

Volume 70 | Supplement 1 | 2024

ACTA MARISENSIS SERIA MEDICA

OFFICIAL PUBLICATION OF THE

GEORGE EMIL PALADE UNIVERSITY OF MEDICINE, PHARMACY, SCIENCE, AND TECHNOLOGY OF TARGU MURES



UMFST – UMCH RESEARCH DAY

March the 15th 2024
Hamburg, Germany

BOOK OF ABSTRACTS

ISSN: 2668-7755 • Online ISSN: 2668-7763 • www.actamedicamarisensis.ro



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The journal publishes high-quality articles on various subjects related to research and medical practice from the all the medical and pharmaceutical fields, ranging from basic to clinical research and corresponding to different article types such as: reviews, original articles, case reports, case series, letter to editor or brief reports. The journal also publishes short information or editorial notes in relation to different aspects of the medical and academic life.

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EVALUATING THE IMPACT OF ALCOHOL CONSUMPTION IN WOMEN ON MENSTRUAL BLEEDING PATTERN

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Background: Every month 1.8 billion women menstruate; this means over 800 million girls and women menstruate every day. Taking up quite an important and dominant role in a woman's life, menstrual complaints may greatly influence their quality-of-life. The menstrual cycle is greatly dependent on hormonal homeostasis, anything that causes a change in hormonal level might lead to a state of imbalance, cycle irregularities, and disturbances. The aim of this study is the evaluation of lifestyle factors, such as alcohol consumption, that might influence the menstrual cycle. Alcohol is known for its impact on health, hormone balance, and body function. According to the WHO, harmful use of alcohol is a causal factor for over 200 diseases and injury conditions. This part of the study aimed to show a relationship between times of alcohol consumption per week and the amount of blood loss per menstrual cycle. **Material and methods:** The data were collected by an online questionnaire, comprising single and multiple-choice questions between 15/01/2024 and 17/02/2024. The questionnaire was distributed among women in their reproductive years in Germany, Romania, and Italy. Distribution was achieved through WhatsApp groups and social media. The participation was voluntary and anonymous. A total of 234 women participated in the study during this period. Inclusion criteria in this evaluation consisted of being female, of reproductive age, and of no alcohol consumption at all up to 5 times per week. Normal bleeding was defined as 40-80 ml per cycle, whereas anything >80 ml, < 40 ml or only spotting was considered abnormal. Women on contraception were excluded from the data analysis since it influences the menstrual cycle and the amount of bleeding. The collected data were statistically analyzed using GraphPad InStat software, and a p-value < 0.05 was considered significant. **Results:** Since the study is still ongoing, the collected data are preliminary. Out of the 234 women 177 met the inclusion criteria and were included in the statistics. The evaluation showed that 17 women stated to consume alcohol 2-5 times per week, 41.17% of them having abnormal bleeding. 98 women consume alcohol ≤1 time per week, with abnormal bleeding occurring in 34.69%. Claiming to consume no alcohol at all were 62 women of whom only 24.19% experienced abnormal bleeding during menstruation. The statistical analysis showed a significant difference (p= 0.0153) between alcohol consumption of 2-5 times per week and no alcohol consumption at all and the occurrence of abnormal bleeding. Alcohol consumption of ≤1 time per week showed no statistically significant difference when compared with 2-5 times per week or no alcohol intake. **Conclusions:** The occurrence of abnormal menstrual bleeding seems to correlate with an increase in alcohol consumption, showing a significant difference between the absence of alcohol and an intake exceeding once a week. While alcohol intake of ≤1 time per week does not make a significant difference statistically, the percentile of abnormal bleeding is still higher compared to abstinent women.

Keywords: menstrual bleeding pattern, alcohol consumption, questionnaire

ENCAPSULATED MESENTERIC FAT NECROSIS MIMICKING AN ABDOMINAL LIPOMA – A CASE PRESENTATION

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Background: Encapsulated mesenteric fat necrosis is a rare condition which falls into the classification of intraperitoneal focal fat infarction (IFFI) and represents a rare inflammatory condition of fat tissue. Although fat necrosis was first described in 1975 in the breast they can occur anywhere in the body. Furthermore, fat necrosis is a benign state, often asymptomatic, which makes it difficult to differentiate it from other diseases like lipoma and liposarcoma. In the literature the encapsulated mesenteric fat necrosis is often described after pancreatitis, trauma, abdominal surgery or diverticulitis. **Material and methods:** A 40-year-old male patient presented for surgical treatment of a mass of unclear etiology in the mesocolon around the right colonic flexure, which was diagnosed during a preventive examination. A 2-phase CT and a colonoscopy were previously performed on an outpatient basis. The segment resection in the right colonic flexure was carried out with a conversion laparotomy.

Due to the nature of the situs and the radical resection target to be achieved, the conversion from the laparoscopic to the open procedure was carried out intraoperatively. The surgical specimen was sent for histopathological examination. **Results:** The CT scan revealed a rounded, encapsulated lesion approximately 5.5 cm in diameter medial to the right lower edge of the liver. The lesion is predominant fatty isodens but shows segmental flat areas of compaction. There was also an increased number of small lymph nodes in the mesenteric fatty tissue. There were signs of an infarction in the mesenteric fatty tissue, but a lipoma or liposarcoma couldn't be ruled out. The pathological examination revealed a 5.7 x 5.6 x 5 cm cystic tumor with a predominantly smooth wall. The microscopic examination revealed shadow cells, fatty tissue necrosis, and foreign body reactions. There was no evidence for malignancy. Additionally, colonoscopy also revealed 2 hyperplastic 3mm polyps and diverticulosis of the entire colon. **Conclusions:** Fat necrosis usually occurs in the breast but can occur anywhere on the body. Due to the radiological characteristics of fat necrosis, its location in the abdomen makes it difficult to exclude a lipoma or liposarcoma. Signs of fat necrosis could be a reduction in the size of the lesion during follow-up investigations. Liposarcoma is also typically located in the retroperitoneum. The exact cause of fat necrosis remains unclear. However, it occurs more frequently after pancreatitis, trauma or abdominal surgery. In our case, the patient had undergone surgery for a right inguinal hernia, but this is difficult to connect due to the different anatomical location. In several literature reviews patients had a history of diverticulosis, which is also present in our patient. The extent to which diverticulosis is related to fat necrosis still needs to be investigated in future studies.

