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OP-1

The Effect of Tocilizumab Use on Antibody Level in COVID-19 patients

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Introduction: Severe acute respiratory infection-coronavirus disease-2 (SARS-CoV-2) causes a hyper-inflammatory response associated with a Macrophage Activation Syndrome (MAS). The use of tocilizumab for treating MAS may affect the level of antibodies. In this study, we investigated whether tocilizumab could affect the antibody response in patients.

Method: Fifty-five coronavirus disease-2019 (COVID-19) patients who developed MAS and 55 patients who did not develop MAS were included in the study. There were 25 patients using tocilizumab in the MAS group. We used the blood, which was taken at the time of discharge. Spike antibodies against COVID-19 were examined from the collected blood. The SARS-CoV-2 immünglobulin G (Abbott, USA) commercial kit will be studied quantitatively with the incandescent microparticle immune analysis (CMIA) method on the Architect i1000 (Abbott, USA) device. Statistical analysis was performed using the student t-test.

Results: There was no statistical difference between the MAS group and the control group. High-level antibody response was statistically higher in the MAS group (>5,000) ($p<0.05$). However, there was no statistical difference in the antibody response between patients who used and did not use tocilizumab ($p>0.05$).

Conclusion: MAS group has increased antibody response. There was no evidence that the use of tocilizumab altered the antibody response. Large-sample studies are needed for more precise effects of tocilizumab.

Key words: Tocilizumab, COVID-19, MAS, antibody response

OP-2

Investigation of Cytotoxic, Apoptotic and Genotoxic Effects of Different Concentrations of Mulberry Seeds (Peganum harmala) Extract on Human Colon Cancer Cells

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Introduction: Colorectal cancer it is the third most common cancer in the world. Peganum harmala active ingredient, whose anti-cancer and immunomodulatory effects have been demonstrated *in vitro* and *in vivo* studies, is a candidate molecule that can be used as an alternative to conventional cancer treatments. In this study, we will investigate the cytotoxic, apoptotic and genotoxic effects of Peganum harmala on human colon cancer cells.

Method: *Peganum harmala seed extract (PHSE)* has been prepared with 80% MeOH:dH_2O solution for two days, MeOH was evaporated by vacuum evaporator and then lyophilized. HT29 colorectal cancer cells and healthy colon epithelial cells (CCD-1072) were incubated with different concentrations of PHSE (200–900 ug/mL) for 24 h. MTT assay was used to measure cytotoxicity of *PHSE* on each cell line. A fluorescent probe, H_2DCF-DA, was used to measure the levels of intracellular reactive oxygen species. Apoptosis was measured using the AO/EB dye using fluorescence microscope. The effect of *PHSE* on DNA damage was evaluated by alkaline single cell gel electrophoresis (Comet assay method) modified by Singh et al.

Results: Peganum harmala seeds extract decrease cell viability and increased intracellular ROS formation in HT29 and CCD cells. The genotoxicity of *PHSE* on colon cancer increased significantly by concentration-dependently damaging the DNA. 300ug/mL and 500 ug/mL doses of *PHSE* showed higher genotoxicity than the control, respectively. Also, it has higher genotoxicity in colon cancer compared to healthy cell.

Conclusion: The results of this study show that the Peganum harmala extract increased intracellular ROS generation in HT29 and CCD cells. It caused the formation of apoptotic and necrotic cells in the body. The Peganum harmala extract showed higher genotoxicity than the control.

Key words: Colon cancer, peganum harmala, cytotoxicity, genotoxicity, apoptosis

OP-3

Comparison of Renal and Metabolic Effects of Empagliflozin and Dapagliflozin on Type 2 Diabetes-Induced Rats

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Introduction: Diabetes mellitus is a disease that affects millions of people worldwide. Extensive randomized clinical studies are ongoing on SGLT-2 inhibitors, Empagliflozin and Dapagliflozin, in patients with heart failure and chronic renal failure. The aim of this study is to investigate the equivalence and superiority of different SGLT2 inhibitors by comparing the metabolic and renal effects.

