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Pınar Soysal
Bezmialem Vakıf University, Faculty of Medicine,
Department of Internal Medicine

OP-1

Investigation of the Anti-inflammatory Effect of *Liquidambar orientalis* Leaf Extract on RAW 264.7 Macrophage Cells

Hümeyra ŞAHİN[1], Zeynep ÖZMAN[2], Abdurrahim KOÇYİĞİT[2]

[1]*Bezmialem Vakıf University, Faculty of Medicine, İstanbul, Turkey*

[2]*Bezmialem Vakıf University, Faculty of Medicine, Department of Medical Biochemistry, İstanbul, Turkey*

Introduction: *Liquidambar orientalis*, or the "Anatolian Sweetgum Tree", native to the southwestern coastal regions of Turkey, has shown antioxidant, antimicrobial, antiulcerogenic, and hepatoprotective effects in various studies. However, its anti-inflammatory effects have not been fully elucidated. This study aimed to demonstrate the anti-inflammatory effect of *L. orientalis* leaf extract (LOLE) in lipopolysaccharide (LPS)-Stimulated RAW 264.7 macrophages.

Method: *L. orientalis* leaves were dried in 40 ºC incubator overnight and extracted using 80% ethanol. The total phenolic and flavonoid contents were assessed using colorimetric methods. Western blot (WB) method was used to determine nuclear factor-kappa B (NF-κB) and nitric oxide synthase (iNOS) levels in LPS-induced RAW 264.7 macrophage cells. ELISA was employed to analyze tumor necrosis factor alpha (TNF-α), interleukin-1 beta (IL-1β), and IL-6 cytokine levels. The cytokine levels of the extract were compared with those of methotrexate.

Results: Total phenolic and flavonoid contents in LOLE were measured as 618.04±6.71 mgGAE/g and 42.81±3.95 mgQE/g, respectively. WB results demonstrated that LOLE suppressed the expression of inflammation-related proteins iNOS and NF-κB in LPS (1 µg/mL) induced RAW 264.7 cells in a dose-dependent manner ($p<0.05$). The ELISA results revealed optimal suppression of IL-1β and TNF-α levels in LPS-induced cell culture at a 0.5 mg/mL LOLE dose, whereas IL-6 was best suppressed at 1 mg/mL ($p<0.001$). When 0.5 mg/mL LOLE was compared with 50 µM methotrexate in LPS-induced cell culture, LOLE showed a greater decrease in IL-1β levels ($p<0.001$).

Conclusion: LOLE decreased inflammatory cytokines IL-1β, IL-6, and TNF-α by regulating the iNOS and NF-κB pathways, suggesting its potential as an alternative anti-inflammatory treatment.

Key words: Anatolian sweetgum tree, Raw 264.7 macrophages, anti-inflammatory effect, methotrexat

OP-2

Investigation of Biomarkers Associated with Intestinal Barrier Permeability in Patients with Migraine

Oğuz Alp KUCUR[1], Aslı YAMAN KULA[2], Şahabettin SELEK[3], Metin DEMİREL[3], Fatmanur GÖKTAŞOĞLU[3]

[1]Bezmialem Vakıf University, Faculty of Medicine, İstanbul, Turkey

[2]Bezmialem Vakıf University, Faculty of Medicine, Department of Neurology, İstanbul, Turkey

[3]Bezmialem Vakıf University, Faculty of Medicine, Department of Biochemistry, İstanbul, Turkey

Introduction: Migraine is a common neurological disorder with no exact pathophysiology. In recent years, studies from the perspective of "Gut-Brain Axis" hypothesis have shown a strong connection between how the Gut and the Brain affect each other in different types of mechanisms such as but not limited to hormones, metabolites, and neuroendocrine factors. From that perspective, there are no studies examining migraine's connection to gut permeability. To examine the aforementioned permeability, two proteins (lipopolysaccharide binding protein and zonulin) were selected.