Keywords: fat, necrosis, lipoma, diverticulosis

NAVIGATING THE DERMATOLOGICAL WEB: A CROSS-SECTIONAL EXAMINATION OF MELANOMA INFORMATION QUALITY FOR LAY AUDIENCES

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Background: Malignant melanoma is a type of cancer with a rapidly increasing incidence worldwide, being known for affecting young and middle-aged individuals and having a high mortality rate. Since patients often rely on web-based information, the quality of online information about melanoma is becoming crucial. **Material and methods:** With the aim of evaluating malignant melanoma information's credibility, completeness, and accuracy on English and Spanish language websites, the research was conducted as an observational cross-sectional study, with a sample of 25 websites for each language. Websites were selected based on specific criteria for inclusion and exclusion. In order to examine credibility, two skilled evaluators assessed each website for completeness and accuracy, using a benchmark for evaluation. Results were reported as relative scores on a scale from 0 to 10. Statistical analyses were performed to test inter-language differences and correlations between the studied characteristics, using appropriate tests such as the Student t-test or Mann-Whitney, Pearson, or Spearman test, with a significance level of 0.05. **Results:** The average scores for credibility, completeness, and accuracy for English language websites were 6.2 ± 1.1 , 4.8 ± 1.6 , and 4.4 ± 1.3 , respectively. On the other hand, the corresponding scores for Spanish language websites were 5.3 ± 1.3 , 4.1 ± 2.7 , and 4.1 ± 1.4 , respectively. Statistical analyses did not show major differences for the considered parameters between the two studied languages, except for English websites, which scored significantly higher ($p=0.0399$) for credibility than Spanish websites. No other significant correlations between Google ranking and credibility versus completeness and accuracy scores were found for any of the languages, except for the Google ranking/completeness score correlation of Spanish websites ($p=0.0217$, $r=-0.4569$). **Conclusions:** The quality of medical information regarding malignant melanoma found on both English and Spanish websites was average. The reliability assessment and Google ranking criteria did not accurately indicate the quality of the information in the analyzed languages.

Keywords: malignant melanoma, infodemiology, consumer health informatics, reliability of online information, internet

SURGICAL OUTCOMES IN PATIENTS WITH GLIOBLASTOMA IDH-WILDTYPE: A SINGLE CENTER PROSPECTIVE ANALYSIS

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Background: Glioblastoma, IDH-wildtype is defined as a WHO CNS grade 4 glioma and constitutes the most common type of primary malignant cerebral tumor, that is a tumor arising from the cells of the central nervous system (CNS), as well as one of the most malignant tumors in humans reflecting its infiltrative nature and severity of clinical presentation. It accounts for approximately 50% of all primary malignant CNS neoplasms. Patients suffering from Glioblastoma often show a rapid decline in cognitive and physical capabilities underlining the tumors grave impact on both longevity as well as quality of life. Therapeutic options are currently limited to surgical resection, radiotherapy and chemotherapy with a mean survival at maximum therapy of just about 12 months, leaving researchers on a quest for maximizing efficacy of current treatment options on one hand while scouting for novel therapeutic remedies on the other. The objective of this paper is the evaluation of GBM patients clinical, imagistic and histopathological presentation and their surgical treatment in the Targu-Mures county hospital.

Material and methods: This single-center study was conducted in a prospective manner over the period of one year (01.01.2023 – 31.12.2023). All patients with suspected malignant glioma admitted to the Emergency County Hospital Targu-Mures to the department of neurosurgery were included in the study. Data was collected on patient demographics, clinical presentation at admission, tumor appearance on MRI, surgical approach and degree of resection, clinical outcome at discharge and tumor histopathology. Other examined factors were patient comorbidities, alcohol/tobacco/drug abuse, and laboratory data. Based on histopathological examination only patients with Glioblastoma IDH-Wildtype were included in the study, while all patients with other types of malignancy and lesions were excluded. **Results:** 22 patients were included in the study, 12 males and 10 females with a mean age of 60,36 years. Mean Tumor volume was 39,45cm³, peritumoral edema volume was measured at a mean of 118,77cm³ diameter and 8 patients (36%) presented significant midline shift > 5mm. The symptomatology was diverse with patients presenting with cephalgia, new-onset epileptic seizures, focal neurological deficits, alteration of personality, behavior or motivation amongst others. Decision to perform surgery was made in 21 patients (95%) with either surgical resection or stereotactic biopsy. Of the 16 cases scheduled for surgical resection in 15 (94%) GTR was achieved. 1 patient required reoperation in which GTR was achieved, amounting to successful GTR in 100% of patients. Clinical improvement was achieved in 18 cases (82%), worsening in 2 cases (9%) and no change in 2 cases (9%). Clinical improvement amongst patients treated with surgical resection was achieved in 100%. **Conclusions:** Statistical analysis of our results showed amongst others significantly improved outcomes of patients treated with surgical resection over those with biopsy or non-surgical treatment alone, underlining both the role of surgery in treatment of malignant gliomas as well as the surgical excellence of the neurosurgery department of the Emergency County hospital Targu-Mures under leadership of Prof. Dr. Adrian Balasa.

Keywords: Glioblastoma IDH-wildtype, Malignant glioma, Neurosurgery, Neurooncology, Neuropathology

DECADAL TRENDS IN SURGICAL APPROACHES: A COMPARATIVE ANALYSIS OF LAPAROSCOPIC AND CLASSICAL SPLENECTOMIES IN A TEMPORAL DATA STUDY.

