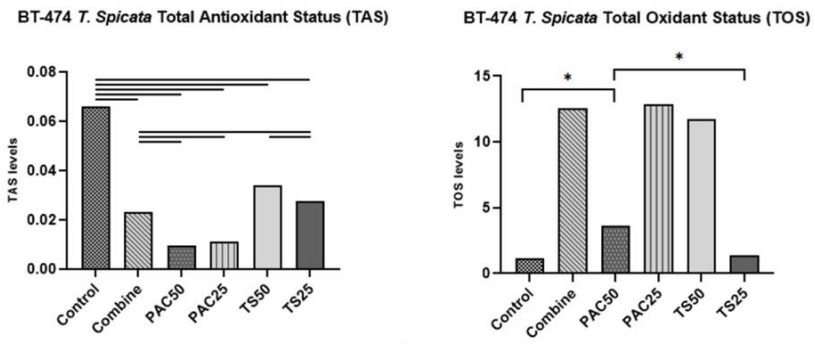

Figure 3. BT-474 Total Antioxidant Status (TAS), Total Oxidant Status (TOS).
The lines between the groups show statistical significance ($p<0.05$).

Finally, Soft-Agar Colony Formation Assay was performed to measure tumorogenic capacity. Large spheroid formations were observed in the control group in both cell lines. (Figure 5, 6). Comparisons between the Control and treatment Groups were determined according to the spheroid, which was accepted as the reference value (The spheroid area considered as a reference is 9 micrometers).

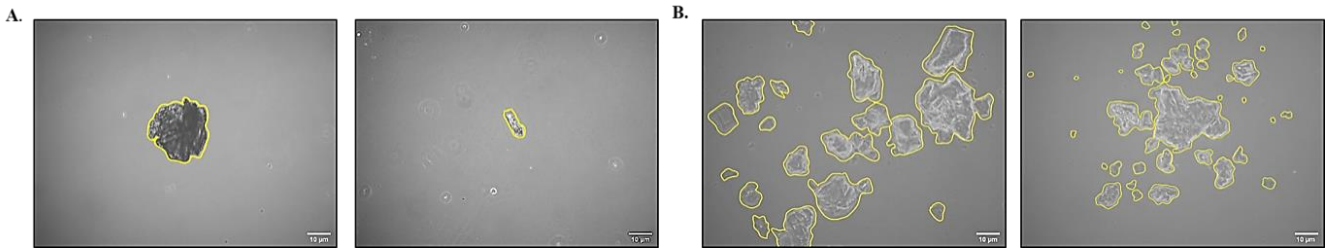

Figure 5. A) MDA-MB-231 cell line Soft-Agar Colony Formation Assay (Sferoid Assay) 7th day Control Group 10X image. B) BT-474 cell line Soft-Agar Colony Formation Assay (Sferoid Assay) 7th day Control Group 10X image.
As can be seen when comparing figures, A and B above, the Soft-Agar Colony Formation Assay formations of the Control Group of BT-474 cell line are larger.

The total spheroid count of the Control Group was statistically significantly higher compared to the PAC50 and *TS*50 Groups. The PAC50 and *TS*50 Group decreased the solid tumor forming capacity compared to the Control Group when applied both separately and in Combination (Figure 6A, B).

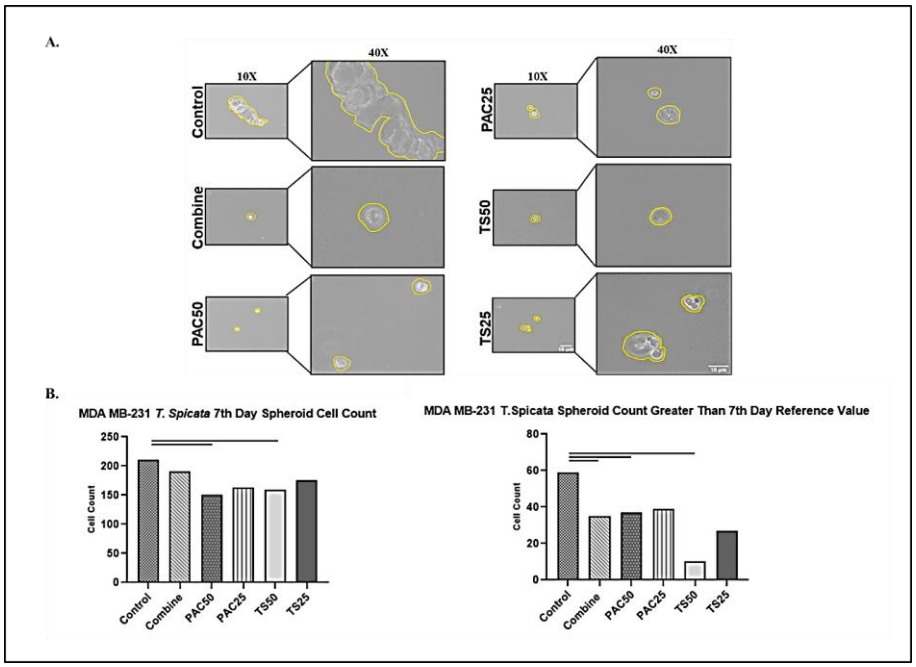

Figure 6. A) Soft-Agar Colony Formation Assay (Sferoid Assay) of the MDA-MB-231 cell lines at 7 days after seeding. B) The lines between the groups show statistical significance (p<0.05).

In BT-474 cell line, it was observed that all treatment groups reduced the total number of spheroids compared to the Control Group.

*TS*50 is successful both in the formation of spheroid formation and in preventing the formation of large formations (Figure 7A, B).

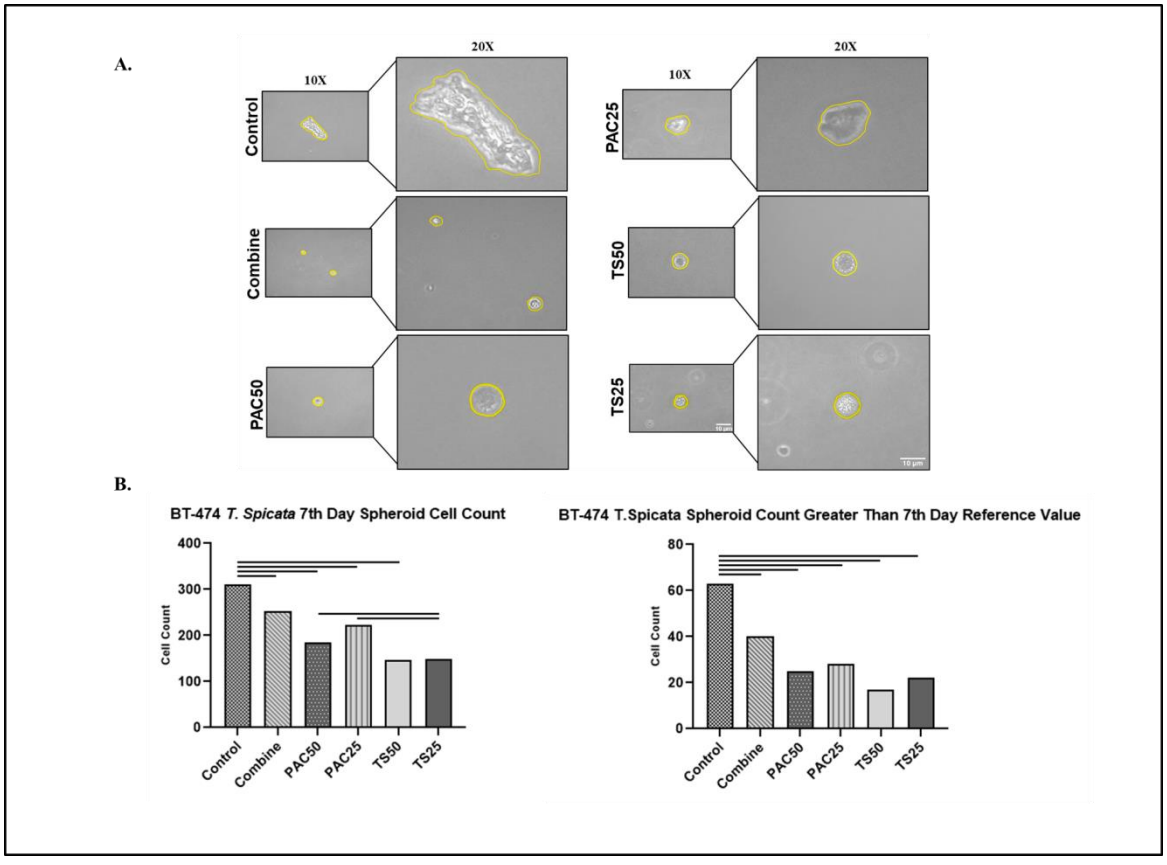

Figure 7. A) Soft-Agar Colony Formation Assay (Sferoid Assay) of the MDA-MB-231 cell lines at 7 days after seeding. B) The lines between the groups show statistical significance (p<0.05).

DISCUSSION

Therapeutic agents used in cancer treatment have toxic effects. PAC is frequently used in first-line therapy of breast cancer [19]. The most common side effects of PAC are alopecia, nausea and vomiting, mucositis, neutropenia, leukopenia, anemia, hypersensitivity reactions, arthralgia, myalgia, and malaise. [19,20]. Resistance to PAC therapy in breast cancer is a major obstacle for clinical applications. Due to existing side effects and drug resistance, more effective and fewer toxic agents are needed as an alternative to standard treatment. In recent years, the interest in endemic plants has increased day by day and it is foreseen to be used as a new therapeutic agent. Our country is very rich in terms of endemic plant reserves. There are around 11,400 plants in total, of which 3,700 are endemic.

Many molecular mechanisms play a role in the development of breast cancer (BC), and now not only immunohistochemical results but also molecular characteristics are evaluated when planning BC treatment. While targeted therapies are developing in the treatment of BC, integrative therapy studies increase continuously. In our study, hexane extract of *Thymbra spicata* (*TS*), an endemic plant species grown in the Eastern Anatolia Region of our country, was used. The effect of this extract was investigated in HER2+, which needs improvement in survival rates despite increasing treatment options, and triple negative breast cancer (TNBC), which has fewer treatment options.

In the case of BC metastasis, the survival time is significantly reduced. Wound healing analysis results are important to evaluate the effect of *TS* on migration and metastasis of BC cells. When the results are evaluated, it is seen that *TS*50 is a potent agent in preventing migration in both cell lines in the wound healing analysis. Especially in the MDA-MB-231 cell line, the *TS*50 group was found to be more successful in preventing migration compared to all other groups. Similar results were obtained in the BT-474 cell line in preventing migration of the combined and *TS*50 group. With these results, we concluded that *TS* may be effective in reducing the development of BC metastases. With these findings, it can be predicted that *TS* may be important in preventing metastasis both in breast cancer patients who have developed metastases and in patients who cancer cell migration and invasion forms the mainstay of tumor biology and is the precursor to metastasis have developed metastases and are receiving treatment [21].

The contribution of oxidative stress developing in the tumor microenvironment to carcinogenesis is known. In current treatment researchs, total oxidant status (TOS) and total antioxidant status (TAS) results are used to evaluate the efficacy of treatment. In this study, it is seen that PAC increases oxidative stress in BT-474 cell line and has a toxic effect on cancer cells. It was observed that the group closest to the cytotoxic effect of PAC was the combination group. At the same time, it was observed that *TS* increased the antioxidant activity of PAC in the combination of PAC25-TS25. In the MDA-MB-231 cell line, it was observed that PAC increased the oxidation level of *TS* in the combined group.

The increased amount of ROS in cancer cells has a higher rate of oxidative stress compared to normal cells [22]. When the results were evaluated, it was confirmed that each cancer cell has its own oxidant and antioxidant properties. Cancer cells progress by using the oxidant or antioxidant mechanism according to the microenvironment in which they are located. The effects of free oxygen radicals on the regulation of tumor progression have been described in the literature. It can be observed that these effects differentiate depending on the subtype of immune cells, the presence of tumor, and the experimental model used. In our study, it is not possible to observe the effects of immune cells such as dendritic cells, myeloid-derived suppressor cells (MDSCs), natural killer cells (NK), and tumor-associated macrophages (TAM). However, it is known that tumor progression is related with these cells which is previously mentioned. It can be concluded that the effect of the reduction in tumor progression observed in cell lines is independent of these cells.

Tumorigenesis refers to the distinguishing features between normal cells and cancer cells. These features are differentiation, differentiated proliferation ability, metastasis, cell death, escape from the immune system, dysregulated metabolism, and epigenetic changes [23]. In our study, it was observed that *TS*50 was effective in reducing the tumorigenesis capacity in the Soft-Agar Colony Formation Assay, which we performed to measure the tumorigenesis capacity. It was observed that the *TS*50 group both reduced spheroid formation and prevented large formations in both cell lines. These results show that *TS* is effective in preventing the development of BC. *TS* may reduce the risk of BC recurrence by preventing tumor re-growth in patients treated with BC. It can also slow or even stop the development of a clinically undetectable tumor. Our findings may also give a preliminary idea that *TS* may have a preventive effect on BC.

In our study, *TS* was found to have antitumoral activity in TNBC and HER2+ BC cell lines. In this study, there are findings that *TS* is a suitable agent to be studied in BC animal experiments, and it is thought that these results will be confirmed by animal experiments. In future studies, it can be expected that *TS* will be included in the preventive and integrative treatment for BC.

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Ethics Statement

The study with file number 6816-GOA was approved by the DEU Non-Interventional Research Ethics Committee on 01.12.2021 (Decision No: 2021/35-16).

OP29: THE EFFECT OF TOLL-INTERANCING PROTEIN ON INFLAMMATORY STATUS OF HEPATOCELLULAR CARCINOMA CELL LINE

[TOLL-ETKİLEŞİMLİ PROTEİNİN HEPATOSELÜLER KARSİNOM HÜCRE HATLARININ İNFLAMASYON DURUMUNA ETKİSİ]

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ABSTRACT

Objectives: Toll-interacting protein (TOLLIP) has an inhibitory effect on Toll-like receptor mediated inflammatory signaling that plays an important role in many cancer types, including hepatocellular carcinoma (HCC). Alpha 7 nicotinic acetylcholine receptors (α7nAChR) play a role in the endogenous suppression of inflammation. In this study, it is aimed to identify the effect of *TOLLIP* expression on several inflammatory pathway related genes in well- and poorly-differentiated HCC cell lines.

Materials-Methods: *TOLLIP* gene expression was increased and silenced by plasmid transfection and siRNA, respectively both in well-differentiated Hep3B and poorly-differentiated SNU449 cell lines. RNA isolation and cDNA synthesis were performed and the expression patterns of *TLR2, TLR4, NFkB, IL6* and *α7nAChR* were evaluated by RT-PCR.

Results: *TOLLIP* overexpression did not change *IL6* and *α7nAChR* expressions while having opposite effects on TLR2 and TLR4 expressions in SNU449 cells. In Hep3B cells, *TOLLIP* overexpression increased IL6 and decreased *α7nAChR*, while having no effect on TLR2 and TLR4 expressions. On the other hand, *TLR2, TLR4, NFkB, IL6* and *α7nAChR* expressions increased *in* SNU449 cells, while decreased in Hep3B cells in the absence of *TOLLIP*.

Conclusions: Silencing the *TOLLIP* gene seems to stimulate the inflammatory status in poorly-differentiated SNU449 cells, while ameliorate the inflammation status in well-differentiated Hep3B cells. Although the results should be confirmed at the protein level and with additional experiments, *TOLLIP* seems to regulate the inflammatory related genes differently in well- and poorly differentiated HCC cell lines and its silencing might have potential therapeutic advantages in early, well-differentiated HCC.

Keywords: tollip; hepatocellular carcinoma; SNU449; Hep3B; inflammation

ÖZET

Amaç: Toll-etkileşimli protein (TOLLIP), hepatoselüler karsinom (HCC) da dahil olmak üzere birçok kanser türünde önemli rol oynayan Toll benzeri reseptör aracılı inflamatuar sinyal yolağı üzerinde inhibitör bir etkiye sahiptir. Alfa 7 nikotinik asetilkolin reseptörleri (a7nAChR) ise inflamasyonun endojen olarak baskılanmasında rol oynamaktadır. Bu çalışmada, iyi ve az diferansiye HCC hücre hatlarında *TOLLIP* ekspresyonunun inflamatuar yolak ile ilgili bazı genler üzerindeki etkisinin belirlenmesi amaçlanmıştır.

Gereç-Yöntem: İyi diferansiye Hep3B ve az diferansiye SNU449 hücre hatlarında, sırasıyla plazmid transfeksiyonu ve siRNA kullanılarak *TOLLIP* gen ekspresyonu arttırılmış ve susturulmuştur. Bu hücrelerden RNA izolasyonu ve cDNA sentezi yapılmış ve *TLR2, TLR4, NFkB, IL6* ve *α7nAChR* ekspresyon kalıpları RT-PCR yöntemi ile kontrol gruplarına göre değerlendirilmiştir.

Bulgular: *TOLLIP* aşırı ekspresyonu, SNU449 hücrelerinde *TLR2* ve *TLR4* ekspresyonları üzerinde zıt etkilere sahipken, *IL6* ve *α7nAChR* ekspresyonlarını değiştirmemiştir. Hep3B hücrelerinde, *TOLLIP* aşırı ekspresyonu, *IL6* ekspresyonunu arttırmış ve *α7nAChR* ekspresyonunu azaltmış, *TLR2* ve *TLR4* ekspresyonlarını değiştirmemiştir. *TOLLIP* geni susturulduğunda ise *TLR2, TLR4, NFkB, IL6* ve *α7nAChR* ekspresyonları SNU449 hücrelerinde artarken, Hep3B hücrelerinde azalmıştır.

Sonuç: *TOLLIP* geninin susturulması, iyi diferansiye Hep3B hücrelerinde inflamatuvar parametreleri azaltmış az diferansiye SNU449 hücrelerinde ise arttırmıştır. *TOLLIP*'in iyi ve kötü diferansiye HCC hücre hatlarında inflamasyon ile ilişkili genleri farklı şekilde regüle ettiği tespit edilmiştir. *TOLLIP* geninin susturulmasının, iyi farklılaşmış HCC'de potansiyel terapötik avantajlarının ileri pre-klinik ve klinik çalışmalar ile araştırılması mekanizmanın anlaşılması için yol gösterici olacaktır.

Anahtar kelimeler: tollip; hepatoselüler karsinom; SNU449; Hep3B; inflamasyon

INTRODUCTION

Toll-interacting protein (TOLLIP), is a 30kDa protein with three domains, where each domain plays a distinct role in its cellular activities [1]. TOLLIP was shown to play role both in pro- and anti-inflammatory processes [2-4]. It acts as an inhibitory molecule in TLR2/4 mediated NF-kB signaling [2], plays role in IL-1 mediated inflammation as well as in autophagy and vacuole trafficking [1]. Therefore, it can be said to be important for the innate immunity. Functional defects of TOLLIP were shown to play role in several disease, such as neurodegenerative diseases [5], inflammatory bowel disease [6] and gastrointestinal adenocarcinoma [7].

Hepatocellular carcinoma (HCC) is the mostly seen type of liver cancer and persistent inflammation is one of the causes of HCC, which can be triggered by viral infections, alcohol consumption, high-fat diet, etc. [8]. TOLLIP has shown to play role both in acute/resolving and chronic/non-resolving inflammation [9]. Due to its regulatory roles in these inflammatory pathways, we wondered how expression changes in *TOLLIP* would affect certain inflammatory parameters in hepatocellular cell lines and decided to evaluate the expression patterns of several genes that play role in inflammatory pathways. Among those are TLR2/4, which are upstream players of TOLLIP in TLR2/4 mediated NF-kB signaling; Nf-KB and IL6 that resides in the downstream of this pathway and *α7nAChR* that mainly suppresses inflammation endogenously. Well and poorly differentiated cell lines were selected and results showed that changes in TOLLIP expression affects inflammation related parameters differently in these cell lines.

MATERIALS AND METHODS

Cell culture and transfections:

Human hepatocellular carcinoma cell lines SNU449 and Hep3B (ATCC) were grown in RPMI-1640 (Gibco, USA, 11875093) and MEM (Sigma Aldrich, Germany, M4655), respectively. Media were supplemented with 10% heat inactivated FBS and 1% penicillin/streptomycin (Gibco, USA, 15140122) at 37°C in 5% CO_2 incubator. The media of each cell was renewed in every other day.

Cells were transfected with either pCMV6-AC-TOLLIP-GFP (Origene, USA, RG200227) for *TOLLIP* overexpression or pCMV6-AC-GFP (Origene, USA, PS1000010) as control. 3ug endotoxin free plasmid DNA was used for transfections. Plasmid transfections were performed with Fugene® HD Transfection Reagent (Promega, USA, E2311) with 3:1 ratio of transfection reagent to DNA as described by the manufacturer with the recommended conditions for 6-well plate. *TOLLIP* gene silencing was performed with siRNA transfection with *TOLLIP* siRNA Silencer Select (5nmoL) (ThermoFisher, USA, Assay ID:29037) and Silencer Select Negative Control No.1 siRNA (ThermoFisher, USA, 4390843) was used as a control. 10uL siRNA and 7,5 uL siRNA Lipofectamine RNAiMax transfection reagent (ThermoFisher, USA, 13778075) was used for transfections.

Total RNA isolation and quantitative real time-PCR analysis:

RNA isolation was performed as described by the manufacturer (ThermoFisher, USA, K0732). RNA concentrations were measured and 1ug RNA was used for cDNA synthesis, which is performed by kit (ThermoFisher, USA, K1622) as described by the manufacturer. The cDNA samples were kept at -20ºC until they are used.

Real Time-PCR (Biorad, USA, CFXconnect) was performed to analyze the mRNA the expressions of *Tollip, α7nAChR, TLR2*, *TLR4*, *NF-κB* and *IL-6* genes. *GAPDH* was used as a reference and relative quantification of mRNA expression was performed through $2^{-\Delta\Delta Ct}$ method and represented as fold changes.

Statistical analysis:

Statistical analysis for Real Time-PCR assays were performed by Students T-test. Results were shown as mean ± S.E.M. p-value <0.05 was considered as statistically significant.

RESULTS

The expression of *TOLLIP* gene at the mRNA level was increased more than 30 folds upon plasmid transfections compared to controls, while decreased 80-90% upon silencing both in SNU449 and Hep3B cells (data not shown) and in these conditions, the changes in expression levels of *TLR2, TLR4*, *NFkB, IL6* and *α7nAChR* genes were evaluated.

TLR2 expression was decreased significantly in SNU449 cells upon *TOLLIP* overexpression while no significant change was observed in Hep3B cells (Figure 1A, B). On the other hand, *TLR2* expression was significantly increased upon silencing of *TOLLIP* in SNU449 cells and decreased significantly in Hep3B cells (Figure 1A, B).

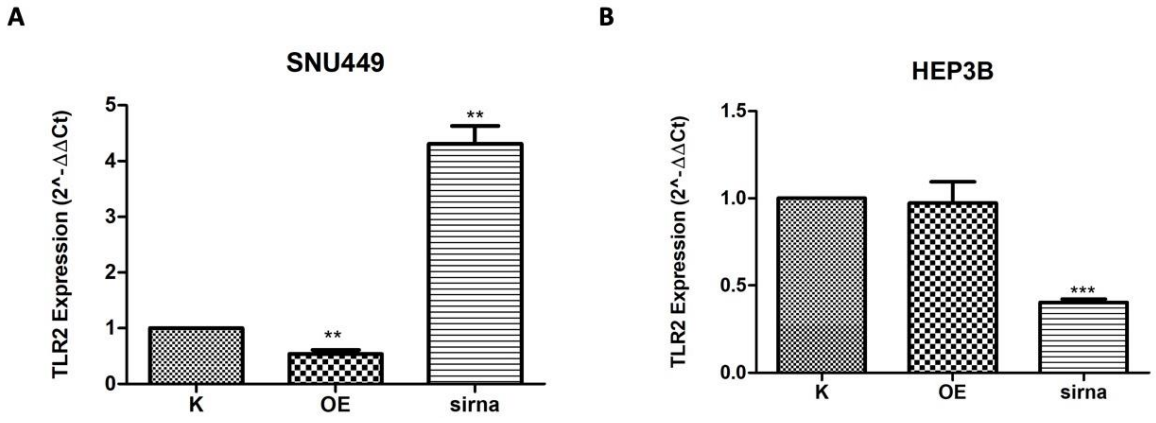

Figure 1. **Expression of *TLR2* gene upon *TOLLIP* expression changes**.
mRNA expression levels of *TLR2* gene **A)** in SNU449 and **B)** in Hep3B cells upon silencing and overexpressing *TOLLIP* gene. The expression levels were indicated as a fold change. (Student's t-test, *: p<0.05; **: p<0.01) (K: Control, OE: Overexpression, sirna: siRNA)

TLR4 expression was increased in SNU449 cells more than two folds upon *TOLLIP* overexpression and two folds upon *TOLLIP* silencing (Figure 2A), while no significant change was observed in *TLR4* upon *TOLLIP* overexpression in Hep3B cells, but a slight significant decrease was observed upon *TOLLIP* silencing (Figure 2B).

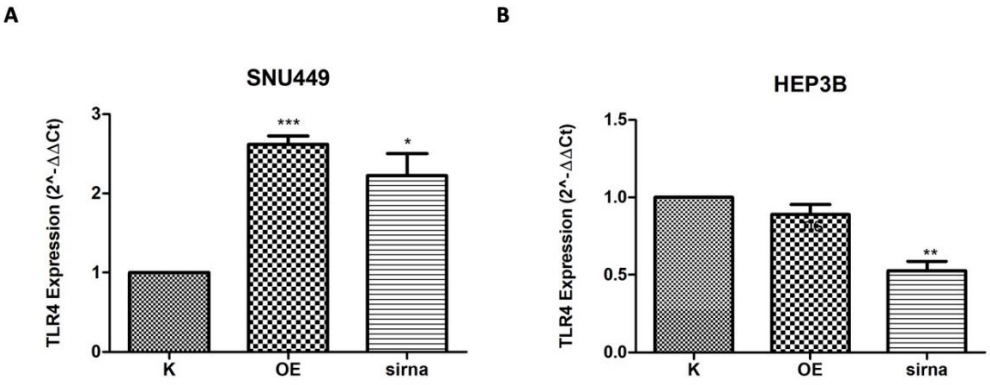

Figure 2. Expression of *TLR4* gene upon *TOLLIP* expression changes.
mRNA expression levels of *TLR4* gene **A)** in SNU449 and **B)** in Hep3B cells upon silencing and overexpressing *TOLLIP* gene. The expression levels were indicated as a fold change. (Student's t-test, *: p<0.05; **: p<0.01, ***: p<0.001) (K: Control, OE: Overexpression, sirna: siRNA)

NF-kB expression was also evaluated since *TOLLIP* gene is known to play an inhibitory role in TLR2/4 dependent NF-kB signaling pathway. It was surprising that upon *TOLLIP* overexpression we could not get any peaks from RT-PCR analysis, although the primers were working therefore, we could not evaluate its expression patterns for this condition. However, upon silencing of *TOLLIP*, *NF-kB* expression was significantly increased in SNU449 cells (Figure 3A) while significantly decreased in Hep3B cells (Figure 3B).

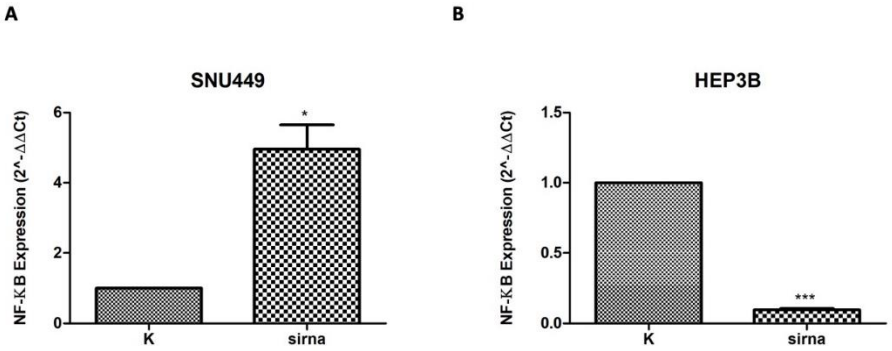

Figure 3. Expression of NF-kB upon silencing of *TOLLIP* gene.
mRNA expression levels of *NK-kB* gene A) in SNU449 and B) in Hep3B cells upon *TOLLIP* gene silencing. The expression levels were indicated as a fold change. (Student's t-test, *: p<0.05; ***: p<0.001) (K: Control, OE: Overexpression, sirna: siRNA)

The changes in *TOLLIP* expression had no significant effect on *IL-6* expression in SNU449 cells (Figure 4A), while *IL-6* expression was significantly increased and decreased in direct correlation with *TOLLIP* expression in Hep3B cells (Figure 4B).

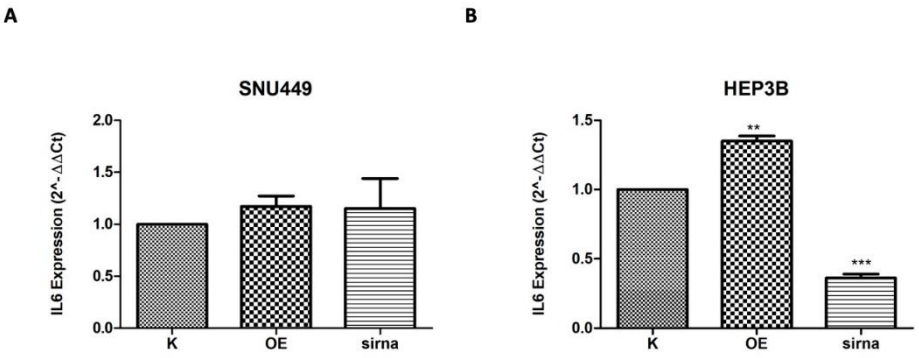

Figure 4. Expression of IL-6 upon upon TOLLIP expression changes.
mRNA expression levels of IL-6 gene **A)** in SNU449 and **B)** in Hep3B cells upon silencing and overexpression of the TOLLIP gene. The expression levels were indicated as a fold change. (Student's t-test, **: p<0.01, ***: p<0.001) (K: Control, OE: Overexpression, sirna: siRNA)

As alpha-7-nicotinic acetylcholine receptors (α7nAChR) have a role in endogenous suppression of inflammation, we also wondered about its expression pattern upon changing *TOLLIP* expression. It was interesting to see that in SNU449 cells α7nAChR expression was increased significantly upon silencing of *TOLLIP* (Figure 5A), while decreased significantly in Hep3B cells both in *TOLLIP* overexpression and silencing conditions (Figure 5B).

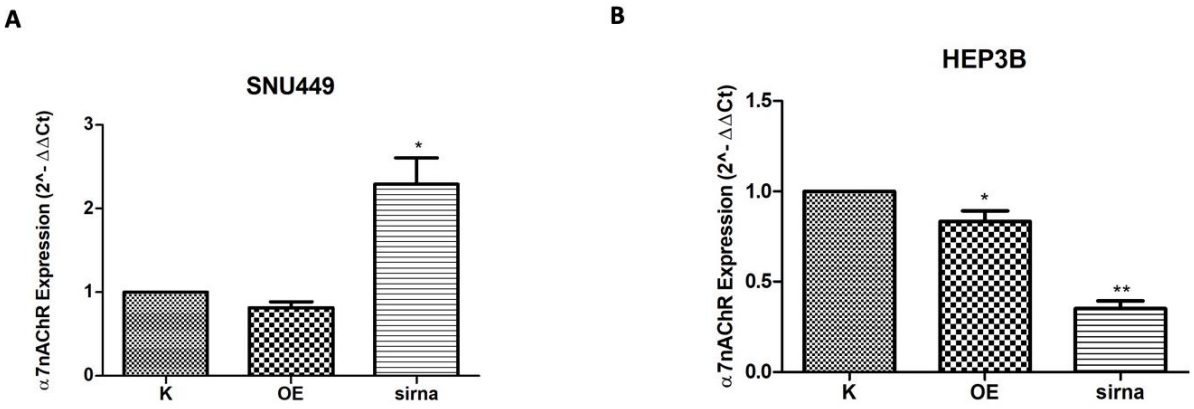

Figure 5. Expression of a7nAChR upon upon *TOLLIP* expression changes
mRNA expression levels of *a7nAChR* gene **A)** in SNU449 and **B)** in Hep3B cells upon silencing and overexpression of the *TOLLIP* gene. The expression levels were indicated as a fold change. (Student's t-test, *: $p<0.05$; **: $p<0.01$)

DISCUSSION

Inflammatory status is known to differ between many cancer types as well as within different stages of HCC [10]. Tollip is known to act as an inhibitory molecule on Toll-like receptor mediated signaling however having opposite roles in several other inflammatory pathways makes this gene an interesting target to understand its exact role-switches in different conditions. When results of this study were evaluated, *TOLLIP* overexpression was observed to had opposite effects on *TLR2* and *TLR4* expressions in SNU449 cells and no significant effect on *IL-6* and *α7nAChR* expressions at the mRNA level. On the other hand, in Hep3B cells, increased *TOLLIP* expression increased *IL-6* expression and decreased *a7nAChR* expression but did not alter *TLR2* and *TLR4* expressions.

In SNU449 cells, *TLR4* expression was increased upon *TOLLIP* overexpression, which can be interpreted as a homeostatic response of the cells since tollip mainly functions as an inhibitory molecule in *TLR4* mediated NF-kB signaling. However, it also gave the same response upon silencing *TOLLIP*, which shows that SNU449 cells give the same response for *TLR4* gene expression to any kind of expression changes in *TOLLIP* gene. Decreased *TLR2* expression in *TOLLIP* overexpression conditions can be a balancing response for the overexpressed *TLR4* (or vice versa) in order to keep the NF-kB pathway in balance. It was surprising that upon *TOLLIP* overexpression we could not get any peaks from RT-PCR analysis for *NF-kB* gene, neither for *GAPDH* nor for *NF-kB* primers. Although the primers were known to be working and intact RNA was isolated from those cells, we could not evaluate *NF-kB* expression patterns for the *TOLLIP* overexpression conditions. Tollip overexpression is known to inhibit NF-kB signaling pathway [1,2] however not getting any *NF-kB* expression data from our study makes it difficult to say if *NF-kB* expression is the same or not compared to control group upon expression changes in TLR2/4 receptors.

There are some contradictory studies performed on mice about the role of α7nAChR in liver cancer pathogenesis. It is both said to play role in carcinogenesis and metastasis [11] and to have anti-inflammatory roles in liver cancer development [12]. When we overexpress *TOLLIP*, the expression of *α7nAChR* did not change in SNU449 cells while slightly decreased in Hep3B cells. However, when we silenced *TOLLIP* gene, *α7nAChR* expression increased in SNU449 cells and decreased in Hep3B cells. These results also show that *TOLLIP* seems to affect the expression of this receptor, especially when it is silenced.

The overall responses of the evaluated genes were more distinct when the *TOLLIP* gene was silenced; *TLR2, TLR4, NF-kB, IL6* and *a7nAChR* expressions were increased in SNU449 cells and decreased in Hep3B cells. Although the results need further confirmations at the protein level, primary mRNA results clearly demonstrate that silencing the *TOLLIP* gene appears to decrease inflammatory parameters in Hep3B cells and increase them in SNU449. Performing further studies would be helpful to understand the exact roles and interactions of *TOLLIP* in HCC cells.

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All authors have accepted responsibility for the entire content of this manuscript and approved its submission.
Competing interests:
Authors state no conflict of interest.
Informed consent:
Not applicable.
Ethical approval:
Not applicable.

ORAL PRESENTATION ABSTRACT [SÖZLÜ SUNUM ÖZETLERİ]

OP1: THYMOL REDUCES THE LIPOPOLYSACCHARIDE-INDUCED ACUTE KIDNEY INFLAMMATION BY MODULATING LYSOSOMAL STRESS

[TİMOL LİZOZOMAL STRESİN MODÜLASYONU YOLU İLE LİPOPOLİSAKKARİT ARACILI İNDÜKLENEN AKUT BÖBREK İNFLAMASYONUNU AZALTIR]

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Objectives: Inflammation-induced overexpression of cytokines can lead to cell death by caspase-dependent or independent signaling pathways. Numerous natural products are used to suppress/re-modulate inflammation. Phenolic monoterpene Thymol is widely used in cosmetics and medical purposes. It has been shown that thymol regulates the anti-inflammatory, antioxidant, and anti-apoptotic responses in LPS-induced in vitro and in vivo models. However, there is still a need to investigate the molecular mechanism of inflammation and the detailed regulatory roles of thymol on inflammation-dependent signal mechanisms. In the present study, the possible protective effects of thymol on inflammation-mediated lysosomal stress in the LPS-induced acute kidney inflammation model were investigated on HEK293 cells.

Materials-Methods: To mimic the inflammation in HEK293 cells, LPS was applied to the cells for 24 hours. Following, cells were treated with various doses of thymol and total protein was isolated from the cells. Inflammation-associated IL-6, TNF-α, Nf-κB and phospho-Nf-κB protein levels, autophagy-related Beclin-1, Atg5, p62/SQSTM1 and LC3-I/II, ubiquitin proteosome system-associated polyubiquitin, cell death-associated caspase-3 and PARP-1 protein levels were examined by immunoblotting.

Results: We find that LPS-induced acute inflammation caused the suppressing of autophagic flux and reducing degradation of polyubiquitinated proteins. Thymol treatment markedly reversed the suppression of autophagy and stacking of poly-ubiquitinated protein by LPS. Also, LPS-induced acute inflammation did not cause caspase activation, it caused an increase in lysosomal stress-related PARP-1 cleavage pattern and thymol administration efficiently reduced PARP-1 cleavage.

Conclusions: Our results suggested that LPS-induced acute inflammation triggers blockage of autophagic flux and thymol has a protective role against LPS-induced lysosomal stress.

Keywords: Autophagy, Inflammation, Lysosomal stress, Thymol

Amaç: İnflamasyonun neden olduğu aşırı sitokin ifadesi kaspaz-bağımlı veya -bağımsız sinyal yolları aracılı hücre ölümüne yol açabilir. Birçok doğal ürün inflamatuar yanıtların baskılanması/yeniden düzenlenmesinde sıklıkla kullanılmaktadır. Fenolik bir monoterpen olan Timol kozmetik ve tıbbi amaçlarla yaygın olarak kullanılmaktadır. Timol'ün, LPS ile indüklenen in vitro ve in vivo modellerde anti-inflamatuar, antioksidan ve anti-apoptotik yanıtları düzenlediği gösterilmiştir. Bununla birlikte, inflamasyonun moleküler mekanizmasının ve Timol'ün inflamasyon-bağımlı sinyal mekanizmaları üzerindeki ayrıntılı düzenleyici rollerinin araştırılmasına hala ihtiyaç vardır. Bu çalışmada, LPS ile indüklenen akut böbrek inflamasyon modelinde Timol'ün inflamasyon aracılı indüklenen lizozomal stres üzerindeki olası koruyucu etkileri HEK293 hücreleri üzerinde araştırılmıştır.