Method: In this particular study, migraine patients (n=52) blood samples were collected at the Neurology Clinic at Bezmialem Vakıf University. The patient group was categorized according to aura history, visual analogue scale (VAS) value, migraine attack frequency per month, onset time, photophobia, sonophobia, pain duration per attack, and nausea and vomiting symptoms. Samples were studied with ELISA Kits at the Biochemistry Laboratory located in Bezmialem University. Their results were compared to healthy controls (n=30) later.

Results: There were no significant differences detected between migraine and healthy control groups in the mean serum zonulin and LPBP levels ($p>0.05$). However, we found a moderately significant correlation between VAS values for both our parameters ($p=0.03$ for zonulin and $p=0.02$ for LPBP).

Conclusion: Our group could not show a significant connection between migraine and gut permeability directly; however, as our results suggest a moderate significance between pain intensity and zonulin and LPBP levels, further studies are needed to elaborate the subject.

Key words: Migraine, gut permeability, zonulin, LPBP

OP-3

Immunotherapeutic Effects of Purple Mulberry (*Morus rubra*) Extract in Colorectal Cancer: Efficacy *in vitro*

Rukiye GÜRLEYEN[1], Ezgi DURMUŞ[2], Abdürrahim KOÇYİĞİT[2]

[1]*Bezmialem Vakıf University, Faculty of Medicine, İstanbul, Turkey*

[2]*Bezmialem Vakıf University, Faculty of Medicine, Department of Biochemistry, İstanbul, Turkey*

Introduction: In this study, we aimed to evaluate the cytotoxic effects of purple mulberry, a red fruit, on colorectal adenocarcinoma cells, to investigate the effect of purple mulberry extract on the expression level of PD-1 protein, and to show how the T cell-mediated cytotoxic effect on colorectal cancer cell lines co-cultured with T cells changed after purple mulberry administration.

Method: In line with these objectives, 80% ethanolic purple mulberry extract was prepared from the purple mulberry fruit. Content analysis of this extract, total phenol, total flavonoid, and total antioxidant determination were measured. The proliferation of colon cancer cell lines (HT-29 and Jurkat-T cells) was evaluated using MTT and WST-1 cell viability assays. ELISA tests were performed according to the user instructions, and cytokine levels in T cell supernatants were measured.

Results: Total phenol, flavone, and antioxidant activities were measured at 125 ug GAEeq/mg, 50 ug QUEeq/mg, and 25% ABTS scavenging capacity, respectively. By MTT cell viability assays, the 48-h 50% cell killing value (IC50) of *Morus rubra* extract at different concentrations (25-2,500 ug/mL) on HT-29 colon cancer was found to be 2,000 UG/mL. The proliferative effect of *Morus rubra* extract on Jurkat T cells was measured by the WST-1 cell viability assay, and the 48-h 50% cell killing value was found to be >3,000 ug/mL, whereas an increase in cell proliferation was observed in the dose range of 1,000-1,500 ug/mL compared with the control. A significant increase in cytokine levels was observed, especially at doses (1,000-2,000 ug/mL) where T cells proliferated.

Conclusion: It was shown that the ethanolic extract of purple mulberry fruit has high phenolic properties and that *Morus rubra* can affect the T cell response as well as its cytotoxic effect against colon cancer cells.

Key words: *Morus rubra,* colon cancer, immunomodulation

OP-4

Effect of Denosumab on MCF-7 Human Breast Cancer Cell Culture

Emre BERİ[1], Vildan Betül YENİGÜN[2], Ahmet Gökhan AKKAN[3], Özlem TOLUK[4]

[1]Bezmialem Vakıf University, Faculty of Medicine, İstanbul, Turkey
[2]Bezmialem Vakıf University, Faculty of Medicine, Department of Biochemistry, İstanbul, Turkey
[3]Bezmialem Vakıf University, Faculty of Medicine, Department of Medical Pharmacology, İstanbul, Turkey
[4]Bezmialem Vakıf University, Faculty of Medicine, Department of Biostatistics, İstanbul, Turkey

Introduction: One common condition encountered in patients receiving hormonal therapy for metastatic breast cancers and breast cancer is bone density loss. Denosumab is one of the bone resorption inhibitors used to prevent these adverse effects. In this study, we investigated the anticancer effects of denosumab on MCF-7 human breast cancer cell culture.