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Background: The rationale behind this study lies in recognizing the distinct advantages of laparoscopic splenectomy, which include smaller incisions, diminished postoperative pain, and expedited recovery periods. Presenting the findings from this retrospective review spanning the past ten years, aiming to shed light on the evolving patterns in the utilization of these surgical modalities, as well as to appreciate the effects of the advancements in haematology towards targeting the splenic pathologies at hand. **Material and methods:** Analysis of the decade-long trends in laparoscopic splenectomy versus classical splenectomy approaches, drawing insights from nearly 500 patient records meticulously archived at the TGM County Hospital's general surgery

department. Our comprehensive review encompassed the medical charts of approximately 500 patients who underwent splenectomies between 2014 and 2023 at TGM County Hospital. We meticulously examined the nature of pathology or lesions, categorizing interventions into classical and laparoscopic splenectomy approaches. In addition, we explored the annual frequency trends, paying special attention to prevalent splenic pathologies such as splenomegaly, thrombocytic purpura, Hodgkin, and non-Hodgkin lymphomas, among others. Moreover, we acknowledged external factors influencing these trends, offering a nuanced understanding of the broader context in which these surgical decisions were made. **Results:** Our main observations, among many others - reveal a noteworthy upswing in laparoscopic splenectomies from 2016 to 2019, with a remarkable peak in 2021. The dip in 2020, attributed to the global SARS-CoV-2 pandemic, exemplifies the impact of external factors on elective surgeries. Following the pandemic, from 2021 to 2023, a consistent decline in laparoscopic splenectomies was noted. This may indicate a paradigm shift, with successful hematological care leading to a reduced reliance on surgical interventions. **Conclusions:** In conclusion, splenectomies remain a reliable last-line treatment for various hematological, traumatic, and neoplastic splenic pathologies. The positive impact of laparoscopic approaches on patient outcomes is evident, as reflected in the overall upward trend observed in splenectomies over the past decade, particularly peaking in 2021. The dip in 2020, influenced by the global pandemic, highlights the delicate balance between patient safety and surgical decision-making during crises. Additionally, the subsequent decline in laparoscopic splenectomies from 2021 to 2023 signifies advancements in hematologic medication and management, offering alternative avenues for effective patient care.

Keywords: Laparoscopy, Splenectomy, General Surgery, Surgical trends, Splenic pathologies

RARE CAUSE OF LOWER LIMB PAIN - POPLITEAL ARTERY ANEURYSM

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Background: Peripheral artery aneurysms are a rare but still underdiagnosed pathology, therefore sometimes being one of the last differential diagnoses considered to determine the cause of lower limb pain. They are defined as a focal dilation in the artery and are often associated with abdominal aortic aneurysms. In this work the goal is to show the benefits of surgical treatment of the popliteal artery aneurysms (PAA), which may represent a cause of lower limb pain. Popliteal aneurysms can be treated by two methods: open surgical repair, in which a bypass is created around the aneurysm to improve the flow of blood, or endovascular popliteal aneurysm repair, where a stent-graft is inserted into the area of the aneurysm. **Material and methods:** This case report presents a 64 years male who was hospitalized at the Vascular Surgery Department, Emergency Mures County Hospital, in September of 2021. The patient was admitted with the following multiple comorbidities: Chronic Venous Disease C2EpAsPr, Peripheral Arterial Disease stage II, Diabetes Melitus type II, Obesity stage 2. He had pain in the lower limb for about three months. The overall diagnostic and investigative process took another three months, inside and outside the hospital, in order to exclude other differential diagnoses. Because of this, the patient suffered from lower limb pain for half of a year before being diagnosed with PAA. It was located in the first part of the popliteal artery and had the size of 36x31x28 mm. The surgical procedures performed was popliteo-popliteal by-pass with reinforced Goretex graft. **Results:** The patient had a good postoperative evolution without any bloodloss and the pulse was consistently present even at the dorsalis pedis artery. The patient also did not have any important pain in the lower limb. The surgical treatment was a good choice with a beneficial outcome for the patient. **Conclusions:** Open surgical treatment of the PAA can solve the cause of the lower limb pain and thereby improves the quality of life. After the long diagnostic time it is usually a big relieve for the patient.

Keywords: aneurysm, vascular, surgery, popliteal artery

PREDICTORS OF MORTALITY IN PULMONARY SEPSIS

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Background: Sepsis has a mortality of up to 50% and accounts for 11 million deaths per year worldwide resulting in the leading cause of death in the ICU and one of the biggest contributors to healthcare costs. Therefore,

emphasis should be put on early mortality prediction and disease progression; for that various scoring systems are currently used, such as the sequential organ failure assessment score. **Material and methods:** A retrospective study was conducted at the EVK Mettmann. It included all patients (n=51) with a main diagnosis of sepsis from December 2022 to December 2023 according to the ICD-A41 criteria. The SOFA score was calculated on the first day, third day, and seventh day of admission to the ICU according to the appropriate criteria including: respiratory, coagulation, liver, cardiovascular, neurological and renal parameters. In patients who spend a prolonged period, more than 7 days, in the ICU the last day of their stay was also included. As the Horovitz index itself is part of the SOFA score it was taken from the same period. Patients who left the ICU in less than 3 days and patients with sepsis not as their main diagnosis were excluded. **Results:** Of the total 51 patients, 32 patients were diagnosed with pulmonary sepsis with a mean age of 75.65 years. In the progression of their ICU stay, 13 needed to be intubated and 8 patients died on the ventilator. The average ICU length was 10.22 days. The mean SOFA scores of patients who died on the ventilator were 10.625, 10.375, 12.333, and 9.000 on the first, third, seventh, and last day, respectively. Day 7 showed the highest SOFA score indicating a mortality risk of 90% and the increase of 2 points from day three to day seven shows that these patients had an extra risk of mortality, making it a valid predictor. The mean values of the Horovitz index of patients on the ventilator were 197.725, 264.625, 202.667, and 106.500 PaO₂/FiO₂ on the first, third, seventh, and last day, respectively. This shows a more in-depth insight into decreased lung function. The comparison of SOFA scores in patients who died versus patients who survived did not show a significant difference. However, the change of PaO₂/FiO₂ in patients on the ventilator who survived showed a favoring prognosis, therefore making it a better tool to predict mortality than the SOFA Score alone. **Conclusions:** The accuracy of the SOFA score as a mortality predictor is limited as it underestimated the mortality risk for pulmonary sepsis patients on the ventilator and showed no significant difference in the final score for patients who survived. A compilation of SOFA scores and the Horovitz index improves the predictability of mortality. Several studies also raise awareness that especially patients with pulmonary sepsis do not exceed scores over 4- 10 and parameters can falsely increase the final score: an elevated baseline creatinine in CKD or only an estimated GCS in patients who are ventilated. It should be considered to include a series of scoring systems to maximize the predictability of mortality in sepsis.