Gereç-Yöntem: HEK293 hücrelerinde inflamasyonu mimik etmek için hücrelere 24 saat süre ile LPS uygulandı. Ardından hücreler çeşitli dozlarda Timol ile muamele edildi ve hücrelerden total protein izole edildi. İnflamasyonla ilişkili IL-6, TNF-α, Nf-κB ve fosforile-Nf-κB protein seviyeleri, otofajiyle ilişkili Beclin-1, Atg5, p62/SQSTM1 ve LC3-I/II, ubikitin-proteozom sistemiyle ilişkili poliubikitin, hücre ölümü ilişkili kaspaz-3 ve PARP-1 protein seviyeleri immünoblotlama ile incelendi.

Bulgular: LPS'nin neden olduğu akut inflamasyonun, otofajik akışın baskılanmasına ve poliubikitine proteinlerin yıkımının azalmasına neden olduğunu bulduk. Timol tedavisi, LPS'nin neden olduğu otofajinin baskılanmasını ve poliubikitine proteinlerin birikimini belirgin şekilde tersine çevirdi. Ayrıca, LPS aracılı akut inflamasyonun kaspaz aktivasyonuna neden olmadığı, lizozomal strese bağlı PARP-1 kesim modelinde artışa neden olduğu belirlenirken Timol uygulaması PARP-1 kesimini verimli tersine çevirdi.

Sonuç: Sonuçlarımız LPS'nin neden olduğu akut inflamasyonun otofajik akışın blokajını tetiklediğini ve Timol'ün LPS'nin neden olduğu lizozomal strese karşı koruyucu bir rolü olduğunu gösterdi.

Anahtar Kelimeler: Otofaji, İnflamasyon, Lizozomal Stres, Timol

OP2: METABOLIC SHIFT OF THE KYNURENINE PATHWAY IN INFLAMMATORY CONDITIONS

[ENFLAMATUAR KOŞULLARDA KİNÜRENİN YOLAĞINDA METABOLİK KAYMA]

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Objectives: Tryptophan is an essential amino acid, and in addition to its participation in protein synthesis, approximately 95% of tryptophan is converted via the kynurenine pathway into a series of metabolites that are biologically active and have physiologically important roles. Recent studies have shown that

kynurenine pathway metabolites are involved in the pathogenesis of psychiatric and neurodegenerative diseases as well as inflammatory diseases and have immunomodulatory properties. However, studies investigating kynurenine metabolites in inflammatory diseases are very limited. Therefore, in our study, we aimed to investigate the kynurenine pathway metabolite levels and the relationship between inflammatory conditions and these metabolites in individuals with acute inflammation.

Materials-Methods: In our study, blood samples were collected from individuals with high C-reactive protein, high sedimentation rate levels and high white blood cell count. Tryptophan, kynurenine, kynurenic acid, 3-hydroxyquinurea and 3-hydroxyanthranilic acid levels were measured using Absciex API 3200 LC-MS/MS.

Results: In this study, kynurenine [267.1 (80.5-3381.0) ng/mL vs. 179.6 (75.6-903.1) ng/ml, p<0.001], kynurenic acid [7.98 (2.85-26.20) ng/mL vs 5.61 (2.84-9.48) ng/mL, p<0.001] levels were statistically significant higher in individuals with acute inflammation compared to the control group, while tryptophan levels [8850 (1740-21200) ng/mL vs 11760 (4020-19660) ng/mL, p<0.001] and Tryptophan/kynurenine ratio [27.59 (3.49-133.19) ng/mL vs 61.13 (17.36-194.73) ng/mL, p<0.001] were statistically significant lower in individuals with acute inflammation compared to the control group. There was a negative correlation between the ratio of tryptophan/kynurenine and WBC (r= -0.309, p<0.001), CRP (r= -0.492, p<0.001) and ESR (r= -0.543, p<0.001) levels.

Conclusions: Our findings revealed that kynurenine metabolism is altered in inflammatory conditions and these metabolites may be potential indicators for inflammatory disorders. In addition, if the diagnostic value of these metabolites can be supported by further studies in more specific subpopulations, we think that these metabolites may be a new therapeutic target in the treatment of inflammatory disorders.

Keywords: Tryptophan, Kynurenine, inflammation, LC-MS/MS

Amaç: Triptofan esansiyel bir amino asit olup protein sentezine katılmasının yanı sıra, triptofanın yaklaşık olarak %95'i kinürenin yolağı ile biyolojik olarak aktif ve fizyolojik olarak önemli rollere sahip bir dizi metabolite dönüşmektedir. Son çalışmalarda triptofanın kinürenin yolağı metabolitlerinin psikiyatrik, nörodejeneratif hastalıkların yanısıra enflamatuvar hastalıkların patogenezine dahil olduğunu ve immunomodulatör özelliklere sahip olduğunu ortaya koymuştur. Bununla birlikte enflamatuvar hastalıklarda kinürenin metabolitlerini araştıran çalışmalar oldukça sınırlıdır. Dolayısıyla, çalışmamızda akut enflamasyonlu bireylerde kinürenin yolağı metabolit düzeylerini ve enflamatuvar koşullarla bu metabolitler arasındaki ilişkiyi araştırmayı amaçladık.

Gereç-Yöntem: Çalışmamızda C-reakif protein, sedimantasyon hızı düzeyleri ve beyaz kan hücresi sayısı yüksek olan bireylerden kan örnekleri toplandı. Triptofan, kinürenin, kinürenik asit, 3-hidroksikinürenin ve 3-hidroksiantranilik asit düzeyleri Absciex API 3200 LC-MS/MS cihazında ölçüldü.

Bulgular: Bu çalışmada kinürenin [267.1 (80.5-3381.0) ng/Ml vs 179.6 (75.6-903.1) ng/ml, p<0.001], kinürenik asit [7.98 (2.85-26.20) ng/Ml vs 5.61 (2.84-9.48) ng/Ml, p<0.001] düzeyleri akut enflamasyonlu bireylerde 41egativ grubuna göre istatiksel olarak anlamlı düzeyde yüksekken, triptofan düzeyleri [8850 (1740-21200) ng/Ml vs 11760 (4020-19660) ng/Ml, p<0.001] ve Triptofan/Kinürenin oranı [27.59 (3.49-133.19) ng/Ml vs 61.13 (17.36-194.73) ng/Ml, p<0.001] düşüktü. Ayrıca, Triptofan/Kinürenin oranı ile WBC (r= -0.309, p<0.001), CRP (r= -0.492, p<0.001) ve ESR (r= -0.543, p<0.001) düzeyleri arasında 41egative korelasyon vardı.

Sonuç: Bulgularımız kinürenin metabolizmasında enflamatuvar koşullarda değişiklik olduğunu ve enflamatuvar bozukluklarda bu metabolitlerin potansiyel birer gösterge olabileceğini ortaya koymuştur. Ayrıca ileri çalışmalarla daha spesifik alt popülasyonlarda yapılacak çalışmalarla bu metabolitlerin tanısal değeri desteklenebilirse bu metabolitlerin enflamatuvar bozuklukların tedavisinde yeni birer terapötik hedef olabileceğini düşünmekteyiz.

Anahtar Kelimeler: Triptofan, Kinürenin, İnflamasyon, LC-MS/MS

OP3: EVALUATION OF HbA1C LEVEL IN PATIENTS WITH COVID-19

[HBA1C DÜZEYİNİN COVID-19'LU HASTALARDA DEĞERLENDİRİLMESİ]

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Objective: Patients with diabetes mellitus (DM) are at serious risk for COVID-19. Studies have reported that the levels of inflammation markers correlate with the clinical severity of COVID-19. The aim of this study is to investigate the relationship between HbA1c values and inflammatory markers that have been shown to closely related to the severity of disease in patients with COVID-19.

Materials-Methods: In this study, cases older than 18 years of age who were hospitalized in Hatay State Hospital, between November 2020 and January 2021, with findings consistent with COVID-19 in RT-PCR (+) or thorax computer tomography were included. In the anamnesis forms of the cases, age, gender, chronic disease, drugs used, smoking and alcohol use were reported. In laboratory findings, both routine biochemistry parameters of the cases and HbA1c, D-Dimer, CRP and Ferritin values were determined. Correlation analyses were performed between HbA1c and CRP, D-Dimer and Ferritin values.

Results: 91 patients who were hospitalized in the COVID-19 service department of the hospital, of which 33 (36.3%) women and 58 (63.7%) men with mean ages 67 (22-84) and 61 (37-89) respectively. The most common diseases observed in the cases were diabetes (90%), hypertension (75.5%) and coronary artery disease (69%), respectively. HbA1c, CRP, D-Dimer and Ferritin levels were 8.70 (7.10-10.00), 14.33 (5.15-59.90), 0.85 (0.38-2.28) and 491.30 (258.90-939.30) respectively. While no

significant correlation was found between HbA1c and levels of inflammatory parameters ($p > 0.05$), a weak correlation was observed between CRP and D-Dimer ($p = 0.045$; $r = 0.211$).
Conclusion: It was observed that most of the patients hospitalized due to COVID-19 were diabetic, and HbA1c levels were not associated with inflammatory parameters.
Keywords: HbA1c, inflammation, diabet, COVID-19
Amaç: Diabetus mellitus'lu (DM) olgular COVID-19 açısından ciddi risk altındadır. Yapılan çalışmalarda COVID-19'un klinik şiddetinin enflamatuvar belirteçlerle ilişkili olduğu bildirilmiştir. Bu çalışmanın amacı, COVID-19' lu hastalarda, HbA1C değerleri ile hastalığın şiddeti ile yakın ilişkili olduğu gösterilen enflamatuvar belirteçler arasındaki ilişkinin araştırılmasıdır.
Gereç-Yöntem: Bu çalışmaya Kasım 2020 ile Ocak 2021 ayları arasında Hatay Devlet Hastanesi'nde yatmış olan RT-PCR (+) veya toraks bilgisayar tomografisinde COVID-19 ile uyumlu bulguları olan 18 yaşından büyük olgular dahil edildi. Olguların anamnez formlarında yaş, cinsiyet, kronik hastalık, kullanılan ilaçlar, sigara ve alkol kullanım bilgileri sorgulandı. Laboratuvar bulgularında olguların rutin biyokimya parametreleri ile HbA1c, D-Dimer, CRP ve Ferritin değerleri belirlendi. HbA1c ile CRP, D-Dimer ve Ferritin değerleri arasında korelasyon analizi yapıldı.
Bulgular: Hastanede COVID-19 servis bölümüne yatmış olan 91 olgunun 33'ü (%36.3) kadın, 58'i (%63.7) erkek olup yaş ortalamaları sırasıyla 67.00 (22-84) ve 61(37-89)'dir. Olgularda en sık gözlenen hastalıkların sırasıyla diyabet (%90), hipertansiyon (%75.5) ve koroner arter hastalığı (%69) olduğu gözlendi. HbA1c, CRP, D-Dimer ve Ferritin düzeyleri sırasıyla 8.70 (7.10-10.00), 14.33 (5.15-59.90), 0.85 (0.38-2.28) ve 491.30 (258.90-939.30) olarak bulundu. Yapılan analizlerde HbA1c ile enflamatuvar parametrelerin düzeyleri arasında anlamlı bir korelasyon gösterilemezken ($p>0.05$), CRP ile D-Dimer arasında zayıf bir korelasyon gözlendiği bulunmuştur ($p=0.045$; $r=0.211$).
Sonuç: Hastaneye COVID-19 nedeniyle yatış yapan olguların çoğunun diyabetik olduğu, HbA1c düzeylerinin enflamatuvar parameterlerle ilişkili olmadığı gözlenmiştir.
Anahtar Kelimeler: HbA1c, enflamasyon, diyabet, COVID-19

OP4: CAN SFRP-4 BE A BIOMARKER OF INFLAMMATION-RELATED ATHEROSCLEROTIC RISK IN PATIENTS WITH ANDROGENIC ALOPECIA?

[SFRP-4, ANDROJENİK ALOPESİLİ HASTALARDA İNFLAMASYONLA İLİŞKİLİ ATEROSKLEROTİK RİSK BİYOBELİRTECİ OLABİLİR Mİ?]

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Objective: Inflammation is an important pathophysiological process in atherosclerosis and plays a very important role in various stages of atherosclerosis. SFRP-4 is an adipokine and has been associated with diseases such as diabetes, CAD, metabolic syndrome. In this study, it was aimed to determine SFRP-4 levels in androgenic alopecia and to investigate its relationship with inflammation-related CAD risk factors.

Materials-Methods: This study was conducted in Selcuk University Faculty of Medicine, Department of Endocrinology in 2016. Forty-one male patients between the ages of 25-45 who started before the age of 30 with male pattern hair loss and 40 male patients without alopecia were included in the study. Androgenic alopecia types were determined by a dermatologist according to the Hamilton-Norward classification (HNS). Specific enzyme-linked immunosorbent assay kits were used for serum SFRP-4 measurement. 24-hour ambulatory blood pressure measurements were made with the oscillometric type Mobil O Graph NG device.

Results: Age, body mass index (BMI), androgen, insulin, 24-hour ambulatory blood pressure measurements, smoking rates, waist and hip circumference measurements did not differ significantly between the two groups ($p>0.05$). The median of SFRP-4 was 1.50 (0.01-21.20) ng/ml in the group with androgenic alopecia, while it was 0.57 (0.04-5.20) ng/ml in the control group ($P=0.025$). Spearman's correlation test, SFRP-4 and hair loss stage according to HNS (rho=0.281, p=0.011), HOMA-IR (rho=0.265, p=0.017), hsCRP (rho=0.274, p=0.013) A positive correlation was found between BMI (rho=0.220, p=0.049) and nighttime pulse rate (rho=0.226, p=0.042) and a negative correlation with HDL-cholesterol (rho=−0.242, p=0.030).

Conclusion: In our study, we found that SFRP-4 levels were significantly increased in men with androgenic alopecia compared to the control group. In addition, SFRP-4 appears to be associated with CVD risk factors at an early age. SFRP-4 may play a role in the pathophysiology of androgenic alopecia and may be an early indicator of insulin resistance, diabetes and hypertension that may develop in the later ages of these patients.

Keywords: SFRP-4, androgenic alopecia, inflammation, atherosclerosis

Amaç: İnflamasyon, aterosklerozda önemli bir patofizyolojik süreçtir ve aterosklerozun çeşitli evrelerinde çok önemli bir rol oynar. SFRP-4 bir adipokindir ve diyabet, KAH, metabolik sendrom gibi hastalıklarla ilişkilendirilmiştir. Bu çalışmada androjenik alopeside SFRP-4 düzeylerinin belirlenmesi ve inflamasyonla ilişkili KAH risk faktörleriyle ilişkisinin araştırılması amaçlanmıştır.

Gereç-Yöntemler: Bu çalışma 2016 yılında Selçuk Üniversitesi Tıp Fakültesi Endokrinoloji Bilim Dalı'nda yapılmıştır. Çalışmaya 30 yaşından önce başlayan erkek tipi saç dökülmesi şikâyeti olan 25-45 yaş arası 41 erkek hasta ve alopesi olmayan

40 erkek hasta alındı. Androjenik alopesi tipleri Hamilton-Norward sınıflamasına (HNS) göre dermatoloji uzmanı tarafından belirlendi. Serum SFRP-4 ölçümü için spesifik enzime bağlı immünosorbent deney kitleri kullanıldı. 24 saat ambulatuvar kan basıncı ölçümleri osilometrik tip Mobil O Graph NG cihazı yapıldı.

Bulgular: Yaş, vücut kitle indeksi (VKİ), androjen, insülin, 24 saat ambulatuvar kan basıncı ölçümleri, sigara içme oranları, bel ve kalça çevresi ölçümleri iki grup arasında anlamlı farklılık göstermedi (p>0.05). Androjenik alopesi olan grupta SFRP-4 medyanı 1.50 (0.01-21.20) ng/ml iken kontrol grubunda 0.57 (0.04-5.20) ng/ml idi (P=0.025). Spearman'ın korelasyon testi, SFRP-4 ile HNS'ye göre saç dökülmesi evresi (rho=0.281, p=0.011), HOMA-IR (rho=0.265, p=0.017), hsCRP (rho=0.274, p=0.013), VKİ (rho=0.220, p=0.049) ve gece nabız hızı (rho=0.226, p=0.042) arasında pozitif korelasyon ve HDL-kolesterol ile negatif korelasyon (rho=−0.242, p=0.030) saptandı.

Sonuç: Çalışmamızda androjenik alopesili erkeklerde SFRP-4 düzeylerinin kontrol grubuna göre anlamlı derecede artmış olduğunu saptadık. Ayrıca SFRP-4, erken yaşlarda KVH risk faktörleri ile ilişkili görünmektedir. SFRP-4 androjenik alopesi patofizyolojisinde rol oynayabilir ve bu hastaların daha sonraki yaşlarında gelişebilecek insülin direnci, diyabet ve hipertansiyonun erken bir göstergesi olabilir.

Anahtar Kelimeler: SFRP-4, androjenik alopesi, inflamasyon, ateroskleroz

OP5: INVESTIGATION OF THE FUNCTION OF C-PEPTİDE IN AN *in vitro* DIABETIC NEPHROPATHY MODEL

[*İn vitro* DİYABETİK NEFROPATİ MODELİNDE C-PEPTİDİN FONKSİYONUNUN ARAŞTIRILMASI]

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Objective: Diabetic nephropathy (DN) is one of the most critical complications resulting from uncontrolled Diabetes Mellitus. C-peptide is an endogenous compound released from the pancreas together with insulin and plays a role in the formation of proinsulin. In recent studies, it has been suggested that C-peptide have essential biological functions and may even have protective effects on diabetic damage. This study aimed to investigate the possible protective role of C-peptide in renal cell damage caused by high glucose concentration in DN.

Materials-Methods: For the in vitro DN model, human renal tubular epithelial cells (HK-2) were used. After 18 hours of serum starvation, the cells were incubated for 24 hours in a medium containing 5.5 and 30mM glucose. Subsequently, 1 and 5 nM C-peptide were applied to the cells for 48 hours. Then, cell viability rate, oxidative stress level, intracellular calcium concentration, and expression of apoptosis-related proteins (Bcl-2, Bcl-xl, Bax, and cleaved PARP) levels were determined by MTT, DCFDA, fluorometrically, and immunoblotting methods, respectively.

Results: It was determined that 1nM C-peptide treatment in HK-2 cells caused a significant decrease in intracellular ROS level, amount of calcium, expressions of Bax, and cleaved PARP compared to control cells, which were found to be significantly increased after high glucose treatment (p<0.01). However, it was determined that cell viability, Bcl-2, and Bcl-xl expressions, which were found to be decreased due to high glucose administration, increased significantly after 1 nM C-peptide treatment (p< 0.01).

Conclusion: The findings indicate that C-peptide has a protective effect against high glucose-induced damage in renal tubular cells. This result suggests that C-peptide may be a potential renoprotective agent in DN treatment.

Keywords: diabetic nephropaty C-peptide HK-2 cells

Amaç: Diyabetik nefropati (DN), kontrol altına alınmamış diyabet hastalığı sonucunda ortaya çıkan en önemli komplikasyonlardan biridir. C-peptid, pankreastan insülin ile birlikte salınan ve proinsülin formunun oluşmasında rol oynayan endojen bir bileşiktir. Son çalışmalarda C-peptit'in önemli biyolojik fonksiyonlara sahip olduğu, hatta diyabetik hasarda koruyucu etkileri olabileceği öne sürülmüştür. Bu çalışmada in vitro DN modelinde yüksek glukoz konsantrasyonunun neden olduğu renal tübüler hücre hasarında C-peptitin olası koruyucu rolünün incelenmesi amaçlanmıştır.

Gereç-Yöntem: İn vitro DN modeli için, insan renal tübüler epitel hücreleri (HK-2) kullanıldı. Hücreler 18 saat serum starvasyonu sonrası, 24 saat 5.5 ve 30 mM glukoz içeren besi yeri ile inkübe edildikten sonra, 48 saat 0, 1 ve 5 nM C-peptit ile muamele edildi. Daha sonra hücrelerde sırasıyla, MTT yöntemi ile hücre canlılığı, DCFDA yöntemi ile oksidatif stres düzeyi, fluorometrik yöntemle hücre içi kalsiyum miktarı ve immünoblotlama yöntemi ile apoptoz ile ilişkili proteinlerin (Bcl-2, Bcl-xl, Bax ve kırpılmış PARP) ekspresyon düzeyleri tayin edildi.

Bulgular: DN modeli oluşturulan HK-2 hücrelerinde 1nM'lık C-peptit uygulamasının, yüksek glukoz uygulaması sonrası artmış olduğu tespit edilen hücre içi ROT düzeyinde, kalsiyum miktarında, Bax ve kırpılmış PARP protein ekspresyon düzeylerinde anlamlı düzeyde azalmaya neden olduğu belirlenmiştir (p<0.01). Bununla birlikte, yüksek glukoz uygulaması sonucu azalan hücre canlılılık oranının, Bcl-2 ve Bcl-xl protein ekspresyonlarının 1 nM'lık C-peptid uygulaması sonrası anlamlı düzeyde arttığı belirlenmiştir (p< 0.01).

Sonuç: Elde edilen bulgular, yüksek glukozun renal tübüler hücrelerde yol açtığı hasara karşı C-peptit uygulamasının koruyucu etkisi olduğuna işaret etmektedir. Bu sonuç, DN tedavisinde C-peptitin potansiyel bir renoprotektif ajan olabileceğini önermektedir.

Anahtar Kelimeler: diyabetik nefropati C-peptit HK-2 hücreleri

OP6: INTERPRETATION OF HEPATOTOXIC SIDE EFFECTS BY RCV (REFERENCE CHANGE VALUE) IN COVID-19 PATIENTS TREATED WITH FAVIPIRAVIR

[FAVIPIRAVİR İLE TEDAVİ EDİLEN COVID-19 HASTALARINDA HEPATOTOKSİK YAN ETKİLERİN RCV (REFERANS DEĞİŞİM DEĞERİ) İLE YORUMLANMASI]

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Objectives: Favipiravir was first used against SARS-CoV-2 in Wuhan at the very epicenter of the pandemic. Its side effects include hyperuricemia, decreased neutrophil counts, diarrhea, and increased alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkalen phospatase ALP, bilirubin. Reference change value (RCV) represents the clinical significance of the variation between the RESULTS of two consecutive tests and laboratory test results exceeding this value are associated with the individual's disease status. In this study, we evaluated the side effects of favipiravir treatment on AST and ALT using RCV.

Materials-Methods: We examined retrospectively 40 patients were administered 1600 mg of favipiravir twice daily on day 1, followed by 600 mg twice daily from day 2 to day 5 (or more if needed). The analytic coefficient of variation (CVA:0,47 for AST 0,42 for ALT) was calculated from internal quality control RESULTS. Intra-individual coefficient of variation (CVI) and inter-individual coefficient of variation (CVG) were obtained from Westgard's website, which was updated in 2014.The RCV% is calculated with the following formula $Zx2^{1/2}x[CVA^2+CVI^2]^{1/2}$ (Using an unidirectional probability of 95%, Z=1.65).

Results: The RCV% results were calculated as %28 for AST and % 45 for ALT.The individuality index (II) was calculated as 0.532 for AST and 0.466 for ALT. ALT and AST values were evaluated as higher than the calculated RCV value in 70%,62,5% of the patients.

Conclusions: The use of RCV is recommended as a valuable tool in the follow-up of patient results and side effects of treatment.

Keywords: reference change values, biological variation, COVID-19, favipiravir.

Amaç: Favipiravir COVİD-19 pandemisinde ilk olarak Wuhan'da kullanıldı. Yan etkileri hiperürisemi, azalmış nötrofil sayısı, diyare ve artan alanin aminotransferaz (ALT),aspartat aminotransferaz (AST), alkalen fosfataz ALP, hiperbilirubinemiyi içerir. Referans değişim değeri (RCV), birbirini izleyen iki testin sonuçları arasındaki varyasyonun klinik önemini temsil eder ve bu değeri aşan laboratuvar test sonuçları, bireyin hastalık durumu ile ilişkilidir. Bu çalışmada, favipiravir tedavisinin AST ve ALT düzeyleri üzerindeki yan etkilerini RCV kullanarak değerlendirdik.

Gereç-Yöntem: 40 hastaya 1. günde günde iki kez 1600 mg favipiravir, ardından 2. günden 5. güne kadar günde iki kez 600 mg (veya gerekirse daha fazla) uygulandı. Analitik varyasyon katsayısı (ALT için AST 0,42 için CVA:0,47) iç kalite kontrol sonuçlarından hesaplanmıştır. Birey içi varyasyon katsayısı (CVI) ve bireyler arası varyasyon katsayısı (CVG) Westgard'ın 2014 yılında güncellenen web sitesindenelde edilmiştir. RCV%, takip eden formül ile $Zx2^{1/2}x[CVA^2+CVI^2]^{1/2}$ (%95 tek yönlü olasılık kullanılarak, Z=1.65) elde edildi.

Bulgular: RCV sonuçları AST için %28, ALT için % 45 olarak hesaplanmıştır. Bireysellik indeksi (II) AST için 0.532, ALT için 0.466 olarak hesaplanmıştır. ALT ve AST değerleri sırasıyla hastaların %70 ve %62,5'inde hesaplanan RCV değerinden yüksek olarak değerlendirildi.

Sonuçlar: Hasta sonuçlarının ve tedavinin yan etkilerinin takibinde RCV kullanımı değerli bir araç olarak önerilmektedir. Anahtar Kelimeler: referans değişim değeri, biyolojik varyasyon, COVID-19, favipiravir.

Anahtar Kelimeler: referans değişim değeri, biyolojik varyasyon, COVID-19, favipiravir.

OP7: MEASUREMENT UNCERTAINTY OF D-DIMER MEASURED BY THE PARTICLE ENHANCED IMMUNOTURBIDIMETRIC ASSAY

[PARTİKÜLLE GÜÇLENDİRİLMİŞ İMMUNOTÜRBİDİMETRİK TEST İLE ÖLÇÜLEN D-DİMER'İN ÖLÇÜM BELİRSİZLİĞİ]

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Objectives: D-dimer is a fibrin degradation product resulting from the degradation of fibrin polymers by plasmin. Although its main use is the evaluation of thromboembolic events, it is also used as an indicator of inflammation. In the recent COVID-19 pandemic, there has been a significant increase in its use as a biomarker. In this study, it was aimed to calculate the measurement uncertainty of D-dimer measured by particle enhanced immunoturbidimetric assay (PETIA).

Materials-Methods: D-dimer measurements were made with the PETIA method (Improgen, Turkey) on the CoagXL (Diagon, Hungary) device installed in the Kulu State Hospital Laboratory. Uncertainty due to calibration and calibrator bias was calculated by running the Procal-D-dimer-DDI0511 (Improgen, Turkey) calibrator 10 times. Serocon external quality control data of the last 3 months were used for uncertainty arising from external quality control. Uncertainty due to repeatability was calculated using internal quality control data from the last 60 days studied with Serocon DDIM.

Results: For D-dimer test, uncertainty due to repeatability was calculated as 0.0168, squared of uncertainty due to external quality control as 0.0123, uncertainty due to calibration 0.0250, and uncertainty due to calibrator deviation 0.0195. The standard uncertainty (uc) was 0.116 and the expanded uncertainty (%U) was calculated as 23%.

Conclusions: In this study, the measurement uncertainty of the D-Dimer test measured by the particle-enhanced immunoturbidimetric assay was calculated as 23%. Interpretation by taking this measurement uncertainty into account, especially at medical decision levels, will contribute to the use of the measurement result for the benefit of the patient.

Keywords: D-dimer, particle enhanced immunoturbidimetric assay, measurement uncertainty

Amaç: D-dimer, fibrin polimerlerinin plazmin tarafından parçalanması ile ortaya çıkan fibrin yıkım ürünüdür. Başlıca kullanım alanı tromboembolik olayların değerlendirilmesi olsa da inflamasyon göstergesi olarak da kullanılmaktadır. Özellikle son yaşanan COVID-19 pandemisinde biyobelirteç olarak kullanımında ciddi artışlar yaşanmıştır. Bu çalışma ile partiküle güçlendirilmiş immünotürbidimetrik test (PETIA) ile ölçülen D-dimer'in ölçüm belirsizliğinin hesaplanması amaçlanmıştır.

Gereç-Yöntem: D-dimer ölçümleri Kulu Devlet Hastanesi Laboratuvarında kurulu bulunan CoagXL (Diagon, Macaristan) cihazında PETIA yöntemi (Improgen, Turkey) temelinde gerçekleştirilmiştir. Ölçüm belirsizliğine etki edebilecek bileşenler kalibrasyon kaynaklı, kalibratör yanlılığı kaynaklı, dış kalite kontrol kaynaklı ve tekrarlanabilirlik kaynaklı olarak belirlenmiştir. Kalibrasyon ve kalibratör yanlılığı kaynaklı belirsizliğin hesaplanmasında Procal-D-dimer-DDI0511 (Improgen, Turkey) kalibratörünün 10 defa çalışılmasıyla elde edilen verilerden yararlanıldı. Dış kalite kontrol kaynaklı belirsizlik için son 3 aya ait Serocon dış kalite kontrol verileri kullanıldı. Tekrarlanabilirlik kaynaklı belirsizlik Serocon DDIM ile çalışılan son 60 günlük iç kalite kontrol verileri kullanılarak hesaplandı.

Bulgular: D-dimer için tekrarlanabilirlik kaynaklı belirsizlik 0.0168, dış kalite kontrol kaynaklı belirsizliğin karesi 0.0123, kalibrasyon kaynaklı belirsizlik 0.0250 ve kalibratör yanlılığından kaynaklı belirsizlik 0.0195 olarak hesaplandı. Standart belirsizlik (uc) 0.116 ve genişletilmiş belirsizlik (%U) %23 olarak hesaplandı.

Sonuç: Bu çalışma ile partikül güçlendirmeli immünotürbidimetrik test ile ölçülen D-dimer testinin ölçüm belirsizliği %23 olarak hesaplanmıştır. Özellikle tıbbi karar düzeylerinde bu ölçüm belirsizliğinin dikkate alınarak yorum yapılması, ölçüm sonucunun hasta yararına kullanımına katkı sağlayacaktır.

Anahtar Kelimeler: D-dimer, partikül güçlendirmeli immunotürbidimetrik test, ölçüm belirsizliği

OP8: INVESTIGATION OF CELLULAR BEHAVIOUR OF HUMAN DERMAL FIBROBLASTS SEEDED ON 3D PRINTED PDMS AND TPU SCAFFOLDS

[3B BASKILI PDMS VE TPU DOKU İSKELELERİNE EKİLEN İNSAN DERMAL FİBROBLASTLARIN HÜCRESEL DAVRANIŞLARININ İNCELENMESİ]

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Objectives: Tissue engineering is a multidisciplinary field that reconstructs the injury or trauma tissue. Three dimensional (3D) scaffolds play a role as support for cells until the natural extracellular matrix (ECM) is regenerated. The aim of this study is to analyze the proliferation and adhesion of human dermal fibroblasts (HDFs) seeded onto 3D printed polydimethylsiloxane (PDMS) and thermoplastic polyurethane (TPU) scaffolds in vitro.

Materials-Methods: 3D PDMS and TPU scaffolds were manufactured using a custom-made fused deposition modelling printer. HDFs were seeded on scaffolds and on tissue culture plastic plates as control and were cultured for 1, 3, 5, 7, 14, and 21 days. The cell viability was measured by WST1 assay. The cell adhesion was evaluated by scanning electron microscopy (SEM).

Results: According to WST-1 results, the viability of HDFs on 3D PDMS and TPU scaffolds on day 1 was 15% and 18%, respectively, compared to the 100% accepted control. The proliferation of HDFs on 3D TPU scaffolds increased to 67,66% on day 21. The proliferation of HDFs on 3D PDMS scaffolds increased to 67% and 63 on days 14 and 21 days, respectively. SEM images revealed that HDFs on 3D PDMS and TPU scaffolds adhered to the surfaces filled the interfiber gaps and maintained their tissue-specific morphology even on days 14 and 21.

Conclusions: Our results show that 3D PDMS and TPU scaffolds create a suitable environment for cell viability and adhesion and may provide a high advantage in tissue engineering applications.

Keywords: Tissue engineering, human dermal fibroblasts, polydimethylsiloxane, thermoplastic polyurethane

Amaç: Doku mühendisliği, yaralanma veya travma dokusunu yeniden yapılandıran multidisipliner bir alandır. Üç boyutlu (3B) doku iskeleleri, doğal hücre dışı matriks (ECM) yenilenene kadar hücreler için destek görevi görmektedir. Bu çalışmanın amacı, 3B baskılı polidimetilsiloksan (PDMS) ve termoplastik poliüretan (TPU) doku iskelelerine ekilen insan dermal fibroblastlarının (HDF'ler) proliferasyonunu ve adezyonunu in vitro olarak analiz etmektir.

Gereç-Yöntem: 3B PDMS ve TPU doku iskeleleri, özel yapım eriyik yığma modelleme yazıcısı kullanılarak üretildi. HDF'ler, iskelelere ve kontrol olarak doku kültürü plastik plakalarına ekilerek 1, 3, 5, 7, 14, ve 21 gün boyunca kültüre edildi. Hücre canlılığı, WST1 testi ile ölçüldü. Hücre adezyonu, taramalı elektron mikroskobu (SEM) ile değerlendirildi.

Bulgular: WST-1 sonuçlarına göre, HDF'lerin 1. günde 3B PDMS ve TPU iskeleleri üzerindeki canlılığı, %100 kabul edilen kontrole kıyasla sırasıyla %15 ve %18 idi. 3B TPU iskelelerinde HDF'lerin proliferasyonu 21. günde %67,66'ya yükseldi. 3B PDMS iskelelerinde HDF'lerin proliferasyonu 14. ve 21. günlerde sırasıyla %67 ve 63'e yükseldi. SEM görüntüleri, 3B PDMS ve TPU doku iskeleleri yüzeylerine tutunan HDF'lerin, iskelelerdeki boşluklar arasını doldurduğunu, 14 ve 21. günlerde bile dokuya özgü morfolojilerini koruduğunu ortaya çıkartmıştır.

Sonuç: 3B PDMS ve TPU doku iskelelerinin insan dermal fibroblast hücre canlılığı ve adezyonu için uygun bir ortam oluşturduğunu ve doku mühendisliği uygulamalarında yüksek avantaj sağlayabileceğini göstermektedir.

Anahtar Kelimeler: Doku mühendisliği, İnsan dermal fibroblastları, Polidimetilsiloksan, Termoplastik poliüretan

OP9: ANTIMETASTATIC POTENTIAL OF CURCUMIN IN ANAPLASTIC THYROID CANCER AND COMBINED ACTIVITY WITH DOCETAXEL

[KURKUMİNİN ANAPLASTİK TİROİD KANSERİNDE ANTİMETASTATİK POTANSİYELİ VE DOCETAXEL İLE KOMBİNE ETKİNLİĞİ]

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Objectives: Anaplastic thyroid cancer (ATC) is one of the most aggressive types of cancer known, with average survival limited to a few months. The disease spreads locally and systemically in a very short time. It is resistant to almost all available cytostatics. There is an urgent need for chemicals with an effective, low toxicity profile. Since Docetaxel (DX) is partially effective in the current routine, it is used to prolong survival in patients with ATK. In this study, the antimetastatic property of tetrahydrocurcumin (THC), the active metabolite of Curcuma Longa, was compared with docetaxel and the presence of synergism in the combination of the two substances was investigated in vitro.

Materials-Methods: IC25 and IC50 concentrations of THC and (DX) in CAL62 and 8505C ATC cells were determined by the modified MTT method we developed in our laboratory. These 2 concentrations were compared with the control in the treatment groups. Cell motility as an indicator of metastatic potential was evaluated by in vitro wound healing method. Free oxygen radicals were evaluated by TAS and TOS analyses.

Results: It was observed that cell adhesions decreased in 8505 cell lines starting from the 2nd hour in the treatment groups, more so in the groups combined with THC and curcumin.
It was found that the combined dose prevented migration and invasion in CAL62 cells in the first hours (24) statistically, and the 72-hour IC25 dose did not have a statistically significant difference with the DX50 dose.
There was no difference in Total Oxidant level between the combination and control groups. It was observed that the most effective dose that significantly reduced the oxidative level was DX50.

Conclusions: THC in ATK cells has an antimetastatic potential close to Docetaxel; It was observed that docetaxel decreased oxidative stress.

Keywords: Anaplastic thyroid cancer (ATC), Docetaxel (DX), tetrahydrocurcumin (THC), Total Antioksidan Status (TAS), Total Antioksidan Status (TOS)

Amaç: Anaplastik tiroid kanseri (ATK) ortalama sağkalım birkaç ayla sınırlı olduğu, bilinen en agresiv kanser türlerinden birisidir. Hastalık oldukça kısa sürede lokal ve sistemik yayılım yapmaktadır. Mevcut sitostatiklerin neredeyse tamamına dirençlidir. Etkin, düşük toksisite profiline sahip kimyasallara acil ihtiyaç bildirlmektedir. Güncel rutinde Docetaksel (DX) kısmen etkinlik gösterdiğinden, ATK lı olgularda sağkalımı uzatmak amacıyla kullanılmaktadır. Bu çalışmada Curcuma Longanın aktif metaboliti olan tetrahidrokurkuminin(THC) antimetastatik özelliği docetaksel ile karşılaştırmak ve iki madde kombinasyonunda sinerjizmin varlığı in vitro incelenmiştir.

Gereç-Yöntem: CAL62 ve 8505C ATC hücrelerinde THC ve (DX) ait IC25 ve IC50 konsantrasyonları, laboratuvarımızda geliştirdiğimiz modifiye MTT yöntemi ile belirlendi. Bu 2 konsantrasyon, tedavi gruplarında kontrol ile karşılaştırıldı. Metastatik potansiyelin bir göstergesi olarak hücre motilitesi in-vitro yara iyileşme yöntemi ile değerlendirildi. Hücresel sitotoksiste TAS ve TOS analizleri ile değerlendirildi.

Bulgular:8505 hücre hattında tedavi gruplarında 2. Saatten itibaren THC ve kurkuminle kombin gruplarda daha fazla olmak üzere hücre adezyonlarının azaldığı gözlendi.