Method: Six week old 44 male Sprague-Dawley male rats were divided into four groups treatment, placebo and control. Throughout the trial, rats had unrestricted access to food and water (ad libitum) and were kept at a standard temperature, humidity and light level.

Streptozotocin was given intraperitoneally after a two-week high-fat diet, and groups were randomly divided based on mean glucose levels. Dapagliflozin and Empagliflozin were administered daily at 13:00, for 1 month. Blood samples and glucose levels were measured at certain intervals. For all groups, urine samples were collected before the treatment and after 1 month of treatment with metabolic cages. Urine samples were analysed with nuclear magnetic resonance.

Results: The Empagliflozin-treated group had considerably decreased blood glucose levels as compared to the Dapagliflozin-treated group ($p<0.001$). In comparison to the placebo group, blood urea nitrogen showed a significant decrease in the Dapagliflozin ($p=0.001$) and Empagliflozin treatment groups ($p<0.001$). Levels of urinary protein and microalbumin increased in the Placebo and Dapa-treated groups ($p=0.002$ and $p=0.006$), but not in the Empa-treated group.

Conclusion: According to the first-ever head-to-head animal model to assess distinct molecules in the same class of SGLT-2 inhibitors, Empagliflozin outperforms Dapagliflozin in terms of blood and urine parameters.

Key words: Empagliflozin, Dapagliflozin, SGLT-2 inhibitor, NMR analysis, diabetic rats

OP-4

Metastatic Breast Cancer: Can Risk of Metastasis be Predicted Through Digital Pathology Images Assessed by Machine Learning?

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Introduction: Breast cancer (BC) is the most frequent malignancy in women worldwide and is curable in ~70%-80% of patients early-stage, non-metastatic disease. Advanced BC with distant organ metastases is considered incurable with currently available therapies and associated with low overall survival. Therefore, the prediction of metastases after resection is clinically important. Detecting metastatic BC earlier and administering new targeted therapies at these earlier timepoints might improve survival and might be our best opportunity to improve patient outcomes.

Method: ***Sample information:*** We included 15 early primary BC and 15 advanced primary BC (in total 30) female patients who underwent mastectomy or breast conserving surgery in Bezmialem Vakıf University. The patients were categorized into two groups: Group 1, early-stage BC patients (12 for training and 3 for test); Group 2, advanced BC patients (12 for training and 3 for test). ***The region of interest (ROI) selection and image size:*** Formalin-fixed, paraffin-embedded HE-stained slides were scanned using BioTek Cytation 5 at x20 image magnification. Under x20 image magnification, 20 and 10 ROIs per sample were selected and annotated by a pathologist in BC and surrounding non-BC areas, respectively. ***ROI feature measurement:*** The morphological features of the ROIs were analyzed using QuPath (https://qupath.readthedocs.io/en/stable/docs/intro/about.html). Each ROI contained 232–1115 nuclei.

Results: We analyzed the nuclear information belonging to Group 1 and Group 2 with 85 QuPath outputted nucleus features. The support vector machine-based prediction method separated the two groups with 91% accuracy.

Conclusion: There has been no other method to predict BC metastases except clinical observations. We developed a metastasis prediction method based on machine learning by using nuclear information (average, standard deviation, heterogeneity) of BC patient tissues. We believe with a featured microscope for digital imaging and bigger sample size, higher accuracy value can be met. Our method shows promise as a novel follow-up method to review the frequency of imaging and determine the need for additional treatment.

Key words: Machine learning, AI, breast cancer, digital pathology

OP-5

Relationship of Carotis Lesions with Thyroid Diseases

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Introduction: Thyroid gland has critical functions for our body with the hormones it secretes. Thyroid gland dysfunction is associated with cardiovascular diseases. Cardiovascular events related to atherosclerotic plaques are seen in patients with abnormal thyroid-stimulating hormone values. Our study aims to examine the relationship between carotid lesions and thyroid diseases.