Keywords: Predictors of mortality, Pulmonary Sepsis, SOFA Score, Horovitz Index

THE STEMI PARADIGM

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Background: Myocardial infarction presents one of the premier emergencies with high mortalities and high time sensitivity. Due to this characteristic of the disease timely diagnosis and treatment are linked strongly to the outcome of patients with myocardial infarction. The most immediate treatment in the form of percutaneous coronary intervention(PCI) has emerged in the last few decades, as the standard of care for most cases. For the decision to catheterise a patient, a solid diagnosis needs to be established and timely. Historically the definition of what constitutes myocardial infarction and the treatment options have changed. Although more diagnostic modalities can be utilised, EKG interpretation remains the primary determinant of initial decision-making due to the time-sensitivity of the diagnosis at hand. This review aims to provide insight regarding the prominence of the STEMI/NSTEMI definition and discuss a possible rationale for broadening the EKG criteria and terminology providing a more accurate basis for decision-making on PCI requiring ischemia. **Material and methods:** Literature review with guidelines and searches on Google Scholar and Pubmed with the key terms myocardial infarction, STEMI, NSTEMI, PCI, OMI <https://hqmeded-ecg.blogspot.com/p/omi-literature-timeline.html> <https://www.escardio.org/> <https://www.heart.org/> **Results:** EKG criteria historically began with the Q-Spike definition (1959) of an already subacute infarction. We have arrived at a more specific definition of the STEMI (ST-Segment elevation myocardial infarction) in the 1990s. STEMI criteria have become the dominant EKG criteria for decision-making in suspected acute coronary syndrome. However other EKG signs of acute catheter-worthy ischemia have been described and researched, exemplarily: Hyperacute T-Waves Wellens signs (A/B) Reciprocal inferior ST-Segment depressions These clear ischemia indicators do not necessarily meet STEMI criteria. There are also so-called STEMI mimics such as benign early repolarisation (BER) meeting STEMI criteria but not representing an ischemia at all. STEMI/NSTEMI criteria are conventionally used as the first distinction line and have essentially become synonymous with myocardial infarction. In praxis, this often causes delayed treatment in favour of further testing, if the patient does not meet "STEMI" criteria. However, the evidence shows

that while correctly applied STEMI criteria give a 97% specificity the overall sensitivity lies only at about 70% due to the aforementioned "exceptions" or other atypical EKG presentations. Further, about 30% of NSTEMI cases with significant/catheter-worthy ischemia are being misdiagnosed due to being outside of the STEMI/NSTEMI definition i.e. Wellens. Recent guidelines have adapted recommendations to account for these exceptions however in praxis are often not applied. Around 2012 a group of physicians began to research these inconsistencies in the diagnosis and treatment of suspected myocardial infarction and coined the term OMI (Occlusion myocardial infarction) as a broader term able to include the atypical EKG patterns and patterns in different stages of perfusion and reperfusion in myocardial infarction as well as the "STEMI mimics". **Conclusions:** The OMI definition should be considered to improve diagnostic and decision-making criteria for patients with suspected acute myocardial infarction. The insistence on STEMI/NSTEMI should be diffused.

Keywords: STEMI, NSTEMI, PCI, OMI, Myocardial infarction

EFFICIENCY ANALYSIS OF EMERGENCY PHYSICIAN DISPATCH IN HAMBURG – STUDY DESIGN

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Background: The German Emergency Services (EMS) is essentially a two-tiered physician-based response system. This means EMS dispatchers decide whether to dispatch an ambulance with a paramedic only or also an emergency physician to the scene. This is based on question algorithms refined by the emergency physician indication catalogue of the German Professional Association of Emergency Medical Services (DBRD e.V.). Due to the scarcity evident of emergency physicians available for dispatch and the volume of 112 calls this is a more practical approach as a) not every emergency call can receive the resource physician and b) many calls don't elicit an EMS response and do not require a physician present to resolve the situation at hand. The limitations of the call/dispatcher setting i.e. limited time to evaluate the situation, only audio contact, laymen as callers, etc. accurate dispatch of resources is difficult. The evidence shows in recent years redundancy regarding the EMS resources (Paramedics and emergency physicians) has declined drastically due to an increase in call volume as well as other factors. Studies in the past have tried to roughly and subjectively evaluate the size of the discrepancy between dispatched and required resources on scene. This study aims to more objectively elicit a state of the dispatch discrepancy to evaluate whether there is a need to adjust the way resources are dispatched. **Material and methods:** A prospective study in the Free and Hanseatic city of Hamburg consisting of a questionnaire completed by Emergency Physicians on operations they have been dispatched to. Three key aspects: - Termination of emergency physician dispatch by on-scene personal before arrival- Dispatch- vs working diagnosis on scene- Medical procedures applied The first two aspects elicit discrepancies in the call-taking and dispatch algorithms from a more subjective point of view. The last aspect will allow us to discern objectively between the need for a physician on scene and sufficient care possibilities by paramedics only, as there are algorithms for the paramedics in Hamburg on what procedures they can perform on their own. Data from the blinded digital documentation of the emergency physicians or - in the event of termination by the ambulance - the paramedics' protocols' data are used for the specific evaluation. **Exclusion criteria:** - Deployments in which the emergency physician is initially canceled and then again requested later. **Results:** **Current literature:** There is no objective literature on the specific issue in the German rescue service. **Conclusions:** Not applicable because it's a study design

Keywords: Emergency physician, Pre-clinical emergency medicine, Study design, Dispatch algorithm, German emergency services

UTILIZING ARTIFICIAL INTELLIGENCE FOR AUTOMATED COBB ANGLE MEASUREMENT IN SCOLIOSIS DIAGNOSIS AND ASSESSMENT

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Background: Scoliosis is defined as a curvature of the spine in the coronal plane, with its idiopathic form being the most frequently encountered. Diagnosis is based on spinal X-Ray imaging, performing a Cobb angle

measurement, which represents the angle calculated between two perpendicular lines traced at the superior margin of the uppermost involved vertebra, and the inferior margin of the lowest affected vertebra. A Cobb angle greater than 10 degrees is considered as positive evidence of spinal deformity and confirms the diagnosis. The traditional Cobb angle measurements are time-consuming and prone to human errors; therefore, an automated measuring algorithm could reduce the diagnostic interval, and hypothetically improve measurement accuracy.