Method: ER+ breast cancer cells (MCF-7) were used in this study to investigate the combination effect of progesterone and denosumab. The MTT cell viability test was used to calculate the half-maximal inhibitory concentrations (IC50) of both drugs and to observe cell viability after they were co-administered. To examine the cell growth rates and progression toward apoptosis, apoptosis analysis acridine orange/ethidium bromide (AO/EB), cell cycle analysis, and Ki-67 staining will be performed.

Results: Cell viability results revealed that low doses of progesterone induced the proliferation of MCF-7 cells, while inducing cytotoxicity at higher doses (starting from 40 µM with an IC50 value of 82.4 µM, $p<0.001$). In addition, approximately 20 µM of denosumab caused half of the cells to die ($p<0.001$). When the non-toxic dose of progesterone (40 µM) was applied to the cells with several doses of denosumab, we did not observe any statistical difference in cell death. Two weeks following the initial test, at the second MTT test, cytotoxicity had decreased to 18%. When denosumab was administered alone, it caused nearly 25% of the MCF-7 cells to undergo apoptosis in the AO/EB analysis, whereas when administered together with progesterone, this rate decreased to 15%.

Conclusion: The results showed that progesterone could counteract the cytotoxic and apoptotic effects of denosumab in MCF-7 cells, but more research is needed to confirm this result.

Key words: Denosumab, RANK-RANKL, progesterone, breast cancer, MCF-7

OP-5

Assessment of PGT-A Outcomes Based on Indications for IVF Treatment

Ege YAĞIBASAN[1], Pınar ÖZCAN[2], Hikmet Tunç TİMUR[3], Fatma Başak TANOĞLU[4], Özge PASİN[5]

[1]*Bezmialem Vakıf University, Faculty of Medicine, İstanbul, Turkey*

[2]*Bezmialem Vakıf University, Faculty of Medicine, Department of Obstetrics and Gynecology, İstanbul, Turkey*

[3]*Urla State Hospital, Clinic of Obstetrics and Gynecology, İzmir, Turkey*

[4]*Çaldıran State Hospital, Clinic of Obstetrics and Gynecology, Van, Turkey*

[5]*Bezmialem Vakıf University, Faculty of Medicine, Department of Biostatistics and Medical Informatics, İstanbul, Turkey*

Introduction: There are multiple reasons to consider preimplantation genetic testing for aneuploidy (PGT-A) for women undergoing *in vitro* fertilization (IVF) treatment. Different indications are anticipated to identify a greater number of aneuploidies than others. Our objective was to assess PGT-A results according to indications regarding the likelihood of identifying aneuploidy.

Method: This retrospective cohort study in a single center was conducted at the IVF center of Bezmialem University Hospital. We analyzed PGT-A results of 446 blasts that underwent PGT-A due to the following indications: advanced maternal age, history of recurrent spontaneous abortion, history of recurrent implantation failure, serious male factor, poor embryo quality, or a combination of two or more of these factors. Next-generation sequencing was used for the PGT-A analysis.

Results: Two thousand and four hundred seven oocytes were retrieved, resulting in the fertilization of 1,300 oocytes. Subsequently, 446 embryos underwent biopsy for PGT-A. The mean ages of the women and men were 34.47±5.83 and 36.5±6.31 respectively. The most common indication for PGT-A was patients with advanced maternal age, accounting for 23.1% of cases; the other indications were as follows: recurrent spontaneous abortion, 20.2%; poor embryo quality, 19.7%; recurrent implantation failure, 15.8%; mixed, 12.3%; and severe male factor, 8.9%. PGT-A analysis indicated that 237 embryos were euploid, while chaotic and aneuploid embryos were 141 and 114 respectively. The rates of euploidy within the indications for PGT-A were 51.1% for advanced maternal age, 82.9% for recurrent spontaneous abortion, 93.8% for recurrent implantation failure, 94.4% for severe male factor, 72.5% for poor embryo quality, and 32% for mixed.

Conclusion: PGT-A results reveal that the ratio of euploidy is lower in advanced maternal age than in other indications. Patients who underwent mixed PGT-A had the lowest rate of euploidy.