CAL62 hücrelerinde kombine dozun ilk saatlerde (24) migrasyonu ve invazyonu istatistiksel anlamlı engellediği, 72 sa lik IC25 dozunun DX50ndozu ile anlamlı istatistiksel farka sahip olmadığı bulgularına ulaşıldı.

Total Oksidan seviyede kombinasyon ve kontrol grupları arasında farki izlenmedi. Oksidatif seviyeyi anlamlı düşüren en etkili dozun DX50 olduğu görüldü.

Sonuç olarak ATK hücrelerinde THC nin Docetaksele yakın antimetastatik potansiyele sahip olduğu; docetaksele ait oksidatif stresi azalttığı gözlendi.

Anahtar Kelimeler: Anaplastik tiroid kanseri (ATC), Dosetaksel (DX), tetrahidrokurkumin (THC), Total Antioksidan Seviyesi (TAS), Total Oksidan Seviyesi (TOS)

OP10: INVESTIGATION OF THE EFFECTS OF PD29 AND UPADACITINIB ON KIDNEY DAMAGE IN A BLEOMYCIN-INDUCED SCLERODERMA MODEL

[BLEOMISINLE OLUŞTURULMUŞ SKLERODERMA MODELINDE PD29 VE UPADACITINIB'IN BÖBREK HASARINA ETKILERININ ARAŞTIRILMASI]

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Objectives: To investigate the effects of PD29 and Upadacitinib on kidney damage in a mouse model of bleomycin (BLM) induced scleroderma. For this purpose, oxidative stress markers from the kidney tissue, such as catalase (CAT) activity, malondialdehyde (MDA) amount, total oxidant status (TOS), total antioxidant status (TAS), and interleukin-13 (IL-13), which are cytokines associated with inflammation, and interleukin-6 (IL-6) studied.

Materials-Methods: Scleroderma Animal model studies were approved by Kütahya Health Sciences University, Faculty of Medicine, Experimental Animals Local Ethics Committee (KSBUTF-DEHYUB) (08.03.2022, decision no. 08). A total of 40 kidney tissues were used as control (n=8), Bleomycin (n=8), Bleomycin+ PD29 (n=8), Bleomycin+Upadacitinib (n=8) and Bleomycin + PD29 + Upadacitinib (n=8). Sacrification was performed at the end of 21 days. Kidney samples were stored at -800 C until the experiment. After homogenization of kidney samples, measurements were made with calorimetric based kit for CAT activity, amount of MDA, TOS, TAS experiments. qPCR method was used to determine IL-13 and IL-6 gene expressions from kidney tissues.

Results: Catalase activity in kidney tissues decreased in the BLM group but increased significantly in the Upadacitinib group only. The amount of MDA increased in the BLM group, but decreased significantly in the PD29, upadacitinib and PD29 + upadacitinib groups. In parallel with this result, TOS increased significantly in the BLM group and decreased significantly in the PD29, upadacitinib and PD29 + upadacitinib groups. TAS decreased in the BLM group and increased significantly in the PD29, upadacitinib and PD29 + upadacitinib groups.

Conclusions: Upadacitinib, a JAK-kinase inhibitor, may have a positive effect against oxidant damage to kidney tissue in scleroderma. In addition, PD29 is also likely to have an effect on oxidative damage and inflammation in scleroderma.

Keywords: Scleroderma, PD-29, Upadacitinib, Oxidative stress

Amaç: Bleomisinle (BLM) oluşturulmuş skleroderma fare modelinde PD29 ve Upadacitinib'in böbrek hasarına etkilerinin araştırılmasıdır. Bu amaç doğrultusunda, böbrek dokusundan oksidatif stres belirteçleri olan katalaz (CAT) aktivitesi , malondialdehit (MDA) miktarı, total oksidan durum (TOS), total antioksidan durum (TAS) ve inflamasyon ile ilişik sitokinler olan interlökin-13 (IL-13) ve interlökin-6 (IL-6) çalışılmıştır.

Gereç-Yöntem: Skleroderma Hayvan modeli çalışmaları, Kütahya Sağlık Bilimleri Üniversitesi, Tıp Fakültesi, Deney Hayvanları Yerel Etik Kurulu (KSBÜTF-DEHYUB) tarafından onaylanmıştır (08.03.2022 tarihli toplantı, 08 no'lu karar). Kontrol (n=8), Bleomisin (n=8), Bleomisin+ PD29 (n=8), Bleomisin+Upadacitinib (n=8) ve Bleomisin + PD29 + Upadacitinib (n=8) olmak üzere toplam 40 böbrek dokusu kullanıldı. 21 gün sonunda sakrifikasyon gerçekleştirildi. Böbrek örnekleri -800 C'de ilgili deney basamağına kadar muhafaza edilmiştir. Böbrek örneklerinin homojenizasyonundan sonra CAT, MDA, TOS, TAS deneyleri için kalorimetrik temelli kit ile ölçüm yapılmıştır. Böbrek dokularından IL-13 ve IL-6 gen ekspresyonlarının belirlenmesi amacıyla qPCR yöntemi kullanılmıştır.

Bulgular: Böbrek dokularında katalaz aktivitesi BLM grubunda azalmıştır ancak sadece Upadacitinib uygulanan grupta anlamlı olarak artmıştır. MDA miktarı, BLM grubunda artmıştır, PD29, upadacitinib ve PD29 + upadacitinib gruplarında ise anlamlı olarak azalmıştır. Bu sonuca paralel olarak TOS, BLM grubunda anlamlı olarak artmıştır, PD29, upadacitinib ve PD29 + upadacitinib gruplarında ise anlamlı olarak azalmıştır. TAS ise BLM grubunda azalmıştır, PD29, upadacitinib ve PD29 + upadacitinib gruplarında ise anlamlı olarak artmıştır.

Sonuç: Bir JAK-kinaz inhibitörü olan Upadacitinib'in, sklerodermada böbrek dokusunda oksidan hasara karşı pozitif etkisi olabilir. Bunun yanında skleroderma'da PD29'un da oksidatif hasara ve inflamasyona etkisi olasıdır.

Anahtar Kelimeler: Skleroderma, PD-29, Upadacitinib, Oksidatif stres, İnflamasyon

OP12: SIGNIFICANCE OF MEASURING THE PROINFLAMMATORY RESPONSE BIOMARKERS IN COVID-19 PATIENTS

[COVID-19 HASTALARINDA PROİNFLAMATUAR YANIT BİYOBELİRTEÇLERİNİN ÖLÇÜLMESİNİN ÖNEMİ]

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Objectives: In the management of COVID-19, bio-inflammatory cytokines (IL-6 and others) can be measured as inflammatory markers to detect conditions in response to treatment, risk assessment, monitoring disease progression, prognosis determination and treatment selection.
The purpose of this study is to identify changes in inflammation markers of COVID-19 patients and to determine whether it

should be used as a prognosis marker.

Materials-Methods: Three groups of the patients consisting of 138 patients (12 non-survived, 35 severe and 91 mild/moderate) aged 16 to 86 years who were diagnosed with COVID-19 by real-time polymerase chain reaction were included in the study. Acute phase serum levels such as CRP, D-Dimer, Ferritin, IL-1B and IL-6 were measured and compared in serum samples taken from these patients. It was examined whether these parameters can be a biomarker that can be monitored for the course of the disease. IL-6 and ferritin were measured with CLIA, D-dimer immunassay, CRP with photometry and IL1-B was measured with flow cytometry methods.

Results: It has been observed that all parameters, except for ferritin (P=0.94), increase significantly during the transition from mild to severe form of the disease. (CRP P:0.005, D-Dimer P<0.0001, IL-1B P:0.03, IL-6 P:0.002). A significant difference was observed in the levels of CRP, IL-6 and D-Dimer in the patient survival. (P=0.003, P=0.03, P:0,0001). According to our results, the use of IL-1B in the prognosis monitoring of patients with severe forms was not found to be significant (P:0.48).

ROC curve analysis showed that the area under the ROC curve (AUC) of CRP, D-Dimer and IL-6 was 0.645 (0,559 to 0,725), 0.637 (0,551 to 0,717) and 0.663 (0,577 to 0,741) respectively, and the cutoff values were >3.77 (sensitivity, 72.3%; specificity, 55%), >0.48 (sensitivity 68.1%; specificity, 57.1%) and <14.9 (sensitivity, 65,9%; specificity, 62.6%), respectively.

Conclusions: Our results confirmed that the dynamic change in IL-6, CRP, D-Dimer can be used as a marker for disease monitoring in patients with severe COVID-19.

Keywords: IL-6, IL-1B, COVID-19

Amaç: COVID-19'un yönetiminde biyo-inflamatuar sitokinler (IL-6 ve diğerleri) tedaviye yanıt olarak durumları saptamak, risk değerlendirmesi, hastalık ilerlemesini izlemek, prognoz tayini ve tedavi seçimi için inflamatuar belirteçler olarak ölçülebilir.

Bu çalışmanın amacı, COVID-19 hastalarının inflamasyon belirteçlerindeki değişiklikleri tanımlamak ve prognoz belirteci olarak kullanılıp kullanılmayacağını belirlemektir.

Gereç-Yöntem: Çalışmaya, gerçek zamanlı polimeraz zincir reaksiyonu ile COVID-19 tanısı alan 16 ila 86 yaşları arasındaki 138 hastadan (12 sağ kalmayan, 35 şiddetli ve 91 hafif/ orta) oluşan üç hasta grubu dahil edildi. Bu hastalardan alınan örneklerinde CRP, D-Dimer, Ferritin, IL-1B ve IL-6 gibi akut faz serum düzeyleri ölçüldü ve karşılaştırıldı. Bu parametrelerin hastalığın seyri açısından izlenebilecek bir biyobelirteç olup olamayacağı incelendi. IL-6 ve ferritin CLIA ile, D-dimer immunassay ile, CRP fotometri ile ve IL1-B ise akım sitometri yöntemleriyle ölçüldü.

Bulgular: Hastalığın hafiften şiddetli formuna geçişte ferritin (P=0.94) hariç tüm parametrelerin anlamlı derecede arttığı gözlenmiştir. (CRP P:0.005, D-Dimer P <0,0001, IL-1B P:0.03, IL-6 P:0.002). Hastanın sağ kalımında CRP, IL-6 ve D-Dimer düzeylerinde anlamlı fark gözlendi. (P= 0,003, P= 0,03, P= 0,0001). Sonuçlarımıza göre, şiddetli formdaki hastaların prognoz izleminde IL-1B kullanımı anlamlı bulunmadı (P=0.48).

ROC analizi sonucunda CRP, D-Dimer ve IL-6 nın sırasıyla AUC değerleri 0.645 (0,559 to 0,725), 0.637 (0,551 to 0,717) ve 0.663 (0,577 to 0,741) iken cut-off değerleri ise >3.77 (sensitivite, 72.3%; spesifisite, 55%), >0.48 (sensitivite 68.1%; spesifisite, 57.1%) and <14.9 (sensitivite, 65,9%; spesifisite, 62.6%) idi.

Sonuç: Sonuçlarımız, IL-6, CRP, D-Dimer düzeylerindeki dinamik değişimin, şiddetli COVID-19 olan hastalarda hastalık izlemesi için bir belirteç olarak kullanılabileceğini doğrulamıştır.

Anahtar Kelimeler:IL-6, IL-1B, COVID-19

OP13: EFFECTS OF PPARγ ACTIVATION ON VARIOUS PATHWAYS IN BRAINSTEM OF HYPERTENSIVE RATS

[PPARγ AKTİVASYONUNUN HİPERTANSİF SIÇANLARIN BEYİNSAPINDA ÇEŞİTLİ YOLAKLARA ETKİSİ]

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Objectives: In this study, we aimed to investigate the alteration in the levels of tight junction proteins and inflammatory proteins (TNFα and IL-1β) in brainstem, a region associated with hypertension, following PPARγ activation

Materials-Methods: Animals were divided into four groups namely spontaneous hypertensive rats (SHR) (n=6), PPARγ agonist (pioglitazone) treated SHRs (n=6), borderline hypertensive rats (BHR) (n=6) and PPARγ agonist (pioglitazone) treated BHRs (n=6). The mRNA levels of tight junction proteins (occludin, claudin-1, claudin-2, claudin-12, ZO-1) were measured in the brainstem using real-time PCR technique. In addition, the effect of the treatment on neuroinflammation was evaluated using the ELISA.

Results: The levels of TNFα and IL-1β in brainstem of pioglitazone-treated SHRs were significantly decreased (p<0.05). Results from this study confirm higher occludin, claudin-2 and claudin-12 mRNA expressions in brainstem of BHRs when compared to SHRs (1.38-fold, 7.50-fold and 1.73-fold, respectively). On the other hand, pioglitazone was found more effective in terms of regulating gene expression in SHR group. Pioglitazone significantly increased mRNA levels of occludin (8.27-fold), claudin-2 (3.16-fold) and claudin-12 (1.89-fold) accompanied with decreased proinflammatory factor levels in SHR group (p<0.05).

Conclusions: Within the scope of this study, the effect of PPARγ activation on tight junction proteins was investigated in hypertension. The responses in indicated parameters were compared in different experimental models of hypertension (spontaneous and borderline). Our work has led us to conclude that alterations in the gene expression of tight junction proteins in the brainstem following PPARγ activation may contribute to

neuroprotection in essential hypertension.

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Keywords: hypertension, neuroinflammation, PPARγ, tight junction proteins

Amaç: Çalışmada hipertansiyonla ilişkili beyin bölgesi olan beyin sapında PPARγ aktivasyonu sonrası sıkı bağlantı proteinleri ve inflamasyon (tümör nekroz faktörüα (TNFα) ve interlökin-1β (IL-1β)) ile ilişkilendirilen birtakım proteinlerdeki değişim incelenmiştir.

Gereç-Yöntem: Çalışmada spontan hipertansif sıçanlar (SHR) (n=6), PPARγ agonisti (pioglitazon) uygulanmış SHR sıçanlar (n=6), borderline hipertansif sıçanlar (BHR) (n=6) ve PPARγ agonisti (pioglitazon) uygulanmış BHR sıçanlar (n=6) olmak üzere 4 grup yer almaktadır. Sıkı bağlantı proteinlerine (occludin, claudin-1, claudin-2, claudin-12, ZO-1) ait mRNA düzeyleri gerçek zamanlı polimeraz zincir reaksiyonu (real-time PCR) tekniği kullanılarak sıçanların beyin sapında ölçülmüştür. Ayrıca uygulamanın nöroinflamatuar süreçlere etkisi IL-1β ve TNFα aracılığıyla ELISA yöntemi kullanılarak değerlendirilmiştir.

Bulgular: Pioglitazon uygulanmış SHR'lerin beyin sapında TNFα ve IL-1β değerleri SHR grubu ile karşılaştırıldığında anlamlı düzeyde düşük bulunmuştur ($p<0.05$). SHR ile karşılaştırıldığında; BHR beyin sapında occludin, claudin-2 ve claudin-12 mRNA düzeyleri sırasıyla 1,38, 7,50 ($p<0.05$) ve 1,73 ($p>0.05$) kat yüksek bulunmakla birlikte pioglitazonun SHR'de daha etkili olduğu tespit edilmiştir. SHR gruplarında pioglitazon; occludin (8,27 kat) claudin-2 (3,16 kat) ve claudin-12 (1,89 kat) mRNA düzeylerini arttırırken proinflamatuvar belirteçleri istatistiksel olarak anlamlı şekilde azaltmıştır ($p<0,05$).

Sonuç: Çalışma kapsamında hipertansiyonda PPARγ aktivasyonunun sıkı bağlantı proteinleri ve beraberinde inflamasyon üzerine etkisi araştırılmış, farklı deneysel hipertansiyon modellerinde (spontan ve borderline) söz konusu parametrelerdeki yanıt karşılaştırılmıştır. Çalışmamız, PPARγ aktivasyonunu takiben beyin sapında sıkı bağlantı proteinlerinin gen ekspresyonundaki değişikliklerin esansiyel hipertansiyonda nöral korumaya katkıda bulunabileceği sonucuna varmamızı sağlamıştır.

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Anahtar Kelimeler: hipertansiyon, nöroinflamasyon, PPARγ, sıkı bağlantı proteinleri

OP14: ASSESSMENT OF THE RELATIONSHIP BETWEEN NEUTROPHIL PERCENTAGE-TO ALBUMIN RATIO AND NEPHROPATHY IN PATIENTS WITH DIABETES MELLITUS

[DIABETES MELLITUS HASTALARINDA NÖTROFİL YÜZDESİ-ALBÜMİN ORANI İLE NEFROPATİ ARASINDAKİ İLİŞKİNİN DEĞERLENDİRİLMESİ]

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Objective: Among patients with diabetic nephropathy (DN), there was no evidence to confirm the prognostic significance of the neutrophil percentage-albumin ratio (NPAR). We hypothesized that NPAR plays a role in the incidence of DN in diabetic patients.

Materials-Methods: We extracted 6 months of diabetes mellitus (DM) data from the hospital database between September 2020 and February 2021, expressed as NPAR, neutrophil percentage/albumin. For statistical analysis, SPSS 15.0 for Windows program was used for the statistical analysis. Descriptive statistics: numbers and percentages for categorical variables; mean, standard deviation, minimum, maximum, median, and interquartile range for numerical variables. Comparisons of numerical variables between two independent groups were made using the Mann-Whitney U test since the normal distribution condition was not met. Cutoff values were analyzed by ROC Curve Analysis. The alpha significance level was accepted as p 0.05.

Results: The areas under the curve of the neutrophil albumin ratio were 0.664 (95% CI: 0.638–690) for proteinuria. A1c Normal-0.682 (95% CI: 0.637-0.726) for A1c Pathological-Proteinuria, 0.617 (95% CI: 0.617-0.683), 0.694 (95% CI: 0.661-0.726) for Microalbuminuria, 0.717 (95% CI: 0.656-0.778) and 0.679 (95% CI: 0.639-0.719) for A1c Pathologic-Microalbuminuria. 61.1% sensitivity and 61.1% specificity of 1,374, A1c Normal-Proteinuria 63.1% sensitivity, 63% specificity, 1,373, A1c Pathological-Proteinuria 60.1% sensitivity, 58.9% specificity, 1,375, for microalbuminuria 64.8% with 64.5% specificity, 1,398, for A1c Normal-Microalbuminuria 0% It was found to be 1,398 with a specificity of 6. The ratio of neutrophil albumin was statistically significantly higher in patients with proteinuria and microalbuminuria compared to patients without, and in patients with a1C pathological compared to those with normal a1C (p 0.001 p 0.001).

Conclusion: The Neutrophil Percent/Albumin Ratio is associated with the risk of the formation of DN in diabetic patients.

Keywords: Diabetes mellitus, diabetic nephropathy, inflammation, neutrophil percent-albumin ratio

Amaç: Diyabetik nefropatili (DN) hastalarda, nötrofil yüzdesi-albümin oranının (NPAR) prognostik önemini doğrulayacak hiçbir kanıt yoktu. NPAR'ın diyabetik hastalarda DN insidansında rol oynadığını varsaydık.

Gereç-Yöntem: Eylül 2020 ile Şubat 2021 arasında hastane veri tabanından 6 aylık Diabetes Mellitus (DM) verilerini çıkardık. İstatistics analiz için SPSS 15.0 for Windows program kullanıldı. Tanımlayıcı istatistikler; kategorik değişkenler için saylar ve yüzdeler, sayısal değişkenler için ortalama, standard sapma, minimum, maximum, medyan, çeyrekler arası aralık. Normal dağılım koşulu sağlanmadığı için iki bağımsız grup arasındaki sayısal değişkenlerin karşılaştırmaları Mann Whitney U testi kullanılarak yapılmıştır. Cutoff değerleri ROC Curve Analysis ile analiz edilmiştir. Alfa anlamlılık düzeyi p 0,05 olarak kabul edildi.

Bulgular: Nötrophil albümin oran eğrisinin altında kalan alanlar proteinuria için 0.664 (%95 GA: 0.638–690) idi. A1c Normal-0.682 (%95 CI: 0.637-0.726), A1c Patolojik-Proteinüri için 0.650 (%95 GA: 0.617-0.683), Microalbuminuria için 0.694 (%95 GA: 0.661-0.726), A1c Normal-için 0.717 (95), A1c Patolojik-Microalbüminüri için % CI: 0.656-0.778) ve 0.679 (%95 GA: 0.639-0.719). Proteinüri için nötrofil albümin oran eşik değerleri %61,1 duyarlık %61,1 özgüllük 1.374, A1c Normal-Proteinuria %63, 1 duyarlk %63 özgüllük 1.373, A1c Patolojik-Proteinüri %60,1 duyarlık %58,9 özgüllük 1.375, Microalbuminuria için %64,8 ile 64,5 % özgüllük 1.398, A1c için Normal-Microalbuminuria için %0 %70,7 ile %66,3 özgüllük. 1.398, A1c için Patolojik, için %62,2 ile %62,6 özgüllük ile 1.398 olarak bulundu. neutrophil albümin oran proteinürisi ve macroalbuminuric olan hastalarda olmayanlara göre ve a1c patolojisi olan hastalarda normal a1c olanlara göre istatistiksel olarak anlamlı derecede yüksekti (p 0,001).

Sonuçlar: Neutrophil Yüzdesi/Albümin Oran diyabetik hastalarda DN oluşumu riski ile ilişkilidir.

Anahtar Kelimeler: Diabetes mellitus, diyabetik nefropati, inflamasyon, nötrofil yüzdesi-albümin oranı

OP15: INVESTIGATION OF RELATIONSHIP BETWEEN PLASMA NITRIC OXIDE LEVELS AND NONSUICIDAL SELF-INJURY BEHAVIOR IN ADOLESCENTS

[PLAZMA NİTRİK OKSİT SEVİYELERİ İLE KENDİNE ZARAR VERME DAVRANIŞI ARASINDAKİ İLİŞKİLİNİN ARAŞTIRILMASI]

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Objectives: Nitric oxide is a small free radical, generated by concurrent release in conversion reaction of arginine to citrulline catalysed by nitric oxide synthases (NOS). NO, as an important signalling molecule performs ubiquitious biological roles in vasodilatation, inflammation, and neurotransmission. Nonsuicidal self-injury (NSSI), which is a common neuropsychiatric disorder especially among adolescents all over the world, is thought to be related with disregulation of endogenous opioid system and particulary β-EP as its neurochemical basis. Both modulation the nitricoxidergic pathway via inhibition in CNS&PNS and impact on endothelial cells (ECs) and peripheral blood mononuclear cells (PBMCs) via μ-1 receptor, β-EP, which levels were decreased in NSSI patients, is responsible for inhibitory control of NO release. In this research it was aim to evaluate the relationship between plasma levels of NO and non-suicidal self-injury behavior in adolescents.

Materials-Methods: All adolescent subjects included in the study received clinical examination and psychiatric assessment in Kocaeli University Child and Adolescent Psychiatry Clinic, between May – October 2020. Participants comprised 31 NSSI patients and 32 non-NSSI control subjects. Plasma samples were obtained and used for biochemical analysis. Plasma NO levels were determined by colorimetric method using the Griess reaction. TNF-α levels were analysed with ELISA method according to the kit manufacturer's instructions (Cat.No E0082Hu, BT-LAB, China). The statistical analysis was performed with GraphpadPrism v9.0 sofware. P values were determined by two independent sample t-test.

Results: Plasma NO levels were found to be statistically higher in NSSI group compared to control group while TNF-α levels were found to be statistically indifferent. Gender and age of the participants were found to be no impact on NO and TNF-a levels as variables.

Conclusions: NSSI, as a neuropschiatric disorder, associated with EOS dysregulation, is also connected to the pathology of nociception and anti-nociception modulation in the central and peripheric nervous system, and non-neuronal cells (ECs, PMBCs). Thus, elevated plasma NO levels may be related to deficient β-EP due to the inability of suppression of NO release.

Keywords: Nitric oxide, neuroinflammation, nonsuicidal self-injury, adolescent, mental health

Amaç: Nitrik oksit (NO), nitrik oksit sentazlar tarafından katalizlenen arjininin sitrüline dönüşüm reaksiyonu sırasında sentezlenen ve saniyeler içerisinde metabolize olan, küçük serbest radikal molekülüdür. Vazodilatasyon, enflamasyon, sinir iletimi vd. çeşitli biyolojik rollerde, intraselüler sinyal iletiminden sorumludur. Dünya genelinde adölesanlarda önemli bir nöropsikiyatrik hastalık olan kendine zarar verme davranışının (KZVD) nörokimyasal patogenezinde endojen opioid sistem (EOS) ve özellikle de beta-endorfin (β-EP) sorumlu tutulmaktadır. SSS'de nitrikoksiderjik yol yanı sıra, endotel hücreleri ve monosit, nötrofil ve lenfosit hücrelerinde μ-1 reseptörleri üzerinden NO salınımını kontrol etmekte olan β-EP'nin KZVD olgularında düşük olduğu bilinmektedir. Bu çalışmada KZVD olan adölesan grupla akranlarının, plazma NO seviyeleri açısından farklı olup olmadıklarının araştırılması amaçlanmıştır.

Gereç-Yöntem: Kocaeli Üniversitesi Çocuk ve Ergen Ruh Sağlığı kliniğinde Mayıs-Ekim 2020 tarihlerinde muayene edilerek KZVD tanısı alan 31 çocuk hasta ile KZVD olmayan 32 adölesan kontrolün dahil edildiği bu çalışmada, katılımcılardan toplanan plazma örneklerinde kolorimetrik yöntemle NO düzeyleri belirlenirken, TNF-α ölçümleri ELİSA yöntemiyle kit kılavuzuna (Kat.no: E0082Hu, BT-LAB, Çin) göre gerçekleştirilmiştir. Verilerin istatistiksel analizi, Graphpad Prism 9.0 yazılımında bağımsız örneklem t testi kullanılarak

gerçekleştirilmiştir.

Bulgular: KZVD olan adölesan grupta NO seviyeleri kontrol grubuna göre istatistiksel olarak anlamlı şekilde yüksek bulunmuştur (p= 0,0393). TNF-α seviyeleri açısından gruplar arasında istatistiksel anlamlı fark saptanmamıştır. Cinsiyet ve yaşın değişken olarak NO ve TNF-α düzeyleri üzerine etkisiz oldukları saptanmıştır.

Sonuç: EOS regülasyon bozukluğuna bağlı bir nöropsikiyatrik hastalık olan KZVD'nin, merkezi ve çevresel sinir sisteminde ağrı ve antinosisepsiyonun modülasyonundaki patolojiye ek β-EP'nin endotel hücreleri ve periferik kan mononükleer hücrelerinde NO sekresyonu üzerindeki inhibitör etkisinin azalması dolayısıyla yüksek plazma NO seviyeleri ile ilişkili olabileceği düşünülebilir.

Anahtar Kelimeler: Nitrik oksit, nöroenflamasyon, kendine zarar verme davranışı, Adölesan, ruh sağlığı

OP16: EVALUATION WITH ROC ANALYSIS, LOGISTICS REGRESSION ANALYSIS AND OTHER STATISTICAL TESTS ANALYSIS OF RETROSPECTIVE RESULTS OF BIOCHEMISTRY LABORATORY RESULTS, ANALYSISED IN COVID-19 INFECTED SERUM OR PLASMA (CRP, PROCALCITONIN, FERRITIN, D-DIMER, FIBRINOGEN, AST, ALT, LDH)

[COVİD-19 İLE ENFEKTE SERUM VEYA PLAZMADA ANALİZ EDİLEN (CRP, PROKALSİTONİN, FERRİTİN, D-DİMER, FİBRİNOJEN, AST, ALT, LDH) BİYOKİMYA LABORATUVAR SONUÇLARININ RETROSPEKTİF OLARAK ROC ANALİZİ, LOJİSTİK REGRESYON ANALİZİ VE DİĞER İSTATİSTİKİ TESTLER İLE DEĞER]

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Objectives: A new type of coronavirus that emerged in Wuhan, China at the end of 2019, caused the Covid-19 (SARS-COV2) pandemic. Common cold symptoms are seen, but in more severe cases, pneumonia, Acute Respiratory Distress Syndrome (ARDS), coagulopathy, multi-organ failure are seen, and it causes death in the course of time. In this study, among the laboratory parameters followed in cases diagnosed with Covid-19 and followed in home isolation, service and intensive care unit; It is aimed to retrospectively evaluate CRP, procalcitonin, ferritin, D-Dimer, fibrinogen AST, ALT and LDH levels with ROC and other statistical analyzes in terms of predicting mortality in the treatment and follow-up of the disease.

Materials-Methods: Between 01.04.2020 and 01.10.2020, the patients who applied to Necmettin Erbakan University Meram Medical Faculty Hospital with cold symptoms and were diagnosed with Covid-19 with RT-PCR positivity, were analyzed from Covid-19 infected serum and plasma. The results of the biomarkers were examined. Demographic data, vital signs and laboratory findings of the cases were compared. The results were statistically evaluated with the SPSS 22.0 package program.

Results: 300 cases who received home isolation, service and supportive treatment in the intensive care unit were included in the study. Crp, Pct, D-dimer, ferritin, fibrinogen, LDH, AST and ALT values were found to be statistically significant. According to the results of ROC (Receiver Operating Characteristic) analysis performed to determine the predictive values of laboratory parameters that were significant as a result of univariate statistical analysis, Crp (0.890775), Pct (0.86795), D-dimer (0.856975), ferritin (0.836975), LDH (0.7829), fibrinogen (0.773925), AST (0.685925) and ALT (0.594025) were found.

Conclusions: The high mutation ability of SARS-CoV-2 makes it difficult to control the pandemic. Therefore, early diagnosis of the disease has gained importance for the treatment of patients with high mortality risk. According to the ROC results we obtained in this study, it supports that CRP, Procalcitonin, Ferritin, D-dimer and LDH levels can be used as effective parameters in determining the prognosis and mortality risk in Covid-19 patients.

Keywords: COVID-19, pandemic, biomarker, ROC analysis

Amaç: 2019 yılı sonlarında Çin'in Wuhan kentinde ortaya çıkan yeni bir koronavirüs türü Covid-19 (SARS-CoV-2) pandemisine yol açmıştır. Yaygın olarak soğuk algınlığı belirtileri görülmekle birlikte daha ciddi vakalarda, pnömoni, Akut Respiratuar Distres Sendromu (ARDS), koagülopati, çoklu organ yetmezliği görülürken ilerleyen süreçte ölüme neden olmaktadır. Bu çalışmada, Covid-19 tanısı alan, evde izolasyon, servis ve yoğun bakım ünitesinde takip edilmiş olan vakalarda izlenen laboratuvar parametrelerinden; CRP, prokalsitonin, ferritin, D-Dimer, fibrinojen AST, ALT ve LDH düzeylerinin hastalığın tedavi ve takibinin mortaliteyi öngörmesi açısından ROC ve diğer istatiksel analizler ile retrospektif olarak değerlendirilmesi amaçlanmıştır.

Yöntem: Çalışmaya 01.04.2020 ile 01.10.2020 tarihleri arasında N. E. Ü. Meram Tıp Fakültesi Hastenesi'ne soğuk algınlığı belirtileriyle başvuruda bulunmuş ve RT-PCR pozitifliği ile Covid-19 tanısı alan vakalardan istenilen, Covid-19 ile enfekte serum ve plazmadan analiz edilen biyobelirteçlerin sonuçları incelenmiştir. Vakaların demografik verileri, vital bulguları, laboratuvar bulguları karşılaştırılmıştır. Sonuçlar SPSS 22.0 paket programı ile istatistiksel olarak değerlendirilmiştir.

Bulgular: Çalışmaya evde izolasyon, servis ve yoğun bakım ünitesinde destek tedavisi alan 300 vaka dahil edilmiştir. Crp, Pct, D-dimer, ferritin, fibrinojen, LDH, AST ve ALT değerleri istatistiksel olarak anlamlı bulunmuştur. Tek değişkenli istatistiksel analiz sonucunda anlamlı çıkan laboratuvar parametrelerinin prediktif değerlerinin belirlenmesi için yapılan ROC (Receiver Operating Characteristic) analizi sonuçlarına göre Crp (0.890775), Pct (0.86795), D-dimer (0.856975), ferritin (0.836975), LDH (0.7829), fibrinojen (0.773925), AST

(0.685925) ve ALT (0.594025) bulunmuştur.

Sonuç: SARS-CoV-2'nin mutasyon yeteneğinin çok yüksek olması pandeminin kontrolünü zorlaştırmaktadır. Dolayısıyla hastalığın erken dönemde tanınması, mortalite riski yüksek

hastaların tedavisi açısından önem kazanmıştır. Bu çalışmada elde ettiğimiz ROC sonuçlarına göre, klinikte CRP, Prokalsitonin, Ferritin, D-dimer ve LDH düzeylerinin Covid-19 hastalarında prognoz ve mortalite riskinin belirlenmesinde efektif birer parametre olarak kullanılabileceğini desteklemektedir.

Anahtar Kelimeler: COVID-19, pandemi, biyobelirteç, ROC analizi

OP17: POSSIBLE PROPHYLACTIC OR THERAPEUTIC EFFECTS OF BORIC ACID ON SEPSIS INDUCED HEPATIC INJURY

[BORİK ASİTİN SEPSİS KAYNAKLI KARACİĞER HASARI ÜZERİNDEKİ OLASI PROFİLAKTİK YA DA TERAPÖTİK ETKİLERİ]

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Objectives: It was aimed to investigate the possible prophylactic or therapeutic effects of boric acid (BA) on sepsis-induced hepatic damage induced by administration of lipopolysaccharide (LPS) in rat livers.

Materials-Methods:32 Spraque-Dawley male rats were divided into four groups. No treatment was applied to the control group, and 1 mg/kg dose of LPS was administered i.p. to the LPS group. For the prophylactic effect, 100 mg/kg BA was given to the animals by gavage one hour before LPS administration (LPS+BAP group). For the therapeutic effect, 100 mg/kg BA was given to the animals by gavage one hour after the LPS administration (LPS+BAT group). MDA, MPO, GSH, IL-6, IL-10, TAS, TOS, cytochrome-c (CYC), caspase-3 (CASP-3), and SEMA3A levels were measured by ELISA for the examination of the inflammatory response, oxidative damage and apoptosis levels in liver tissues taken from rats. For histopathological changes, 4 µm thick sections from paraffin-embedded liver samples were stained with H&E, examined under a light microscope.

Results: MDA, MPO, IL-6, CYC, CASP-3, SEMA3A, and TOS levels were significantly higher in the LPS group. GSH, IL-10 and TAS levels were significantly reduced in the LPS group inversely. It was observed that the application of BA caused statistically significant changes in these parameters compared to the LPS group. Also, the ameliorative effect of BA was higher in the prophylactic group compared to the therapeutic group histopathologically and biochemically.

Conclusions: In our study, it has been shown that the application of BA in sepsis-induced hepatic injury has better prophylactic effectiveness.

Keywords: Boric acid, sepsis, hepatic injury, prophylactic, therapeutic

Amaç: Bu çalışmada, sıçan karaciğerlerinde lipopolisakkarit (LPS) uygulaması ile oluşturulan sepsis kaynaklı karaciğer hasarında borik asidin (BA) olası profilaktik ya da terapötik etkilerinin araştırılması amaçlanmıştır.

Gereç-Yöntem: 32 Spraque-Dawley erkek sıçan dört gruba ayrıldı. Kontrol grubuna herhangi bir uygulama yapılmazken LPS grubu hayvanlara 1 mg/kg dozda LPS i.p olarak uygulandı. Profilaktik etki için hayvanlara LPS uygulamasından bir saat önce gavaj yoluyla 100 mg/kg BA verildi (LPS+BAP grubu). Terapötik etki için hayvanlara LPS uygulamasından bir saat sonra gavaj yoluyla 100 mg/kg BA verildi (LPS+BAT grubu). İnflamatuar cevap, oksidatif hasar ve apoptoz seviyelerinin incelenmesi için sıçanlardan alınan karaciğer dokularındaki MDA, MPO, GSH, IL-6, IL-10, TAS, TOS, sitokrom-c (CYC), kaspaz-3 (CASP-3) ve SEMA3A düzeyleri ELISA ile ölçüldü. Histopatolojik analizler için, parafine gömülmüş karaciğer örneklerinden alınan 4 µm kalınlığındaki kesitler H&E ile boyandı ve ışık mikroskobu altında incelendi.

Bulgular: MDA, MPO, IL-6, CYC, CASP-3, SEMA3A ve TOS düzeyleri LPS grubunda anlamlı olarak yüksekti. GSH, IL-10 ve TAS seviyeleri ise anlamlı olarak azalmış olarak bulundu. BA uygulamasının LPS grubuna göre bu parametrelerde istatistiksel olarak anlamlı değişikliklere neden olduğu gözlendi. Ayrıca hem histopatolojik hem de biyokimyasal olarak terapötik gruba göre profilaktik grupta BA'nın etkisinin daha yüksek olduğu görüldü.

Sonuç: Çalışmamızda sepsis kaynaklı karaciğer hasarında BA uygulamasının daha iyi profilaktik etkinliğe sahip olduğu gösterilmiştir.

Anahtar Kelimeler: Borik asit, sepsis, karaciğer hasarı, profilaktik, terapötik

OP19: THE ASSESSMENT OF PREANALYTICAL ERRORS BY FAILURE REPORTING AND CORRECTIVE ACTION SYSTEM

[PREANALİTİK HATALARIN ARIZA RAPORLAMA VE DÜZELTİCİ FAALİYET SİSTEMİ İLE DEĞERLENDİRİLMESİ]

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Objectives: Preanalytical errors constitute significant errors within the total testing process. The present study was aimed to conduct the risk analysis of a public health laboratory's preanalytical errors.

Materials-Methods: The frequencies of eight preanalytical errors belonging to 2021 were obtained from laboratory information and management software. Failure Reporting and Corrective Action System (FRACAS) was implemented on these errors according to the Clinical and Laboratory Standards Institute EP18A2 document using error frequency and severity. Then, the Pareto graph was drawn to determine which errors contributed to over 80 percent of the preanalytical errors. Next, the risk matrix was generated in the line of ISO 22367 to figure out acceptable and unacceptable errors. Finally, the risk priority number (RPN) was calculated to incorporate detectability into risk analysis for each error.

Results: Errors including clotted samples, hemolyzed samples, insufficient sample volume, inappropriate storage conditions, wrong sample collection device, and inappropriate transportation were contributed to at least 80 percent of preanalytical errors and found to be considered within acceptable risk if reasonably reduced according to the risk matrix. In addition, when detectability was included in risk analysis via RPN calculation, all errors were found within the acceptable low-risk category (RPN <25).

Conclusions: The present study showed our public health laboratory's most critical preanalytical errors, which were regarded to have acceptable low risk.