Objective: The aim of this study is to investigate and test the application of artificial intelligence (AI), and its existing algorithms, for automated Cobb angle measurement and scoliosis assessment. **Material and methods:** Radiographic images of 197 patients have been obtained from the database of a private clinic from Targu-Mures, spanning the period between 30/11/2023 and 20/02/2024. The acquired images underwent processing using the AI Open-Source Software "Cobb Angle Calculator". Additionally, a manual calculation was performed using the "RadiAnt DICOM Viewer" software to ensure a comparison between automated and manual methods. Statistical analysis was carried out utilizing the GraphPad InStat software to statistically assess differences between the automated and the manually calculated measurements. **Results:** Out of the 197 analyzed X-Ray images, the manual measurement of the Cobb angle led to a diagnosis of scoliosis in 170 patients. The measurements were conducted three times, in order to minimize errors. Among these, 52 patients were diagnosed with thoracic scoliosis, 51 with lumbar deformities, and 67 with combined thoraco-lumbar curvatures. The roentgenograms were then processed with the AI software "Cobb Angle Calculator", and the outcomes compared with the ones calculated manually. Statistical analysis demonstrated that the difference in accuracy of the two methods is extremely significant (p value=0.0002), thus rejecting the null hypothesis. Subsequently, each X-ray image underwent a contrast-enhancing process to improve visualization of the skeletal structures, and the results were compared a second time. The obtained p value of 0.3019, considered not statistically significant, confirmed the null hypothesis, therefore proving the valuable aid of AI in Cobb angle quantification as an alternative to manual evaluation. **Conclusions:** Automated Cobb angle measurement, being at the beginning of its era, lacks sufficient accuracy when employed without a specific image contrast-enhancing procedure, hence displaying high probability of scoliosis misdiagnosis. Integrating an image contrast-enhancing process is a pivotal step forward in measurement automation, and consequently offers a crucial alternative, and possibly future substitution, to the available standard techniques.

Keywords: scoliosis, artificial intelligence, Cobb angle, radiology

INDICATIONS FOR LABOR INDUCTION IN GERMANY: CLINICAL GUIDELINES AND REPRODUCTIVE RESULTS

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Background: Induction of labor (IoL) involves the medical and/or mechanical stimulation of the uterus to induce labor and facilitate a vaginal delivery. The rate of labor induction in Germany has increased from 16.50 % in 2015 to 20.0 % in 2023, highlighting the importance of evaluating the reproductive results. In 2022 the rate of cesarian sections in Germany was 30.90%. **Material and methods:** All cases of IoL (n=99) documented at the Klinikum Leer in the time interval June 2023 to November 2023 were evaluated in a retrospective study. Variables included gravidas age, gestation, indication for induction, type of delivery, APGAR score, uterine artery pH, base deficit, neonatal and postpartum complications. The indications for inductions were classified according to the 2020 German, Swiss and Austrian guideline program including 11 indications with a strong recommendation for employment. Only singleton pregnancies were considered. **Results:** The most common indication for IoL was overdue pregnancy (n=39) with a mean gestational age of 41+6.28. A secondary cesarian sections was conducted in 33.30% of those patients, mainly indicated by a pathological CTG or obstructed labor. Neonatal parameters compromised a mean uterine artery pH of 7.25, mean APGAR score of 8.79/9.69/9.97 and a mean base excess of -3.94. Neonatal adverse outcomes included two cases of an abnormal base excess >12 mmol/L, two cases of neonatal acidemia, defined by an uterine artery pH below 7.10 and one case of amniotic infection syndrome. No post-partum complications were documented. The second most common indication for IoL was preterm premature rupture of membranes (PPROM) (n=35). A secondary cesarian section was performed in 28.57%, indicated by pathological CTGs or an obstructed delivery. Neonatal parameters included mean uterine artery pH of 7.25, mean APGAR score of 8.83/9.68/9.94, mean base excess of -3.9. Neonatal adverse outcomes included one case of neonatal acidemia and 3 cases of amniotic infection syndrome. One case of post-partum atony was present. Less common indications included gestational diabetes (n=6), intrauterine growth retardation (n=3), gestational

hypertension (n=2), HELLP syndrome (n=2), others (n=4). IoL indications that were not compliant with the German guidelines included pathological cardiotocograph (CTG) (n=6), fetal anemia (n=1) and placental insufficiency (n=1), neonatal adverse outcomes included one case of neonatal acidemia. In 31.31% of cases a secondary cesarian sections was performed. Maternal atony was documented in 2 cases. Neonatal adverse outcomes included five cases of neonatal acidemia and two cases of an abnormal base excess >12 mmol/l. **Conclusions:** Labor induction following the 2020 German, Swiss and Austrian guideline program does not increase neonatal or maternal adverse outcomes. In total 91.92% of all induction indications were included in the guideline program, supporting its applicability in German hospitals. Indications not compliant with the guidelines showed an increased risk of 12.50% of neonatal acidemia. The rate of cesarian sections in Germany in 2022 was comparable to the rate of secondary cesarian sections under IoL. In conclusion the leading causes of labor induction are an overdue pregnancy and PPRM.

Keywords: Labor induction, Induction guidelines Germany, Umbilical artery pH

ASSESSING THE COST-EFFECTIVENESS OF NEGATIVE PRESSURE WOUND THERAPY VERSUS CONVENTIONAL DRESSINGS FOR LOWER LIMB WOUNDS: AN INVESTIGATIVE PROSPECTIVE STUDY

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Background: Non-healing lower limb wounds, especially in diabetic patients, pose significant challenges that conventional therapies often struggle to address. Negative Pressure Wound Therapy (NPWT) has emerged as a promising solution by stimulating angiogenesis, vascularization, and oxygenation while effectively reducing edema, promoting granulation tissue formation, enhancing local blood flow, and lowering bacterial burden. However, despite its proven efficacy, the adoption of NPWT has been hindered in some regions due to perceived high costs.