Method: Computed tomographic angiography (CTA) was used to collect data. All CTA scans were performed on a 128-row multidetector CT scanner (Somatom Definition, Flash; Siemens Healthcare, Erlangen, Germany). The plaques formed in the carotid interna artery were analysed as soft, calcific, and mixed type. It was determined on which side the plaques were located. The relationships between these patients with hypertension, diabetes, hyperlipidemia and smoking were examined. The normal TSH value of these patients was evaluated as 0.5–4 mIU/L and T4 value as 0.6–12 mIU/L. Values in between were evaluated as subclinical. The relationship of carotid plaques between subclinical and clinical hypothyroidism and hyperthyroidism was examined.

Results: Ninety patients aged between 18 and 80 years were analysed with CTA. 54 of 90 patients were male and mean age was 61,57. Results of plaque types: Normal 36.7%, Calcific 38.9%, Soft 4.4%, Mixt 20%. Results of side: Normal 36.7%, Right ICA 5.6%, Left ICA 10%, Bilateral 47.8%. Results of hypertension (HT), diabetes mellitus (DM), hyperlipidemia (HL) and cigarette: HT 64.4%, DM 62.2%, HL 31.1% and cigarette 17.8%. Results of thyroid clinical outcomes: Normal 33.3%, Subclinical hypothyroidism 2.2%, Subclinical hyperthyroidism 50%, hyperthyroidism 11.1% hypothyroidism 3.3%. The result we obtained is subclinical, and clinical hypothyroidism and hyperthyroidism do not differ in meaning.

Conclusion: In conclusion, thyroid gland dysfunction is related to carotid plaque formation. However, the types of plaque may not be correlated to the level of TSH.

Key words: Carotid lesions, plaque, hypothyroidism, hyperthyroidism, CTA

OP-6

The Effect of Bemiparine Na and Hyaluronic Acid on Postoperative Adhesions in Rat Uterine Horn Model

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Introduction: Pelvic adhesions are abnormal fibrous connections between tissues and are one of the main causes of infertility. Barrier agents prevent the formation of these adhesions. Low-molecular-weight heparin has an effect that inhibits adhesion formation by decreasing the thrombin formation. This study aims to observe the independent effects of Bemiparine Na and hyaluronic acid (HA) on pelvic adhesion formation, and to observe the possible synergistic effects of their combined use.

Method: Twenty non-pregnant female Sprague-Dawley rats weighing 180–220 g were used for postoperative adhesion formation. The rats were randomized into four groups after ten standard lesions were inflicted in a right uterine horn using bipolar cauterization with 10w power. The rats were treated with 700 U Bemiparine Na, 0.5 mL HA and both agents. No medication was given to the control group. The uterine horns of 20 rats were evaluated for the type, tenacity and extent of the adhesions and fibrosis. Vascular endothelial growth factor (VEGF) and TGF-B immunohistochemical stains were studied on the tissue samples.

Results: Macroscopic adhesion scores, including type, extent and total scores in the Bemiparine Na+HA group were significantly lower than those in group Control and group HA ($p<0.05$). Among these three categories of scoring, group Bemiparine Na + HA had a significantly lower score than group HA in adhesion type ($p<0.01$) and group Bemiparine Na had a slightly lower score than group HA in adhesion extent ($p<0.05$). There were no statistical differences across all four groups in the microscopic inflammation, fibrosis, and immunohistochemistry staining.

Conclusion: Thus, Bemiparine Na and HA combination is effective on pelvic adhesions by macroscopic evaluation but there were not significant differences between groups in terms of immunohistochemistry and microscopic evaluation.

Key words: Pelvic adhesions, bemiparine Na, hyaluronic acid, VEGF, TGF-B

OP-7

COVID-19 Associated Sleep Disorders and the Role of Inflammation in the Pathogenesis

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Introduction: Coronavirus disease-19 (COVID-19) activates the inflammatory pathways and have high levels of circulating tumor necrosis factor (TNF)-α, interleukin (IL)-1β, IL-6, IL-10. Insomnia is a common sleep disorder in COVID-19 patients. Previous research has demonstrated that extreme elevations in IL-1β and TNF-α can impair sleep. Based on these findings, we hypothesized that COVID-19 and insomnia cooperation developing on an inflammatory background. Our purpose is to research immunopathologies of insomnia and COVID-19 patients and to reveal their association.