Keywords: Risk, Risk Assessment, Laboratory, Quality Management

Amaç: Preanalitik hatalar, toplam test süreci içerisinde önemli rol oynamaktadır. Bu çalışmada, bir halk sağlığı laboratuvarının preanalitik hatalarının risk analizinin yapılması amaçlamıştır.

Gereç-Yöntem: 2021 yılına ait sekiz preanalitik hatanın sıklıkları laboratuvar bilgi ve yönetim yazılımından elde edilmiştir. Bu hatalar üzerinde, Klinik ve Laboratuvar Standartları Enstitüsü EP18A2 rehberine uygun olarak hata sıklığı ve şiddeti kullanılarak Arıza Raporlama ve Düzeltici Faaliyet Sistemi uygulandı. Ardından, preanalitik hataların yüzde 80'inden fazlasına hangi hataların katkıda bulunduğunu belirlemek için Pareto grafiği çizildi. Sonrasında, 53abul edilebilir ve 53abul edilemez risk oluşturan hataları tespit etmek için ISO 22367 doğrultusunda risk matrisi oluşturuldu. Son olarak, her hata için tespit edilebilirlik, risk analizine dahil ederek risk öncelik numarası hesaplanmıştır.

Bulgular: Pıhtılı numuneler, hemolizli numuneler, yetersiz numune hacmi, uygun olmayan saklama koşulları, yanlış numune toplama tüpü ve uygun olmayan taşıma gibi hataların, preanalitik hataların en az yüzde 80'ini oluşturduğu tespit edildi ve risk matrisi uygulandığında makul ölçüde azaltılırsa 53abul edilebilir risk içerisinde değerlendirilebileceği gösterildi. Ayrıca, risk öncelik numarası hesabı yoluyla risk analizine tespit edilebilirlik dahil edildiğinde, tüm hataların 53abul edilebilir düşük risk kategorisinde (<25) bulunduğu tespit edildi.

Sonuç: Bu çalışmada, halk sağlığı laboratuvarımızda kayıt altına alınanan preanalitik hataların kritik olanları tespit edilmiş ve tümünün 53abul edilebilir düşük risk kategorisinde yer aldığı gösterilmiştir.

Anahtar Kelimeler: Risk, risk değerlendirme, laboratuvar, kalite yönetimi

OP20: COULD MARESIN-1 (MAR1) BE A NEW BIOMARKER IN THE DIAGNOSIS OF HIRSUTISM?

[HİRSUTİZM TANISINDA MARESİN-1 (MAR1) YENİ BİYOBELİRTEÇ OLABİLİR Mİ?]

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Objectives: Maresin-1 (MaR1) is an endogenous anti-inflammatory molecule produced by macrophages. Inflammation is one of the main endocrinological and biochemical events accompanying hirsutism. Therefore, it was aimed in this study to reveal whether there is a correlation between MaR-1 and idiopathic hirsutism (initial diagnosis).

Materials-Methods: This study was conducted with 30 patients with idiopathic hirsutism and 30 healthy women (control), a total of 60 voluntary participants with compatible BMI and age. Hirsutism assessments were made using the modified Ferriman Gallwey score. Those with a score of 8 or higher were considered hirsutism patients. After overnight fasting, 5 ml blood samples were collected from the patients. The amount of MaR1 in blood samples was measured by enzyme-linked immunosorbent assay (ELISA) test method. The luteinizing hormone (LH), follicle-stimulating hormone (FSH) dehydroepiandesteronesulphate (DHEA-S), and free testosterone, glucose, insulin, CRP, and lipid values of the participants were obtained from the hospital records.

Results: The amounts of (MaR1) and CRP in the control group were 1.09 ± 0.02 ng/mL and 3.2 ± 0.03 mg/L, respectively; in the idiopathic hirsutism group, they were 0.065±0.02 ng/mL and 0.048±0.01 mg/L, respectively (<0.05). There was an inverse correlation between the amounts of MaR1 and C-RP in hirsutism. In addition, DHEA-S, free testosterone, glucose and insulin values of the participants with hirsutism were significantly higher than the control group, and they were negatively correlated with MaR1 values and positively correlated with CRP values.

Conclusions: Compared to the control values, significantly decreased MaR1 and increased CRP values in the idiopathic hirsutism group are promising as new endocrinological and biochemical parameters that may have a role in the diagnosis and follow-up of this disease, in addition to the classical parameters (LH, FSH, DHEA-S, and testosterone).

Keywords: Maresin-1, Hirsutism, CRP

Amaç: Maresin-1 (MaR1) makrofajlar tarafından üretilen endojen bir anti-inflamatuar moleküldür. Inflamasyon hirsutizme eşlik eden endokrinolojik ve biyokimyasal başlıca olaylardan biridir. Dolayısı ile bu çalışmada MaR-1 ile idiyopatik 53estoster (ilk tanı) arasında bir ilişkinin olup olmadığının ortaya çıkarılması amaçlandı.

Gereç-Yöntem: Bu çalışma VKİ ve yaşları birbiri ile uyumlu 30

idiyopatik hirsutizmi olan ve 30 sağlıklı kadın (54estost) toplam 60 gönüllü katılımcı ile yapıldı. Hirsutizm değerlendirmeleri modifiye Ferriman Gallwey skoru kullanılarak yapıldı. 8 veya üstü skoru olanlar 54estoster hastası olarak 54esto edildi. Hastalardan bir gece açlığı takiben 5 Ml kan örnekleri alındı. Kan numunelerinde MaR1 miktarları enzyme-linked immunosorbent assay (ELISA) test yöntemi ile ölçüldü. Katılımcıların lütenize edici 54estost (LH), folikül stimüle edici 54estost (FSH) dehidroepiandesteronsülfast (DHEA-S) ve serbest 54estosterone, glukoz, 54estost, CRP ve lipit değerleri ise hastane kayıtlarından elde edildi.

Bulgular: Kontrol grubunda (MaR1) ve CRP miktarları sırası ile 1.09 ± 0.02 ng/Ml ve 3.2 ± 0.03 mg/L; idiyopatik 54estoster olan grupta ise MaR1 ve CRP miktarları sırası ile 0.065±0.02 ng/Ml ve 0.048±0.01 mg/L idi (<0.05). Hirsutizmde MaR1 ve CRP miktarları arasında ters bir korelasyon vardı. Ek olarak 54estost grubuna göre hirsutizmli katılımcıların DHEA-S, serbest testesteron, glukoz ve 54estost, değerleri anlamlı olarak yüksek ve MaR1 değerleri ile 54estoste CRP değerleri ile ise pozitif korelasyon göstermekteydi.

Sonuç: Kontrol değerlerine göre idiyopatik hirsutizminde kayda değer bir şekilde azalan MaR1 ve artan CRP değerleri klasik parametrelere ek olarak (LH, FSH, DHEA-S ve 54estosterone) bu hastalığın tanı ve takibinde yeri olabilecek yeni endokrinolojik ve biyokimyasal parametreler olarak umut vaat etmektedirler.

Anahtar Kelimeler: Maresin-1, Hirsutizm, CRP

OP21: DEVELOPMENT OF A NEW LC-MS/MS METHOD FOR THE DETECTION OF ALPHA-1 ANTITRYPSIN DEFICIENCY

[LC-MS/MS İLE ALFA-1 ANTİTRİPSİN EKSİKLİĞİNİN TESPİTİNDE YENİ ANALİZ YÖNTEMİ GELİŞTİRİLMESİ]

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Objectives: Alpha-1 antitrypsin deficiency is the most common genetic cause of childhood liver disease and adult pulmonary emphysema caused by mutations in the A1AT gene. In the diagnosis of A1AT deficiency, it is necessary to determine both the low level of A1AT and the specific variant. A combination of nephelometry, genotyping and/or phenotyping methods is used to diagnose A1AT deficiency. In our study, we aimed to distinguish between wild type and mutated (S and Z) alleles in the A1AT gene by liquid chromatography mass spectrometry (LC-MS/MS) method for the phenotyping of A1AT.

Materials-Methods: According to the results of immunonefelemetry analysis, patients with low A1AT were selected. The A1AT protein in the serum samples was digested with trypsin. The samples were combined with labeled peptide standards and measured with LC-MS/MS. Phenotyping was determined based on the presence/absence of variant peptides. The concordance of the results was compared by genotyping analysis.

Results: Allele detection in the A1AT gene was confirmed by genotyping analysis of a patient with a homozygous ZZ mutation and a control patient without S and Z mutations as a result of LC-MS/MS analysis. These findings showed that the LC-MS/MS results were in agreement with the genotyping results.

Conclusions: In this study, we developed a cost-effective, sensitive, and high analytical performance method to detect A1AT deficiency. This method has the potential to improve the diagnosis of A1AT deficiency for clinical laboratories.

Keywords: alpha 1- antitrypsin deficiency, LC-MS/MS, phenotyping, genotyping analysis

Amaç: Alfa-1 antitripsin eksikliği, A1AT genindeki mutasyonların neden olduğu çocuklukta karaciğer hastalıklarının ve erişkinlerde akciğer amfizeminin en sık görülen genetik nedenidir. A1AT eksikliğinin tanısında, A1AT düzeyinin düşüklüğüyle beraber spesifik varyantın tanımlanması gereklidir. A1AT eksikliğinin teşhisi için nefelometri, genotipleme ve/veya fenotipleme yöntemlerinin kombinasyonu kullanılır. Çalışmamızda, A1AT'nin fenotiplemesi için sıvı kromatografi kütle spektrometrisi (LC-MS/MS) yöntemi ile A1AT genindeki vahşi tip ve mutasyona uğramış (S ve Z) alellerini ayırt etmeyi amaçladık.

Gereç-Yöntem: İmmunonefelemetri analiz sonuçlarına göre düşük A1AT hastaları seçildi. Serum örneklerindeki A1AT proteini, tripsin ile peptitlerine parçalandı. Örnekler, işaretli peptit standartlarıyla birleştirildi ve LC-MS/MS ile ölçüldü. Fenotipleme, varyant peptitlerin varlığına/yokluğuna göre belirlendi. Sonuçların uyumu, genotipleme analizi ile karşılaştırıldı.

Bulgular: A1AT genindeki alel tespitinde, LC-MS/MS analizi sonucunda homozigot ZZ mutasyonuna sahip hasta ve S ve Z mutasyonuna sahip olmayan kontrol hastası genotipleme analiziyle doğrulanmıştır. Bu bulgular, LC-MS/MS sonuçları ile genotipleme sonuçlarının uyumlu olduğunu gösterdi.

Sonuç: Bu çalışmada, A1AT eksikliğini tespit etmek için uygun maliyetli, duyarlı ve yüksek analitik performansa sahip bir yöntem geliştirdik. Bu yöntemin, klinik laboratuvarlar için A1AT eksikliği tanısını iyileştirme potansiyeline sahip olduğu gösterilmiştir.

Anahtar Kelimeler: alfa-1-antitripsin eksikliği, LC-MS/MS, fenotipleme, genotipleme analizi

OP22: THE ASSOCIATION BETWEEN OBESITY, LIVER ENZYMES, AND SQUALENE SYNTHASE IN NON-ALCOHOLIC FATTY LIVER DISEASE

[NON-ALKOLİK YAĞLI KARACİĞER HASTALARINDA OBEZİTE, KARACİĞER ENZİMLERİ VE SKUALEN SENTAZ İLİŞKİSİ]

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Objectives: Obesity plays an important role in the pathogenesis of non-alcoholic fatty liver disease (NAFLD) by contributing to chronic low-grade inflammation. The strong correlation between obesity and inflammation marker CRP has been known. Squalene synthase (SS), one of the key regulators in cholesterol synthesis, is among the potential targets in the treatment of NAFLD. In our study, we aimed to investigate the relationship between obesity, CRP, liver enzymes, SS, and rs2645424-SNP of the FDFT1 gene which encodes SS in NAFLD patients.

Materials-Methods: SS levels were evaluated by ELISA method and FDFT1 rs2645424 genotypes were detected by real-time PCR in 64 NAFLD patients and 77 controls.

Results: In the comparison of BMI≥27.5 and BMI<27.5 subgroups, waist and hip circumference, CRP (p<0.001), AST (p=0.047), SS levels (p=0.006) were higher in BMI≥27.5 patients; while waist and hip circumference (p<0.001), glucose (p=0.019), CRP (p=0.026), ALT (p=0.002) and GGT (p=0.001) were higher in controls. FDFT1 rs2645424(C/T) genotype distributions was similar between groups (p>0.05). In patients with BMI ≥27.5, the T allele is associated with higher HbA1c (p=0.014) and HDL-C (p=0.001), and the C allele with low HbA1c (p=0.034) levels. in BMI≥27.5 patients, SS levels was positively correlated with waist circumference (r^2=0.29;p=0.043), hip circumference (r^2=0.32;p=0.027) and AST (r^2=0.3; p=0.042), but negatively correlated with triglyceride (r^2=-0.4;p=0.005). In patients with BMI<27.5, SS levels was positively correlated with HbA1c (r^2=0.7;p=0.037) and GGT (r^2=0.8;p=0.016), and there was a negative correlation between CRP and HDL-C (r^2=(-)0.8;p=0.014).

Conclusions: In our study, the rare T allele of the rs2645424 SNP, which was defined in the literature to be associated with increased SS activity in overweight/obese NAFLD patients, was observed to be associated with poor glycemic control. Correlation analyses showed that SS level was positively related to obesity parameters in overweight/obese patients, while it was associated with poor glycemic control and liver enzymes (GGT) in overweight/non-obese patients. Elevations in liver enzymes in obese controls were correlated with high CRP. In conclusions, we suggest that SS, one of the regulators of liver cholesterol metabolism, may potentially contribute to hepatic inflammation secondary to NAFLD, based on its relationship with obesity, glycemic control, and liver enzymes.

Keywords: Obesity, Squalene Synthase (FDFT1), Inflammation, Liver function markers, Body mass İndex

Amaç: Obezite kronik düşük dereceli inflamasyona katkısıyla non-alkolik yağlı karaciğer hastalığı (NAFLD) patogenezinde önemli rol oynamaktadır. Obezite ile inflamasyon belirteci CRP arasındaki güçlü korelasyon bilinmektedir. Kolesterol sentezinde anahtar regülatörlerden biri olan Skualen sentaz (SS), NAFLD tedavisinde potansiyel hedefler arasındadır. Çalışmamızda NAFLD hastalarında SS'yi kodlayan FDFT1 genindeki rs2645424-SNP, CRP, SS, karaciğer enzimleri ve obezite ilişkisini araştırmayı hedefledik.

Gereç ve Yöntem: 64 NAFLD hastası ve 77 kontrolde SS düzeyleri ELISA yöntemiyle, FDFT1 rs2645424(C/T) SNP gerçek-zamanlı PZR'la incelenmiştir.

Bulgular: VKİ≥27,5 ve VKİ<27,5 alt gruplarındaki karşılaştırmada, VKİ≥27,5 NAFLD hastalarında bel ve kalça çevresi, CRP (p<0,001), AST (p=0,047), SS düzeyleri (p=0,006); Kontrollerde ise bel ve kalça çevresi (p<0,001), glukoz (p=0,019), CRP (p=0,026), ALT (p=0,002) ve GGT (p=0,001) yüksektir. FDFT1 rs2645424 (C/T) genotip dağılımları gruplar arasında benzerdir (p>0,05). VKİ≥27,5 hastalarda, T alleli yüksek HbA1c (p=0,014) ve HDL-K (p=0,001) ile, C alleli düşük HbA1c (p=0,034) düzeyleriyle ilişkilidir. VKİ≥27,5 hastalarda, SS düzeyleri, bel çevresi (r^2=0,29;p=0,043), kalça çevresi (r^2=0,32;p=0,027) ve AST ile (r^2=0,3;p=0,042) pozitif, trigliseritle negatif korelasyonda idi (r^2=(-)0,4;p=0,005).VKİ<27,5 hastalarda ise SS, HbA1c (r^2=0,7;p=0,037) ve GGT (r^2=0,8;p=0,016) ile pozitif korelasyonda idi, ve CRP ve HDL-K arasında negatif korelasyon vardı (r^2=(-)0,8;p=0,014).

Sonuç: Çalışmamızda aşırı kilolu/obez NAFLD hastalarında literatürde artmış SS aktivitesiyle ilişkili tanımlanmış rs2645424 SNP'nin nadir T alleli zayıf glisemik kontrol ile ilişkili gözlenmiştir. Korelasyon analizleri aşırı kilolu/obez hastalarda SS düzeyinin obezite parametreleriyle pozitif ilişkisini gösterirken, aşırı kilolu/obez olmayan hastalarda zayıf glisemik kontrol ve karaciğer enzimleriyle (GGT) ilişkisine işaret etmektedir. Obez kontrollerde karaciğer enzimlerindeki yükselmeler, yüksek CRP ile koreledir. Sonuç olarak, karaciğer kolesterol metabolizmasının düzenleyicilerinden SS enziminin obezite, glisemik kontrol ve karaciğer enzimleriyle olan ilişkisine dayanarak, NAFLD'ye ikincil gelişen hepatik inflamasyona potansiyel katkıda bulunabileceğini önermekteyiz.

Anahtar Kelimeler: Obezite, İnflamasyon, Skualen Sentaz (FDFT1), Vücut kitle indeksi, Karaciğer fonksiyon belirteçleri

OP23: IMPACT OF HEMATOCRIT LEVEL AND CHROMATOGRAPHIC EFFECTS ON BIOTINIDASE MEASUREMENTS FROM DRIED BLOOD SPOTS

[HEMATOKRİT SEVİYESİ VE KROMATOGRAFİK ETMENLERİN, KURUTULMUŞ KAN ÖRNEKLERİNDEN BİYOTİNİDAZ ÖLÇÜMÜNE ETKİSİ]

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Objectives: Effect of hematocrit (HCT) level of the blood sample, chromatographic effects on filter paper and the presence of biotinidase (BTD) bearing white blood cells (WBC) on biotinidase enzyme activity (BEA) measurements from dried blood samples (DBS) were investigated.

Material-Methods: BEAs of 3.2mm diameter samples punched from the centre or periphery of DBSs of 4 clinically important biotinidase levels (BTD-0, BTD-50, BTD-100, BTD-200) that were prepared from blood pools created by altering the hematocrit level (HCT34%, HCT50%) and/or removing WBCs were measured with fluorometric neonatal biotinidase kit. Statistical significance analyses were performed by ANOVA and Student-t-test, and effect sizes were determined by CohenD.

Results: BEA measurements of DBSs with lower hematocrit level were significantly higher than those with higher hematocrit ($p<0.05$). BEAs of peripheral punches from DBSs without WBC were significantly lower than their counterparts with preserved WBC ($p<0.05$). BEAs measured from peripheral punches was significantly higher than that of centre punches ($p<0.05$). Depending on the chromatographic effects, HCT ratio and WBC presence, fold differences between the BEA measurements of centre- vs peripheral-punches ranged between 9.1-14.3%, 10.7-12.7% and 7.9-12.6% at BTD-50U, BTD-100U and BTD-200U respectively. The greatest fold diference between BTD measurements from centre/peripheral punches was observed in samples with lower haematocrit (11.8%-14.3%). Total precision for the samples bearing BTD enzyme was between 6.0%-8.7%. Throughout the study, the average precision of centre and peripheral punches were 5.9% and 8.2%, respectively. CohenD effect sizes of BEA differences between centre/peripheral punches were ~1.0-2.6.

Conclusion: It is observed that, throughout the study, the variation in BEA measurements attributable to HCT ratio, WBC presence and chromatographic effects remained within the preanalytical total error rate, which is 15% for DBS measurements. Since preliminary information on HCT level of the sample is often not available during neonatal screening, possible variations between centre/peripheral punches should be considered particularly around the clinical threshold level.

Keywords: Biotinidase deficiency, Neonatal screening, Dried Blood Spots (DBS), haematocrit level, chromatographic effects

Amaç: Kan numunesinin hematokrit(HCT) seviyesi, biyotinidaz(BTD) aktivitesine sahip beyaz kan hücrelerinin(WBC) varlığı ve filtre kağıdı üzerindeki kromatografik etkilerin, kurutulmuş kan örneklerinden(DBS) gerçekleştirilen biyotinidaz enzim aktivitesi(BEA) ölçümleri üzerindeki etkisi incelendi.

Gereç-Yöntem: Hematokrit seviyesi değiştirilip (HCT34%, HCT50%), beyaz kan hücrelerinin korunması/çıkarılmasıyla oluşturulan kan stoklarından, klinik olarak önemli 4 farklı biyotinidaz seviyesine (BTD0, BTD50, BTD100, BTD200) sahip DBSler hazırlanmış ve DBSlerin merkez veya kenar alanlarından delinen 3.2mm çapındaki numunelerde (punch), florometrik yenidoğan biyotinidaz kitiyle BEA ölçülmüştür. İstatistiksel anlamlılık analizleri ANOVA ve Student-t testi, etki büyüklüğü analizleri CohenD ile belirlenmiştir.

Bulgular: Düşük hematokritli DBS'lerin BEA ölçümleri, yüksek hematokritlilerden istatistiksel anlamlı yüksektir ($p<0.05$). WBCsi uzaklaştırılmış kan numuneleriyle hazırlanmış DBSlerden alınan kenar punchların BEAsı, WBCsi korunan eşleniklerinden istatistiksel anlamlı düşüktür($p<0.05$). DBSlerin kenar punchlarından ölçülen BEA, merkez punchlarınkinden istatistiksel anlamlı yüksektir($p<0.05$). Merkez/kenar punchların BEA ölçümleri arasındaki sapma; kromatografik etkiler, HCT oranı ve WBC mevcudiyetine bağlı olarak farklılık göstermekle birlikte; BTD50U, BTD100U ve BTD200U seviyelerinde sırasıyla 9.1-14.3%, 10.7-12.7% ve 7.9-12.6% oranında gerçekleşmiştir. Merkez/kenar BEA ölçümleri arasındaki en yüksek sapma, düşük hematokritli numunelerde gözlenmiştir(11.8%-14.3%). BTDenzimine sahip numunelerin total tekrarlanabilirlikleri 6.0%-8.7% arasındadır. Çalışma genelinde merkez ve kenar punchların ortalama tekrarlanabilirlikleri sırasıyla 5.9% ve 8.2%'dir. Merkez/kenar BEA farklarının CohenD etki büyüklükleri 1.0-2.6 arasındadır.

Sonuç: HCT oranı, WBC mevcudiyeti ve kromatografik etkilere bağlı olarak, DBSlerin BEA ölçümlerinde gözlemlenen sapmanın, DBSten ölçüm için tanımlanan %15lik preanalitik hata bütçesi içinde kaldığı gözlenmektedir. HCT seviyesine dair öncül bilginin genellikle mevcut olmadığı yenidoğan taramalarında özellikle de klinik karar eşik değerinde; merkez/kenar punchlar arasındaki muhtemel sapma, değerlendirmeler sırasında göz önünde bulundurulmalıdır.

Anahtar Kelimeler: Biyotinidaz eksikliği, Yenidoğan taraması, Kuru Kan Örnekleri (Dried Blood Spots - DBS), Hematokrit Seviyesi, Kromatografik Etkiler

OP24: THE IMPORTANCE OF ACUTE PHASE PROTEINS IN THE EVALUATION OF CRITICAL COVID-19 PATIENT PROGNOSIS

[KRİTİK COVID-19 HASTA PROGNOZUNUN DEĞERLENDİRİLMESİNDE AKUT FAZ PROTEİNLERİNİN ÖNEMİ]

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Objectives: Identifying COVID-19 patients with risk of adverse outcomes at first admission to the intensive care unit has several diagnostic challenges. The concentration of acute phase proteins synthesized by the liver increases or decreases markedly in the serum following inflammation and infection. This study aimed to investigate the predictive value of acute phase proteins in critically ill COVID-19 patients and to evaluate the efficacy of inflammatory markers in predicting mortality risk in the intensive care unit.

Material-Methods: A retrospective study was conducted in critically ill COVID-19 patients treated in the intensive care unit. Overall, 123 patients with ARDS and/or multi-organ dysfunction were included in the first 24 hours of admission to intensive care unit. After 28 days, groups of survived (n=54) and dead patient (n=69) or groups of patients with (n=83) and without (n=40) invasive mechanical ventilation were formed. Serum amyloid A, C-reactive protein, albumin, and prealbumin values considered as acute phase proteins within the first 24 hours of admission to the intensive care unit were compared between groups.

Results: Albumin and prealbumin levels significantly decreased in dead patients (p=0.011, p<0.001, respectively) and were mechanically ventilated patients (p=0.010, p=0.006, respectively). The Serum amyloid A levels in mechanically ventilated patients significantly increased (p=0.022).

Conclusions: Low prealbumin and albumin levels and high serum amyloid A levels during admission to ICU can be used as a prognostic marker of disease severity and mortality.

Keywords: Acute-phase proteins, COVID-19, mechanical ventilation, mortality

Amaç: Yoğun bakım ünitesine ilk kabulde kötü prognoz riskine sahip COVID-19 hastalarını belirlemenin çeşitli tanısal zorlukları vardır. Karaciğer tarafından sentezlenen akut faz proteinlerinin konsantrasyonu inflamasyon ve enfeksiyonu takiben serumda artar veya azalır. Bu çalışmada, kritik COVID-19 hastalarında akut faz proteinlerinin prediktif değerini belirleme ve yoğun bakım ünitesinde mortalite riskini öngörmede inflamatuar belirteçlerin etkinliğini değerlendirme amaçlanmaktadır.

Gereç-Yöntem: Retrospektif olarak tasarlanan bu çalışma yoğun bakım ünitesinde tedavi gören kritik COVID-19 hastalarında yapıldı. Çalışmaya yoğun bakım ünitesine kabulün ilk 24 saatinde ARDS ve/veya çoklu organ disfonksiyonu olan 123 hasta dahil edildi. Yoğun bakım ünitesindeki 28 günün sonunda sağ kalan (n=54) ve ölen (n=69) hasta grupları veya invaziv mekanik ventilasyon (n=83) uygulanan ve uygulanmayan (n =40) hasta grupları oluşturuldu. Gruplar arasında akut faz proteinleri olan serum amiloid A, C-reaktif protein, albümin ve prealbüminin yoğun bakım ünitesine kabulün ilk 24 saat içerisindeki değerleri karşılaştırıldı.

Bulgular: Albümin ve prealbümin düzeyleri ölen (sırasıyla p=0.011, p<0.001) ve mekanik ventilasyon uygulanan (sırasıyla p=0.010, p=0.006) hastalarda anlamlı olarak azaldı. Mekanik ventilasyonlu hastalarda serum amiloid A düzeyleri anlamlı olarak arttı (p=0.022).

Sonuç: Yoğun bakım ünitesine kabul sırasında düşük prealbümin ve albümin seviyeleri ve yüksek serum amiloid A seviyeleri, hastalık şiddeti ve mortalitenin prognostik bir belirteci olarak kullanılabilir.

Anahtar Kelimeler: COVID-19, mekanik ventilasyon, mortalite, akut faz proteinler

OP25: POTENT PROBIOTICS ATTENUATE NEUROINFLAMMATION THROUGH THE SEMAPHORIN PATHWAY AND FERROPTOSIS IN THE GUT-BRAIN AXIS

[GÜÇLÜ PROBİYOTİKLER SEMAFORİN YOLU ÜZERİNDEN NÖROİNFLAMASYONU VE BAĞIRSAK-BEYİN EKSENİNDEKİ FERROPTOZİ AZALTIR]

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Objective: The aim of this study was to examine the effects of Lactobacillus salivarius (LAC) and Bifidobacterium bifidum (BIF), potent probiotics, on LPS-induced neuroinflammation and ferroptosis in the Gut-Brain axis through the Semaphorin-3A.

Materials-Methods: Twenty-five Wistar Albino female rats were divided into five groups; Control, lipopolysaccharide (LPS, 100 µg/kg), LPS+LAC, LPS+BIF, and LPS+LAC+BIF (4×10^9 ml CFU). Incubation was performed according to the manufacturer's protocol for commercially purchased bifidobacteria and lactobacilli species. 1 mL of probiotics were added to the drinking water daily for 21 days for the rats. LPS was applied to rats intraperitoneally on the 17th day. Brain tissues of all groups were taken four days after LPS application. Fecal calprotectin levels of rats were measured as an important biomarker in determining intestinal flora disruption. GPx4 and ACLS4 levels of ferroptosis, TNF-a and IL-10 of inflammation, apoptotic proteins as caspase 3 (CASP3) and caspase 7 (CASP7) were measured with ELISA. BDNF and SEMA3A mRNA expression were analyzed RT-PCR and Western Blot. The immunohistochemistry, H&E, and apoptosis examinations were carried out with light microscopy for Histopathological assessments

Results: Calprotectin levels were high in the LPS group

(p<0.05). ACSL4, TNF-a, CASP3, and CASP7 levels were higher in LPS groups (p<0.05). These levels were statistically decreased in the probiotic groups compared to the LPS group, as demonstrated in both biochemical and histological analyzes (p<0.05). While BDNF mRNA expression decreased in LPS groups, SEMA3A levels increased in the same group. What's more, BDNF/actin rates were proven by western blot and the damage caused by neuroinflammation in the brain tissue and the preservation of the intestinal microbiota were visualized histopathologically on the morphological structures in all groups

Conclusion: The use of probiotics against LPS-induced inflammatory responses and impaired gut microbiota showed anti-inflammatory effects through semaphorin and ferroptosis signaling pathways.

Keywords: Neuroinflammation, lipopolysaccharide, lactobacillus, bifidobacterium, probiotics

Amaç: Bu çalışmanın amacı, güçlü probiyotikler olan Lactobacillus salivarius (LAC) ve Bifidobacterium bifidum'un (BIF), Semaphorin-3A aracılığıyla Gut-Beyin ekseninde LPS kaynaklı nöroinflamasyon ve ferroptozis üzerindeki etkilerini incelemektir.

Gereç-Yöntem: Yirmi beş Wistar Albino dişi sıçan beş gruba ayrıldı; Kontrol, lipopolisakkarit (LPS, 100 µg/kg), LPS+LAC, LPS+BIF ve LPS+LAC+BIF (4× 10^9 ml CFU). İnkübasyon, ticari olarak satın alınan bifidobakter ve laktobasil türleri için üreticinin protokolüne göre yapıldı. Sıçanların içme suyuna 21 gün boyunca günde 1 mL probiyotik eklendi. Sıçanlara 17. günde intraperitonal olarak LPS uygulandı. LPS uygulamasından dört gün sonra tüm grupların beyin dokuları çıkarıldı. Sıçanların dışkı kalprotektin seviyeleri, bağırsak florasının bozulmasının belirlenmesinde önemli bir biyobelirteç olarak ölçülmüştür. GPx4 ve ACLS4 ferroptozis, TNF-a ve IL-10 inflamasyon, kaspaz 3 (CASP3) ve kaspaz 7 (CASP7) apoptoz üzerine biyobelirteçler olarak belirlendi ve ELISA ile ölçüldü. BDNF ve SEMA3A mRNA ekspresyonu, RT-PCR ve Western Blot yöntemiyle analiz edildi. Histopatolojik değerlendirmeler için ışık mikroskobu ile immünohistokimya, H&E ve apoptoz incelemeleri yapıldı.

Bulgular: LPS grubunda kalprotektin düzeyleri yüksekti (p<0.05). ACSL4, TNF-a, CASP3 ve CASP7 düzeyleri LPS gruplarında kontrol grubuna kıyasla daha yüksekti (p<0.05). Bu seviyeler, hem biyokimyasal hem de histolojik analizlerde gösterildiği gibi, LPS grubuna kıyasla probiyotik verilen gruplarda istatistiksel olarak azaldı (p<0.05). LPS gruplarında BDNF mRNA ekspresyonu azalırken, aynı grupta SEMA3A ekspresyonu arttı. Ayrıca western blot ile BDNF/aktin oranları ispatlanmış ve tüm gruplarda nöroinfamasyonun beyin dokusunda oluşturduğu hasar ve bağırsak mikrobiyotasının korunması histopatolojik olarak morfolojik yapılar üzerinde görüntülenmiştir.

Sonuç: LPS ile indüklenen inflamatuar yanıtlara ve bozulmuş bağırsak mikrobiyotasına karşı probiyotik kullanımı, semaforin ve ferroptoz sinyal yolakları aracılığıyla anti-inflamatuar etki göstermiştir.

Anahtar Kelimeler: Nöroinflamasyon, lipopolisakkarit, laktobasil, bifidobakter, probiyotikler

OP26: EVALUATION OF THE EFFECT OF FAVIPIRAVIR USE ON INR, PT, APTT TESTS IN COVID-19 PATIENTS

[FAVIPIRAVIR KULLANAN VE KULLANMAYAN COVID-19 HASTALARDA INR, PT, APTT TESTLERININ DEĞERLENDIRILMESI]

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Objective: Studies have shown that high mortality rates associated with abnormal coagulation response, bleeding and coagulation disorders in COVID-19 patients. In our study, it was aimed to investigate the effect of the use of favipiravir on coagulation tests such as INR, PTT and Aptt.

Materials-Methods: 50 patients who had a positive RT-PCR in nasal and throat swabs result and were diagnosed with COVID-19 using favipiravir and 50 non-users favipiravir COVID-19 patients were included. INR, PT, Aptt data were evaluated for all patients.

Results: Results of patients using favipiravir; INR 1.3±0.2, PT(s) 16.4±3.4, Aptt(s) 40.7±10.1, while the results of patients who did not use favipiravir were INR 1,2±0.2, PT(s) 14.6±2.5, Aptt(s) was found 38.4±7.8. While PT and INR were found to be significantly higher in patients using favipiravir (p<0.05), the elevation in Aptt values was not significant.

Conclusions: As a result, it was observed that favipiravir prolongs the clotting time. In the light of these **RESULTS**, it is recommended to consider this in anticoagulant therapy used for treatment.

Keywords: COVID19, PTT, INR

Amaç: COVID-19 hastalarında, anormal koagülasyon yanıtı ile ilişkili yüksek mortalite oranları, kanama ve pıhtılaşma bozukluklarının geliştiği yapılan çalışmalarla gösterilmiştir. Çalışmamızda COVID-19 tedavisinde favipiravir kullanımın koagulasyon testleri olan INR, PT, aPTT testleri üzerine etkisinin araştırılması amaçlanmıştır.

Gereç-Yöntem: Çalışmaya, alınan nazal ve boğaz sürüntülerinde COVID-19 RT-PCR testi pozitif olan, favipiravir kullan 50 hasta ve kullanmayan 50 hasta dahil edildi. Tüm hastalara INR, PT, aPTT verileri değerlendirildi.

Bulgular: Favipiravir kullanan hastaların sonuçları; INR 1,3±0,2, PT(sn) 16,4±3,1, aPTT(sn) 40,7±10,1 gelirken, favipiravir kullanmayan hastaların sonuçları INR 1,2±0,2, PT(sn) 14,6±2,5, aPTT(sn) 38,4±7,8 olarak bulunmuştur. Favipiravir kullanan hastalarda PT ve INR anlamlı yüksek bulunurken (p<0.05), aPTT değerlerindeki yükseklik anlamlı bulunmamıştır.

Sonuç: Sonuç olarak favipiravirin pıhtılaşma zamanını uzattığı görüldü. Bu sonuçlar ışığında tedavi için kullanılan antikoagulan tedavide bunu göz önünde bulundurulması önerilir.

Anahtar Kelimeler: COVID19, PTT, INR

OP-27: A COMPARATIVE PROTEOMIC ANALYSIS FOR THE IDIOPATHIC GRANULOMATOUS MASTITIS: DISCOVERY OF PUTATIVE DIAGNOSTIC BIOMARKERS FOR DIAGNOSIS

[İDİYOPATİK GRANÜLAMATÖZ LOBÜLER MASTİT HASTALIĞININ KARŞILAŞTIRMALI PROTEOMİK ANALİZİ: HASTALIĞIN TEŞHİSİ İÇİN OLASI BİYOBELİRTEÇLERİN ARAŞTIRILMASI]

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ABSTRACT

Idiyopathic Granulomatosis Lobular Mastitis (IGLM) is a inflammation related disease that mostly mimics breast cancer. Clinical indications of IGLM are pain, edema, erythema, nipple discharge, nipple retraction, inflammation on breast skin and fistula. Even if the etiology of the disease is still not clear, possible explanations for causes of IGLM in the literature can be classified as autoimmune basis of IGLM, infection relation of IGLM and breast cancer resemblance. However, there is need to clarify disease cellular molecular mechanisms underneath. Therefore, this study is aimed to investigate possible disease molecular mechanisms in the formation, progress and recurrence of IGLM at the protein level. For this, two different proteomic approaches as MALDI TOF-TOF analysis following 2D-SDS-PAGE gels and nHPLC coupled LC-MS/MS analysis.

In MALDI analysis, 50 differentially regulated spots were identified in the IGLM compared to controls. Bioinformatic analysis (STRING and GProfiler Analyses) revealed that cellular response to superoxide radicals and detoxification mechanisms were downregulated. The inhibition in those mechanisms result accumulation of reactive oxygen species and genome instability. Which in turn may explain the tumorigenic behavior of the disease. Additionally, oxidative phosphorylation and citric acid cycle pathways inhibited. That results may be explained there may be Warburg Effect like mechanism. Like being in cancer, in IGLM, energy may be produced by glycolysis with lactate production and mitochondrial respiration even in the presence of oxygen.

In the label-free quantitative (LFQ) analyses of LC-MS/MS results,1455 master proteins were identified, among them 482 were found differentially regulated (>2-fold change) in the comparison of IGLM and control groups. Bioinformatics analysis performed with STRING, DAVID, PANTHER and GProfiler indicated that 26 proteins were related to immune system processes. Within those, 5 proteins, PNP, TAP1, ITGAL, PRKDC, and PTPRC were related to combined immunodeficiency. Upregulations in those genes can be conducted that there is an immune system uplift in IGLM tissues. These results may be an explanation for immunity-related symptoms of IGM tissues such as edema, nipple discharge, etc. Since IGM is also considered a cancer-like disease, results were evaluated by indicating their cancer relation by DAVID analysis. To that, 20 of 60 differentially regulated proteins in IGLM was related to the cancer metabolisms. Two proteins, TAP1 and PRKDC, which we have previously found to be associated with immunity, were also found to be associated with the cancer. Additionally, there was also upregulation insulin response elements which may explain the disease relation with inflammation, hormone imbalance and insulin related diseases like Diabetes Mellitus. Moreover, there was an upregulation in neutrophil degranulation proteins. That may explain which immune system mechanisms were activated and inflammation triggered.