Objective: This study aims to assess the cost-effectiveness of NPWT compared to conventional dressings in the treatment of lower limb wounds, particularly in diabetic patients. **Material and methods:** Conducted at Surgery Clinic 2 of the Emergency County Hospital in Targu Mures, Romania, the study enrolled 53 patients with lower limb wounds, divided into two groups: 21 receiving NPWT (Group A) and 32 receiving conventional therapy (Group B). Demographic characteristics, wound location, hospitalization duration and cost, wound healing duration and cost as well as patient survival were analyzed. Group A patients underwent necrectomy and debridement before transitioning to NPWT using specialized kits. Dressing changes were performed every three days. Group B patients received traditional dressings with hydrogen peroxide or Betadine, changed once or twice daily. Statistical analysis using IBM SPSS 17.0 compared various parameters between the two groups. **Results:** Both groups exclusively presented lower limb wounds, with no significant differences in gender distribution or mean age. Group A had longer hospital stays but shorter local healing durations compared to Group B. Despite longer hospitalization, Group A incurred lower total costs for hospitalization and local healing. Correlation analysis revealed positive correlations between hospitalization duration and costs, as well as between local healing duration and overall wound recovery process in both groups. ROC Curve analysis confirmed the cost-effectiveness of NPWT, showing shorter healing durations and higher efficiency in Group A despite higher costs and longer hospitalization. Three deaths occurred during the study, unrelated to anticoagulant therapy. **Conclusions:** Managing devitalized and infected chronic wounds in the lower limb post-surgery is time-intensive. Traditional therapy is effective but requires ongoing care and attention post-discharge until complete healing. NPWT demonstrates greater efficiency in healing lower limb wounds compared to conventional dressings, with lower overall expenses and patient comfort. Despite longer treatment duration and increased costs, NPWT reduces local therapy expenses by approximately 26% and improves complete wound healing by 30%, with minimal complications.

Keywords: Lower Limb Wounds, Negative Pressure Wound Therapy (NPWT), Cost-Effectiveness

ALZHEIMER DISEASE AND PERIODONTAL DISEASE - TWO SIDES OF THE SAME STORY?

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Background: Alzheimer's disease is a neurodegenerative disease that significantly increases with age and is characterized by inflammation which plays a pivotal role in the onset and progression of the disease. Periodontitis is a common dental disease that triggers local inflammation but can also propagate systematically through blood and nerve pathways, instigating systemic inflammation. The aim of this search was to delineate the most important common pathways involved in the pathogenesis of both Alzheimer's disease and Periodontitis. **Material and methods:** A comprehensive search was conducted on PubMed utilizing the key words "Alzheimer" "Periodontitis" "Inflammatory markers" and "Oxidative stress". **Results:** The search revealed elevated levels of inflammatory markers including interleukin-6 (IL-6), C-reactive protein (CRP), tumour necrosis factor-alpha (TNF- α), and lipopolysaccharide (LPS) in both conditions. The pathophysiology of periodontitis involves the activation of pro-inflammatory cytokines which can penetrate the brain through either a compromised blood-brain barrier or via neuronal pathways, such as the trigeminal nerve. Within the brain tissue, this process triggers the activation of microglia, inducing neuroinflammation. This will further increase Amyloid- β production and deposition, as well as phosphorylation of tau proteins. Consequently this cascade precipitates a loss of neuronal synapses and neurodegeneration and is a major contributor to deterioration seen in Alzheimer's disease. It is noteworthy that it is not only the direct damage caused by Amyloid- β plaques and tau protein aggregates that contributes to brain tissue damage, but also the chronic inflammatory response elicited by them and associated with systemic increased cytokine expression of the neuro-inflammatory biomarkers CRP, TNF- α , and others. **Conclusions:** Inadequate oral hygiene contributes to the development of periodontitis and can thereby increase the risk for Alzheimer's disease. Conversely, individuals afflicted with Alzheimer's disease often present impaired ability to maintain adequate oral hygiene which heightens the susceptibility to development of periodontitis. Considering the current absence of curative therapy for Alzheimer's disease, preventive measures such as maintaining an optimal oral hygiene could hold a substantial role in the management of dementia.

Keywords: Alzheimer, Periodontitis, Inflammation, Oxidative stress

RISK FACTORS IN HEALTHCARE-ASSOCIATED CLOSTRIDIODES DIFFICILE INFECTION

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Background: Clostridioides Difficile, a toxigenic anaerobic bacterium, is an infectious pathogen often associated with severe infectious colitis that causes significant morbidity and mortality globally, especially in the elder patients. Also, Clostridioides Difficile represents one of the main agents that can cause health-care associated infections, making this specific type of disease a public health issue, requiring a multifaceted approach, including spread control, mindful usage of antibiotics, patient education, also requiring future research to develop more effective treatments and prevention strategies. **Material and methods:** A retrospective study was carried over a period of 4 years (2020-2023), in which there were included 232 patients hospitalized in the Internal Medicine Clinic of the Emergency County Clinical Hospital of Tîrgu Mureș. Inclusion criteria consisted of bacteriological confirmed diagnosis of Clostridioides difficile enterocolitis, treated in the clinic, with some of further being transferred to a Infectious Diseases Clinic. Data collection was made by reviewing existing documentation in all discharge notes and clinical observation sheets from admissions and consultations of patients with Clostridioides difficile enterocolitis. **Results:** With a cohort of 232 patients, aged between 26 and 96 years, analysis revealed that the infection is more common in the elder population, with an average age of affected patients being around 73 years old. Most patients developed the infection during hospitalization. Intravenous antibiotic treatment was strongly associated (87% cases). Another result highlighted is that the use of broad-spectrum antibiotic therapy represents the main risk factor for the development of this condition. Combined pharmacotherapy was common, with more than half of patients (52%) receiving two or more different classes of antibiotics, particularly cephalosporins. The analysis of the association between the antibiotic

therapy combination and the patient's survival rate revealed that cases of death most often occurred when the patient received a combination of antibiotics (23%), compared to monotherapy in those who survived (30%). The analysis of the duration of antibiotic treatment revealed that the deceased individuals received treatment for a longer period. Another noteworthy aspect is that one-fifth of the patients had undergone surgical intervention prior to developing the infection, and a history of pseudomembranous colitis was a significant predictor for the recurrence of the infection ($p < 0.05$). The mortality rate following *Clostridioides difficile* infection was 33%, with a positive correlation between the duration of broad-spectrum antibiotic treatment and mortality ($p < 0.05$). These findings emphasize the relevance of appropriate management of antibiotic therapy and associated pathologies in the prevention and treatment of *Clostridioides difficile* infection. **Conclusions:** This study has examined the dynamics and risk factors of *Clostridioides difficile* infection among a cohort of patients hospitalized in the Internal Medicine department. Most patients originate in rural areas, as low income and socioeconomic status play an important role in the occurrence of this infection. Beyond demographic characteristics, the use of broad-spectrum antibiotics was identified as a major risk factor, involved in over 80% of cases. This paper aims to highlight the risk factors associated with *Clostridium Difficile*, while presenting valuable correlations with the particularities of the affected patients.