Method: The number of people participating in this study was determined as 96. Three groups: 1) COVID-19 patient with insomnia, 2) COVID-19 patient without insomnia, 3) Healthy people were designed. Socio-demographic Form, Epworth Sleepiness scale (ESS), Pittsburgh Sleep Quality index (PSQI), Beck Anxiety Inventory (BAI), Insomnia Severity index (ISI) was applied. BDNF, IL-6, TNF-α, IL-1β, IL-10, MMP-9 levels were measured in the volunteers' blood.

Results: Based on blood samples from 96 volunteers; BDNF ($p<0.001$), IL-6 ($p<0.001$), TNF-α ($p<0.001$) ($p<0.036$), IL-1β ($p<0.001$), IL-10 ($p<0.001$) values were shown a significant difference in insomnia patients compared to COVID-19 patients without insomnia and control group ($p<0.001$). Insomnia patients were increased cytokine levels than the other groups. Wherewithal COVID-19 patients without insomnia were increased cytokine levels than the control group. MMP-9 levels were not shown a significant difference between insomnia patients compared to COVID-19 patients without insomnia ($p=1$). But MMP-9 levels were not shown a significant difference between the control group and COVID patients ($p<0.001$). ESS, PSQI, BAI, ISI scores were shown a significant difference in insomnia patients compared to COVID-19 patients without insomnia and control group ($p<0,001$).

Conclusion: Based on the data obtained, the basis of insomnia is inflammatory pathogenesis. Insomnia patients had increased inflammatory cytokines and PUKI, BAI, ESS, ISI scores. Our results should be confirmed with further experimental and clinical studies.

Key words: COVID-19, insomnia, cytokines

OP-8

Quorum-Sensing Inhibition by Furanone Compounds and Therapeutic Effects on *Pseudomonas Aeruginosa* Keratitis Rabbit Model

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Introduction: Keratitis is the inflammation of the cornea and associated with both infectious and non-infectious diseases. A mechanism called Quorum Sensing (QS) is the communication between bacterial cells reliant on cell density and the concentration of specific signaling molecules. Inhibitors of QS are an advanced strategy discovered to decrease *P. aeruginosa* pathogenesis and its virulence. Based on the previous studies and proven effects of furanones as a QS inhibitor on pseudomonas infection, this study aims to investigate QS inhibition by furanone compounds in *P. aeruginosa* keratitis rabbit model.

Method: Thirty adults New Zealand white rabbits were used in this study. Corneas of anesthetized rabbits were intrastromally injected with bacteria. Rabbits were randomly divided into six groups. Control group only infected with *P. aeruginosa*. Starting 1 hour after inoculation 0.1 mg/mL (B), 0.2 mg/mL (C), 0.3 mg/mL (D) Furanone, 50 mg/mL ceftazidime (A) and 20% dimethyl sulfoxide (E) were used with one drop per hour. Rabbits were sacrificed 3 days later and corneas were collected.

Results: Collected samples were evaluated clinically, histologically and biochemical. In all evaluations, the therapeutic response in the antibiotic group was better than other groups. Slit lamp examination score of Group C was significantly lowered compared to the control ($p=0.009$). Histological evaluation shows that inflammation is decreased in B, C, and D groups. Reactive oxygen species values were significantly lower in group B ($p=0.001$) and C ($p=0.01$). And there was no statistical significance among Superoxide dismutase values.

Conclusion: The comprehensive findings demonstrate that furanone showed an anti-inflammatory effect. However, its therapeutic effect has not been observed to be sufficient compared to antibiotics. Further investigation is necessary to explore the protective effects and mechanism of furanones on pseudomona keratitis.

