

BEZMİÂLEM SCİENCE

5th ANNUAL MEDICAL STUDENTS' RESEARCH DAY 04 JUNE 2021

ORAL PRESENTATIONS

Guest Editor

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Investigation of Factors Affecting Daily Life Activities in Geriatric Patients

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Introduction: The world is ageing and people are living longer with their comorbid diseases which cause a decrease in functional capacity. In this study, we aimed to find out how much the functional capacities of geriatric patients were affected by specific diseases through an age classification.

Method: Age, gender, education year, number of drugs used, comorbidities of hypertension, coronary artery disease (CAD), chronic obstructive lung disease (COPD), cerebrovascular disease, chronic heart disease, peripheric vascular disease (PVDs), dementia, Parkinson's disease and osteoarthritis (OA), and functional tests were recorded. Functional tests based on the Barthel Index for Activities of Daily Living and The Lawton Instrumental Activities of Daily Living were used. The analysis was made according to the functional dependence levels and comorbid diseases of the patients.

Results: The study included 768 outpatients who were admitted to one geriatric outpatient clinic in Turkey between January 2019 and September 2020. The mean age was 79 ± 7.61 years (13.9% 60-70, 36% 70-80, 43% 80-90, 7.1% 90 and older, female 69.30%) and the mean frequency of comorbidities was 2.09 ± 1.33 . The Barthel index was evaluated through diseases, the results of CAD, COPD and PVDs (p>0.05) were insignificant, and the Lawton index, was evaluated by diseases, the results of CAD, COPD, PVDs and OA (p<0.01) were insignificant and other comorbidities were significant (p<0.01) for both indexes. Logistic regression was performed for diseases that caused a decrease in scores by adjusting for age, comorbidities, gender and education level. Logistic regressions of Barthel index and Lawton index found the following to be a significant risk of full dependency: dementia [odds ratio (OR): 12.9; 95% confidence interval (CI) -18.9 \pm -6.9)] (OR: -5.27; 95% CI -7.08 \pm -3.46) (p<0.05), Parkinson's disease (OR: -23.85; 95% CI -31.32 \pm -16.38) (OR: -3.77; 95% CI -6.02 \pm -1.52) (p<0.05).

Conclusion: Urinary incontinence is a problem that starts before the age of 65 years, and neurodegenerative diseases cause a diffuse decrease in daily living activities. Further investigations should be done in line with these results.

Key words: Disability, comorbidities, age classification



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The Potential Role of Alternative Transcript Isoforms in Developmental Gene Expressions in Ants

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Introduction: Alternative transcript isoforms can differ in their translated and/or untranslated regions (UTRs), which can lead to differences in proteins or their expression. Alternative UTRs can affect a gene's function through their effects on the subcellular localization and the timing of their translation. In ants, the highly conserved Homeobox containing transcription factors *Ultrabithorax* (*Ubx*) and abdominal-A (abd-A) has acquired novel spatiotemporal expression patterns and roles, in addition to their conserved expression and function. The highly specific novel subcellular localizations of *Ubx* and abdA transcripts have been shown to be involved in early embryonic patterning and the developmental integration of cellular endosymbionts into their hosts. These data suggest the possibility of structural differences in the transcripts of different developmental-stage specific expressions of these genes. This project aims to determine whether alternative transcript dependent mechanisms have played any role in the evolution of novel gene expressions and functions of *Ubx* and abdA.

Method: Camponotus floridanus embryos were collected and separated into two developmental stage specific groups (stage 1 and 12; n=10 per stage). Total RNA was obtained using the TRIzol method for each stage. cDNA libraries were synthesized using reverse transcriptase and Rapid Amplification of cDNA Ends was conducted to acquire Ubx and abdA transcripts. The obtained transcripts were DNA sequenced and were aligned to the annotated gene sequences using Muscle algorithm.

Results: The protein-coding sequences that we obtained from developmental stage-specific transcripts of Ubx and abd-A were discovered to be near identical. The discovered minor differences were interpreted to be due to Sanger sequencing.