Key words: PGT-A, euploidy, aneuploidy, IVF

OP-6

Comparative Effects of Vitamin C, Curcumin, and *Sambucus nigra* Extract on Cell Viability and Cytokine Levels in Cigarette-exposed Lung Epithelium Cell Cultures

Abdullah Eren ÖZKAYA[1], Hanife Sevgi VARLI[2], Nelisa Laçin TÜRKOĞLU[2], Ayşegül YABACI TAK[3], Fatmanur KARAKÖSE OKYALTIRIK[4]

[1]*Bezmialem Vakıf University, Faculty of Medicine, İstanbul, Turkey*
[2]*Yıldız Technical University, Department of Molecular Biology and Genetics, İstanbul, Turkey*
[3]*Bezmialem Vakıf University, Faculty of Medicine, Department of Biostatistics and Informatics, İstanbul, Turkey*
[4]*Bezmialem Vakıf University, Faculty of Medicine, Department of Pulmonary Diseases, İstanbul, Turkey*

Introduction: Cigarettes contain harmful chemicals leading to diseases such as lung cancer and coronary artery diseases, causing deaths globally. Smoking depletes antioxidants crucial for immune function. Inflammation involving cytokines is a natural defensemechanism. Antioxidants such as *Sambucus nigra*, curcumin, and vitamin C reduce oxidative stress. However, higher doses of antioxidants may have a potential pro-inflammatory aspect, revealing a complex relationship between antioxidants and inflammation.

Method: Human lung epithelium (BEAS-2b) cells were cultured in T25 flasks until 90% confluence at 37 °C. Cigarette smoke extract (CSE) was prepared. Tumor necrosis factor alpha (TNF-α) and interleukin-6 (IL-6) cytokine levels from CSE-stimulated cells were measured using ELISA kits. The effects of vitamin C, *Sambucus nigra*, and curcumin were tested through MTT analysis at varying concentrations. CSE-treated cells were supplemented with antioxidants, and cytokine levels were assessed using ELISA kits.

Results: After 24 h of incubation with various concentrations of CSE, the highest concentration (resulting in the lowest viability) was selected for subsequent stages. BEAS-2b cells stimulated with CSE for 24 h showed no IL-6 stimulation, and TNF-α measured positive at 6.06 ng. Antioxidant exposure for 24, 48, and 72 h yielded varying viability percentages, with higher viability rates observed in the vitamin C groups. Seven groups were selected for cytokine level analysis, and IL-6 or TNF-α stimulation was not measured.

Conclusion: The impact of substances on cells depends on dose and exposure duration. Higher vitamin C doses were correlated with lower cell viability, indicating potential pro-inflammatory effects. *Sambucus nigra* and curcumin consistently exhibited lower viability rates. Adjusting doses in future studies may clarify the healing effects. CSE uniquely increased TNF-α cytokine levels, revealing its inflammatory effects, whereas other substances suppressed inflammation, reducing cytokine levels.

Key words: Cigarette smoke, cell viability, cytokine, antioxidant

OP-7

Gamma Knife Radiosurgery for Arteriovenous Malformations: Efficiency, Outcomes, and Possible Side Effects

Mehmet Denizhan YURTLUK[1], Mehmet Hakan SEYİTHANOĞLU[2]

[1]Bezmialem Vakıf University, Faculty of Medicine, İstanbul, Turkey

[2]Bezmialem Vakıf University, Faculty of Medicine Hospital, Department of Neurosurgery, İstanbul, Turkey

Introduction: Arteriovenous malformations (AVM) can present challenges in terms of obliteration and debilitating outcomes. Stereotactic radiosurgery (SRS), embolization, and microsurgical resection can be used, but the treatment strategy should be tailored to the patient. Our study aimed to examine the effectiveness of SRS on AVMs in a large population of patients in a large size range and evaluate obliteration rates and patient outcomes after SRS.