Key words: Keratitis, *P. aeruginosa*, quorum-sensing, furanone

OP-9

Whole Genome Sequencing Analysis of *Neisseria gonorrhoeae* Isolates From Turkey: An Observational Study

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Introduction: *Neisseria gonorrhoea,* the agent of sexually transmitted infections, remains a major public health concern. Whole genome sequencing (WGS) of the agent can provide insights on antimicrobial resistance, pathogenicity, and epidemiology of the bacteria, among others. The aim of this study is to sequence and characterize the whole genome of nine *Neisseria gonorrhoeae* strains and to understand their epidemiological origins, and the resistance determinant genes.

Method: *N. gonorrhoeae* strains were obtained from different clinical microbiology laboratories. The isolates were cultured on Thayer-Martin medium and antimicrobial susceptibility test was done using disk diffusion method. DNA was extracted from bacterial suspensions using the DNA Kit and WGS sequencing was done. Genes involved in antimicrobial resistance were detected using various bioinformatics tools. Phylogenetic analysis based on 50S ribosomal protein L6 was carried out to determine the evolutionary origin of the isolates. Basic Local Alignment Search Tool search with the protein identified close homologs, which were aligned for maximum likelihood tree generation (bootstrap of 100).

Results: Six of the *N. gonorrhoeae* isolates were susceptible to ceftriaxone and three of them were resistant or intermediate to penicillin. All *N. gonorrhoeae* isolates possessed *norm, mtrC, mtrR, mtrF, mtrA, farB, DfrA42, macA,* and *macB* genes as genetic resistance determinants. Only one isolate contained *tetM* gene, a tetracycline-resistant determinant. Phylogenetic analysis revealed that our strains formed a statistically significant clade with isolates from Korea, Canada, USA and Russia.

Conclusion: The nine *N. gonorrhoeae* strains circulating in Turkey do not appear to pose a significant threat to public health since they do not have any novel antimicrobial resistance features. Phylogenetic analysis revealed that our clinical strains share common origin with isolates from diverse regions of the world.

Key words: *N. gonorrhoeae,* whole genome sequencing, antimicrobial resistance, evolution

OP-10

Investigating the Role of Biomarkers Using Liquid Biopsy for Diagnosis and Surveillance in Meningioma Patients

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Introduction: Meningiomas are the most common primary brain tumors in adults. The diagnosis of meningioma can be made using magnetic resonance imaging of brain. However, there are difficulties differentiating the grades of the tumor, which is important for choosing the right treatment (follow, surgical resection, Gamma Knife) and extent of tumor resection if surgery is preferred. However, there is no established method for meningioma grading. Although the expression of c-MYC, FABP7, GATA4, and MAOB have been investigated in meningioma tissues, their expression in serum has not been described. Therefore, this study aimed to evaluate the role of liquid biopsy by investigating the expression of these genes in meningioma patients.

Method: Twenty patients who underwent surgical resection of intracranial meningiomas were enrolled. Tumor and serum samples were obtained during the surgery. Real time polymerase chain reaction was performed to assess the expression of FABP7, GATA-4, c-MYC, and MAOB in tumor tissue and in serum. Patients' clinical data including age, gender, radiological findings, simpson grade were retrospectively collected.

Results: The expression levels of FABP7 and MAOB in serum of meningioma patients were significantly higher than healthy controls ($p<0.05$). The expression levels of MAOB in serum of grade 2 meningioma were significantly higher than those with grade 1 ($p=0.032$). *MAOB, c-MYC* and *GATA4* genes were expressed significantly higher ($p=0.031$, $p=0.041$, $p=0.003$,respectively) in tumor tissues from grade 2 meningioma patients compared to grade 1. We did not observe any of these genes to be correlated with patients' clinical data and local tumor control.

Conclusion: Our results suggested that expressions of *FABP7* and *MAOB* genes in serum could be implemented as diagnostic marker for meningiomas. However, further studies are required.

Key words: Biomarker, liquid biopsy, meningioma