Conclusion: The results suggest that the origin of the novel expression is a result of changes in either the untranslated regions or the cis-regulatory sequences of these genes. Future studies will unravel the origin of novel functional changes in these genes.

Key words: Hox genes, alternative transcript isoforms, embryonic development



Investigation of Cytotoxic, Genotoxic and Apoptotic Effects of Thymoquinone-oxime on Glioma Cells

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Introduction: Glioma is one of the malignant tumors of the brain. Although many studies have been carried out so far to treat glioma and to increase the survival time, an effective method has not been found yet, and treatment is difficult. It is known that Thymoquinone (TQ), an important bioactive component of black seed (*Nigella sativa*) oil, has antioxidant, anti-inflammatory, and antineoplastic effects. The lipophilic structure and low molecular weight of TQ passes through the blood-brain barrier. Although it showed toxicity against cancer cells in *in vitro* studies, the expected effect was not seen *in vivo* models. Therefore, it is the aim of our project to examine the cytotoxic, genotoxic, and apoptotic effects of TQ-oxime (TQ-ox), which will be obtained by chemical synthesis, on gliomas in vitro.

Method: In this study, we used mouse glioma cell line: GL261. We synthesized TQ-ox from TQ. Then the structure was confirmed with nuclear magnetic resonance. After 24h incubation, we determined cytotoxicity and glutathione (GSH) by different luminometric methods, iROS, and iCa^{2+,} by different fluorometric methods, mitochondrial membrane potential (MMP) by flow cytometry, DNA damage by comet assay, apoptosis by fluorescence microscopy. SPSS 25 was used for statistical analysis.

Results: When TQ and TQ-ox were evaluated together, the cytotoxic, genotoxic, and apoptotic effects of TQ-ox were found to be significantly (p<0.001) higher than TQ. While cytotoxicity, DNA damage, apoptosis, iCa $^{2+}$, and iROS levels increased significantly (p<0.001) in both TQ-ox and TQ, GSH and MMP levels decreased significantly (p<0.001) with increasing dose.

Conclusion: According to the results, we propose that TQ-ox has cytotoxic, genotoxic, and apoptotic effects on glioma in a dose-dependent manner, and therefore, TQ-ox can be one of the options that can be used for glial cancer treatment.

Key words: Glioma, thymoquinone, thymoquinone-oxime, cytotoxicity



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Investigation of *in vitro* Wound Healing Properties of Metformin and Coenzyme Q10

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Introduction: Previous studies have shown that Metformin and Coenzyme Q10 (CoQ10) increase fibroblast cell proliferation, collagen synthesis, and epithelization in wound healing process. This study aimed to observe wound healing, antioxidant and anti-inflammatory activities of Metformin and CoQ10 on cultured human dermal fibroblasts and keratinocytes.

Method: Single and combined doses of Metformin and CoQ10 were examined separately in dermal fibroblasts and keratinocytes. Initially, anti-genotoxicity, anti-apoptotic effects, intracellular ROS, intracellular calcium, and glutathione levels were investigated. Afterward, the wound model was created using the CytoSelect™ 24-Well Wound Healing Assay plate and apparatus. Metformin and CoQ10 were applied to the model after 24 hours of incubation. The migration/proliferation of cells and wound closure areas were recorded at different times, and the dose/response ratio was evaluated by calculating the wound area. The supernatants of the 24-plate wound model were collected at 24 hours, and growth factors [(epidermal growth factor (EGF), vascular endothelial growth factor (VEGF)] and inflammatory [interleukin (IL)-1β, IL6, TNFα)] biomarkers were measured.

Results: After the 24-hour incubation of Metformin and Coenzyme Q10 in single and combined doses in dermal fibroblasts and keratinocytes, the maximum proliferating doses were found to be 100 μ M for both substances. In all groups, the inflammatory biomarkers including IL1 β , IL6, and TNF α decreased by the increasing doses of Metformin and CoQ10, while the levels of EGF and VEGF increased significantly (p<0.001). The wound areas were reduced considerably by the increasing doses of Metformin and CoQ10 in both single and combined cell groups of fibroblasts (p<0.001) and keratinocytes (p<0.001).