Method: A total of 115 (74 female) patients were included, and the median age was 38 years (range: 6-73 years) for all patients. The median AVM volume was 2.9 cc (range: 0.009-49.38 cc). One hundred and three patients underwent one fraction of SRS with a median marginal dose of 20 Gy (range: 14-25 Gy), 11 patients underwent two fractions of Gamma knife radiosurgery with a median marginal dose of 16 Gy (range: 15-22 Gy) and 1 patient underwent three fractions of SRS with a marginal dose of 18 Gy. The median total follow-up period was 25 months (range: 3-72 months). Patient outcomes were evaluated using the Modified Rankin Scale.

Results: In the end, thirty-four (19 female, 30.4%) patients achieved complete obliteration in a median time of 40 months (95% confidence interval: 36-49), and the median AVM volume was 1.91 cc (range: 0.11-45.5 cc). The obliteration rate was 41%, 70%, and 85% at 3, 4, and 5 years, respectively, after one fraction or two fraction volume-staged SRS. Patients presented with various complications, including hemorrhage, seizure, and neurological deficits.

Conclusion: SRS provides a noninvasive treatment method for AVMs. Although the preferred outcome is not achieved immediately, it is a relatively safer method for suitable patients.

Key words: Arteriovenous malformation, gamma knife radiosurgery, stereotactic radiosurgery

OP-8

Role of Thrombospondin-2 in Refractory Epilepsy

Serra SAĞLAM[1], Şahabettin SELEK[2], Türkan UYGUR ŞAHİN[3], Ufuk SARIKAYA[4]

[1]Bezmialem Vakıf University, Faculty of Medicine, İstanbul, Turkey
[2]Bezmialem Vakıf University, Faculty of Medicine, Department of Biochemistry, İstanbul, Turkey
[3]Medical Park Hospital, Clinic of Pediatric Neurology, İstanbul, Turkey
[4]Bezmialem Vakıf University, Faculty of Medicine, Department of Biochemistry, İstanbul, Turkey

Introduction: Epilepsy is a common chronic disease characterized by repetitive convulsions related to sudden, abnormal discharges of neurons that unfavorably influence neurobiological, cognitive, psychological, and social abilities. Although some treatment choices, including medical and surgical procedures, exist, there are refractory cases as well. Our aim was to explain the role of thrombospondin-2 (TSP), a glycoprotein produced by astrocytes in the central nervous system, in refractory epilepsy.

Method: In this prospective study, 82 children (<18 years old) -regardless of their sex- that attended Bezmialem Vakıf University Hospital between August 2023 and January 2024 were included and classified into three groups: an epilepsy group (n=34) whose convulsions were under control with 1 drug, a refractory epilepsy group (n=28) that still had convulsions despite using two or more drugs, and a healthy group (n=20) that had no chronic disease. Children who had any chronic disease other than epilepsy or any lesion detected in cranial MR were excluded. TSP-2 levels in serum samples were analyzed using a commercial ELISA kits and compared between each group using the Kruskal-Wallis H test.

Results: Mean age was 2.17±0.66 in epilepsy group, 2.02±0.80 in refractory epilepsy group and 2.15±0.43 in control group. There was no significant difference between the mean ages of the groups (p=0.55). The mean TSP-2 level was 2.73±0.75 in epilepsy group, 2.31±0.73 in refractory epilepsy group and 1.77±0.80 in control group. There was a statistically significant difference between the TSP-2 levels of the groups (p<0.001).

Conclusion: The TSP-2 levels of both epilepsy and refractory epilepsy patients were increased, whereas the mean TSP-2 levels of the epilepsy group were higher than those of the refractory epilepsy group. Further studies are essential to confirm our results.

Key words: Refractory, epilepsy, thrombospondin-2, convulsion

OP-9

Impact of Nutritional Status, Loss of Weight or Appetite, Dysphagia, and Micronutrient Deficiencies on All-Cause Mortality in Older Patients

Elifnur AYDIN[1], Pınar SOYSAL[2], Özge PASİN[3]

[1]*Bezmialem Vakıf University, Faculty of Medicine, İstanbul, Turkey*

[2]*Bezmialem Vakıf University, Faculty of Medicine, Department of Internal Medicine, Division of Geriatrics, İstanbul, Turkey*

[3]*Bezmialem Vakıf University, Faculty of Medicine, Department of Statistics, İstanbul, Turkey*

Introduction: This study aimed to evaluate the effect of different indicators of nutritional status, including undernutrition, risk of malnutrition, malnutrition, weight loss or loss of appetite, dysphagia, and deficiencies of vitamin B12, folate, and vitamin D, on mortality in older patients.