Keywords: healthcare-associated infections, antibiotic use, pseudomembranous colitis, elder patients, toxin-mediated pathogenic processes

ASSESSING THE QUALITY OF ONLINE MEDICAL INFORMATION. A DEEP DIVE INTO FRENCH NEUROLOGICAL DISORDERS WEBSITES.

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Background: The leading cause of disability worldwide are the neurological disorders, which affect a significant part of the world population and are considered the second leading cause of death. The number of patients diagnosed with neurological diseases has been increasing for the last 30 years. The internet is accessible to anyone and many patients are using the internet instead of making medical appointments. Some websites may contain errors that can expose readers to certain risks. The primary purpose of this study was to evaluate the information about Alzheimer's disease, Parkinson's disease, and multiple sclerosis found on the internet by French-speaking general users employing quality criteria such as credibility, completeness, accuracy, and the Brief DISCERN tool. In addition, the study tested whether the websites' Google Ranks and credibility scores could be useful indicator of website content quality. **Material and methods:** Based on inclusion and exclusion criteria, a sample of 75 websites was selected, 25 websites for each disease. Compliance with credibility requirements was assessed using a set of 12 widely accepted criteria. Completeness and accuracy of the information were assessed by cross-checking the website content against diseases-specific evidence-based quality benchmarks developed in collaboration with specialists in the respective field. The assessment procedure followed a protocol described in previously published works. Credibility, completeness, and accuracy were expressed as scores ranging from 0 to 10. The brief DISCERN tool was applied to measure the quality of information about treatment choices as described by its authors. Overall and disease-specific means and standard deviations of quality scores were computed. Correlations between scores were tested using Spearman correlation test. This study is a component of a larger project, encompassing analyses exploring the quality of information on medical websites, covering various pathologies in different languages. **Results:** The overall means and standard deviations of the credibility, accuracy, completeness, and Brief DISCERN scores for the neurological disorder websites were 5.2 (1.5), 4.0 (2.6), 5.4 (2.1), and 15.3 (6.0), respectively. The disease-specific scores, presented in the same order, were 5.2 (1.0), 3.6 (2.8), 6.2 (1.6), and 13.5 (6.2) for Alzheimer's websites, 5.2 (1.7), 4.8 (2.5), 4.1 (1.6), and 17.0 (5.8) for Parkinson's websites, and 5.2 (1.8), 3.6 (2.5), 5.9 (2.3), and 15.5 (5.7) for multiple sclerosis websites. The results of the correlations test showed the following values: credibility vs. completeness score: $\rho=0.1971$, $p=0.901$; credibility vs. accuracy score: $\rho=0.0775$, $p=0.5202$; credibility vs. brief DISCERN score: $\rho=0.1883$, $p=0.1056$; Google rank vs. completeness score: $\rho=-0.2967$, $p=0.0097$; Google ranks vs. accuracy score: $\rho=0.1661$, $p=0.1662$; Google rank vs. brief DISCERN score: $\rho=-0.3506$, $p=0.002$. **Conclusions:** Overall, the average credibility, accuracy, completeness, and brief DISCERN scores for the neurological disorder websites in French were moderate, indicating substandard quality of available information. The statistically significant correlations between Google ranks and two quality scores suggest a trend where higher-ranked websites offer more comprehensive and accurate content. However, considering the low strength of the correlations observed, the

practical significance of Google rankings as a reliable indicator of information quality becomes uncertain.

Keywords: Infodemiology, consumer health informatics, Alzheimer's disease, Parkinson's disease, multiple sclerosis

UTILITY OF COMPLETE BLOOD COUNT DERIVED INFLAMMATORY INDEXES IN THE MANAGEMENT OF ACUTE KIDNEY INJURY

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Background: Complete blood count derived inflammatory indexes have gained popularity in the recent years as easily available, cost-efficient-tools of assessing inflammation aside the traditional biomarkers. Indexes such as Neutrophil-to-Lymphocyte Ratio (NLR), derived Neutrophil-to-Lymphocyte Ratio (dNLR)= Neutrophil / (Leukocyte – Neutrophil), Systemic Immune-Inflammation Index (SII) = Platelet x NLR, Platelet-to-Lymphocyte Ratio (PLR), Neutrophil-to-Erythrocyte Ratio (NER), and Hemoglobin-to-Platelet Ratio (HPR) can be easily calculated from the standard complete blood count (CBC). Their utility and significance in the setting of acute kidney injury (AKI) is yet to be clearly established. **Objectives** The present study aimed to compare AKI patients' laboratory data between hospital admission and discharge moment in order to assess the inflammation markers and their evolution during the medical attempt to reverse the acute kidney injury. **Material and methods:** A retrospective study was conducted collecting data from 175 patients hospitalized at Mures County Clinical Hospital, Nephrology Ward between January 2017 and October 2023. The data sheets of 175 people were subjected to manual review, followed by anonymization, digitization and electronic documentation. Demographic details and comorbidities as well as laboratory data at hospital admission and discharge were registered, including CBC, CBC-derived inflammatory indexes, serum creatinine (SCr), estimated glomerular filtration rate (eGFR) (using the CKD-EPI equation) and blood urea nitrogen (BUN) values. Data analysis was performed using Microsoft Excel (Version 16.54), R statistical-software (Version 4.2.3). Normal distribution was checked by visual inspection using calculated histograms and quantile-quantile plots (Q-Q plots). Not all CBC-parameters were distributed normally. Patients-data were presented as mean±standard deviation, CBC-data as medianIQR. Differences between admission and discharge values for each CBC-parameter were tested by Wilcoxon-Test. Associations between studied parameters were tested by Spearman's correlation. p values < 0.05 were considered statistically significant. **Results:** The study enrolled 84 male and 91 female patients, mean age at admission of 70±15 years old, length of hospital stays of 10±4 days. Comorbidities included hypertension (n=148), diabetes (n=54), obesity (n=36), and cancer (n=28). CBC-parameters and CBC-derived-inflammation-indexes variation during hospital stay included a statistically significant increase/decrease of Hemoglobin 10.8(9.5-12.4) to 9.9(8.8-11.6) (g/dL), p< 0.01; Leukocytes 9.4(7.0-11.9) to 8.0 (10³/µL), p< 0.01; Neutrophils 6.9(4.9-9.4) to 5.4(3.8-7.5) (10³/µL), p< 0.01; Lymphocytes 1.4(1.0-2.0) to 1.5(1.1-2.0) (10³/µL), p< 0.05; Erythrocytes 3.6(3.2-4.1) to 3.4 (3.0-3.8) (10⁶/µL), p< 0.05. NLR 5.21(3.0-9.4) to 3.27(2.2-5.7), p< 0.01; dNLR 3.29(3.3-5.3) to 3.27(1.5-3.5), p< 0.01; SII 1108.21(555-2053) to 794,35(478-1450), p< 0.01; NER 1.97(1.4-2.8) to 1.47(1.0-2.3), p< 0.01; HPR 0.05(0.04-0.07) to 22.10(16.8-29.6), p< 0.01. eGFR 14.24(7.9-25.5) to 24.48(12.1-45.2), p< 0.01; BUN 58.38(39.8-84.4) to 40.86(23.8-58.6), p< 0.01. Result for creatinine: 3.2(1.9-5.8) to 2.1(1.3-4.1) (mg/dL), p< 0.01. Correlation analysis revealed robust and statistically significant associations between the differences observed between admission and discharge values. NLR, dNLR, SII, NER, PLR significant positive correlation with temporal changes (r>0.75, p< 0.01); eGFR-BUN, r=0.7, p< 0.01, eGFR-NLR, r=0.4, p< 0.05. Additionally, GFR and BUN stage changes also demonstrated significant correlations to CBC-derived inflammation indexes (r=0.7; p< 0.01), suggesting their potential usefulness as prognostic indicators. **Conclusions:** The working hypothesis that CBC-derived biomarkers may provide additional prognostic information in kidney disease status was confirmed.