Conclusion: Increasing single and combined doses of Metformin and CoQ10 were found to be effective in reducing inflammation and increasing proliferation in *in vitro* wound model. Further formulations and animal studies should be conducted to obtain better knowledge.

Key words: Metformin, cell culture, Coenzyme Q10, wound healing



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The Investigation of the Effectiveness of *Urtica Dioica* in the Streptozotocin-Induced Neurodegeneration Model

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Introduction: Nowadays, researches of phytotherapeutics for preventing the Alzheimer's disease (AD)-related neuronal damage have gained momentum. *Urtica dioica* (UD) is one of these phytotherapeutics because of its memory-improving effect. Therefore, we aimed to investigate the effects of UD on the hippocampus of streptozotocin (STZ) induced-rats.

Method: The rats were divided into the control, sham control, STZ (3 mg/kg, i.c.v) and STZ-UD [STZ injection and oral administration of UD (50 mg/kg/day)] groups. Morris Water Maze (MWM) and Passive Avoidance Task were applied for cognitive functions. After behavioral experiments, the concentrations of proteins related to AD pathology (PSEN, pTau, Amyloid beta, BACE, reelin) and the functioning of hippocampal tissue (nNOS, brevican, CAMKII, prealbumin, NMDR) were examined in hippocampus.

Results: In the MWM training, UD treatment attenuated STZ-induced learning deficiencies (p<0.05). On the MWM probe trial and the passive avoidance task which measured the memory capacity, no significant differences were observed among the groups. According to Nissl staining results, STZ injection decreased the number of neurons and UD treatment increased the viable neurons in hippocampus. At the molecular analysis, there was no change in the amount of PSEN both due to STZ injection and UD treatment. Compared to the control groups, STZ injection increased the amount of BACE and nNOS (p<0.005) which were ameliorated by the UD treatment (p<0.05). Due to STZ injection, the level of prealbumin which could "sequester" A β to prevent neuronal damage decreased (p=0.030). In addition, STZ injection disrupted the normal functioning of hippocampus by decreasing the level of CAMKII and NMDR which were responsible for learning and memory signaling mechanisms (p<0.001). The treatment effect of UD was especially observed in these proteins and the level of cytoskeletal protein Brevican.

Conclusion: UD has a neuroprotective role in the functioning of the hippocampal neurons to recover the neuropathology of AD by restoring neuron viability.

Key words: Alzheimer's disease, streptozotocin, urtica dioica, neuroprotective, rat



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Research of Chronotype and Sleep Quality in Infertile Population and Comparison with Non-infertile Population

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Introduction: In humans, the sleep-wake cycle, body temperature, hormone levels, affect and some cognitive functions depend on a daily rhythm called circadian rhythm. This circadian rhythm determines a person's chronotype. Chronotype refers to the period of the day when the person is physically and cognitively active and is divided into three types: morning, evening, intermediate type. There is not enough data about the effect of chronotypes in the infertile population and whether they affect the treatment.

Method: The MEQ morningness-eveningness questionnaire was used to determine chronotypes. Pittsburgh Sleep Quality Index which provides a quantitive measurement of sleep quality, was used to define good and bad sleep. One hundred three infertile and 103 fertile patients who participated in this study were divided into groups according to their MEQ and PSQI scores, and they were compared in terms of disease severity based on the clinical data we have collected.

Results: Two hundred twenty seven patients that met the inclusion criteria were enrolled for the study. The mean PSQI score of infertile women and healthy fertile women were, 5.00 ± 2.11 , 4.00 ± 1.54 respectively. There are a significant differences in the mean PSQI score of women between groups (p<0.001). In terms of subcategories PSQI score, sleep latency, sleep duration, sleep efficiency scores were significantly different between the groups (p<0.05), others were insignificant. The mean MEQ score of infertile women and healthy fertile women were, 50.00 ± 9.17 , 56.00 ± 6.87 respectively. There are a significant differences in the mean MEQ scores of women between groups (p<0.001).