In conclusion, there is no doubt that IGLM is inflammation related disease, however it is not clear that, whether IGM is immunity-related or is a cause after microbial infection. Immunity related aforementioned regulated proteins may be candidate biomarker proteins for IGLM yet they has to be supported by additional studies. Also, IGLM resembles cancer by disease formation and progress. It seems that there are common energy metabolisms between cancer and IGLM but molecular basis and related proteins have to be well investigated with further studies.

This study can be a base to clarify disease formation and progress. Also, previously mentioned proteins can be offered as molecular targets. However, further detailed analyses are still needed to reveal baseline disease mechanisms.

"The data regarding the abstract presented at this congress is a part of Merve Gülsen Bal Albayrak's doctoral dissertation."

ÖZET

Idiyopatik Grabülamatöz Lobüler Mastit (IGLM) klinik olarak meme kanserini taklit eden inflamasyon ilişkili bir hastalıktır (1). IGLM hastalığının klinik belirtileri ağrı, ödem, eritem, meme başı akıntısı, meme başı retraksiyonu, meme derisinde iltihaplanma ve fistüldür (2). Hastalığın etiyolojisi tam olarak bilinmemesine rağmen, literatüre göre hastalığın olası nedenleri; IGLM'nin otoimmün temeli, IGLM'nin enfeksiyon ilişkisi ve meme kanseri benzerliği olarak sınıflandırılabilir (3-8). Ancak IGLM hastalığının temelinde yatan moleküler mekanizmaların açığa çıkarılmasına ihtiyaç vardır. Bu nedenle, bu çalışma protein düzeyinde IGLM'nin oluşumu, ilerlemesi ve tekrarlanmasındaki olası moleküler mekanizmaları protein seviyesinde araştırmak için planlanmıştır. Bunun için 2D-SDS-PAGE jel akabinde MALDI TOF-TOF analizi ve nHPLC akabinde LC-MS/MS analizi olmak üzere iki farklı proteomik yaklaşım planlanmıştır.

MALDI analizinde, IGLM'de kontrole kıyasla regüle olan 50 protein beneği belirlenmiştir ve bu beneklerin tanımlaması yapılmıştır. Elde dilen verinin biyoinformatik analizi (STRING ve GProfiler Analizleri), hücrenin süperoksit radikallerine verdiği cevap ve detoksifikasyon mekanizmalarının aşağı regüle olduğunu ortaya çıkarmıştır. Bu mekanizmalardaki inhibisyon, reaktif oksijen türlerinin birikmesine ve sonuç olarak genom instabilitesine neden olur. Bu da hastalığın tümörijenik

davranışını açıklayabilir. Ayrıca, oksidatif fosforilasyon ve sitrik asit döngüsü yolakları da inhibe görülmektedir. Bu sonuç IGLM hastalığında kanserdeki Warburg Hipotezi benzeri bir mekanizmanın olabileceği şeklinde yorumlanabilir. Kanserde olduğu gibi, IGLM'de de enerji, oksijen varlığında bile laktat üretimi ve mitokondriyal solunum ile glikoliz aracılı olarak üretiliyor olabilir.

LC-MS/MS sonuçlarının etiketsiz kantitasyon (label-free quantitative-LFQ) analizinde, 1455 ana protein tanımlandı, bunlardan 482'si IGLM ve kontrol gruplarının karşılaştırılmasında regüle bulundu (>2 kat fark). STRING, DAVID, PANTHER ve GProfiler programları ile gerçekleştirilen biyoinformatik analizler, 26 proteinin immün sistem süreçleriyle ilgili olduğunu gösterdi. Bunlardan 5 protein, PNP, TAP1, ITGAL, PRKDC ve PTPRC, kombine immün yetmezlik ile ilişkili bulundu. Bu genlerdeki yukarı regülasyonlar, IGLM dokularında immün sistemde artış olarak yorumlanabilir. Bu sonuçlar, IGLM dokularındaki, ödem ya da meme başı akıntısı gibi inflamasyon ilişkili semptomlar için bir açıklama olabilir. IGLM ayrıca kanser benzeri bir hastalık olarak kabul edildiğinden, sonuçlar DAVID analizi ile hastalığın kanser ilişkisini ortaya çıkarmak için değerlendirilmiştir. Buna göre, IGLM'deki 60 regüle proteinin (>10 kat artış) 20'si kanser metabolizması ile ilişkili bulunmuştur. Daha önce immünite ile ilişkili olduğunu saptadığımız iki protein olan TAP1 ve PRKDC'nin kanserle de ilişkili olduğu tespit edildi. Ayrıca inflamasyon, hormon dengesizliği ve Diabetes Mellitus (11-13) gibi insüline bağlı hastalıklarla IGLM ilişkisini açıklayabilen insülin yanıt elemanlarının da yukarı regüle olduğu saptanmıştır. Ek olarak nötrofil degranülasyon proteinlerinde de artış bulunmuştur. Bu, immün sistem artışında hangi mekanizmaların aktif olup inflamasyonun tetiklendiğini açıklayabilir.

Sonuç olarak, IGLM'nin inflamasyonla ilişkili bir hastalık olduğuna şüphe yoktur, ancak IGLM'nin doğrudan immünite ile ilişkili olup olmadığı ya da mikrobiyal enfeksiyon sonrası immün sistemin tetiklenip tetiklenmediği net değildir. İmmünite ile ilgili yukarıda bahsedilen regüle proteinler, IGLM için aday biyobelirteçler olabilir, ancak bunların ek çalışmalarla desteklenmesi gerekmektedir. Ayrıca IGLM, hastalık oluşumu ve ilerlemesi ile kansere benzemektedir. Elde edilen bulgular ışığında, kanser ve IGLM'de ortak enerji metabolizmaları bulunmaktadır, ancak bu mekanizmaları açıklayan moleküler temel ve bu mekanizmalarda rol oynayan proteinlerin daha ileri çalışmalarla araştırılması gerekmektedir.

Bu çalışma, IGLM oluşumunu ve ilerlemesini netleştirmek için bir temel niteliğindedir. Ayrıca, daha önce bahsedilen proteinler moleküler hedefler olarak sunulabilir. Bununla birlikte, hastalığında temelinde yatan mekanizmaları ortaya çıkarmak için daha ayrıntılı analizlere ihtiyaç vardır.

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OP28: EFFECT OF BIOTRANSFORMATION AND EXTRACTION METHODS ON THE ANTI-INFLAMMATORY EFFECT OF PROPOLIS IN THP-1 CELL-LINE

[BİYOTRANSFROMASYON VE EKSTAKSİYON YÖNTEMLERİNİN ETKİSİYLE PROPOLİSİN THP-1 HÜCRE HATTI ÜZERİNDEKİ İNFLAMATUVAR ETKİSİ]

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Objectives: Recently it has been shown that propolis has various biological activities such as antioxidant, anti-inflammatory, antibcterial, antifungal, antiviral, antimutagenic, antitumoral, anticancer, cytotoxic, anti-proliferatie, anti-angiogenic, and immunomodulataroy. The extraction method has demonstrated that biotransformation of propolis by specific strains of Lactobacillus plantarum might decrease the amount of allergenic molecules in propolis.

The aims of our study were to demonstrate the most suitable extraction methods/ solvents to get the highest anti-inflammatory effect and to determine the effect of biotransformation by L. plantarum strains on its antiinflammatory effect in THP-1 cell-line.

Materials-Methods: Propolis samples were subjected to biotransformation by different L.plantarum strains (ISLG-2, ATCC-8014 and Visbyvac) at different concentration (1,5%; 2,5%; 3,5%) prior to extraction procedure by using different solvents (ethanol; poly-ethylene glycol - PEG; water) and ultrasound treatments (300 W / 40 Hz (5, 10 and 15 minutes). The phenolic profiles of samples were analyzed by liquid chromatography-mass spectrometry/mass spectrometry (LCMS/MS).

Results: Demonstrated that four of propolis samples reduced all cytokine levels except NFk-B. The anti-inflammatory activity of propolis was observed to be closely associated with its biologically active constituents especially caffeic acid, kaempferol, ferulic acid, quercetin, pelargonin and naringenin. Decreasing of allergen molecules in propolis via biotransformation resulted in no change of anti-inflammatory effects of propolis.

Conclusions: The highest anti-inflammatory effect of propolis was determined in the samples bio transformed by L. plantarum ATCC®8014 and extracted in ethanol+biotransformed, in water and in water + sonicated for 15 minutes.

Keywords: LPS, inflammation, propolis, biotransformation, extraction

Amaç: Son zamanlarda propolisin antioksidan, antiinflamatuar, antibakteriyel, antifungal, antiviral, antimutajenik, antitümöral, antikanser, sitotoksik, antiproliferasyon, antianjiyogenik ve immünomodülatör gibi çeşitli biyolojik aktiviteleri olduğu gösterilmiştir. Ekstraksiyon yöntemi, propolisin spesifik Lactobacillus plantarum suşları tarafından biyotransformasyonunun propolisteki alerjenik moleküllerin miktarını azaltabileceğini göstermiştir.

Çalışmamızın amacı, propolisin en yüksek anti-inflamatuar etkiyi elde etmek için en uygun ekstraksiyon yöntemlerini/solventleri göstermek ve L. plantarum suşlarının biyotransformasyonun THP-1 hücre hattı üzerindeki antiinflamatuar etkisini belirlemekti.

Gereç-Yöntem: Propolis numuneleri ekstraksiyon öncesinde farklı L.plantarum suşları (ISLG-2, ATCC-8014 ve Visbyvac) ile farklı konsantrasyonlarda (%1,5; %2,5; %3,5) biyotransformasyona tabi tutulmuştur. Farklı solventler (etanol; polietilen glikol - PEG; su) ve ultrason işlemleri (300 W / 40 Hz (5, 10 ve 15 dakika) kullanılarak örneklerin fenolik profilleri sıvı kromatografi-kütle spektrometrisi/kütlesi spektrometri (LCMS/MS) ile analiz edildi..

Bulgular: Dört propolis numunesinin NFk-B hariç tüm sitokin seviyelerini azalttığını gösterdi. Propolisin anti-inflamatuar aktivitesinin biyolojik olarak aktif bileşenleri, özellikle kafeik asit, kaempferol, ferulik asit, kersetin, pelargonin ve naringenin ile yakından ilişkili olduğu gözlemlendi. Propolisteki alerjen moleküllerinin biyotransformasyon yoluyla azalması, propolisin antiinflamatuar etkilerinde herhangi bir değişiklik oluşturmamıştır.

Sonuç: Propolisin en yüksek anti-inflamatuar etkisi L. plantarum ATCC®8014 ile biyo transforme edilmiş ve etanol+biyotransforme edilmiş, suda ve su+sonikasyonda 15 dakika ekstrakte edilen örneklerde belirlendi.

Anahtar Kelimeler: LPS, inflamasyon, propolis, biyotransformasyon, ekstraksiyon

OP30: EVALUATION OF THE RELATIONSHIP BETWEEN FRAILTY AND INFLAMMATORY MARKERS IN OLDER ADULTS

[YAŞLI HASTALARDA KIRILGANLIK İLE İNFLAMATUAR BELİRTEÇLERİN İLİŞKİSİNİN DEĞERLENDİRİLMESİ]

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Objectives: Irregularities in inflammatory processes occur with advancing age. It causes an increased chronic, sterile inflammatory response in older adults. The damage caused by increased inflammation of the organism can lead to geriatric syndromes. On the other hand, frailty is a geriatric syndrome that can lead to the development of dependence and mortality due to the difficulty in maintaining the homeostatic balance that develops with age. In our study, the relationship between inflammatory markers and frailty was examined.

Materials-Methods: Our study is cross-sectional and retrospective. The files of patients over the age of 60 who applied to Dokuz Eylul University Geriatrics Clinic were examined. Patients with evidence of infection and acute or chronic inflammatory disease were excluded. A total of 892 patients were included in the study. For the evaluation of inflammatory status, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), albumin, and ferritin levels were evaluated. FRAIL and FRIED indices were used for the frailty and the SPSS program was used for statistical analysis.

Results: The mean age of the patients was 75.26±7.53, the frequency of female gender was 63.70% and the frequency of frailty was 43.27%. ESR, CRP levels were higher in the frail group, and albumin levels were lower (<0.001, for each). When regression analysis is performed according to inflammatory parameters and factors that may be associated with frailty; ESR, CRP, and albumin levels were found to be associated with frailty (OR: 1.015 95% CI 1.005-1.026 p=0.005, OR: 1.043 95%CI 1.021-1.066 <0.001 and OR: 0.304 95% CI 0.190-0.485 p<0.001, respectively).

Conclusions: In our study, it was shown that there is a relationship between serum ESR, CRP, and albumin levels and frailty. Prospective studies are needed to support these results, clarify their causes, and prevent frailty.

Keywords: Frailty, inflammation, inflammation, erythrocyte sedimentation rate, albumin

Amaç: İlerleyen yaş ile inflamatuar süreçlerde düzensizlikler meydana gelmektedir. Bunun sonucunda yaşlı erişkinlerde artmış kronik, steril bir inflamatuar yanıt oluşmaktadır. Artmış inflamasyonun organizmaya verdiği hasar ise birçok geriatrik sendromun oluşumuna yol açabilmektedir. Kırılganlık, yaşla birlikte gelişen homeostatik dengenin sağlanmasında güçlüğe bağlı olarak bağımlılık ve mortalite gelişimine yol açabilecek bir sendromdur. Çalışmamızda inflamatuar belirteçler ile kırılganlık arasındaki ilişki incelenmiştir.

Gereç-Yöntem: Çalışmamız kesitsel ve retrospektiftir. Dokuz Eylül Üniversitesi Geriatri Kliniğine başvuran 60 yaş üstü hastaların dosyaları incelenmiştir. Enfeksiyon bulgusu, akut veya kronik inflamatuar hastalığı olan hastalar dışlanmıştır. Toplamda 892 hasta çalışmaya dahil edilmiştir. İnflamatuar durum değerlendirilmesi için eritrosit sedimantasyon hızı (ESH), C reaktif protein (CRP), albümin ve ferritin düzeyi değerlendirilmiştir. Kırılganlık için FRAIL ve FRIED indeksleri ve istatiksel analiz için SPSS programı kullanılmıştır.

Bulgular: Hastaların yaş ortalaması 75,26±7.53, kadın cinsiyet sıklığı %63,70 ve kırılganlık sıklığı %43,27 idi. ESH, CRP düzeyleri kırılgan grupta daha yüksek, albümin düzeyi ise daha düşüktü (<0,001, her biri için). İnflamatuar parametreler ve kırılganlık ile ilişkili olabilecek faktörlere göre regresyon analizi yapıldığında; kırılganlık ile ESR, CRP ve albümin düzeyi ilişkili bulundu (OR: 1,015 %95 CI 1,005-1,026 p=0.005, OR: 1.043 %95CI 1,021-1,066 <0,001 ve OR: 0.304 %95 CI 0,190-0,485 p<0,001, sırası ile).

Sonuç: Çalışmamızda serum ESH, CRP ve albümin düzeyleri ile kırılganlık arasında ilişki olduğu gösterilmiştir. Bu sonuçların desteklenmesi, nedenlerinin aydınlatılması ve kırılganlığın önüne geçilmesi için prospektif çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: inflamasyon, eritrosit sedimantasyon hızı, albümin, kırılganlık

OP31: EVALUATION OF INFLAMMATION WITH NEW INFLAMMATORY INDICES IN OBESITY PATIENTS THAT LOSE WEIGHT OBJECTIVES

[KİLO VEREN OBEZ HASTALARDA İNFLAMASYONUN YENİ İNFLAMATUVAR İNDEKSLERLE DEĞERLENDİRİLMESİ]

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Objectives: Obesity is a chronic pathology in which subclinical inflammation can be observed with many psychosocial, metabolic, vascular, and oncological complications. In the last few decades, many indices have been used in the literature, which are accepted by the mathematical relationship of simple laboratory parameters which have been associated with inflammation, nutrition, disease progression, mortality, and increased cardiovascular risk.
In this study, it was aimed to evaluate whether simple laboratory parameters and inflammation indicator indices make a difference after weight loss in patients followed up for obesity.

Materials-Methods: The data of 216 patients admitted to our hospital's obesity center were evaluated retrospectively. The parameters and indices used in our study are as follows; WBC, platelet, lymphocyte, monocyte, neutrophil, HOMA-IR, insulin, HbA1C, TSH, PLR(platelet/lymphocyte ratio), NLR(neutrophil/lymphocyte ratio), MLR(monocyte/lymphocyte ratio), GLR(GGT/lymphocyte ratio), Systemic Immune Inflammation index(SII)(platelet countxNLR), ANRI=(AST/neutrophil), SIRI=(monocyte xNLR), Prognostic Nutritional Index((10×albumin(g/L)+(0.005×total lymphocyte count)), APRI((AST/35)x100/platelet), ALRI(AST/lymphocyte), De Ritis Ratio(AST/ALT), ALT/ASTratio, LDH/Alb Ratio, ALBI((-0.085xAlb)+0 ,66×log(bilirubin)), Alb/GGT ratio, AIP(log (TG/HDL-C)) Patients' admission and 2nd control values were compared.

Results: The patients included in our study (age=45.9±11.4; BMI=40.2±6.3; F/M=201/15) lost an average of 6.2±4.2 kg. With weight loss a significant difference was detected in terms of GLR, SII, PNI, APRI, ALRI, De Ritis, ALT/AST, ALBI, Alb/GGT ratio, AIP, HOMA-IR, T-CHOL, LDL-CHOL, TG, HbA1C, AST, ALT, ALP, GGT, T.Bilirubin, albumin, and TSH values(P<0.005).

Conclusions: New inflammatory indices such as GLR, SII, PNI, APRI, ALRI, De Ritis, ALT/AST, ALBI, Alb/GGT ratio are calculated from inexpensive and easily accessible parameters, can show the degree of inflammation in obese individuals, and can be used to determine positive response with treatment.

Keywords: Obesity, İnflammation, Weight Lost

Amaç: Obezite psikososyal, 62lbumin62c, vasküler, onkolojik birçok komplikasyona sahip subklinik enflamasyon gözlenebilen kronik bir patolojidir. Son birkaç dekaddır literatürde basit laboratuvar parametrelerinin birbiriyle matematiksel ilişkisi ile 62lbum gören çok sayıda indeks kullanılmaya başlanmış; inflamasyon, nutrisyon, hastalık progresyonu, mortalite, artmış kardiyovasküler risk ile ilişkilendirilmişlerdir. Bu çalışmada, obezite nedeni ile takip edilen hastalarda, kilo kaybı sonrasında, basit laboratuvar parametreleri ile inflamasyon göstergesi indekslerin fark oluşturup oluşturmadığının değerlendirilmesi amaçlandı.

Gereç-Yöntem: Hastanemiz obezite merkezine başvuran 216 hastanın verileri retrospektif olarak değerlendirildi. Çalışmamızda kullanılan bazı rutin biyokimyasal parametrelere ek olarak kullanılan parametreler ve indeksler şunlardır; WBC, platelet, lenfosit, monosit, nötrofil, HOMA-IR, 62lbumin, HbA1C, TSH, PLR(platelet/lenfosit oranı), NLR(nötrofil/lenfosit oranı), MLR(monosit/lenfosit oranı), GLR(GGT/lenfosit oranı), Sistemik Immün İnflamasyon indeksi(SII)(platelet sayısıx NLR), ANRI=(AST/nötrofil), SIRI=(monosit xNLR), Prognostik Nutrisyonel İndeks((10×albümin(g/L)+(0,005×toplam lenfosit sayısı)), APRI((AST/35)x100/platelet), ALRI(AST/lenfosit), De Ritis Oranı(AST/ALT), ALT/AST oranı, LDH/Alb Oranı, ALBI ((-0,085xAlb)+0,66×log(bilirubin)), Alb/GGT oranı, AIP(log (TG/HDL-C)). Hastaların başvuru ve 2. 62lbumin değerleri kıyaslandı.

Bulgular: Çalışmamıza alınan hastaların (yaş=45,9±11,4; VKİ=40,2±6,3; K/E=201/15) ortalama 6.2±4.2 kg ağırlık kaybettiği tespit edildi. Hastalarda ağırlık kaybı ile; GLR, SII, PNI, APRI, ALRI, De Ritis, ALT/AST, ALBI, Alb/GGT oranı, AIP, HOMA-IR, T-KOL, LDL-KOL, TG, HbA1C, AST, ALT, ALP, GGT, T.Bilirubin, 62lbumin, TSH değerlerinde anlamlı fark tespit edildi (P<0,005)

Sonuç: GLR, SII, PNI, APRI, ALRI, De Ritis, ALT/AST, ALBI, Alb/GGT ratio gibi yeni inflamatuvar indeksler ucuz ve kolay ulaşılabilen parametrelerden hesaplanmakta olup, obez bireylerde inflamasyon derecesini gösterebilir, tedavi ile olumlu cevabı tespitte kullanılabilirler.

Anahtar Kelimeler: Obezite, İnflamasyon, Kilo Kaybı

OP32: INVESTIGATION OF THE EFFECTS OF HORSE-BACK RIDING ON CORE MUSCLES IN ADOLESCENTS

[ADÖLESANLARDA BİNİCİLİĞİN KOR KASLARI ÜZERİNDEKİ ETKİLERİNİN İNCELENMESİ]

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Objectives: The aim of the study is to examine the effects of riding on the core strength and endurance in healthy adolescents.

Materials-Methods: Twenty participants, aged between 10-19 years, research (n=5) and control (n=5) groups, were included in the study. The socio-demographic information and clinical characteristics of the participants were recorded. The study group (n=5) received riding training for eight weeks. Core strength (stabilizer pressure biofeedback device), core endurance (isometric endurance tests) assessments were performed on the study group before and after the riding training.

Results: There was no statistically significant difference between the two groups in terms of core strength and core endurance measurements at the beginning of the study ($p>0.05$). Although better scores were obtained in the trunk flexor test in the study group as a result of the riding training, the difference was not statistically significant ($p>0.05$). Statistically significant difference was found in prone and supine core strength measurement, trunk extensor test, right lateral bridge test, left lateral bridge test, and prone bridge test measurements ($p<0.05$).

Conclusions: As a result of our study, it was shown that horse riding continued for eight weeks in healthy adolescents increased core strength and core endurance. However, there is a need for studies to be carried out by increasing the number of samples in this area.

Keywords: Adolescent, Horse-back riding, Core stability, Muscle strength

Amaç: Çalışmanın amacı sağlıklı adölesan bireylerde biniciliğin kor kuvveti ve enduransı üzerindeki etkilerinin incelenmesidir.

Gereç-Yöntem: Araştırmaya yaşları 10-19 yaş aralığında olan, çalışma (n=5) ve kontrol (n=5) grubu olmak üzere 10 katılımcı dahil edildi. Katılımcıların sosyo-demografik bilgileri ve klinik özellikleri kaydedildi. Çalışma grubu (n=5) sekiz hafta binicilik eğitimi aldı. Çalışma grubuna binicilik eğitimi öncesi ve sonrası, kor kuvvet (stabilizer pressure biofeedback cihazı), kor endurans (izometrik endurans testleri) değerlendirmeleri yapıldı.

Bulgular: Çalışmanın başlangıcında kor kuvvet ve kor endurans ölçümleri açısından iki grup arasında istatistiksel olarak anlamlı fark bulunmadı ($p>0.05$). Çalışma grubunda binicilik eğitimi sonucunda gövde fleksör testinde başlangıca göre daha iyi skorlar elde edilmesine rağmen aradaki fark istatistiksel olarak anlamlı bulunmadı ($p>0.05$). Yüzüstü ve sırtüstü kor kuvvet ölçümü, gövde ekstansör testi, sağ lateral köprü testi, sol lateral köprü testi, yüzüstü köprü testi ölçümlerinde ise istatistiksel olarak anlamlı fark bulundu ($p<0.05$).

Sonuç: Çalışmamızın sonucunda sağlıklı adölesanlarda sekiz hafta boyunca devam edilen biniciliğin kor kuvvetini ve kor enduransını arttırdığı gösterildi. Ancak bu alanda örneklem sayısını arttırarak yapılacak çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Adölesan, Binicilik, Kor stabilite, Kas kuvveti

OP33: THE RELATIONSHIP BETWEEN C-REACTIVE PROTEIN AND THE LEVEL OF LOW BACK PAIN AND BACK PAIN RELATED PHYSICAL IMPAIRMENT AND DISABILITY

[KRONİK BEL AĞRILI HASTALARDA C-REAKTİF PROTEİN İLE BEL AĞRISI VE BEL AĞRISI KAYNAKLI FİZİKSEL YETERSİZLİK VE ÖZÜRLÜLÜK DÜZEYİ ARASINDAKI İLİŞKİ]

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Objective: Low back pain is a common musculoskeletal disorder that 70-80% of adults experience at least once in their lifetime. The aim was to investigate the relationship between the severity of pain and the level of physical impairment and disability due to pain, and CRP (C-Reactive Protein) in patients with chronic low back pain.

Materials-Methods: Thirty-four patients with chronic low back pain who applied to the Özel Izmir Avrupa Cerrahi Tıp Merkezi Physical Therapy and Rehabilitation outpatient clinic were evaluated. Demographic data and serum CRP levels of the cases were recorded. Low back pain was assessed using the Low Back Pain Rating Scale (LBPRS). LBPRS is an outcome measure that is evaluated over a total of 130 points and includes sub-parameters of pain, disability and physical impairment. The relationship between LBPRS and its sub-parameters and CRP was examined.

Results: The mean age of 34 patients (19 women, 15 men) evaluated was 53.7±2.5. The mean LBPRS scores of the patients were 81.47±14.7, pain parameters were 40.21±9.7, disability scores were 18.62±6.3, and physical impairment scores were 26.41±7.4. Serum CRP levels were found to be 6.9±2.4(mg/l). According to Spearman correlation analysis, a strong correlation was found between BADS and CRP ($r=0.784$ $p<0.05$).

Conclusions: In patients with chronic low back pain, an increase in the level of CRP, which is one of the indicators of inflamation, may cause more pain, disability and physical impairment.

Keywords: Low Back Pain, CRP, LBPRS, Inflamation

Amaç: Bel ağrısı, yetişkinlerin %70-80 inin hayatları boyunca en az bir kez yaşadığı yaygın bir kas iskelet sistemi hastalığıdır. Çalışmanın amacı kronik bel ağrılı hastalarda ağrı şiddeti ve ağrıya bağlı fiziksel yetersizlik ve özürlülük seviyesi ile CRP (C-Reaktif Protein) arasındaki ilişkinin araştırılmasıydı.

Gereç-Yöntem: Özel Izmir Avrupa Cerrahi Tıp Merkezi Fizik Tedavi ve Rehabilitasyon polikliniğine başvuran kronik bel ağrılı

34 hasta değerlendirildi. Olguların demografik verileri ve serum CRP düzeyleri kaydedildi. Bel ağrısı, Bel Ağrısı Derecelendirme Ölçeği (BADÖ) kullanılarak değerlendirildi. BADÖ toplam 130 puan üzerinden değerlendirilen ve ağrı, özürlülük ve fiziksel yetersizlik alt parametrelerini içeren bir sonuç ölçümüdür. BADÖ ve alt parametreleri ile CRP arasındaki ilişki incelendi.

Bulgular: Değerlendirilen 34 hastanın (19 kadın, 15 erkek) yaş ortalaması 53,7±2,5 tir. Olguların BADÖ toplam puan ortalamaları 81,47±14,7, ağrı parametresi 40,21±9,7, özürlülük puanları 18,62±6,3 ve fiziksel yetersizlik puanları 26,41±7,4 olarak bulunmuştur. Serum CRP seviyeleri ise 6,9±2,4(mg/l) olarak bulundu. Spearman korelasyon analizine göre BADÖ ile CRP arasında güçlü ilişki bulundu ($r=0,784$ $p<0,05$).

Sonuç: Kronik bel ağrılı hastalarda inflamasyon göstergelerinden biri olan CRP düzeyindeki artış daha fazla ağrı, özürlülük ve fiziksel yetersizliğe neden olabilir.

Anahtar Kelimeler: Kronik Bel Ağrısı, CRP, BADÖ, İnflamasyon

OP34: IMMUNE AND INFLAMATORYRESPONSE HETEROGENEITY IN NEUROBLASTOMA

[NÖROBLASTOMDA İMMUN VE İNFLAMATUAR CEVAPTA HETEROJENİTE]

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Objectives: Immunity and inflammatory response are the most important features in cancer development, progression, and survival. Prognostic significance of immune and inflammation-related markers in neuroblastoma before and after treatment and during the follow-up period has not been adequately investigated. The aim of this study is to investigate the prognostic importance of immune and inflammation-related markers in neuroblastoma.

Materials-Methods: In 1750 neuroblastoma cases examined between 2012-2022, achievable blood albumin, CRP values and ratio (Glascow Prognostic score), diversity and amount of immune cell infiltration in tumor tissue and surrounding tissue, immunohistochemical CTLA-4, PDL-1, PD-1, PDL-2 expression was evaluated. RESULTS were tested with analysis of variance and survival at $p<0.05$ significance.

Results: The mean age of the cases was 36.23±39.90 (1-217 months) and 48.6% were girls and 51.4% were boys. 28% of the cases are in low risk, 23.3% in medium risk, 48.7% in high-risk class. Lymphocyte infiltration was detected in 6% and a low number in neuroblastoma cases before treatment. No heterogeneity was detected in the expression of CTLA-4, PDL1, PD1. After multimodal chemotherapy, lymphocyte infiltration was found significantly more in tissues with differentiated ganglioneuroma. It was noted that immunity did not show intertumoral heterogeneity.

Conclusions: Neuroblastoma was found to be weak in immune and inflammatory response. Absence of intratumoral heterogeneity in immune response, increased immune cell increase after chemotherapy were interpreted in favor of metachronous immune heterogeneity. In vitro, ex vivo and in vivo studies are needed to determine the immune profile changes in tumors after radiotherapy and chemotherapy, in short, whether neuroblastomas can be converted from cold tumors to hot tumors for immunotherapy.

Keywords: Neuroblastoma, heterogeneity, immune response, inflamatory response

Amaç: Kanser gelişim progresyon ve sağkalımında immunite ve inflamatuar yanıt, başlıca önemli özelliklerden birisidir. Nöroblastomda tedavi öncesi ve tedavi sonrası ve izlem sürecindeki immun ve inflamasyon ilişkili belirteçlerin prognostik önemi yeterince araştırılmamıştır. Bu çalışmanın amacı nöroblastom olgularında immun ve inflamasyon ilişkili belirteçlerin prognostik önemini araştırmaktır.

Gereç-Yöntem: 2012-2022 yıllarında incelenen 1750 adet nöroblastom olgusunda, ulaşılabilen kan albümin, CRP değerleri ve oranı (Glascow Prognostik skoru), tümör dokusu ve çevre dokuda immun hücre infiltrasyon çeşitliliği ve miktarı, dokuda immunhistokimyasal CTLA-4, PDL-1, PD-1, PDL-2 ekspresyonu değerlendirilmiştir. BULGULAR varyans analizi ve sağkalım analizi $p<0,05$ anlamlılığı ile test edilmiştir.

Bulgular: Olguların yaş ortalaması 36,23±39,90 (1-217 ay) ad olup %48,6 olgu kız, %51,4 olgu erkek çocuktur. Olguların %28'i düşük risk, %23,3'ü orta risk, %48,7'si yüksek risk sınıfındadır. Tedavi öncesi nöroblastom olgularında lenfosit infiltrasyonu % 6 yüzdede ve düşük sayıda saptanmıştır. CTLA-4, PDL1, PD1 ekspresyonunda heterojenite saptanmadı. Multimodal kemoterapi sonrası diferansiye ganglionörom histolojisindeki dokularda lenfosit immun hücre infiltrasyonu belirgin fazla saptanmıştır. İmmunitenin intertümöral heterojenite göstermediği dikkati çekmiştir.

Sonuç: Nöroblastom immun ve inflamatuar yanıt olarak zayıf olarak saptanmıştır. İmmun cevapta intratümöral heterojenite olmaması, kemoterapi sonrası artan immun hücre artışı, metakron immun heterojenite lehine yorumlanmıştır. Radyoterapi ve kemoterapi sonrası tümörlerde immun profilin değişip değişmediğinin, kısaca nöroblastomların immunoterapi için soğuk tümörden sıcak tümöre çevrilmesinin olası olup olmadığı yönünde in vitro, ex vivo ve in vivo deney hayvanı çalışmalarına ihtiyaç vardır.

Anahtar Kelimeler: Nöroblastom, heterojenite, immun yanıt, inflamatuar yanıt

OP35: THE RELATIONSHIP BETWEEN DISEASE ACTIVITY SCORE AND DIAPHRAGM FUNCTION IN PATIENTS WITH ANKYLOSING SPONDILITIS: PILOT STUDY

[ANKİLOZAN SPONDİLİTLİ HASTALARDA HASTALIK AKTİVİTE SKORLARI İLE DİYAFRAGMA FONKSİYONU ARASINDAKİ İLİŞKİ: PİLOT ÇALIŞMA]

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Objectives: BASDAI (Bath Ankylosing Spondylitis Disease Activity Index) and ASDAS (Ankylosing Spondylitis Disease Activity Score) are frequently used disease activity scores in AS, and ASDAS also includes objective serological markers of inflammation (ESR or CRP). Although the limitation of chest expansion is an important problem in AS, studies examining diaphragmatic functions are limited. The aim of the study was to examine the relationship of disease activity scores used in AS with diaphragmatic muscle function and chest expansion.

Materials-Methods: Six (male, age: 48 years) AS patients were included in the study. The disease activities of participants were evaluated with BASDAI, ASDAS-CRP, and ASDAS-ESR; chest expansion with tape measure; and diaphragmatic function with ultrasonography from the 8th intercostal space. The thickness of the diaphragm was measured at the end of calm expiration and during deep inspiration, and the thickening rate (%) was calculated. While descriptive statistics were given as median, the relationship was evaluated with Spearman Correlation analysis.

Results: As BASDAI (3.40) and ASDAS (ASDAS-CRP:2.85, ASDAS-ESR:2.40) scores increased, thickening rate (157.75%) and chest expansion (4.25 cm) indicating diaphragmatic function decreased. However, no statistically significant relationship was found ($p>0.05$).

Conclusions: Although this pilot study showed that there is no relationship between disease activity scores and diaphragmatic function, we think that there may be effects on diaphragmatic functions and even compensatory activities in AS due to the limitation of thoracic cage mobility and kyphosis. There is a need for studies with large samples in which motion analysis and imaging methods are used together.

Keywords: Ankylosing Spondylitis, disease activity, Diaphragm

Amaç: BASDAI (Bath Ankilozan Spondilit Hastalık Aktivitesi İndeksi) ve ASDAS (Ankilozan Spondilit Hastalık Aktivite Skoru) AS'de sık kullanılan hastalık aktivitesi skorlarından olup ASDAS ayrıca inflamasyonun objektif serolojik belirteçlerini de (ESR veya CRP) içermektedir. AS'de göğüs ekspansiyonunun limitasyonu önemli bir problem olmasına rağmen diyafragma fonksiyonlarının incelendiği çalışmalar sınırlıdır. Çalışmanın amacı, AS'de kullanılan hastalık aktivitesi skorlarının diyafragma kas fonksiyonu ve göğüs ekspansiyonu ile ilişkisini incelemekti.

Gereç-Yöntem: Çalışmaya 6 (erkek, yaş: 48 yıl) AS hastası alındı. Katılımcıların hastalık aktiviteleri BASDAI, ASDAS-CRP, ASDAS-ESR; göğüs ekspansiyonu mezura; diyafragma fonksiyonu 8. interkostal aralıktan ultrasonografi ile değerlendirildi. Diyafragma kalınlığı sakin ekspirasyon sonunda ve derin inspirasyonda ölçülerek kalınlaşma oranı (%) hesaplandı. Tanımlayıcı istatistikler ortanca olarak verilirken ilişki Spearman Korelasyon analizi ile değerlendirildi.

Bulgular: BASDAI (3,40) ve ASDAS (ASDAS-CRP:2,85, ASDAS-ESR:2,40) skorları arttıkça diyafragma fonksiyonunu gösteren kalınlaşma oranı (%157,75) ve göğüs ekspansiyonu (4,25 cm) azalmasına rağmen istatistiksel olarak anlamlı bir ilişki bulunmadı ($p>0,05$).

Sonuç: Bu pilot çalışma hastalık aktivitesi skorlarıyla diyafragma fonksiyonu arasında ilişki olmadığını gösterse de AS'de göğüs kafesi mobilitesindeki kısıtlılığa ve kifoza bağlı olarak diyafragma fonksiyonlarında etkilenimler ve hatta kompanse edici aktiviteler olabileceği görüşündeyiz. Hareket analizi ile görüntüleme yöntemlerinin birlikte kullanıldığı geniş örneklemli çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Ankilozan Spondilit, hastalık aktivitesi, Diyafragma

POSTER PRESENTATION FULL TEXT
[POSTER SUNUMU TAM METİNLERİ]

PP2:D-DIMER/ALBUMIN AND FIBRINOGEN/ALBUMIN RATIOS TO PREDICT COVID 19 MORTALITY IN INTENSIVE CARE UNIT PATIENTS: A PRELIMINARY STUDY

[YOĞUN BAKIMDA YATAN HASTALARDA COVİD 19 MORTALİTESİNİ ÖNGÖRMEK İÇİN D-DİMER/ ALBÜMİN VE FİBRİNOJEN/ALBÜMİN ORANLARI; ÖN ÇALIŞMA]

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ABSTRACT

Objective: COVID-19 is life-threatening, and the main cause of mortality is immune organ damage, especially ARDS, which develops because of an uncontrolled inflammatory response. Although a timely and effective anti-inflammatory treatment reflects positively on the prognosis, early markers are needed for aggressive treatment. Therefore, we examined the predictive role of fibrinogen/Albumin ratio (FAR) and D-dimer/Albumin ratio (DAR), which are suggest as valuable markers in systemic inflammation, for COVID-19 mortality in intensive care patients.

Materials-Methods: In our study, patients hospitalized in the intensive care unit with the diagnosis of COVID-19 between 20.10.2021-27.03.2022 were evaluated retrospectively and 101 patients were included in the study. Fibrinogen, D-dimer, and albumin (ALB) levels of the patients during admission to and discharge from the intensive care unit (discharge- at most one day before death) were recorded. Our patients were divided into two subgroups as surviving (n: 53) and non-surviving (n: 48). DAR and FAR were calculated as ug/g and mg/g units respectively. The SPSS IMB program was used for statistical analysis.