Method: This retrospective cohort study enrolled 1911 older outpatients (81.0±13.0, 70.8% female). Mini Nutritional Assessment, Eating Assessment Tool-10, and the Council on Nutrition Appetite Questionnaire were used to determine nutritional status, dysphagia, and loss of appetite, respectively. The patient or the caregiver was asked whether the patient had lost weight in the last 3 months. Vitamin B12 and folate deficiencies were defined as <200 pg/mL and <3 ng/mL, respectively.

Results: In terms of survival analyses, the results obtained from Cox regression analysis showed that the effects of folate and B12 vitamin deficiencies on the hazard ratio (HR) were not significant ($p<0.05$), but vitamin D deficiency was related to 1.57 times higher mortality ($p<0.001$). The HR value for individuals with undernutrition, risk of malnutrition, and malnutrition were 2.94, 2.19, and 4.46 times higher, respectively ($p<0.001$). Individuals with dysphagia have a 1.83-fold higher HR ($p<0.001$). Reduced appetite leads to a 1.63 times higher HR ($p<0.001$). For individuals with a weight loss of 3 or more, the hazard risk is 2.42 times higher ($p<0.001$).

Conclusion: The results of this study show that nutritional status, loss of weight or appetite, dysphagia, and micronutrient deficiencies are associated with all-cause mortality.

Key words: Elderly patient, malnutrition, mortality

OP-10

Electrophysiology in the Early Diagnosis of Chemotherapy-Induced Distal Symmetric Polyneuropathy

Melih Mete KARAAĞAÇ[1], Zeliha MATUR[2]

[1]Bezmialem Vakıf University, Faculty of Medicine, İstanbul, Turkey
[2]Bezmialem Vakıf University, Faculty of Medicine, Department of Neurology, İstanbul, Turkey

Introduction: Many drugs used in cancer treatment exert toxic effects on peripheral nerves, often resulting in distal symmetric sensory polyneuropathy (DSP). Early diagnosis of polyneuropathy is crucial for guiding treatment. This project establishes a new electrophysiological ratio for the early diagnosis of DSP.

Method: Sixteen patients with chemotherapy-induced DSP (34-78 years) and 23 healthy volunteers (35-78 years) were included in the study. The patient group comprised cancer patients referred to the electromyography (EMG) laboratory with a preliminary diagnosis of chemotherapy-induced polyneuropathy. EMG examination involved radial, median, ulnar, superficial peroneal, sural, medial femoral cutaneous, and mixed medial plantar sensory; as well as motor nerve conduction studies. Sensory amplitude ratios, including sural/radial (SRR), medial femoral cutaneous/radial (MFCRR), and medial plantar/radial (MPRR), were calculated.

Results: All patients reported burning or numbness of the feet or hands. Neurological examination revealed hypoalgesia/paresthesia in the distal lower extremities, loss of distal deep tendon reflexes, and decreased or absent vibration sensation in the distal lower extremities. The MNST-A scores had a median of 5, and the MNST-B scores had a median of 4.5. Medial plantar responses were bilaterally absent in 10 patients and unilaterally absent in one. SRR, MFCRR, and MPRR mean values were significantly lower in patients than in the control group ($p<0.001$). MPRR demonstrated the highest sensitivity (45%) and specificity (90%) in discriminating patients from normals.

Conclusion: In this study, it was observed that chemotherapy-induced neuropathy occurs most frequently in sensory nerves, with less impact on motor nerves. The most significant impact was observed in the distal medial plantar response, which was measured at the most distal point in the lower extremities. In mild cases, MPRR was found to be the most useful ratio for differentiating patients from volunteers.

Key words: Chemotherapy, medial plantar/radial amplitude ratio, polyneuropathy, nerve conduction studies