Conclusion: The results showed that poor sleep quality with a high PSQI score and an evening-type with a low MEQ score are associated with a high prevalence of infertility. The results revealed that there is a potential connection between these two conditions and infertility. More extensive research should be done to confirm these results and to demonstrate the impact of chronotype and sleep quality on fertility success.

Key words: Infertile, chronotype, sleep quality



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The Effect of Augmented Reality Technology on Preoperative Anxiety in Children and Parents

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Introduction: The surgical operations may cause serious anxiety in children, leading to physiological and psychological problems. Some techniques are used to reduce pre-surgical anxiety. This study aims to analyze the effect of pre-surgical use of augmented reality technology in children on child and parental anxiety.

Method: Thirty-nine children between the ages of 4 and 11 years, who would undergo a surgery, and their parents were included in this study. Participants were divided into 2 groups: a study group of 18 children and the control group of 21 children. The study group did painting and saw their pictures in the form of augmented reality while the control group did nothing. Afterwards, we assessed the anxiety levels of children through Modified Yale Preoperative Anxiety Scale (mYPAS), and of parents through the State Trait Anxiety Inventory (STAI). Also, saliva samples were taken before and 20-35 minutes after the application in the study group and every 20-35 minutes in the control group.

Results: It was observed that the anxiety level (Total mYPAS score) of children in the control group was significantly higher (p=0.01). The "vocalization" and "emotional expression" categories of the mYPAS were found to be significantly higher in the control group. Although the state score indicating the level of anxiety in the STAI was lower in the study group than in the control group, no significant difference was observed (p>0.05). While there was a significant decrease between the 1^{st} and 2^{nd} salivary cortisol values in the study group (p=0.01), there was no significant decrease in the control group.

Conclusion: The fact that, in the study group, the stress level was found to be significantly less with the mYPAS and that the salivary cortisol level significantly decreased showed that the use of augmented reality technology could reduce children's anxiety preoperatively.

Key words: Augmented reality, anxiety, salivary cortisol, child surgery



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The Importance of Postpartum Kleihauer-Betke Test in Low Risk Rh-Incompatible Pregnant Population

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Introduction: Prevalence of Rh disease is estimated to be 276 per 100,000 live births, which is significant considering its relationship with conditions like fetal anemia, hydrops fetalis, fetal death and recurrent fetal demises in future pregnancies. In order to prevent these, anti-D immunoglobulin should be given after inciting events, in a dose sufficient. In Turkey and some other countries, anti-D dose is given on "one shot fits for all" principle. Here, we challenge the conventional wisdom and evaluate the amount of fetomaternal hemorrhage (FMH) and adjusted the dose of anti-D accordingly.

Method: In our study, Rh incompatible women who gave birth between October 2020 and March 2021 were included. FMH was determined by the Kleihauer-Betke test in the blood sample taken from the mothers after delivery. Blood smears were fixed with ethyl alcohol and incubated in citric acid buffer solution. In acid medium, HbF becomes resistant to elution, while other types are removed from erythrocytes. The smears are then taken under a microscope to examine the percentage of cells containing fetal hemoglobin. We used Oski-Naiman method to count fetal cells present, then estimated FMH using Mollison's formula. Clinical data were available at hospital's digital system.

Results: Seventy patients got tested during study period. Twenty-five (39.6%) of cases had more than 4 mL of FMH. Among them, one (1.6%) case was found to have more than 30 mL of FMH, and was given an additional dose. This case had no obstetrical risk factor such as antepartum bleeding, preeclampsia, or manual removal of placenta. The rate of smoking was significantly higher in cases with more than 4 mL of FMH (p=0.001). There were no other variables differed significantly in women having more than 4 mL of FMH.

Conclusion: FMH requiring more than 300 mcg of anti-D is significantly high in low-risk pregnant women in Turkey. Implementation of quantitative FMH testing with Kleihauer-Betke or flow cytometry test is necessary.