Results: In our study, the mean age of our patients was 71.1±.16.5 (69.9±17.8 for women, 72.4±15.3 for men). 51% (n:52) of the patients were female, 49% (n:49) were male, and 12% had no additional disease. The mean hospital stay of the patients was 23.90 (3-108) days, and there was no significant difference between the surviving and non-surviving groups (0.765). When we compared the survivor and non-survivor patient groups, there was no significant difference between the hospitalization FAR and DAR of the patients. However, a significant difference was found between the output FAR and DAR. (P = 0.012 and P = 0.001, respectively). The area under the curve (AUC) to predict COVID-19 mortality for DAR was higher than the FAR. In the multivariate Cox regression analysis, the odds ratio was 1.003 (1.000-.1.005) for FAR and 1.001 (1.000-1.002) for DAR and was determined as an independent risk in predicting mortality.

Conclusion: DAR may be more useful than FAR in the early differentiation of mortality in COVID-19 patients, but the explanatory power of DAR is not high enough. In addition, our study is a preliminary study.

Keywords: Covid -19, fibrinogen/ALB ratio, D-dimer/ALB ratio, Mortality

ÖZET

Amaç: COVID-19, yaşamı tehdit etmekte olup mortalitenin ana nedenini kontrolsüz inflamatuvar yanıt sonucu gelişen başta ARDS olmak üzere immun organ hasarı oluşturmaktadır. Zamanında ve etkin bir anti-inflamatuvar tedavi prognoza olumlu yansımakla birlikte agresif tedavi için erken belirteçlere ihtiyaç vardır. Sistemik inflamasyonda önemli belirteçler olan Fibrinojen/Albümin oranı (FAR) ve D-dimer/Albümin oranının (DAR) yoğun bakım hastalarında COVID-19 mortalitesi için preditif rolünü inceledik.

Gereç-Yöntem: Çalışmamızda COVID-19 tanısı ile 20.10.2021-27.02.2022 tarihleri arasında yoğun bakıma yatan hastalar retrospektif olarak değerlendirildi ve 101 hasta çalışmaya dahil edildi. Hastaların yoğun bakıma yatış ve çıkış (taburculuk- ölüm öncesi en fazla bir gün öncesi) sırasındaki fibrinojen, D-dimer ve Albumin (ALB) düzeylerine bakıldı. Hastalarımız yaşayan (n:53) ve ölen (n: 48) olarak iki gruba ayrıldı. FAR mg/g ve DAR ug/g ünite olarak hesaplandı. İstatistiksel analizde SPSS IMB programı kullanıldı.

Bulgular: Çalışmamızda hastalarımızın yaş ortalaması 71.1±.16.5 (kadınlar için 69.9±17.8, erkekler için 72.4±15,3) idi. Hastaların %51 (n:52)'i kadın, %49 (n:49)'u erkekti ve %12'sinin ek bir hastalığı yoktu. Hastaların ortalama yatış süresi 23,90 (3- 108) gündü ve survivor ve non-survivor gruplar arasında anlamlı fark yoktu (0.765). Hasta gruplarını karşılaştırdığımızda hastaların yatış FAR ve DAR arasında anlamlı fark görülmedi. Ancak çıkış FAR ve DAR arasında anlamlı fark saptandı. (Sırasıyla P=0,012, P<0.001). Covid-19 mortalitesini öngörmek için çıkış DAR için eğrinin altındaki alan (AUC), FAR'dan daha yüksekti. Multivarite Cox regresyon analizinde Odds oranı DAR için 1.001 (1.000-1.002) ve FAR için 1.003 (1.000-.1.005) saptandı ve mortaliteyi öngörmede bağımsız risk olarak belirlendi.

Sonuç: DAR, COVİD-19 hastalarında mortalitenin erken ayrımında FAR'dan daha faydalı olabilir, ancak DAR'ın mortaliteyi öngörme açıklama gücü yeterince yüksek değildir.Ayrıca çalışmamız bir ön çalışmadır.

Anahtar kelimeler: COVİD -19, fibrinojen/ALB oranı, D-dimer/ALB oranı, Mortalite

INTRODUCTION

The coronavirus disease (COVID-19) begins with clinical symptoms of upper respiratory tract infection, then causes disseminated organ damage and thrombotic complications, including diffuse intravascular coagulopathy, and coagulopathies, which develop because of an increased hyperinflammatory response. COVID-19 constitutes a serious global health problem due to the increased risk of mortality [1, 2]. The clinical course of COVID-19 progresses very rapidly in some patients, and effective treatment is delayed. It can reduce

mortality by identifying risky patients beforehand. In this sense, biochemical parameters that can be applied easily, cost-effectively, and quickly to predict mortality are necessary [2].

D-dimer is a fibrin degradation product that is frequently employed as a biomarker for thrombotic disorders. D-dimer levels below 500 μg/L, FEU is generally considered normal. As the severity of coagulation disorders increases, the D-dimer level also increases. Following the outbreak of the COVID-19 pandemic, D-dimer has been identified as a potential indicator for prognosis in patients with COVID-19 [3,4].

Fibrinogen, known as one of the acute phase proteins, is synthesized in high amounts by the liver in response to inflammation and takes part in fibrin formation as the last step of coagulation. It has emerged as a research topic due to the close relationship between COVID-19 and disseminated intravascular coagulation. The fibrinogen levels of COVID-19 patients undergo remarkable and significant changes [5].

Serum albumin has antioxidant properties and is a negative acute phase protein. Its level varies depending on many clinical conditions. Specifically, hypoalbuminemia has been found to be associated with poor prognosis and increased mortality [6].

D-dimer and fibrinogen, which are indicators of hypercoagulation, have been found to be predictors of prognosis in hospitalized COVID-19 patients [7]. It is thought that instead of using D-dimer and fibrinogen alone, the utilize of D-dimer/albumin (DAR) and fibrinogen/albumin (FAR) combined with albumin, which is a negative acute phase reactant, will be more valuable in-patient management. In some studies, on COVID-19 patients, DAR and FAR were found to be more sensitive and specific than only D-dimer and fibrinogen in showing hypercoagulation and microthrombotic damage [5,6]. However, there are no definitive conclusions about the prognosis of patients with COVID-19 or their association with mortality.

This study's objective is to examine the predictive value of DAR and FAR, which are biomarkers of hypercoagulopathy in COVID-19, for COVID-19 mortality in intensive care patients.

MATERIAL AND METHODS:

Study Population

This study was carried out in the Medical Biochemistry Laboratory of the Ankara Training and Research Hospital. In this study, medical records of patients over the age of 18 who were admitted to the intensive care unit with the diagnosis of COVID-19 (PCR positive) between 20.10.2021 and 27.02.2022 were examined. Patients whose fibrinogen, albumin, and D-dimer levels were studied in the patient follow-up were included. Our patients were divided into two subgroups as surviving and non-surviving. The study was approved by the Ankara Training and Research Hospital clinical research ethics committee of Health Sciences University (Acceptance date: 11/08/2022, No: 1026/2022) according to the principles of the Helsinki Declarations.

Methods and Analysis of Biochemical tests

Serum albumin levels and D-dimer were analyzed with commercial reagents (Roche Cobas 6000 c501, Roche Diagnostic, Indianapolis, IN, U.S.A.). Fibrinogen were analyzed with commercially reagents (Stago STA R Max, Diagnostica Stago SAS, France). Fibrinogen, D-dimer, and albumin levels of the patients were measured during admission to and discharge from the intensive care unit (discharge-at most one day before exitus). Fibrinogen, D-dimer, and albumin levels of the patients were measured during admission to and discharge from the intensive care unit (discharge at most one day before death). DAR as ug/g (D-Dimer /Albumin) and FAR was calculated as mg/g (Fibrinogen/Albumin). COVID-19 was diagnosed only in patients identified as SARS-CoV-2 by RT-PCR in nasopharyngeal and oropharyngeal swabs.

Coefficient of variation (CV%) of arameters in the study were obtained from the internal quality controls results were low and high levels, respectively: fibrinogen: 3.7-3.98%, D-dimer: 2.35%-1.12%, albumin: 2.13%-1.19%.

Statistical analysis

Data analysis was performed using SPSS IMD software (SPSS Inc., Chicago, IL) or XLSTAT- Statistical Software for Excel (Addinsoft Inc., New York, USA). Normal distribution analysis of the data was done with the Kolmogorov-Smirnov test. The data are presented as percentages for categorical variables, means and standard deviations for parametric variables, and medians (interquartile ranges) for non-parametric variables. Parametric (independent sample T test) or non-parametric (Mann Whitney U test) statistical analyses were used to estimate the statistically significant difference between groups, and the Chi-squared test was conducted for categorical variables. Cox regression analysis was performend in multivariable survival analysis. ROC (receiver operation characteristic) analysis was performed to determine the optimal cutoff levels of the parameters. AUC (area under the curve), specificity, sensitivity, and positive/negative predictive value values were calculated. A P value less than 0.05 will be considered statistically significant.

RESULTS

In this study, 101 patients were included [subgroups as surviving (n: 53) and non-surviving (n: 48)] in the study, and the age mean age of our patients was 71.1±16.5 (69.9±17.8 for female, and 72.4±15.3 for male). 51% (n:52) of the patients were female, 49% (n:49) were male, and 12% there are not different for additional disease between subgroups (Table 1). The mean hospital stay of the patients was 23.90 (3-108) days, and there was no significant difference between the surviving and non-surviving groups (0.765) (Table 1). When we compared the surviving and non-surviving groups, there was no significant difference between the admission DAR and FAR of the patients. However, a significant difference was found between the DAR and FAR results according to discharge or exitus (P=0.012, P<0.001, respectively) (Table 2). Specificity, sensitivity, and positive/negative predictive value values for all parameters are shown in Table 3. The area under the curve (AUC) for COVID-19 mortality was 0. 0.662 (95% CI: 0.557-0.767) for D-dimer, which was higher than the AUC for all other parameters (Table 4, Figure 1). In the multivariate Cox regression analysis, the odds ratio was 1.003 (95% CI: 1.000-1.005) for FAR and 1.001 (95% CI: 1.000-1.002) for DAR and was determined as an independent risk in predicting mortality.

Table 1. Evaluation of patients' demographic information

	Surviving N:53	**Non-surviving N: 48**	***P* Value**
Age	66.4±15.7	76.2±16.4	<0.001[a]
Female, n (%) Male, n (%)	28 (57%) 25 (48%)	21 (43%) 27 (52%)	<0.365[b]
Additional diseases (Hypertension, Coronary artery disease, Diabetes, Chronic lung disease, Chronic kidney, other diseases), n (%)	46 (86%)	42 (87%)	0.501[b]
ICU hospitalization period, Day	17.0 (19.2)	18.0 (17.0)	0.765[c]

a, Independent-samples T test; b, Chi-squared test; c, Mann-Whitney U test; ICU, Intensive care unit. Data are presented as number (percentages), mean±standart deviation, and median (inter quartile range).

Table 2. Comparison of biochemical parameters between Surviving and Non-surviving groups.

	Surviving N:53	**Non-surviving N: 48**	**P-value**
Fibrinogen, mg/dL			
Hospitalization	539±136	518±187	0.370 [a]
Final results	451±165	457±187	0.849 [a]
D- dimer, µg/L, FEU			
Hospitalization	1000 (1710)	1640 (2700)	0.034 [c]
Final results	2324 (2180)	7780 (6580)	<0.001[c]
Albumin, g/L			
Hospitalization	33 ±6	31 ± 5	0.245 [a]
Final results	31 ±5	25 ±5	<0.001 [a]
FAR, mg/g			
Hospitalization	166.21(65.8)	160.9(77,8)	0.871 [c]
Final results	131.0(90,5)	208 (146.1)	0.003 [c]
DAR, µg/g			
Hospitalization	31.25(63,7)	52.5 (81,7)	0.069 [c]
Final results	33.71 (90.9)	196.1 (391,7)	<0.001 [c]

a, Independent-samples T test; b, Chi-squared test; c, Mann-Whitney U test; DAR, D-dimer/Albumin ratio; FAR, Fibrinogen/Albumin ratio. Data are presented as mean± standart deviation, and median (inter quartile range).

Table 3: Diagnostic performance of parameters to predict COVID 19 mortality

	Albumin, (95%, CI)	D-dimer, (95%, CI)	Fibrinogen, (95%, CI)	DAR, (95%, CI)	FAR, (95%, CI)
Cutoff	<2,4 g/d	>500, µg/L, FEU	>450, mg/dL	>10, µg/g	>132.1, mg/g
Sensitivity	0,915 (0.80-0.96)	0.92(0.81-0.96)	0.70(0.56-0.81)	0.97(0.88-0.99)	0.74 (0.58-0.83)
Specificity	0,074 (0.053-0.156)	0,352 (0.24-0.49	0,28(0,18-0.41)	0.22 (0.13-0.35)	0.26 (0.16-0.39)
PPV	0.46(0.44-0.49)	0.55.(0.56-0.59)	0.46(0.41-0.51)	0.55 (0.49-0.55)	0.46 (0.41-0.50
NPV	0,50(0.28-0.75)	0.83(0.67-0.92)	0.52(0.39-0.64)	0.92 (0.69-0.98)	0.52 (0.39-0.65

CI, Confidence interval; DAR, D-dimer/Albumin ratio; FAR, fibrinogen/Albumin ratio; NPV, negative predictive value; PPV, positive predictive value.

Table 4: ROC analysis results to predict COVID 19 mortality

				Asymptotic 95% Confidence Interval	
Parameters	AUC	Std. error	P Value.	Lower limit	Upper limit
Albumin (g/L)	0.586	0.057	0.132	0.109	0.289
D-Dimer (ug/L, FEU)	0.662	0.054	0.002	0.557	0.767
Fibrinogen (mg/dL)	0.517	0.060	0.774	0.440	0.674
DAR (µg/g)	0.655	0.054	0.004	0.579	0.761
FAR (mg/g)	0.509	0.059	0.602	0.393	0.625

AUC, Area under the curve; ROC, receiver operating characteristic; DAR, D-dimer/Albumin ratio; FAR, Fibrinogen/Albumin ratio.

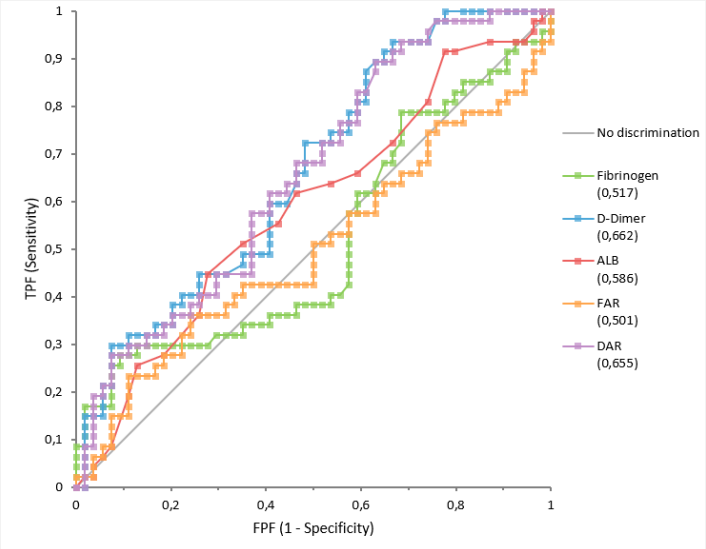

Figure 1: ROC (receiver operating characteristic) to predict COVID 19 mortality.

DISCUSSION

In this study, we investigated the relationship between D-dimer, fibrinogen, DAR and FAR levels and mortality in intensive care patients. According to the results of our study, DAR and FAR values were found to be higher in the non-surviving group. The mortality prediction performance of DAR and FAR was like that of D-dimer and fibrinogen. Hypercoagulability is common in COVID-19 patients. This leads to an increase in D-dimer and fibrinogen concentrations. For this reason, these two markers are used in the follow-up of poor prognosis in COVİD- 19 patients. Transforming biochemical parameters used in routine practice into easily applicable indices increases its diagnostic efficiency. Studies have shown that the DAR and FAR indices, which are made by dividing these two markers by albumin, can predict a poor prognosis and early death in COVID-19 [7,8,9].

When we look at the literature, there are many studies for FAR for COVID-19, while the literature information for DAR is very limited, only one study has been identified [7,10]. Küçükceran et al. evaluated both DAR and FAR. As a result of the study, it was suggested that DAR according to FAR could be employed to indicate of COVID-19 mortality [7]. There was a situation like our study. The predictive power of DAR was higher than that of

FAR. In our study, d-dimer and DAR performances were also found to be similar. Apart from COVID-19 for DAR, in the study of Seo et al., it was suggested that it can be applied with other scoring indices in the risk assessment of acute variceal bleeding [11].

In a meta-analysis for FAR [12], eight studies were included. In thi, FAR was proposed as a candidate marker for predicting mortality in COVID-19 patients [combined AUC: 0.73 (95% CI: 0.64-0.81)]. Another meta-analysis by Hung et al. [13], which included ten studies, found a positive association between the FAR rate and poor prognostic outcomes of COVID-19 [combined sensitivity: 0.74 (95% CI: 0.70-0.79)], specificity: 0.64 (95% CI:0.60-0.72) and AUC: 0.77 (95% CI: 0.74-0.81)]. In our study, the predictor power of FAR for mortality was not very good [sensitivity: 0.74 (95%CI: 0.58-0.83)], specificity: 0.26 (95%CI: 0.19-0.36), and AUC: 0.509 (95% CI: 0.393-0.625)]. This may have been caused by the limitations of our study.

Different cut-off values have been determined in previous studies for DAR and FAR. While the only study for DAR used 5.66 (µg/g) cut-off to evaluate mortality, we determined a >10 (µg/g) cut-off in our study (7). As can be seen in the meta-analysis for FAR, values of 111–150 (mg/g) were used for cut-off in the included studies [14]. According to our research, this rate is 132,1 (mg/g). Additionally, the absence of a standard unit for D-dimer, fibrinogen, and albumin results in different in cut-off values for DAR and FAR. Presumably, these conditions may cause heterogeneity among studies.

The current study had several limitations. These limitations were the small number of cases, the retrospective and single-center design, and the inability to evaluate treatment protocols. Because of the limitations of this study, additional investigations are required to support our findings.

CONCLUSION

Based on our study findings, DAR may be more useful than FAR in the early differentiation of mortality in COVID-19 patients, but the explanatory power of DAR is not high enough. In addition, our study is a preliminary study, which will make an significant contribution to the literature, and a further a with larger- scale investigation is planned.

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PP16: COMPARISON OF THE EFFECTS OF *PISTACIA VERA* INNER SHELL OBTAINED FROM DIFFERENT REGIONS OF TURKEY ON OXIDATIVE STRESS AND PROLIFERATION IN INVASIVE BREAST CANCER CELL LINE

[TÜRKİYE'NİN FARKLI BÖLGELERİNDEN ELDE EDİLEN *PISTACIA VERA* İÇ KABUĞU EKTRESİNİN, İNVAZİV MEME KANSERİ HÜCRE HATLARINDAKİ OKSİDATİF STRES VE PROLİFERASYON ÜZERİNDEKİ ETKİSİNİN KARŞILAŞTIRILMASI]

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ABSTRACT
The efficacy of extracts obtained from the inner bark of *P. vera* plants collected from different regions was investigated in invasive breast cancer cell lines.
In our study, inhibitory concentrations of plant extracts were determined by MTT method. Total antioxidant and oxidant levels were determined, and oxidative stress indices were examined. Migration test was performed to investigate the effect of the agents used on the motility of the cells. Colony formation test was performed to investigate the effect of extracts on colony forming properties. In our study, we observed that *P. vera* Urfa Extract was the most effective in reducing migration in MDA MB 231 cell line among the groups.
Keywords: *P. vera*; cytotoxicity; Oxidative Index; Migration; Colony Formation

ÖZET
Farklı bölgelerden toplanan *P. vera* bitkilerinin iç kabuğundan elde edilen ekstraktların etkinliği, invaziv özellikli meme kanseri hücre hatlarında araştırılmıştır. Çalışmamızda bitki ekstraktlarının inhibitör konsantrasyonları MTT yöntemi ile belirlenmiştir. Toplam antioksidan ve oksidan düzeyleri belirlenmiş, oksidatif stres indeksleri incelenmiştir. Kullanılan ajanların, hücrelerin hareketliliği üzerine etkisini araştırmak için migrasyon testi yapıldı. Ekstraktların koloni oluşturma özelliği üzerindeki etkisini araştırmak için koloni oluşum testi yapılmıştır. Çalışmamızda gruplar arasında MDA MB 231 hücre hattında, migrasyonu azaltmada en etkili olanın *P. vera* Urfa Ekstresi olduğunu gözledik.
Anahtar Kelimeler: *P. vera*; sitotoksisite; Oksidatif İndeks; Göç; Koloni Oluşumu

INTRODUCTION
Cancer is uncontrolled cells that can be induced by carcinogens such as viruses, chemicals, radiation, and genetic predisposition and examples can occur [1]. It is estimated that breast cancer may develop in approximately one in eight women all over the world, and one out of every 30 women will die from breast cancer [2].
There are many subtypes of breast cancer. In addition, the negativity of hormone receptors is limited to a poor prognosis. For this reason, MDA MB-231 breast cancer cell line, which is estrogen, progesterone receptor and human epidermal growth factor receptor 2 (HER-2) negative, was used in our study.
Pistacia vera (*P. vera*) is a fruit tree species belonging to the genus Pistacio and originating from Central Asia [3].
Extracts obtained from the resin, bark, leaf, oil and seed of *P. vera*; has been investigated for its anticancer, antiangiogenic, antioxidant, and cytotoxic effects [4–14]. In another study by Seifaddinipour M. et al., it was reported that extracts from *P. vera* decreased the UGDP-glucose dehydrogenase activity in breast cancer cell lines [15]. According to the study by Seifaddinipour M. et al., *P. vera* has been shown to play a therapeutic role in HepG2 hepatoma cell lines, human breast cancer cell line and colon carcinogenesis [16]. In line with this literature information, the effectiveness of *P. vera* we obtained from Antep, Siirt and Urfa regions in the invasive character cell line; comparing it with Docetaxel (DTX), which is one of the standard treatment agents used in evidence-based medicine on patients in the clinic; We aimed to demonstrate their effectiveness with in vitro experiments, if any.

MATERIALS AND METHODS
All methods used in the research are schematized (Figure 1).

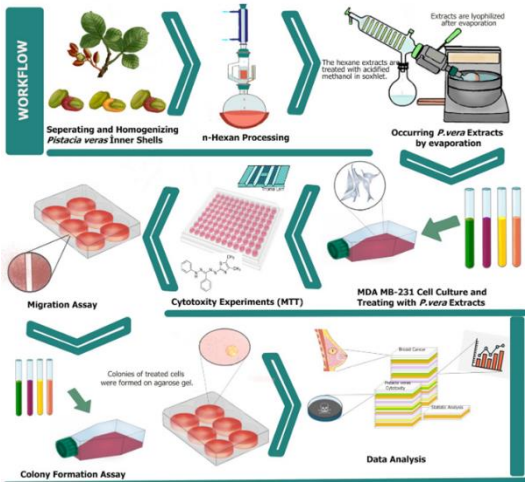

Figure 1. Workflow of investigation

Pre-Extraction with Hexane

The inner bark of *P. vera* collected from Antep, Siirt and Urfa regions was ground (Figure 2).

The ground shells were pre-extracted with hexane in a soxlet device (6 - 8 h). Evaporation was performed to remove n-hexane from the obtained extracts. Lyophilization was performed to completely remove humidity [17].

Preparation of *P. Vera* Extraction

Ground *P. vera*, was extracted with methanol-water (3:1) solution (4-6 h) in soxlet [17]. Filtering was done to remove the residues. The methanol and water phases of the extract were removed by evaporator and lyophilization was performed (Figure 2). Antep, Siirt and Urfa *P. vera* extracts (A.*P. vera*, S.*P. vera*, U.*P. vera*) were prepared at a concentration of 1 mg/mL with the medium used in cell culture [17].

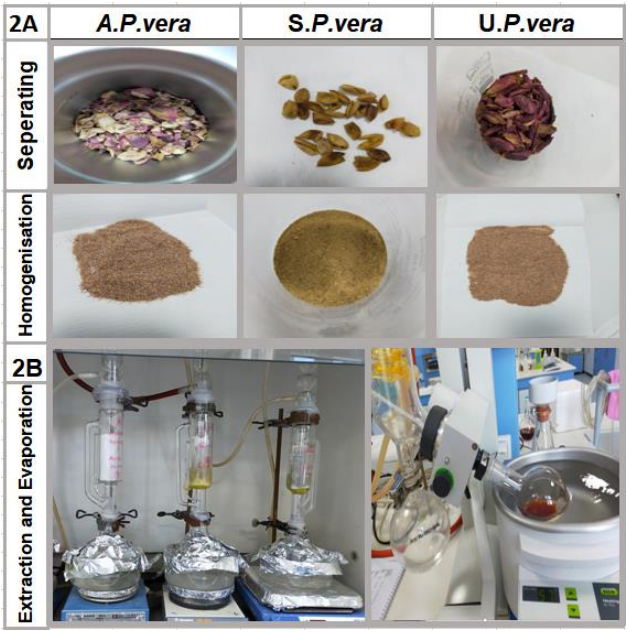

Figure 1. Preparation of P. vera extracts (A) P. vera inner shells and homogenization (B) *P. vera* extractions with soxhlet and evaporation processing

Cell Culture

MDA MB-231 cell line was used in the study. Cells were maintained in DMEM/F12 medium (Gibco) with 1% penicillin/streptomycin, 1% amphotericin B, 1% L-glutamine, and 10% Fetal Bovine Serum (FBS-Gibco). Cells were grown using T75 cell culture dishes (Corning Co.) at 37°C, in an atmosphere of 5% CO 2 and 95% humidity. Ethical approval for the research use of the MDA MB-231 cell line was obtained from the Institutional Ethics Committee (Dokuz Eylul University Non-Interventional Research Ethics Committee, Ref. no: 2021/14-30) [18].

Cell Viability and *P. Vera* / Dtx Therapies

MTT was used for cell viability analysis. Briefly, MDA MB-231 cells were transferred to 96-well plates at a density of 10,000 cells/well. Then, *P. vera* extracts (50, 100, 200, 400, 600, 800, 1000 µg) and DTX (0.1, 1, 10, 100 nM) were added to the cells at different concentrations in different wells. Absorbance was measured at 570 nm using a microplate reader (Thermo Electron Corporation). Inhibitor Concentration (IC50) values were determined by 72 h incubation [19–27].

Cell Lysate Preparation

Cells incubated with *P. vera* extracts and DTX for 72 hours were removed using a cell scraper and centrifuged with the addition of PBS. Supernatants were removed and pellets were resuspended with 3 mL of PBS. Cell suspensions were sonicated at twenty-second intervals for a total of one minute. Care was taken to keep the samples on ice during sonication. Obtained cell lysates were stored at -20 ºC to investigate oxidative stress parameters [18].

Oxidative Stress Parameters

Cell lysates stored at -20 ºC were thawed at 37 ºC. Colorimetric analysis kits (Rel Assay Diagnostics, Gaziantep, Turkey) developed by Erel O. were used for TAS and TOS analyzes [28]. Oxidative Stress Index (OSI) was calculated using the ratio between Total Oxidant Capacity (TOS) and Total Anti Oxidant Capacity (TAS).

[OSI = TOS (µmol H2O2 Eq/L)/TAS (µmol Trolox Eq/L)].

Wound Healing Assay

Cell migration; determined by "in vitro wound healing analysis". Cell groups incubated with both *P. vera* extracts and DTX for 72 h; seeded in a six-well plate (5x104 cells/well). Cells were allowed to confluence with 24 h incubation. Later on, Lines were created at the bottom of each well with a 200 µL micropipette tip. Cells were treated with *P. vera* extracts or DTX alone or in combination. Migration of cells was observed for 30 h by reversed phase microscopy and photographs were taken at 15 min and 8, 12, 24 and 30 h of treatments. Images were then processed and analyzed using the Image J program [29].

Colony Formation Assay

Colony formation analysis was performed to determine the colony formation potential of the cells. 1.2% agarose was prepared for the bottom layer (2.5 mL/well). 0.7% agarose was prepared for the top layer. Cells were suspended with the prepared top layer and transferred onto the bottom layer (2.5 mL/well). Once the agarose solidified, cells were treated with *P. vera* extracts (with IC50 doses). Images were recorded periodically.

Statistical Analysis

Data were evaluated statistically with the licensed SPSS program. The conformity of the variables to the normal distribution (Kolmogorov-Smirnov/Shapiro-Wilk tests) was examined. Descriptive statistics: The mean ± standard deviation values of the variables were given. ANOVA was used to compare the groups. Significance was assessed with the Holm-Sidak test, and p-Value <0.05 was considered statistically significant [18].

Results Of Cell Viability

IC_{50} values of cells treated with DTX, A. *P. vera*, S. *P. vera* and U. *P. vera* as a result of MTT analysis, respectively; 0.25 nM, 630.2 µg/mL, 480 µg/mL, 509.8 µg/mL (Figure 3).

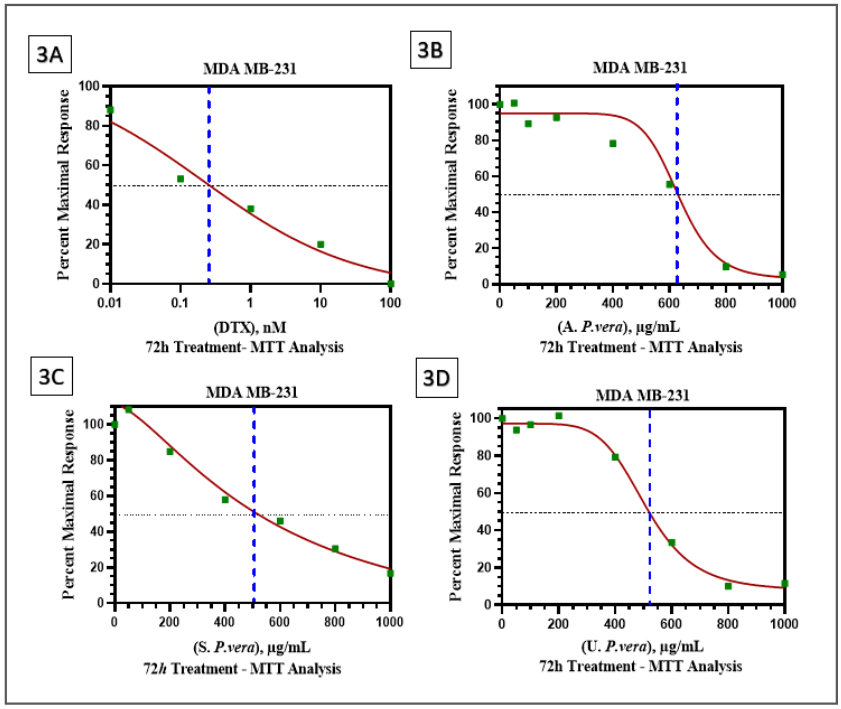

Figure 3. Graphical representation of IC_{50} values determined by MTT analysis with a four-parameter logistic regression model (4PL).

Results of Oxidative Stress Parameters

When *P. vera* extracts were combined with DTX, the TAS values of the cells were increased. When S. *P. vera* and U. *P. vera* extracts are combined with DTX; A decrease was observed in TOS values of the cells, and an increase was observed in the DTX combination of A. *P. vera* extract. The increase in OSI was only seen in the groups treated with S. *P. vera* and U. P. vera extracts. Despite this increase, oxidative stress decreased in other treatments (Figure 4).

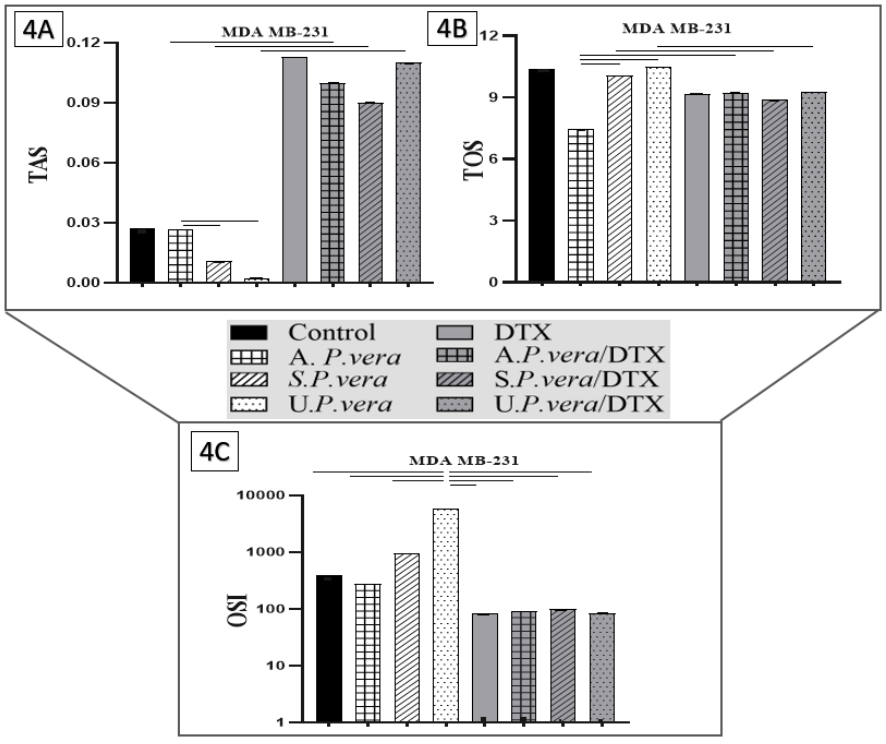

Figure 4. (A) *P. vera* extracts TAS analysis. (B) *P. vera* extracts TOS analysis. (C) *P. vera* extracts OSI.
In the graphics, horizontal lines indicate statistical significance between the groups (P<0.05, ANOVA followed by Holm–Sidak).

Migration Analysis Findings

In the migration analysis, it was seen that the treatment group with the least mobility was the cell group treated with A.P. vera extract (Figure 5A). It was observed that the cells treated with U.*P. vera* did not adhere to the flask surface. Therefore, migration could not be observed in these cells. It was determined that there was no significant difference in mobility of cells over time in terms of treatment groups, but the difference in migration rates in the last four time intervals became evident (Figure 5B). In addition, by examining the motility, it was observed that U.*P. vera* and A.*P. vera* extract showed antisynergistic effects with DTX.

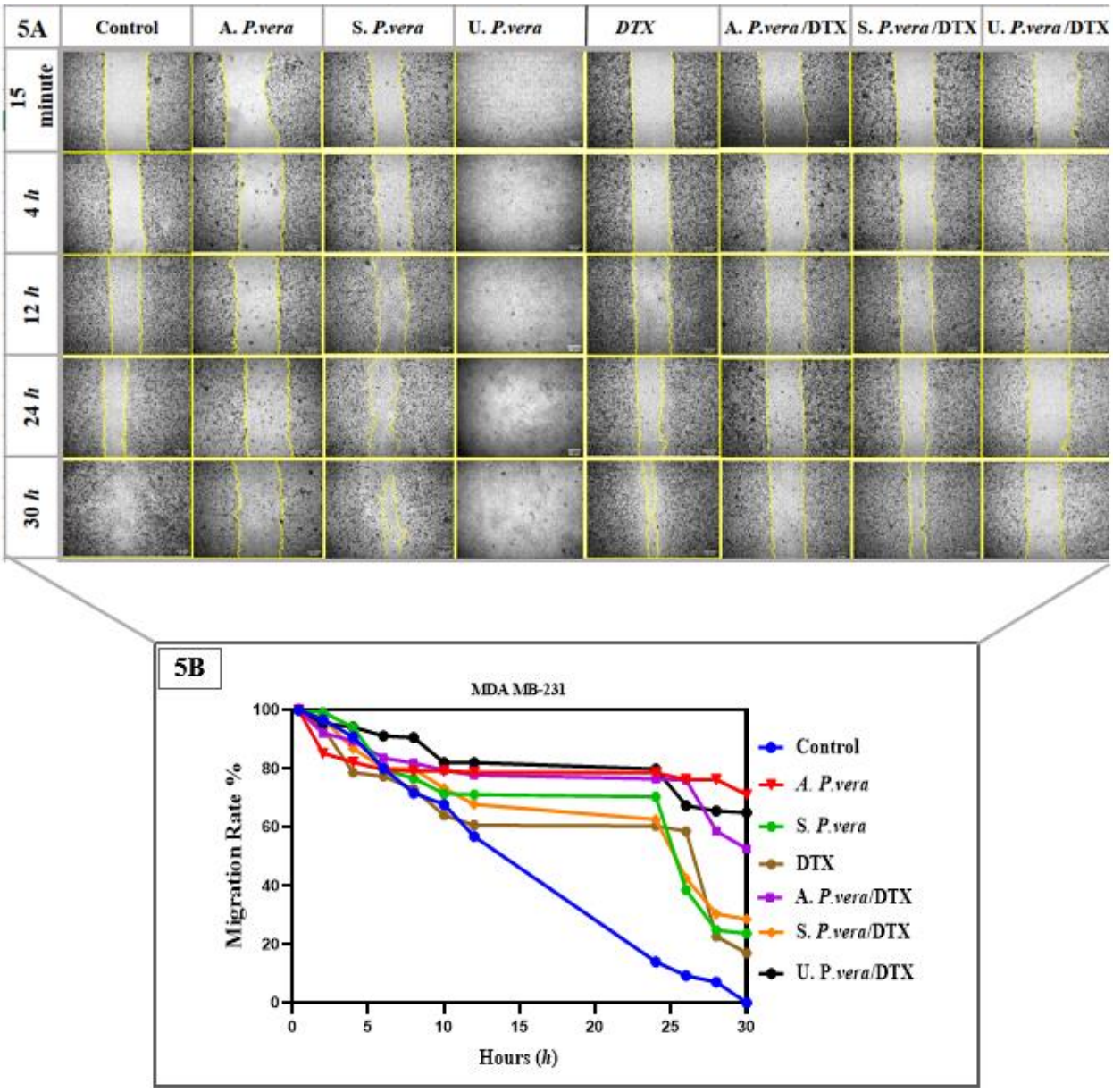

Figure 5. Migration after treatment with *P. vera* extracts.

(A) Migration observations with inverted microscopy (x10 Magnification, 50 µm scale bar) (B) Migration rate % according to time.

Colony Formation Assay Findings

It was observed that the largest colonies were formed in the control group. The A. *P. vera*-treated group had more colonies than the other *P. vera* groups. Colonies formed by cells treated with U. *P. vera*/DTX combination were found to be microtubular. It was predicted that this structuring was caused by the DTX effect. Colony formation results showed the least colony formation in the S. *P. vera* and A. *P. vera*/DTX treatment groups (Figure 6).