Key words: Fetomaternal hemorrhage, Rh incompatibility



Oxidative Stress and Neural Damage Parameters in Parkinson's Disease

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Introduction: Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by motor symptoms and loss of dopaminergic neurons in the substantia nigra pars compacta (SNpc) and accumulation of alpha synuclein (α Syn). There is no diagnostic test for PD, so the diagnostic criteria of PD are highly dependent on the typical motor symptoms which manifest long after the beginning of the pathology in SNpc. This research aims to study biochemical parameters such as α Syn and free radicals that might be helpful in the early diagnosis of PD and thus, to make preventive treatment possible.

Method: Sixty-two patients with PD and 62 healthy individuals with similar ages and genders were enrolled in the study. Blood samples were collected from participants and the levels of plasma αSyn were measured using ELISA. Total antioxidant status and total oxidant status were measured using TRAP assay. Iron (Fe), high density lipoprotein, low density lipoprotein, and triglyceride levels were measured with routine biochemical methods. The levels of the parameters were compared between patients and healthy individuals. The results were also compared within the experimental group in terms of the duration of the disease, treatment methods, and Hoehn-Yahr scale.

Results: The plasma levels of α Syn oligomer in patients were significantly higher than in healthy individuals (p<0.001). Plasma Fe levels were significantly lower in the experimental group (p<0.05). A positive correlation between the duration of the PD and plasma α Syn, and LDL levels was found in the experimental group (p<0.05).

Conclusion: Plasma α Syn and Fe levels might be helpful in the early diagnosis of PD. α Syn and LDL may illustrate more severe prognosis of the disease.

Key words: Early diagnosis, Parkinson's disease, a-synuclein, oxidative stress



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Ideal Unclamping Order at Carotid Endarterectomy Procedures: Ex Vivo Study

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Introduction: Higher than 70% stenosis of the carotid artery poses a significant risk for stroke. Carotid endarterectomy (CEA) is a standard procedure for carotid artery stenosis. However, it carries a high risk for mortality and morbidity. The risk of perioperative embolism has been shown to be 1-3%. The unclamping procedure is one of the most critical stages. Different authorities use different sequences. After all, there is no consensus. This study aims to indicate the ideal order of unclamping the carotid arteries to prevent a cerebrovascular accident, to emphasize this matter, and to be a reference to this desideratum.

Method: In this study, 5 Bovine aortic bifurcations, which represented common carotid artery (CCA), internal carotid artery (ICA) and external carotid artery (ECA), have been prepared. Aorta and iliac artery pieces were carefully removed and prepared upon special request from animals slaughtered for consumption. Collateral branches on the arteries were ligated with surgical silk ties. CCA has been tied to the pump via a transparent medical grade PVC tube. ICA and ECA were tied to the lip of the balloons with T infusion connectors. Fifteen beads with a diameter of 2 mm representing the remnant tissue were taken into the system. All arteries were clamped with vascular clamps. Seven combinations, including one textbook combination, were used, and unclamping alternatives were examined ten times for each combination. The same beads were used throughout the entire experiment, and it was ensured that all 15 beads were present each time. 10 seconds after unclamping, the number of beads was recorded. A total of 3 vessels were used due to deformation for this procedure.

Results: The number of beads in the ICA median value was 4. The number of beads distributed in ICA had a statistically significant difference between each combination (p<0.001). The statistically significant difference occurred between 1st and 2nd combinations (p<0.001), 1st and 4th (p=0.001), 1st and 7th (p<0.001), 2nd and 5th (p=0.025), 3rd and 4th (p=0.008), 3rd and 7th (p=0.002). After getting the post hoc test results, it was found out that the best combination among the combinations formed was the 2nd combination which had the lowest median value 3.

Conclusion: Considering the statistical data obtained, a significant difference has been demonstrated among combinations. The combination with the CCA-ECA-ICA unclamping sequence has preferable results in terms of remnant tissues leading to ICA and causing a potential stroke. According to the result, the CCA-ECA-ICA unclamping sequence would be recommended during CEA procedures.

Key words: Carotid endarterectomy, embolism, stroke, clamping



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