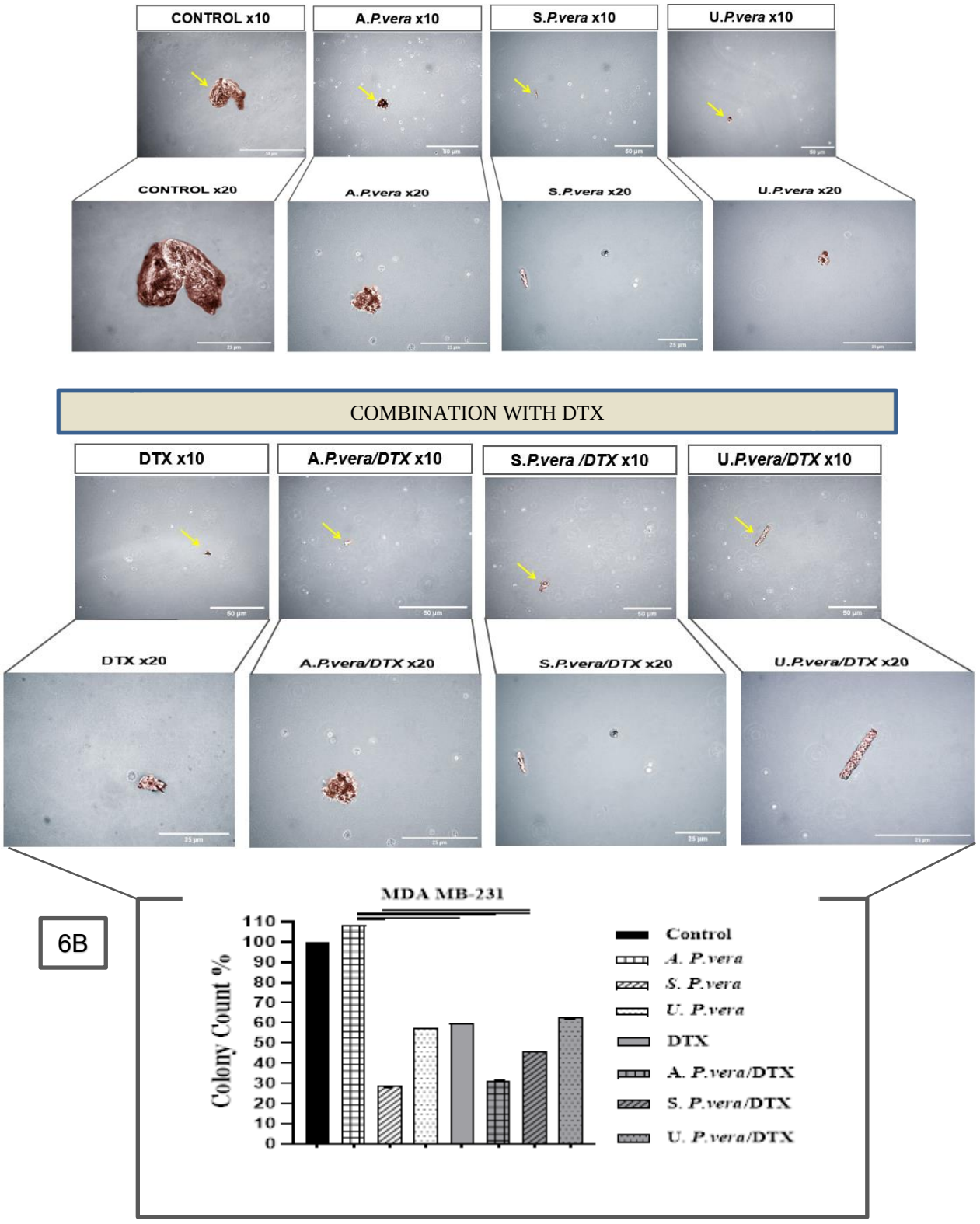

Figure 6. Colony formation analysis results.
Colony formation images after seven days of treatments [x 10 Magnification (inverted microscope), 50 μm scale bar; and x 20 Magnification (inverted microscope), 25 μm scale bar. Colony counts (%) of cells that treatment for seven days (*P. vera* Extracts and DTX combinations). In the graphics, horizontal lines indicate statistical significance between the groups (P≤0.01, Kruskal-Wallis One Way Analysis of Variance on Ranks).

DISCUSSION

Pistachios have been part of our diet since prehistoric times. It has a long history of use in different regions around the world. Emerging research aims to explore the benefits associated with the many bioactive compounds found in pistachios that have antioxidant, anti-inflammatory and anticarcinogenic properties. Emerging research is also reviewed showing that pistachio consumption may play a role in cognitive function, in modulating the human gut microbiota and may have beneficial effects on the skin and the health of the retina. Pistachio polyphenols have antimicrobial and antiviral potential.

Antioxidant and anti-inflammatory effects of pistachio consumption have been carried out in animal and clinical studies. Although the results of the conducted studies on the inflammatory markers and metabolic syndrome of pistachio are inconsistent, more research is needed in this area [30].

Tomaino et al. In vitro studies have shown that pistachio shells have a higher antioxidant activity and a higher content of antioxidant phenolic compounds than kernels [31].

The main objective of our study was to determine the activities of extracts obtained from the inner shell of P.vera collected from three different regions of Turkey (Antep, Siirt and Urfa) on aggressive breast cell line and to investigate their anticarcinogenic potential.

In the literature, Pistachios have been shown to reverse cognitive and motor damage and prevent memory impairments caused by two neurotoxic anticancer drugs, cisplatin and vincristine [32].

When used in induced experimental memory disorders of a pistachio ethanolic extract at a concentration of 200 and 400 mg/kg; It has been observed to lead to cognitive improvements in Swiss Albino mice. [33]

The effectiveness of extracts prepared from the inner shell of P.vera on cell lines is limited in the literature. Anticancer properties of pistachio have also been studied in a small number. For this purpose, the aggressive character MDA MB-231 cell line, which is estrogen, progesterone and HER2 receptor negative was selected.

In our study, DTX, which is used in the treatment of breast cancer and is the standard chemotherapeutic in these patients, was also used. When examining the oxidative stress parameters, in the groups in which P.Vera was combined with DTX; It is clearly observed that it increases the antioxidant capacity. In TOS and OSI analysis, Data consistent with these findings were obtained. Antioxidant properties of pistachios are frequently mentioned in the literature.

When our migration test findings are examined; We found that pistachio inner shells delayed wound healing in all groups where they were used alone or together.Although the migration analysis was also repeated 3 times in the UP vera group; It was determined that the cells did not adhere to the flask. We hypothesize that this finding may be due to its effect on adhesion molecules.

As seen in the coloni formation analysis findings in Figure 6; Except for AP vera, it was observed that all groups significantly reduced coloni formation compared to the control group.

In the literature, studies on the outer shell and kernel of pistachio are mentioned.

There are also studies on Nutrient-Bioactive Composition and its antioxidant effects.

According to our research, especially the UP vera inner bark extract; We found that it is most effective in invasive breast cancer cell lines and has a synergistic effect with DTX.

Pistachio, which benefits different population groups by contributing to a healthy, balanced, more plant-based diet; We think that it should also be examined in the treatment of diseases. In these studies, we foresee that it will be very valuable to consider and research the inner shell extracts as well.

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- The authors wish to thank Prof. Dr. Leman TARHAN, Prof. Dr. Raziye OZTURK and graduate student Aylin ONER for their help in collecting *T. spicata* (TS) and preparing the hexane extract.
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POSTER PRESENTATION ABSTRACT [POSTER SUNUM ÖZETLERİ]

PP1: IN DELAYED ONSET MUSCLE SORENESS, EFFECTS OF THE NEURODYNAMIC MOBILIZATION TECHNIQUE ON INFLAMMATION BIOMARKERS, AND PAIN, PRESSURE PAIN THRESHOLD, RANGE OF MOTION, MUSCLE STRENGTH, AND FUNCTIONAL STATE

[GECİKMİŞ KAS AĞRISINDA NÖRODİNAMİK MOBİLİZASYON TEKNİĞİNİN İNFLAMASYON BİYOBELİRTEÇLERİ İLE AĞRI, BASINÇ AĞRI EŞİĞİ, NORMAL EKLEM HAREKETİ, KAS KUVVETİ VE FONKSİYONEL DURUM ÜZERİNE ETKİSİNİN ARAŞTIRILMASI]

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Objectives: In this study, it was aimed to investigate the effects of neurodynamic mobilization (NM) technique on inflammation biomarkers, and pain, pressure pain threshold, range of motion, muscle strength, and functional status in delayed onset muscle soreness.

Materials- Methods: In the study, 32 healthy sedentary male volunteers were randomly divided into two groups as NM (n = 16) and placebo-NM (n = 16). After the initial evaluation of the individuals, femoral nerve NM and placebo NM techniques were administered three sets a day with ten repetitions for three days a week for three weeks. Then, a delayed muscle pain induction protocol was started for the quadriceps femoris muscle was initiated. Initial assessments were repeated immediately after the onset of delayed muscle pain and at hours 24, 48, and 72. Serum inflammation (IL-6, IL-10, IL-1 beta, TNF-alpha, and C reactive protein) biomarkers, pain (rest and activity), pressure pain threshold, range of motion, muscle strength (QF, hamstring eccentric/concentric) and performance (one-leg jump, vertical jump) parameters were measured.

Results: In the interaction of time by the group, in IL-6 level (η^2: 0.162), activity pain intensity (η^2: 0.165-0.110), pressure pain thresholds (η^2: 0.219-0.162), active knee flexion range of motion (η^2: 0.097), and one leg forward jump distance (η^2: 0.156), statistically significant differences were detected with varying effect size levels ($p < 0.05$). Individuals in the NM group had higher recovery rates at IL-6, IL-10, IL1-β, TNF-α, pain intensity, and QF eccentric muscle strength levels.

Conclusions: It is thought that the NM technique can be applied as a preventive treatment method in reducing and controlling the symptoms caused by delayed onset muscle soreness.

Keywords: Delayed onset muscle soreness, Neurodynamic mobilization, Inflammation

Amaç: Çalışmada, gecikmiş kas ağrısında nörodinamik mobilizasyonun (NM) inflamasyon biyobelirteçleri ile ağrı, basınç ağrı eşiği, normal eklem hareketi, kas kuvveti ve fonksiyonel durum üzerine etkilerinin araştırılması amaçlanmıştır.

Gereç-Yöntem: Çalışmaya 32 sağlıklı sedanter erkek gönüllü randomize edilerek NM (n=16) ve plasebo NM (n=16) grubu olarak ikiye ayrıldı. Bireylerin başlangıç değerlendirmeleri yapıldıktan sonra üç hafta boyunca haftada üç gün, günde üç set ve on tekrar olacak şekilde femoral sinir NM ve plasebo NM teknikleri uygulandı. Ardından, kuadriseps femoris kasına yönelik gecikmş kas ağrısı oluşturma protokolüne geçildi. Gecikmiş kas ağrısı oluşumunun hemen ardından ve 24, 48, 72. saatlerde başlangıç değerlendirmeleri tekrarlandı. Serum inflamasyon biyobelirteçleri (IL-6, IL-10, IL-1 beta, TNF-alfa ve C reaktif protein) değerlendirildi. Ağrı (istirahat ve aktivite), basınç ağrı eşiği, normal eklem hareketi, kas kuvveti (KF, hamstring eksantrik/konsentrik) ve performans (tek ayak sıçrama, dikey sıçrama) parametrelerine bakıldı.

Bulgular: Gruba göre zamanın etkileşiminde iki grup arasında IL-6 düzeyi (η^2:0.162), aktivite ağrı şiddetleri (η^2:0,165-0,110), basınç ağrı eşikleri (η^2:0.219-0.162), aktif diz fleksiyon normal eklem hasarı (η^2:0,097) ve tek ayak öne sıçrama mesafesinde (η^2:0.156) değişen düzeylerde etki büyüklüğü ile istatistiksel olarak anlamlı farklılıklar tespit edildi ($p<0.05$). Serum IL-10, IL1-β, TNF-α, ağrı şiddeti ve KF eksantrik kas kuvveti düzeylerinde NM grubundaki bireylerin toparlanma hızının daha yüksek olduğu görüldü.

Sonuç: NM tekniğinin gecikmiş kas ağrısı sonucu ortaya çıkan semptomların azaltılmasında ve kontrol edilmesinde koruyucu tedavi yöntemi olarak uygulanabileceği düşünülmektedir.

Anahtar Kelimeler: Gecikmiş kas ağrısı, Nörodinamik mobilizasyon, Inflamasyon

PP3: EVALUATION OF BIOTIN INTERFERENCE FOR BNP TEST

[BNP TESTİ İÇİN BİYOTİN İNTERFERANSININ DEĞERLENDİRİLMESİ]

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Objectives: Biotin is a common over-the-counter supplement that acts as a coenzyme in various carboxylation reactions. Its known effects include strengthening hair and nails, regulation of blood sugar, and positive effects on peripheral neuropathy. Immunoassay systems include tests that are analyzed using the strong interaction between biotin and streptavidin, and high-dose biotin-containing preparations may cause interference in these tests. In our study, we aimed to evaluate the interaction of biotin for the BNP test, which has been shown to be triggered by inflammation in recent studies.

Materials - Methods: Biotin (Sigma-Aldrich, USA) at 6 different levels (10-20-50-100-200-500 ng/mL) was added to serum pools containing 2 different levels of BNP (38.04-247.54 pg/mL). Serum BNP measurements were performed using chemiluminescent immunoassay on ADVIA Centaur XPT (Siemens Healthcare Diagnostics Inc, Tarrytown, NY, USA) analyzer. Following the addition of biotin, the change of the recovery value that exceeds>10 % (acceptable bias) is accepted as an interference.

Results: Following the addition of 100 ng/mL biotin in the serum pool containing 38.04 pg/mL BNP, and the addition of 200 ng/mL biotin in the serum pool containing 247.54 pg/mL BNP, interference began.

Conclusion: The use of biotin has increased in recent years, and false low values may be encountered in BNP results due to biotin interference. When a low BNP test is encountered that does not comply with the clinical situation, it should be considered whether the patient is taking supplements containing biotin.

Key Words: Biotin interference, BNP, streptavidin

Amaç: Biotin reçetesiz satılan yaygın bir takviye olup, çeşitli karboksilasyon reaksiyonlarında bir koenzim olarak işlev görür. Bilinen etkileri arasında, saç ve tırnakları güçlendirme, kan şekerinin regülasyonu ve periferik nöropatide olumlu etkileri yer almaktadır. İmmunoassay sistemlerinde biyotin ve streptavidin arasındaki güçlü etkileşimi kullanarak analiz edilen testler yer almakta olup, yüksek doz biyotin içeren preparatlar bu testlerde interferansa neden olabilmektedir. Çalışmamızda son yıllarda yapılan çalışmalarda inflamasyonun tarafından salınımının tetiklendiği ortaya konan BNP testi için, biyotin etkileşimini değerlendirmeyi amaçladık.

Gereç-Yöntem: 2 farklı düzeyde BNP (38,04-247,54 pg/mL) içeren serum havuzlarına 6 farklı düzeyde (10-20-50-100-200-500 ng/mL) biyotin (Sigma-Aldrich, ABD) eklendi. Serum BNP ölçümleri ADVIA Centaur XPT (Siemens Healthcare Diagnostics Inc, Tarrytown, NY, ABD) analizöründe kemiluminesan immunoassay kullanılarak gerçekleştirildi. Biyotin eklenmesini takiben geri elde değerindeki > % 10 (kabul edilebilir bias) değişiklik interferans olarak kabul edildi.

Bulgular:38,04 pg/mL BNP içeren serum havuzunda 100 ng/mL biyotin eklenmesini takiben; 247,54 pg/mL BNP içeren serum havuzunda ise 200 ng/mL biyotin eklenmesini takiben test sonucunda interferans başladı.

Sonuç: Biyotin kullanımı son yıllarda artmış olup, biyotin interferansı nedeniyle BNP sonuçlarında hatalı düşük değerlerle karşılaşılabilinir. Klinik duruma uymayan düşük BNP testi ile karşılaşıldığında hastanın biyotin içeren takviyeleri alıp almadığının göz önünde bulundulmalıdır.

Anahtar Kelimeler: Biyotin interferansı, BNP, streptavidin

PP4: THE RELATION BETWEEN DIETARY INFLAMMATORY INDEX, PHYSICAL ACTIVITY, SERUM LIPIS AND ABDOMINAL OBESITY

[DİYET İNFLAMATUVAR İNDEKS, FİZİKSEL AKTİVİTE, SERUM LİPİDLERİ VE ABDOMİNAL OBEZİTE İLİŞKİSİ]

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Objectives: Evaluation of inflammatory load of adherence to Mediterranean Diet and the relation with physical activity, serum lipids and abdominal obesity.

Materials-Methods: The 95 (Female: 77, Male: 18) volunteers who live in Famagusta/North Cyprus were included in the study by random sampling method. Mediterranean Diet Score (MDS) and Dietary Inflammatory Index (DII) were calculated from food frequency questionnaire. International Physical Activity Questonnarie-short form has been used to assess physical activity level. Body weight and composition was analysed by Tanita 420MA, waist circumference and height were measured by non-strech tape. Serum total cholesterol, triglyceride, LDL, HDL and VLDL levels were analysed. IBM SPSS 26.0 was used for statistical analysis.

Results: The mean age of individuals was 35.8±12.77 years. DII scores of individuals whose adherence to MD is high were lower than whose low ($p<0.05$). There were a negative correlation between MD and DII ($r=-0.234$, $p=0.022$). The individuals whose adherence to MD is low ($p>0.05$) and the individuals have abdominal obesity have higher serum triglyceride and VLDL levels ($p<0.05$). In addition, serum triglyceride and VLDL levels, waist circumference, body fat mass and percentage were lower in individuals whose physical activity level is high active compare to inactive ($p<0.05$).

Conclusions: The increased adherence to MD is related with increased anti-inflammatory potential of diet. Low physical activity level and abdominal obesity are related with increased serum triglyceride and VLDL levels. It is important to design further studies for analyzing relation between inflammatory load of the diet and specific inflammatory parameters with widen sample selection.

Keywords: Mediterranean diet, dietary inflammatory index, physical activity, triglyceride, abdominal obesity

Amaç: Akdeniz Diyeti'ne uyumun inflamatuvar yük açısından değerlendirilmesi ve fiziksel aktivite, serum lipidleri ve abdominal obezite ilişkisinin değerlendirilmesidir.

Gereç-Yöntem: Rastgele örnekleme yöntemiyle Mağusa, Kuzey Kıbrıs'ta yaşayan 95 (Kadın:77, Erkek:18) gönüllü birey örnekleme dahil edilmiştir. Bireylerin miktarlı besin tüketim sıklık kaydı ile Akdeniz Diyet Skoru ile Akdeniz Diyeti'ne uyumu, Diyet İnflamatuvar İndeks ile diyetin inflamatuvar yükü ve Uluslararası Fiziksel Aktivite Anketi-kısa formu ile fiziksel aktivite düzeyleri değerlendirilmiştir. Bireylerin vücut ağırlığı ve vücut kompozisyonu Tanita 420MA cihazı ile ölçülmüş ve

esnemeyen mezura ile bel çevresi ve boy uzunluğu ölçümleri yapılmıştır. Ayrıca, serum total kolesterol, trigliserit, LDL, HDL, VLDL düzeyleri analiz edilmiştir. İstatistiksel analizler için IBM SPSS 26.0 kullanılmıştır.

Bulgular: Bireylerin yaş ortalaması 35.8±12.77 yıldır. Akdeniz Diyeti'ne uyumu yüksek olanların düşük olanlara kıyasla Diyet İnflamatuvar İndeks puanları düşüktür ($p<0.05$). Akdeniz Diyet Skoru ile Diyet İnflamatuvar İndeks puanı arasında negatif bir koreaslyon saptanmıştır ($r=-0.234$, $p=0.022$). Akdeniz Diyeti'ne uyumu yüksek olanların ($p>0.05$) ve abdominal obezitesi olan bireylerin serum trigliserit ve VLDL düzeylerinin daha yüksek olduğu belirlenmiştir ($p<0.05$). Ayrıca fiziksel aktivite düzeyi çok aktif olan bireylerin inaktif bireylere kıyasla serum VLDL, trigliserit, bel çevresi, vücut yağ kütlesi, vücut yağ oranı daha düşüktür ($p<0.05$).

Sonuç: Akdeniz Diyeti'ne uyum arttıkça diyetin anti-inflamatuvar potansiyeli artmaktadır. Düşük fiziksel aktivite düzeyi ve abdominal obezite serum trigliserit ve VLDL düzeylerindeki artış ile ilgilidir. Diyetin inflamatuvar yükünün spesifik inflamatuvar belirteçler ile ilişkisine yönelik daha geniş örneklem büyüklüğüne sahip daha kapsamlı çalışmalar yapılması önemlidir.

Anahtar Kelimeler: Akdeniz diyeti, diyet inflamatuvar indeks, fiziksel aktivite, trigliseri, abdominal obezite

PP5: SERUM ALBUMIN TO GLOBULIN RATIO AS A BIOMARKER IN INFLAMMATUAR BOWEL DISEASES

[İNFLAMATUVAR BAĞIRSAK HASTALIKLARINDA BİYOMARKER OLARAK SERUM ALBÜMİN/GLOBÜLİN ORANI]

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Objective: Albumin and globulin are two important components of serum proteins and have been proven to play a role in systemic inflammation. The role of serum albumin-globulin ratio (AGR) as a marker of inflammatory disease in inflammatory bowel disease (IBD) is unknown. The main purpose of this research is to investigate the relationship between serum AGR and inflammatory bowel disease (IBD).

Material-Methods: 60 patients with ulcerative colitis (UC) diagnosis, 49 patients with Crohn's disease (CD) diagnosis, and 154 non-IBD controls (age and gender-matched controls who were healthy) were enrolled in the study. Patients' baseline characteristics including demographics, laboratory data and comorbidities were collected for statistical adjustments. The albumin to globulin ratio (AGR) is calculated according to the following formula: AGR = albumin/globulin. **Results:** Serum AGR was significantly lower among IBD patients compared with non-IBD controls ($P<0.000001$). The area under the curve (AUC) for AGR to distinguish UC was 0.734 (sensitivity: 41.7%, specificity: 98.1%) optimal cutoff value for serum AGR is <1.0 and the AUC of CD was 0.626 (sensitivity: 55%, specifity: 79.2%) optimal cut off value for serum AGR is <1.12.

Conclusion: Serum AGR may become a promising test to help clinicians diagnose and differentiate IBD and assess IBD disease activity. Evaluation of serum AGR value together with other inflammation parameters in IBS patients will provide more accurate results in terms of differential diagnosis and prognosis. Therefore, in this group of patients, low-cost serum AGR measurement can be used as a convenient prognostic tool that can be measured by routine clinical practice.

Keywords: IBD, Serum AGR, UC, CD

Amaç: Albümin ve globülin başlıca serum proteinleridir ve sistemik inflamasyonda rol oynadığı kanıtlanmıştır. İnflamatuar barsak hastalıklarında (IBD) serum albümin-globulin oranının (AGR) inflamatuar hastalık belirteci olarak rolü bilinmemektedir. Bu araştırmanın temel amacı serum AGR ile IBD arasındaki ilişkiyi araştırmaktır.

Gereç-Yöntem: Çalışmaya retrospektif olarak ülseratif kolit (UC) tanısı alan 60 hasta, Crohn hastalığı (CD) tanısı alan 49 hasta ve 154 sağlıklı olan IBD dışı kontrol (yaş ve cinsiyet eşleşmeli kontroller) alındı. İstatistiksel analiz için hastaların demografik özellikleri, laboratuvar verileri ve komorbiditeleri içeren temel özellikleri toplandı. AGR = albümin / globülin formüle göre hesaplandı.

Bulgular: Serum AGR, IBD hastaları arasında IBD olmayan kontrollere kıyasla önemli ölçüde daha düşük bulundu ($P<0.000001$). AGR'nin UC'yi ayırt etmesi için eğrinin altındaki alan (AUC) 0,734 (duyarlılık: %41,7, özgüllük: %98,1), serum AGR için optimal eşik değeri <1,0 ve CD'nin AUC'si 0,626 (duyarlılık: %55, özgüllük: %79.2) serum AGR için optimal eşik değeri <1.12'dir.

Sonuç: Serum AGR, klinisyenlerin IBD tanı ve hastalığın aktivitesinin değerlendirmesine yardımcı olmak için umut verici bir test olabilir. IBS hastalarında serum AGR değerinin diğer inflamasyon parametreleri ile birlikte değerlendirilmesi ayırıcı tanı ve prognoz açısından daha doğru sonuçlar sağlayacaktır. Serum AGR ölçümü düşük maliyeti ve rutin klinik uygulamalarla kolay ölçülebilen uygun bir prognostik araç olarak kullanılabilir.

Anahtar Kelimeler: İBD, Serum AGR, ÜK, CD

PP6: ASSOCIATION OF TOLL-LIKE RECEPTOR 7 AND 8 POLYMORPHISMS WITH COVID-19 SEVERITY

[TOLL-BENZERİ RESEPTÖR 7 VE 8 POLİMORFİZMLERİNİN COVID-19 ŞİDDETİ İLE İLİŞKİSİ]

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Objectives: Toll-like receptors (TLRs) are an important family of receptors that recognize infectious agents and play an important role in the innate immune system. TLRs are a potential candidate to control infection in the early stages of the disease and to produce vaccines against SARS-CoV-2. In addition, studies have suggested that TLR polymorphisms are also associated with antiviral responses against SARS-CoV-2. Therefore, we aimed to investigate the relationship of TLR7 and TLR8 polymorphisms with COVID-19 disease prognosis.

Materials-Methods: A total of 120 COVID-19 patients, including 40 outpatients, 40 patients with mild and moderate clinical status, hospitalized and severe pneumonia, and 40 patients followed in the intensive care unit (ICU), were included in the study. The classification of disease severity was made according to WHO criteria. TLR7 (rs179009), TLR8 -129 C/G (rs3764879) and TLR8 Met1Val (rs3764880) polymorphisms were genotyped using the PCR-RFLP method.

Results: Since TLR7 and TLR8 are located on the X chromosome, men and women were analyzed separately. There was no significant difference between the groups in terms of 3 polymorphisms in males. On the other hand, in women, individuals carrying AG genotype and G allele for TLR8 Met1Val polymorphism were found at a higher rate in patients hospitalized in ICU than in patients followed in the service ($p < 0.05$). In terms of the other two polymorphisms, no significant difference was found between the groups in women.

Conclusions: We suggest that the AG genotype and G allele of TLR8 Met1Val polymorphism can be considered as an important risk factor that increases the severity of the disease in women.

Keywords: Toll-like receptor, Covid-19, Polymorphism, TLR7, TLR8

Amaç: Toll benzeri reseptörler (TLR'ler), enfeksiyöz ajanları tanıyan ve doğuştan gelen bağışıklık sisteminde önemli bir rol oynayan önemli bir reseptör ailesidir. TLR'ler, hastalığın erken evrelerinde enfeksiyonu kontrol etmek ve SARS-CoV-2'ye karşı aşı üretmek için potansiyel bir adaydır. Ayrıca yapılan çalışmalarla TLR polimorfizmlerinin SARS-CoV-2'ye karşı antiviral cevaplarla da ilişkili olduğu öne sürülmüştür. Bu nedenle, TLR7 ve TLR8 polimorfizmlerinin KOVİD-19 hastalığının prognozu ile ilişkisini araştırmayı amaçladık.

Gereç-Yöntem: 40 ayaktan takip edilen hasta, 40 Hafif, orta derecede kliniği olan ve hastaneye yatırılarak takip edilen ve ağır pnömonisi olan hasta ve 40 yoğun bakım ünitesinde takip edilen hasta olmak üzere toplam 120 KOVİD-19 hastası çalışmaya dahil edildi. Hastalık şiddetinin sınıflandırılması WHO kriterlerine göre yapıldı TLR7 (rs179009), TLR8 -129 C/G (rs3764879) ve TLR8 Met1Val (rs3764880) polimorfizmleri PCR-RFLP metodu kullanılarak genotiplendirildi.

Bulgular: TLR7 ve TLR8 X kromozumu üzerinde bulunduğundan erkekler ve kadınlar ayrı ayrı analiz edildi. Erkeklerde 3 polimorfizm açısından da gruplar arasında anlamlı bir farklılık saptanmadı. Buna karşın kadınlarda TLR8 Met1Val polimorfizmi AG genotipi ve G allelini taşıyan bireylerin yoğun bakıma yatan hastalarda serviste takip edilen hastalara göre daha yüksek oranda bulunduğu saptanmıştır ($p < 0.05$). Diğer iki polimorfizm açısından gruplar arasında kadınlarda anlamlı bir farklılık saptanmamıştır.

Sonuç: TLR8 Met1Val polimorfizminin AG genotipi ve G alelinin kadınlarda hastalık şiddetini artıran önemli bir risk faktörü olarak değerlendirilebileceğini öneriyoruz.

Anahtar Kelimeler: Toll-benzeri reseptör, Kovid-19, Polimorfizm, TLR7, TLR8

PP7: RHEUMATIC DISEASES AND INFLAMMATION [ROMATİZMAL HASTALIKLAR VE İNFLAMASYON]

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Objectives: We wanted to share three different vasculitis cases and three different skin involvements based on inflammation.

Materials-Methods: The files of the patients were reviewed retrospectively and their clinical, laboratory and pathological features were recorded, and vasculitic rashes of two patients were photographed before and after the treatment.

Results: Our first patient: 60-year-old female patient, A case of pyoderma gangrenosum on the left leg while being followed up with a diagnosis of connective tissue disease

Our second patient: 69-year-old female patient, Granulomatous Polyangiitis was found while investigating for the etiology of malignancy due to the existing masses in the internal organs of the patient, who had purplish erythema, papules, nodules, and plaques on the skin with an increase in temperature, and ulcerations with granulation tissue on the ground in some areas.

Our third patient: 45-year-old female patient, The patient, who has multiple wounds with necrotic tissue on the distal one-third of the leg for about 5 months, is being followed in our clinic with the diagnosis of Polyarteritis nodosa.

Conclusions: Inflammation is characterized histologically by the accumulation of leukocytes in the affected tissue due to migration of circulating leukocytes out of the vasculature. It is an actively mediated process controlled by leukocytes, the cytokines they produce, and the vascular endothelium. However, excessive, or uncontrolled inflammatory responses can lead to the pathological inflammation seen in many rheumatological diseases.

Keywords: Inflammation, vasculitis, skin involvement

Amaç: Temelinde inflamasyon olan üç farklı vaskülit ve üç farklı cilt tutulumlu vakamızı paylaşmak istedik.

Gereç-Yöntem: Hastaların dosyaları retrospektif olarak incelenerek klinik, laboratuvar ve patolojik özellikleri kaydedildi, 2 hastanın tedavi öncesi ve tedavinin devamında vaskülitik döküntülerinin fotoğrafı çekildi.

Bulgular: 1. hastamız: 60 yaşında, kadın hasta, Bağ doku hastalığı tanısıyla takip edilirken sol bacakta gelişen pyoderma

gangrenosum vakası

2. hastamız: 69 yaşında,kadın hasta, Cildinde üzerinde ısı artışı olan morumsu eritemli, papül, nodül ve plaklar, bazı alanlarda zemininde granülasyon dokusu izlenen ülserasyonlar saptanan hastanın iç organlarındaki mevcut kitleleler nedeniyle malignite etyolojisi için araştırılırken Granülomatöz Polianjitis saptandı.

3. hastamız: 45 yaşında, kadın hasta, Yaklaşık 5 aydır olan bacak 1/3 distalinde üzerinde nekrotik doku bulunan çok sayıda yaraları mevcut olan hasta Poliarteritis nodosa tanısıyla kliniğimizde takip edilmektedir.

Sonuç: İnflamasyon, histolojik olarak, dolaşımdaki lökositlerin damar sistemi dışına göçü nedeniyle, etkilenen dokuda lökositlerin birikmesiyle karakterizedir, lökositler, onların ürettiği sitokinler ve vasküler endotel tarafından aktif aracılı yolla kontrol edilen bir süreçtir. Ancak aşırı veya kontrolsüz inflamatuar yanıtlar birçok romatolojik hastalıkta görülen patolojik inflamasyona yol açabilmektedir.

Anahtar Kelimeler: İnflamasyon, Vaskülit, Cilt tutulumu

PP8: INVESTIGATION OF IN-VIVO EFFECT OF ST. JOHN'S WORTH (HYPERICUM PERFORATUM) IN LUNG CANCER

[AKCİĞER KANSERİNDE SARI KANTARON'UN (HYPERICUM PERFORATUM) *in-vivo* ETKİSİNİN ARAŞTIRILMASI]

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Objectives: The aim of this study is to investigate the anti-cancer effects of SJW in an in vivo experimental animal model of lung cancer.

Matherials-Methods: In the in-vitro part of the study, the 5µg/ml-50mg/ml dose range of SJW on the LLC lung cancer cell line was applied at 24,48,72 hours incubation times and WST-1 cell viability test was performed. After that, the effect of the effective dose of SJW on invasion and migration was examined.

In the research, 5 groups (Control, DOX, 0,2 cm+SJW, 0,8cm+SJW, DOX+SJW) were created.

Biochemical analyzes in serum and urine samples obtained during the sacrification of animals were performed using veterinary in vitro diagnostic (IVD) tests and devices. The blood glucose, creatinine, AST and ALT measurements of the animals were measured spectrophotometrically with the Vetscan VS2 Chemistry Analyzer device (Abaxis) in DEU Bio Izmir, using the Preventive Care Profile Plus kit (ABAXIS, Germany), which is IVD for veterinary medicine. Urine microalbumin and creatinine measurements of the animals were measured with the Clintek Status Analyzer device (Siemens) available in DEU Bio Izmir, using the IVD Clintek Microalbumin kit (SIEMENS, Germany) for veterinary medicine.

Results: The LD50 value of SJW was determined to be 50 µg / ml for 24 hours. It was observed that invasion and migration decreased significantly in 24 hours in the SJW group and 48 hours in the combined drug group. When SJW was applied to a 8mm tumor, no reduction in tumor size was observed. However, it caused necrotic cell death in tumor tissue. When comparing the control group with SJW, it was observed that tumor cell necrosis was statistically different in the SJW group. This necrotic effect was observed both on 1.5 cm3 tumors and when SJW was given after 0.5cm3 tumor formation. Similar tumor necrosis was observed in the SJW + DOX group. However, no synergistic effect was observed in the combination of SJW with DOX. Although the apoptotic effect is higher in the combination group than the control group, the necrotic effect is lower than the control group. This apoptotic effect occurred both through intrinsic and extrinsic pathway. SJW application increased Ang1 expression slightly, while DOX application increased Ang1 expression more. Ang2 expression has not changed.

Conclusion: SJW has been shown to have an anti-tumoral effect similar to DOX in the in-vivo experimental animal subcutaneous lung cancer model. No synergistic effect was observed in application with DOX.

Keywords: in-vivo lung cancer animal model, Hypericum perforatum, nude mice, anticancer drug

Amaç: Bu çalışmada, akciğer kanserinin tedavisinde, anti-proliferatif ve pro-apoptotik etkileri çeşitli çalışmalarla kanıtlamış olan Sarı Kantaron (St. John's Worth= SJW= Hypericum Perforatum)'un in-vivo deney hayvanı modelinde anti kanser etkilerinin araştırılması amaçlanmıştır.

Gereç Yöntem: İn-vitro basamakta ilk olarak SJW, LLC akciğer kanseri hücre hattı üzerinde 5µg/ml-50mg/ml doz aralığında, 24,48,72 saatlik inkübasyon sürelerinde uygulandı. Hücre canlılığı WST-1 testi ile değerlendirildi. Devamında, SJW'nin etkin dozunun invazyon ve migrasyon üzerine etkisi de incelendi.

In vivo çalışmalar için 5 grup (Kontrol, Dox, 0,2 cm+SJW, 0,8cm+SJW, DOX+SJW) oluşturuldu.

Her grupta 7 hayvan olmak üzere 35 hayvan kullanıldı. Ajan uygulamasından 7 gün sonra hayvanlar sakrifiye edildi. Hayvanların sakrifikasyonu sırasında elde eldilen serum ve idrar örneklerindeki biyokimyasal analizler, veterinerlik için in vitro diagnostik (IVD) testler ve cihazlar kullanılarak gerçekleştirildi.Hayvanların kan glukoz, kreatinin, AST ve ALT ölçümleri, veterinerlik için IVD olan Preventive Care Profile Plus kiti (ABAXIS, Almanya) kullanılarak, DEU Bio Izmir'de bulunan Vetscan VS2 Chemistry Analizör cihazıyla (Abaxis) spektrofotometrik olarak ölçüldü. Hayvanların idrar mikroalbümin ve kreatinin ölçümleri veterinerlik için IVD olan Clintek Microalbumin kiti (SIEMENS, Almanya) kullanılarak strip bazlı olarak DEU Bio İzmir'de bulunan Clintek Status Analizör cihazında (Siemens) ölçüldü.

Bulgular: SJW'nin LD50 değeri 24 saat için 50 µg/ml olarak saptandı. LD50 dozu uygulanan SJW grubunda 24 saatte, kombin ilaç grubunda ise 48 saatte invazyon ve migrasyonun önemli ölçüde azaldığı gözlendi. SJW kontrol grubuna kıyasla istatistiksel anlamlı düzeyde tümör hücre nekrozu oluşmuştur. SJW-DOX grubunda da benzer tümör nekrozu oluşmuştur. Ancak DOX ile kombinasyonda sinerjistik etki gösterilmemiştir. Apoptotik etki hem interensek hem de ekstrensek yolak üzerinden gerçekleşmiştir. SJW uygulaması Ang1

ekspresyonunu hafif düzeyde arttırmıştır, DOX uygulaması ise daha fazla arttırmıştır. Ang2 ekspresyonu değişmemiştir.

Sonuç: SJW'nin in-vivo deney hayvanı subkutan akciğer kanseri modelinde DOX ile benzer anti-tümöral etkisi olduğu gösterilmiştir. DOX ile birlikte uygulamada sinerjistik etki gözlenmemiştir.

Anahtar Kelimeler: in-vivo akciğer kanseri modeli, Hypericum perforatum, Nude fare, Anti-kanser ilaç

PP9: SIT-AND-REACH TEST FOR THE EVALUATION OF SPINAL MOBILITY IN ANKYLOSING SPONDYLITIS PATIENTS

[ANKİLOZAN SPONDİLİT HASTALARINDA SPİNAL MOBİLİTENİN DEĞERLENDİRİLMESİNDE OTUR-UZAN TESTİ]

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Objectives: The aim of this study is to examine the relationship between sit-and-reach test (SRT) and the Bath Ankylosing Spondylitis Metrology Index (BASMI), sub-parameters of BASMI (cervical rotation, tragus-wall distance, lumbar lateral flexion, modified Schober's test, and intermalleolar distance) and to evaluate whether SRT is appropriate for the measuring spinal mobility in ankylosing spondylitis (AS).

Materials-Methods: 54 AS patients (29 male,25 female) were included. Age, weight and height were recorded. Bath AS Disease Activity Index (BASDAI), Bath AS Functional Index (BASFI) and BASMI were used. The SRT was administered with a standard protocol. Spearman's correlation coefficient was used. Statistical significance value was accepted as $p<0.05$.

Results: The mean age of the participants was 43.31±8.04, weight 78.29±15.35 kg, height 1.7±0.1 m, BASDAI score 2.9±1.9, BASFI score 2.15±1.77, BASMI score 1.91±1.56, SRT score 18.6±12.4 cm. SRT results were statistically better in women than men ($p<0.05$). SRT had negative moderate relationship with BASMI and with tragus-wall distance. There was a negative low-moderate correlation between SRT and lumbar lateral flexion, modified Shober's test, cervical rotation. There was no significant correlation between SRT and intermalleolar distance. Both BASMI and the SRT were not correlated with BASDAI. There was a low correlation between SRT and BASFI, while a moderate correlation was found between BASMI and BASFI.

Conclusions: The sit-and-reach test can provide insight into patients' spinal mobility, as there is a moderate correlation with BASMI. It can be used in patient follow-up and evaluation of the effectiveness of interventions in AS patients.

Keywords: ankylosing spondylitis, spinal mobility, sit-and-reach test, BASMI

Amaç: Bu çalışmanın amacı otur-uzan testi ile Bath Ankilozan Spondilit Metroloji Indeksi (BASMI), BASMI'nin alt parametreleri (servikal rotasyon, tragus-duvar mesafesi, lateral lumbar fleksiyon, modifiye Schober testi ve intermalleolar mesafe) arasındaki ilişkinin incelenmesi ve otur-uzan testinin ankilozan spondilit(AS) hastalarında spinal mobilitenin değerlendirilmesinde uygun olup olmadığının belirlenmesidir.

Gereç-Yöntem: 54 AS hastası (29 erkek, 25 kadın) dahil edildi. Yaş, kilo ve boy kaydedildi. Bath AS Hastalık Aktivite İndeksi (BASDAI), Bath AS Fonksiyonel Indeksi (BASFI) ve BASMI kullanıldı. Otur-uzan testi standart bir protokolle uygulandı. Spearman korelasyon katsayısı kullanıldı. İstatistiksel anlamlılık değeri $p<0.05$ olarak kabul edildi.

Bulgular: Katılımcıların ortalama yaşı 43.31±8.04, kilosu 78.29±15.35 kg, boyu 1.7±0.1 m, BASDAI puanı 2.9±1.9, BASFI puanı 2.15±1.77, BASMI puanı 1.91±1.56, otur-uzan test sonucu 18.6±12.4 cm olarak hesaplandı. Otur-uzan test sonucu kadınlarda erkeklere göre istatistiksel olarak daha iyiydi ($p<0.05$). Otur-uzan testinin BASMİ ve tragus-duvar mesafesi ile negatif yönde orta derecede ilişkisi bulundu. Otur-uzan testi ile lateral lumbar fleksiyon, modifiye Schober testi, servikal rotasyon arasında negatif yönde düşük-orta derecede korelasyon bulundu. Otur-uzan testi ile intermalleolar mesafe arasında anlamlı bir ilişki yoktu. Hem BASMI hem de otur-uzan testi, BASDAI ile korele değildi. Otur-uzan testi ile BASFI arasında düşük bir korelasyon varken, BASMI ile BASFI arasında orta derecede bir korelasyon bulundu.

Sonuç: Otur-uzan testi ile BASMI arasında orta derecede bir korelasyon bulunduğundan otur-uzan testi hastaların spinal mobilitesi hakkında fikir verebilir. AS hastalarında hasta takibinde ve müdahalelerin etkinliğinin değerlendirilmesinde kullanılabilir.

Anahtar Kelimeler: ankilozan spondilit, spinal mobilite, otur-uzan testi, BASMİ

PP10: DETERMINATION OF CYTOKINE PROFILES OF M1 AND M2 POLARIZED MACROPHAGES DIFFERENTIATED FROM U937 MONOCYTIC CELLS BY CHEMICAL INDUCTION

[U937 MONOSİT HÜCRELERİNDEN KİMYASAL UYARIMLA FARKLILAŞTIRILAN M1 VE M2 POLARİZE MAKROFAJ HÜCRELERİNİN SİTOKİN PROFİLLERİNİN BELİRLENMESİ]

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Objectives: U937 cells, human hematopoietic cell line with pro-monocytic properties were derived from the pleural effusion of a 37-year-old male patient with histiocytic lymphoma. U937 cells can be differentiated into different forms of macrophages with various activation and polarization protocols based on chemical induction. This cell line is used in many in vitro studies with the

aim to investigate the different polarized macrophages and their effects. In this study, it was aimed to differentiate U937 cells into M1 and M2 polarized macrophages by chemical induction and subsequent quantitative analysis of secreted pro-inflammatory and anti-inflammatory cytokines in order to perform metabolic characterization of differentiated cells.

Materials-Methods: Early passage U937 monocytic cells (ATCC® CRL-1593.2) are firstly differentiated into nonpolarized M0 mature macrophages with the treatment of phorbol-12-myristate-13-acetate (PMA). M0 macrophages were treated with lipopolysaccharide (LPS) and interferon-gamma (IFN-γ) to obtain M1 polarization. Whereas, M2 polarization was carried out with the interleukin 4 (IL-4) treatment of the M0 macrophages. Cell culture mediums for both groups were collected after 24 hours of induction. Analysis of cytokines IL-1β, IL-6, TNF-α, TGF-β, IL-10, and IL-12p70 in the medium was performed by ELISA method, kit (E0143Hu, E0090Hu, E0082Hu, E3051Hu, E0099Hu, E0102Hu; BT-LAB, China). Statistical analysis of data was conducted using with Graphpad Prism 9.0 software. Independent samples t-test was used to compare the means between groups.

Results: As pro-inflammatory cytokines, IL-1β and IL-12p70 levels were found to be statistically significantly higher in M1 polarized macrophage group compared to the M2 polarized macrophage group, while IL-6 levels were higher in M2 group. Moreover, IL-10 levels and IL/10/IL-12p70 ratio as anti-inflammatory profile, were higher in M2 group compared to the M1 group. While TGF-β levels were higher in M2 group, a statistically significant difference was not revealed between groups to some extent apart from the assumption.

Conclusions: In particular, our findings support IL10/IL12p70 ratio might serve as a reliable indicator to distinguish polarization state of the macrophages.Macrophages have differentiation plasticity in response to environmental stimuli, transform into M1 and M2 polarized macrophages and exhibite distinct effector functions.

Keywords: U937, cellular differentiation, M1 polarized macrophages, M2 polarized macrophages, inflammation

Amaç: U937 hücreleri 37 yaşındaki histiyositik lenfomalı bir erkek hastanın plevral efüzyonundan elde edilmiş, pro-monositik özellikler sergileyen insan hematopoietik hücre hattıdır. U937 hücreleri farklı kimyasal uyarım protokolleri ile farklı polarize aktif makrofaj hücrelerine farklılaştırılabilmektedir. Farklı polarize makrofajların etkilerinin araştırıldığı in vitro desendeki birçok araştırmada kullanılan temel hücre hattıdır. Bu çalışmada, U937 hücrelerinin kimyasal uyarımla M1 ve M2 farklı polarize makrofajlara farklılaştırılması ve sonrasında bu aktif makrofajlar tarafından sekrete edilen pro-enflamatuar ve anti-enflamatuar sitokinlerin kantitatif analizleri ile metabolik karakterizasyonlarının gerçekleştirilmesi amaçlanmıştır.

Gereç-Yöntem: Öncelikle, erken pasaj U937 monosit hücreleri (ATCC® CRL-1593.2) phorbol-12-myristate-13-acetate (PMA) ile nonpolarize M0 matür makrofaj hücrelerine farklılaştırılır. M0 makrofajlar, lipopolisakkarit ve interferon-gama ile uyarılarak M1 polarize makrofajlara; interlökin-4 ile uyarılarak M2 polarize makrofaj diferansiyasyonu gerçekleştirilir. 24 saatlik indüksiyon sonunda hücre kültür medyum içeriğindeki IL-1β, IL-6, TNF-α, TGF-β, IL-10 ve IL-12p70 sitokinleri ELİSA yöntemiyle, kit (E0143Hu, E0090Hu, E0082Hu, E3051Hu, E0099Hu, E0102Hu; BT-LAB, Çin) talimatlarına uygun şekilde analiz edilmiştir. Verilerin istatistiksel analizinde, GraphPad Prism 9.0 yazılımı kullanılmıştır. Bağımsız örneklem t testi ve pearson korelasyon analizi uygulanmıştır.

Bulgular: M1 polarize makrofaj grubunda pro-enflamatuar sitokinlerden IL-1β ve IL-12p70 düzeyleri M2 grubuna göre istatistiksel anlamlı şekilde daha yüksek iken, IL-6, M2 grubunda yüksektir. M2 grubunda IL-10 düzeyleri ile IL/10/IL-12p70 oranı M1 grubuna göre anlamlı şekilde daha yüksektir. TGF-β düzeyleri, gruplar arasında istatistiksel olarak anlamlı bir fark olmadan M2 grubunda daha yüksektir.

Sonuç: Makrofajlar plastisite özelliğine sahip bağışıklık hücreleri olarak farklı çevresel uyarılar neticesinde pro-enflamatuar veya anti-enflamatuar karakterlere sahip M1 ve M2 polarize makrofajlara farklılaşabilmektedirler. Bu farklılaşmada, IL10/IL12p70 oranı güvenilir bir belirteç olarak düşünülebilir.

Anahtar Kelimeler: U937, hücre farklılaşması, M1 polarize makrofaj, M2 polarize makrofaj, enflamasyon

PP11: BETAINE EXHIBITS ANTI-INFLAMMATORY AND ANTI-PROLIFERATIVE EFFECTS ON HEPG2 CELLS IN DOSE-DEPENDENTLY

[BETAİN DOZA BAĞIMLI OLARAK HEPG2 HÜCRELERİ ÜZERİNDE ANTİ-İNFLAMATUAR VE ANTİ-PROLİFERATİF ETKİ SERGİLER]

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Objective: This study sought to investigate the competence of betaine in antiproliferative and anti-cancer effects on HepG2 cells and explore underlying potential mechanisms through inflammatory cytokines.

Materials-Methods: The cytotoxic activity and cell viability of Betaine (0.25 - 50 mM) in HepG2 cells were tested at 24, 48 and 72 hours using 3-(4,5-dimethylthiazol, 2-yl)-2,5-diphenyl tetrazolium bromide (MTT) in a different dose. Then, cell lysates at IC25, IC50 and IC75 concentrations of betaine were used for biochemical and morphological analysis. IL-35, IL-10, and IL-6 levels of cytokines and cytochrome c (CYC) and caspase-3 (CASP3) of apoptotic markers were measured with ELISA.

Results: The IC50 concentration of Betaine at 3.9 mM was found in the MTT assay. In ELISA analyses, Interleukin-35 levels (ng/L) were decreased in the IC50 dose group of Betaine (33.98 ± 2.25) compared to untreated cell (40.73 ± 0.89) ($p<0.05$). Proinflammatory cytokines such as IL-6 levels (pg/mL) were increased in betaine groups compared to the control. However, it was not statistically significant. Anti-inflammatory cytokines such as IL-10 (pg/mL) levels were slightly decreased in the

betaine groups compared to the control, as demonstrated in both biochemical and morphological analyzes ($p<0.05$). CASP3 levels increased in a dose-dependent manner at IC25 (0.523±0.02) and IC50 (0.552±0.07). On the other hand, cytochrome c levels decreased statistically when compared to the control group at the IC25 dose ($p<0.05$).

Conclusion: Our present study highlights evidence for the therapeutic effects of betaine on the hepatocellular cancer model. This anticancer effect can be predominantly attributed to the inflammation pathway of betaine at certain doses.

Keywords: Inflammation, cancer, betaine, liver, apoptosis

Amaç: Bu çalışma, HepG2 hücresi üzerinde Betain'in anti-proliferatif ve anti-kanser etkilerini araştırmayı ve altta yatan potansiyel mekanizmaları inflamatuar sitokinler aracılığı ile keşfetmeyi amaçladı.

Gereç-Yöntem: HepG2 hücrelerinde Betain'in (0.25 - 50 mM) farklı dozlarda sitotoksik aktivitesi ve hücre canlılığı, MTT 3-(4,5-dimetiltiazol, 2-il)-2,5-difenil tetrazolyum bromür) kullanılarak 24, 48 ve 72. saat boyunca test edildi. Daha sonra, Betain'in IC25, IC50 and IC75 konsanstrasyonundaki hücre lizatları biyokimyasal ve morfolojik analizler için kullanıldı.

Bulgular: MTT analizinde, Betain'in IC50 konsantrasyonu 3.9 mM olarak bulundu. ELISA analizlerinde, Betain'in IC50 doz grubunda (33.98 ± 2.25) tedavi edilmeyen hücreye (40.73 ± 0.89) göre interlökin-35 seviyeleri (ng/L) azalmıştır ($p<0.05$). Kontrole kıyasla Betain gruplarında pro-inflamatuar sitokin olan IL-6 seviyeleri (pg/mL) arttı. Ancak istatistiksel olarak anlamlı değildi. Hem biyokimyasal hem de morfolojik analizlerde gösterildiği gibi, kontrol grubuna kıyasla Betain gruplarında anti-inflamatuar sitokin olan IL-10 (pg/mL) seviyeleri kısmen azalmıştır ($p<0.05$). CASP3 seviyeleri, IC25 (0.523±0.02) ve IC50'de (0.552±0.07) doza bağlı bir şekilde arttı. Öte yandan IC25 dozunda sitokrom c seviyeleri kontrol grubuna göre istatistiksel olarak azaldı.

Sonuç: Mevcut çalışmamız, Betain'in hepatoselüler kanser modeli üzerindeki terapötik etkilerine dair kanıtları vurgulamaktadır. Bu antikanser etkisi, ağırlıklı olarak, belirli dozlarda Betain'in inflamasyon yolağına atfedilebilir.

Anahtar Kelimeler: İnflamasyon, kanser, betain, karaciğer, apoptoz

PP12: THE EVALUATION OF ANTIINFLAMMATORY ACTIVITIES OF METHYLTHIAZOLE DERIVATIVES

[METİLTİYAZOLTÜREVLERİNİN ANTİİNFLAMATUAR AKTİVİTELERİNİN DEĞERLENDİRİLMESİ]

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Objectives: Cyclooxygenases (COXs) and lipoxygenases (LOX) are important target enzymes of various chemical compounds in anti-inflammatory drug research because they are key molecules involved in the formation of an inflammatory response. Thiazole derivative compounds are important structures that researchers focus on because they have strong anti-inflammatory effect potential. For this reason, in our study, nine new compounds with a 4-methylthiazol-2-acetamide part in their main structures were synthesized, and it was aimed to investigate the anti-inflammatory effects of these compounds.

Materials-Methods: Methylthiazole derivative compounds were synthesized within the scope of this study. They were synthesized for the first time and their structures were elucidated by high resolution mass spectrometry (HRMS, LC/IT-TOF), 1H-NMR, and 13C-NMR methods. The inhibitory effects of the compounds on COX-1 and COX-2 enzymes were measured with the "Cayman COX Inhibitor Screening Assay Kit," (catalog no: 701050) and their anti-inflammatory potentials were determined. The cytotoxicity values of the compounds on NIH/3T3 cell lines were calculated by the MTT method.

Results: Inhibition values of compound 3c containing 2-thiazoline on COX-1 and COX-2 enzymes at 100µM concentration were determined as 98,11±0,56%; %12,63±0,76 % respectively. The percent inhibition values of compound 3h on COX-1 and COX-2 enzymes were determined as 90.47±2.14; 25.75±0.91 respectively. The cytotoxicity of compounds were determined as %329±79.70; %5,94±0,49 respectively.

Conclusıons: The findings obtained from our study show that among the compounds tested for COX-1, COX-2, and LOX enzyme inhibition effects and cytotoxicity, 3c and 3h compounds have a significant inhibitory effect on the COX-1 enzyme. Our in vitro study results indicate that compound 3h is a promising compound for further studies as an anti-inflammatory agent due to its strong COX-1 inhibition effect and low toxicity.

Keywords: Methylthiazole derivatives, Anti-inflammatory, Cyclooxygenase, Lipoxygenase, NIH/3T3 cell line.

Amaç: Siklooksijenazlar (COXs) ve Lipoksijenaz (LOX) inflamatuar yanıt oluşumunda rol oynayan anahtar moleküller olmaları nedeniyle anti-inflamatuar etkili ilaç araştırmalarında çeşitli kimyasal bileşiklerin önemli hedef enzimleridir. Tiyazol türevi bileşikler, güçlü anti-inflamatuar etki potansiyeline sahip olmalarından dolayı araştırmacıların üzerinde odaklandıkları önemli yapılardır. Bu nedenle çalışmamızda, ana yapısında 4-metiltiyazol-2-asetamit parçası bulunan dokuz yeni bileşik sentezlenmiş ve bu bileşiklerin antiinflamatuar etkilerinin araştırılması hedeflenmiştir.

Gereç-Yöntem: Bu çalışma kapsamında sentezlenen Metiltiyazol türevi bileşikler; ilk defa sentezlenmiş olup, yapıları yüksek çözünürlüklü kütle spektrometresi (HRMS, LC/IT-TOF), 1H-NMR ve 13C-NMR yöntemleriyle aydınlatılmıştır. Bileşiklerin COX-1ve COX-2 enzimleri üzerinde inhibitör etkileri "Cayman COX Inhibitor Screening Assay Kit, (katalog no:701050)" ile ölçülerek anti-inflamatuar potansiyelleri belirlenmiştir. Bileşiklerin NIH/3T3 hücre dizileri üzerindeki sitotoksisite değerleri MTT yöntemi ile hesaplanmıştır.

Bulgular: 2-tiyazolin içeren 3c bileşiğinin 100µM konsantrasyonda COX-1 ve COX-2 enzimleri üzerindeki inhibisyon değerleri sırasıyla %98,11±0,56; %12,63±0,76 olarak belirlendi. 4-Methyl-triazol kalıntısı içeren 3h bileşiğinin COX-1 ve COX-2 enzimleri üzerindeki inhibisyon değerleri sırasıyla %90.47±2.14; %25.75±0.91olarak tespit edildi. 3c ve 3h bileşiklerinin NIH/3T3 hücre dizileri üzerindeki sitotoksisiteleri sırasıyla %329±79.70; %5,94±0,49 olarak hesaplandı.

Sonuç: Çalışmamızdan elde edilen bulgular, COX-1, COX-2 ve LOX enzim inhibisyon etkileri ve sitotoksisiteleri test edilen bileşikler arasında 3c ve 3h bileşiğinin COX-1 enzimi üzerinde önemli derecede inhibitör etkiye sahip olduğunu göstermektedir. In vitro çalışma sonuçlarımız, 3c bileşiğinin güçlü COX-1 inhibisyon etki ve düşük toksisite gostermesinden dolayi anti-inflamatuar ajan olarak daha ileri çalışmalar için umut verici bir bileşik olduğuna işaret etmektedir.

Anahtar Kelimeler: Metiltiyazol türevleri, Antiinflamatuar, Siklooksijenaz, Lipoksijenaz, NIH/3T3 hücre dizisi.

PP13: EVALUATION OF THE CORRELATION OF INFLAMMATION MARKERS AND PROGNOSTIC FACTORS IN MULTIPLE MYELOMA

[MULTIPLE MYELOMDA INFLAMASYON BELİRTEÇLERİNİN PROGNOSTİK FAKTÖRLERLE İLİŞKİSİNİN DEĞERLENDİRİLMESİ]

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Objectives: Inflammation markers are used to predict the morbidity and mortality risk of many chronic diseases and malignancies. We aimed to evaluate the relationship between systemic immune inflammation index (SII) and prognostic factors in patients diagnosed with Multiple Myeloma (MM).

Materials-Methods: 30 MM patients was included. Diagnostic laboratory data were evaluated for comparison with other systemic inflammation-based prognostic indicators such as SII, neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio(PLR). SII was calculated with the formula SII=(PxN)/L, NLO=N/O, PLO=P/L; P, N, and L are platelet, neutrophil, and lymphocyte counts, respectively. In addition to beta2-microglobulin and albumin as prognostic markers, C-reactive protein (CRP) Erythrocyte Sedimentation Rate (ESR), used in the follow-up of inflammation, the plasma cell ratio of bone marrow (BM-PCR) at the time of diagnosis were also examined. The median values of the data were calculated. The correlation of the parameters were evaluated. **Results:** The median age was 63(43–84), with a F/M ratio of 18/12. 23 patients were evaluated as Stage-III, five patients as Stage-II, and two patients as Stage-I. Median(minimum-maximum) values of the parameters as follows; platelet 237,50/mm3(41,000-558,000), leukocytes 6655/mm3(1490-15660), neutrophil 3725/mm3(100-9050), lymphocyte 1650/mm3(220-7950), BM-PCR was 50%(10-95), ESR 94.5mm/hr(13-148), CRP 3.9mg/L(0.3-98), beta-2 microglobulin 4.8mg/L(1.6-15), albumin 3.5g/L(1.3-4,4) SII 384.4(51.7–6854), NLR 2(0.1–14.4), and the PLO was 0.1(0–0.6). In the correlation of SII, NLR, and PLR with all parameters, only the platelet count and CRP were correlated.

Conclusion: Considering the limited number of patients, sufficient evidence could not be found fort he usage of SII, NLR and PLO in the determination of prognosis in MM patients.

Keywords: Myeloma; systemic immune-inflammation index; prognosis

Amaç: Inflamasyon belirteçleri birçok kronik hastalığın ve malinitenin morbidite ve mortalite riskini öngörmekte kullanılmaktadır. Biz de Multiple Myelom (MM) tanılı hastalarda, sistemik immün inflamasyon indeksinin (SII) prognostik faktörlerle ilişkisini değerlendirmeyi amaçladık.

Gereç-Yöntem: Multiple Mylelom (MM) tanılı 30 hastanın retrospektif analizi yapıldı. Tanıdaki laboratuvar verileri, Sistemik inflamasyon indeksi (SII), nötrofil-lenfosit oranı (NLO) ve trombosit-lenfosit oranı (PLO) gibi diğer sistemik inflamasyona dayalı prognostik göstergelerle karşılaştırmak için değerlendirildi. SII, SII = (P x N)/L, NLO=N/L, PLO=P/L formülüyle hesaplandı; P, N ve L, sırasıyla periferik trombosit, nötrofil ve lenfosit sayılarıdır. Prognostik belirteç olarak beta2 mikroglobulin ve albümin yanısıra inflamasyon izleminde kullanılan C reaktif protein (CRP) Eritrosit Sedimentasyon Hızı (ESR) verileri tanı anındaki plazma hücre oranına da bakıldı. Verilerin ortanca değerleri hesaplandı ve birbirleri ile korelasyonuna bakıldı.

Bulgular: Ortanca yaş 63(43–84), Kadın/Erkek oranı 18/12 idi. 23 hasta Evre-III, beş hasta Evre-II, iki hasta Evre-I olarak değerlendirildi. Parametrelerin ortanca (minimum-maksimum) değerleri her bir parametre sırasıyla; trombosit için 237.500/mm3(41.000-558.000), lökosit 6655/mm3(1490-15660), nötrofil 3725/mm3(100-9050), lenfosit 1650/mm3(220-7950), kemik iliği-plazma hücre oranı(Kİ-PHO) %50(10-95), ESR 94.5mm /saat(13-148), CRP 3.9mg/L(0.3-98), beta-2 mikroglobulin 4.8mg/L(1.6-15), albumin 3.5g/L(1.3–4,4). SII 384.4(51.7–6854), NLO 2(0.1–14.4), PLO 0.1 (0–0.6) bulundu. SII, NLO ve PLO'nun diğer parametreler ile korelasyonunda sadece trombosit sayısı ve CRP ile korelasyon gösterirken diğer parametreler ile korelasyon göstermedi.

Sonuç: SII, NLO ve PLO için hasta sayısının kısıtlı olması göz önüne alınmakla birlikte MM hastalarında prognoz tayininde kullanılmak üzere yeterli kanıt bulunamamıştır.

Anahtar Kelimeler: Myelom, sistemik immun-inflamatuar indeks, prognoz

PP14: A CASE OF COVID-19 WITH ISOLATED THROMBOCYTOPENIA

[İZOLE TROMBOSİTOPENİ İLE SEYREDEN COVID-19 OLGUSU]

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CASE REPORT ABSTRACT: COVID-19 can affect many systems out of the respiratory system. In this article, a COVID-19 case with fever and isolated severe thrombocytopenia without pulmonary involvement is presented. A 25-year-old male patient admitted to our hospital with complaints of fever and headache was hospitalized for close follow-up because of severe thrombocytopenia in peripheral blood and a positive result of SARS-CoV-2 PCR in the combined nasal and throat swab sample. Daily hemogram follow-up was done. The patient, whose fever decreased under COVID-19 treatment and whose thrombocyte count tended to increase, was discharged on the 5th day of treatment. Other tests performed in terms of thrombocytopenia etiology were negative. In particular, it is not enough to suspect COVID-19 in patients with only respiratory system findings and fever, but rarer presentations should be kept in mind.

Keywords: COVID-19, Thrombocytopenia, Fever

OLGU SUNUM ÖZETİ: COVID-19 solunum sistemi dışında birçok sistemi tutabilmektedir. Akciğer tutulumu olmadan,ateş ve izole ağır trombositopeni ile seyreden bir COVID-19 olgusu sunulmuştur. Ateş ve baş ağrısı şikâyetiyle hastanemize başvuran 25 yaşerkek hasta periferik kanda ağır trombositopeni saptanması ve kombine burun boğaz sürüntü örneğinde SARS-CoV-2 PCR testinin pozitif sonuçlanması nedeniyle yakın takip amacıyla yatırıldı. Günlük hemogram takibi yapıldı. Akciğer tutulumu izlenmedi. COVID-19 tedavisi altında ateşi düşen ve trombosit sayısı yükselme eğiliminde olan hasta tedavisinin 5.gününde taburcu edildi. Trombositopeni etiyolojisi açısından yapılan tetkikler negatif sonuçlandı. Özellikle içinde bulunduğumuz süreçte sadece solunum sistemi bulguları ve ateşi olan hastalarda COVID-19'dan şüphelenmek yeterli olmamakla birlikte daha nadir prezentasyonları akılda tutulmalıdır.

OLGU: 25yaş erkek hasta,2 gündür devam eden ateş ve baş ağrısı şikâyeti ile hastanemiz acil servisine başvurdu.COVID-19 için temas öyküsü yoktuAteş 36,7C,nabız 95 vuru/dk,Tansiyon 127/62 mm/Hg, oda havasında (SpO2)%97,solunum sayısı 14/dk idi.Laboratuvarlökosit sayısı 5.050/mm3,lenfosit sayısı 1.365/mm3 (%27),trombosit sayısı 14.300/mm3,üre 22 kreatinin 0,99 mg/dL, AST/ALT 16/11 U/L,CRP <2 mg/L, ferritin 131 µg/L, d-dimer 0,42 mg/L olarak saptandı. Periferik yaymasında dev trombositler mevcuttu, atipik hücre ve blast görülmedi ve trombosit sayısı 20.000/mm3 ile uyumluydu. SARS-CoV-2 PCR testi pozitif sonuçlandı. Toraks BT'de, her iki akciğerde aktif infiltrasyon ve yer kaplayan lezyon saptanmadı.Yatışı yapılan hastaya seftriakson 2x1 gr ıV, favipiravir 2x1600 mg yükleme,2x600 mg idame oral başlandı.Hematoloji konsültasyonu istendi, günlük hemogram takibi yapıldı.Trombositopeni etiyolojisi amacıyla gönderilen vitamin B12,folik asit,ferritin,demir, TDBK testleri normal sonuçlandı. RoseBengal, Brusella aglütinasyon testleri, HBsAg, Anti-HCV, HIVAg/Ab, CMV IgM, Parvovirüs IgG, EBV IgM, ANA, Anti-dsDNA, Direkt Coombs, indirekt Coombs negatif bulundu. Takiplerinde ateş yanıtı alındı,tedavi altında trombosit sayısında yükselme görüldü.Tedavi 5.günü hemogramda trombosit sayısının 67.000/mm3'e çıktığı,kontrol periferik yaymasında 100.000/mm3 ile uyumlu saptandı.Taburculuk sonrası poliklinik takiplerinde 4.ayda patoloji saptanmadı.

Anahtar Kelimeler: COVİD 19, Trombositopeni, Ateş

PP15: DEVELOPMENT OF APTASENSOR FOR THE DIAGNOSIS OF COVID-19

[COVID-19 TANISI İÇİN APTASENSÖR GELİŞTİRİLMESİ]

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Objectives: The objective is to develop a low-cost, practical, portable aptasensor platform for the diagnosis of COVID-19.

Materials -Methods: Amino-terminated aptamers to be used for the design of an aptasensor were synthesized by SELEX method, and interaction of aptamers with SARS-CoV-2 S1 protein was investigated by isothermal titration calorimetry (ITC). Gold electrodes were used to design the biosensor platform. After the electrode surface was functionalized with cysteamine, the amino-terminated aptamer was conjugated to the surface via glutaraldehyde crosslinker. Then, the surface characterization and analytical parameters of the designed sensing platform were determined by adding commercial S1 proteins on the surface using differential pulse voltammetry (DPV), cyclic voltammetry (CV) and impedance spectroscopy (EIS). To evaluate the working performance of the system, S1 proteins were added to the synthetic serum samples using the standard addition method and the measurements were repeated.

Results: Surface characterization of the platform designed with EIS and CV measurements was performed and it was found that the modification was successfully performed. In addition, DPV results and analytical parameters of the platform (calibration plot, limit of detection(LOD) , repeatability, coefficient of variation) were determined and the working performance of system was evaluated. Moreover, working performance of the biosensor in real samples and its specificity for COVID -19 were determined by experiments with synthetic serum and influenza A and B proteins.

Conclusions: According the results, the system has potential to be used for the detection of COVID -19, and also it can be rapidly adapted in different pandemic situations that may occur in the future.

Keywords: COVID-19, Aptasensor, Electrochemical biosensor, Aptamer

Amaç: COVID-19 tanısına yönelik düşük maliyetli, pratik, taşınabilir bir aptasensör platformunun geliştirilmesi hedeflenmiştir.

Gereç-Yöntem: Aptasensör tasarımında kullanılmak üzere amino uçlu aptamerler, SELEX yöntemi ile sentezlendi ve aptamerlerin SARS-CoV-2 S1 proteini ile etkileşimi izotermal titrasyon kalorimetre (ITC) ile değerlendirildi. Biyosensör platformunun tasarımı için altın elektrotlar kullanıldı ve elektrot yüzeyi sisteamin ile fonksiyonel hale getirildikten sonra, glutaraldehit çapraz bağlayıcı aracılığıyla amino-uçlu aptamer yüzeye konjuge edildi. Ardından ticari olarak temin edilen S1 proteinleri yüzeye eklenerek tasarlanan sensör platformunun yüzey karakterizasyonu ve analitik parametreleri diferansiyel puls voltammetrisi (DPV), döngüsel voltammetri (CV) ve impedans spektroskopisi (EIS) ölçümleri ile belirlendi. Geliştirilen aptasensör test sisteminin, çalışma performansının değerlendirilmesi için sentetik serum örneklerine standart katma yöntemi ile S1 proteinleri eklendi ve ölçümler tekrarlandı.

Bulgular: EIS ve CV ölçümleri ile tasarlanan biyosensör platformunun yüzey karakterizasyonu yapılmış ve modifikasyonun başarılı şekilde gerçekleştirildiği belirlenmiştir. Ayrıca DPV sonuçları ile sensör platformunun analitik parametreleri (kalibrasyon grafiği, belirtme sınırı (LOD), tekrarlanabilirlik, varyasyon katsayısı) belirlenmiş olup geliştirilen sistemin çalışma performansı değerlendirilmiştir. Bunlara ek olarak, sentetik serumda ve influenza A ve B proteinleri ile yapılan denemeler ile biyosensörün gerçek örneklerdeki çalışma performansı ve COVID-19'a spesifikliği belirlenmiştir.

Sonuç: Çalışma kapsamında, elde edilen sonuçlara göre tasarlanan aptasensör sisteminin, COVID-19 tespitinde kullanım potansiyeli olmakla birlikte, ileride karşılaşılabilecek olan farklı pandemi durumlarında hızlıca adapte edilerek kullanım potansiyeli taşımaktadır.

Anahtar Kelimeler: COVİD-19, Aptasensör, Elektrokimyasal biyosensör, Aptamer

CASE REPORT FULL TEXT
[VAKA SUNUMU TAM METİN]

OP36: CHASING THE ETIOLOGY OF HYPONATREMIA

[HİPONATREMİ ETYOLOJİSİNİN PEŞİNDEN KOŞARKEN]

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ABSTRACT

Primary Empty Sella (PES) syndrome is characterized by the herniation of the subarachnoid space within the sella, which is often associated with variable degrees of flattening of the pituitary gland in patients without previous pituitary pathologies [1] It is often seen in pseudo tumor cereberi, obese, chronic autoimmune thyroiditis (Hashimoto's thyroiditis), and multiparous females. [2] We present a case of 66 years old female who has partially primary empty sella manifested dizziness and hyponatremia. After some investigations, we found that the etiology of hyponatremia was not related with PES; but due to heart failure, and hypervolemia; however neurological complaints were thought to be due to PES.

Keywords: Hyponatremia, Empty Sella syndrome, Hypervolemia, Heart Failure

ÖZET

Primer Boş Sella (PES) sendromu, primer hipofiz patolojisi olmayan hastalarda sıklıkla hipofiz bezinin değişken derecelerde düzleşmesi ve sella içine subaraknoid boşluğun herniasyonu ile karakterizedir.[1] Sıklıkla psödo tümör cereberi, obez, kronik otoimmün tiroidit (Hashimoto tiroiditi) ve multipar kadınlarda görülür. [2] Vakamızda baş dönmesi ve hiponatremi kliniği ile kendini gösteren parsiyal primer boş sella sendromlu 66 yaşında bir kadın olguyu sunuyoruz. Yapılan tetkikler sonucunda hiponatreminin etiyolojisinin PES ile ilişkili olmadığı kalp yetmezliği ve hipervolemiye sekonder olduğu ancak nörolojik şikayetlerin PES'e bağlı olabileceği kanısına varıldı.

Anahtar Kelimeler: Hiponatremi, Boş Sella sendromu, Hipervolemi, Kalp Yetmezliği

Introduction:

Hyponatremia is the most common electrolyte disorder and always develops due to a secondary cause. [3] Hence, finding the cause is important for both preventing recurrence and managing treatment. Hyponatremia treatment differentiates according to cause. Investigating etiology begins with determining volume situation. There are various causes in etiology of hyponatremia and sometimes, even a well-known cause may be unobserved. Herein, a patient with hyponatremia with unknown origin is presented.

Material-methods:
In our study, a 66-year-old diabetic, hypertensive multiparous female patient with hyponatremia was examined. The patient's body mass index was in the normal range at the time of examination, but she had obesity in the past. She had been diagnosed with hypothyroidism many years ago and was using Levothyroxine sodium regularly.
Routine biochemical blood parameters (and hormones, including pituitary) were taken every morning at 8 am and analyzed in the hospital's general biochemistry laboratory. Magnetic resonance (MRI) for brain and computer tomography (CT) for thorax-abdominal imaging performed for further investigation. Contrast material could not be used during imaging due to the patient's chronic renal failure.

Case Presentation:
A 66-year-old multiparous woman admitted to emergency department with dizziness and her blood sodium was found 108 mEq/L. The patient was hypotonic and euvolemic. So, for the etiology, her thyroid (TSH 3,25 U/L) and adrenal functions were examined and found normal. There was indapamide among her medications and although the diuretic was discontinued, hyponatremia kept going. Her urine sodium was normal (97 mmol/day N: 40 to 220), so SIADH was excluded. She did not have nausea, vomiting, polyuria, polydipsia, hypo/hyperkalemia. She also had normal renin (3.42 ng/ml/h) and slightly increased aldosterone levels (248.5 pg/mL). The etiology of hyponatremia could not be found. The patient also described that she had suffered from headache, imbalance, and dizziness for many years.
On the other hand, since the patient had heart failure in her history, a control echocardiography was performed for routine check-up and found that she had asymptomatic pericardial effusion (5 mm). A thorax CT showed bilateral pleural effusion in 1 cm size. But, on physical examination, there was no sign or symptom for hypervolemia. After treatment with diuretics and fluid restriction, serum sodium level normalized. Later, the patient was referred to the cardiology clinic for the treatment of chronic heart failure.
Neurological examination was found to be normal when the blood sodium level was above 130; while still complaining of dizziness. She was examined by neurology and otolaryngology and no pathology was found. Pituitary MRI showed findings compatible with partial empty sella. Pituitary hormone levels were in the normal range (LH: 28.7 IU/L, FSH: 83 mlU/mL, progesterone: 0.45 units, estradiol: 1.2 ng/L, Growth hormone: 0.317 ng/mL and IGF-1: 43.5 ng/mL). Serum ACTH and morning fasting serum cortisol level were between normal ranges (16,7 pg/mL and 14.3 ug/dL, respectively).

DISCUSSION

Empty sella is characterized by the herniation of the subarachnoid space within the sella[1], and classified into two groups, primary or secondary. Secondary causes are intracranial surgery, radiotherapy, adenoma. However, primary empty sella (PES) is defined with cases unknown etiology (4). Risk factors for PES are female gender (F/M ratio 5:1) (5), obesity, diabetes mellitus, auto-immune diseases such as Hashimoto’s thyroiditis, hypertension and multiparity. Patients with PES can have headache, and neurological symptoms (6). Since this patient had those risk factors and symptoms, at first, the etiology was considered as PES. But after excluding hypopituitarism, she was diagnosed as chronic heart failure related hypervolemic hyponatremia. On the other hand, neurological complaints of the patient may be caused by PES. Headache is one of the most prevalent symptoms in PES reported in about 60-80 % of cases (7).

CONCLUSION

Diagnosis and treatment of the patient was delayed. So, although physical examination shows euvolemia, patients with chronic heart failure should be examined with radiological methods in selected cases. Also, in the etiology of headache, rare causes such as PES, should be considered.

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