Keywords: acute kidney injury, complete blood count, inflammation

NON-ANTIBIOTIC COMPOUNDS FOR THE PREVENTION OF RECURRENT URINARY TRACT INFECTIONS IN HEALTHY ADULT WOMEN

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Background: Urinary tract infections (UTIs), or cystitis, are one of the most frequent bacterial infections worldwide – in 2019, 404.61 million cases were reported globally, with actual numbers potentially much higher. UTIs occur when gut-resident bacteria or bacteria residing in the periurethral area, such as *Escherichia Coli*, but also other bacteria such as *Klebsiella pneumoniae*, *Proteus mirabilis*, *Staphylococcus saprophyticus* and *Enterococcus faecalis*, migrate and colonize the urethra, bladder, ureters, and kidneys. In this paper, an emphasis is placed on the prevention of recurrent infection amidst the threat of antibiotic resistance. The treatment of repeating episodes of UTIs may cause the creation of multidrug resistant organisms. Thus, the use of natural treatment options for prophylaxis like cranberry extract, D-mannose, and methenamine hippurate, alone or in combination, will be examined for effectiveness. **Material and methods:** A review of existing literature on the compounds was done through PubMed and similar data banks to assess the action mechanism and effects of cranberry extract, D-mannose, and methenamine hippurate on UTIs by using keywords including 'UTI', 'cranberry extract', 'D-mannose' and 'methenamine hippurate'. Clinical double-blind trials and large data bank reviews were selected with preference. **Results:** Cranberry extracts (anthocyanins, flavonols, and proanthocyanidins) and D-mannose effectively prevented and inhibited the adherence of bacteria to urinary tract epithelium and reduced bacterial colonization through bactericidal mechanisms like inhibition of bacterial adherence proteins and acidification of the urine. Methenamine hippurate produced formaldehyde in acidic pH, which worked as a potent disinfectant within the urinary tract. Additionally, behavioural changes such as ingesting 1.5-2 Litres of fluids per day, emptying the bladder fully, (temporary) abstinence from sexual activity, avoidance of contraceptives such as spermicides or diaphragms, preventing hypothermia, and normal body weight, also showed to reduce the incidence rate. **Conclusions:** The non-antibiotic treatment options were shown to effectively help reduce the incidence rate of UTIs in women who suffered from recurrent infections. However, in none of the three cases could antibiotic treatment be replaced in case of active infection. In addition to prophylaxis, a combined intake could be beneficial to reduce antibiotic exposure time. There is a need for further research: future studies should be more long-term, with larger groups, and should take place under better-defined parameters to make higher evidence conclusions.

Keywords: Urinary tract infection, Cranberry extract, D-mannose, Methenamine hippurate

URTICARIA IN CHILDREN - A CHALLENGE IN FINDING ETIOLOGY

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Background: Urticaria is a skin disorder manifested by an erythema with characteristics of having a reddish color and an intense pruritic feeling. Wheals, also known as hives, are local temporary transient plaques on skin or mucosal membranes with edema of the subcutaneous or interstitial tissue which appears in urticaria. Almost 20 % of the world's population will get urticaria in their life. Around 20% is the lifetime prevalence of urticaria. Acute urticaria has many potential causes even though no specific etiology of urticaria can be diagnosed. The study aims to determine the causes of urticaria and evaluate this dermatological skin disorder in pediatric patients from the clinic. **Material and methods:** Based on data from medical records of pediatric patients the retrospective study was performed on a sample of 30 pediatric patients with acute urticaria admitted to Spital Clinic Judetean Mures, Clinica Pediatrie II of Târgu Mureș (România) between January 2018 and March 2023. **Results:** The study population has 13 (43%) male pediatric patients and 17 (57%) female pediatric patients. The average age of the sample is 6,15 years old. The prevalence of infection as the most common cause among pediatric patients with acute urticaria in the study group is 47%. Interestingly among the infectious causes are some cases of SARS-CoV-2 infections. The second most common cause of acute urticaria is different types of foods with 33% of the patient's sample. Then it is followed by idiopathic urticaria with 23% of the pediatric patients. A cause is not always detectable in idiopathic urticaria. The last trigger that causes urticaria in pediatric patients is a medication with

10%. **Conclusions:** Many triggers can cause urticaria with infections being the most common cause followed by food, allergies, medications, psychogenic factors, and physical stimuli. A cause might not always be detectable in idiopathic cases making the etiological clarification and treatment options challenging. Many triggers can cause urticaria and identifying the etiology is crucial for treatment as well as the prevention of relapse since the disease might reduce the quality of life for patients. Thus pediatricians should be aware of possible avoidable causes.

Keywords: urticaria, infections, dermatology, allergic reactions

EXAMINING PARENTAL REFUSAL TO VACCINES AND DEVELOPING A PLAN FOR GLOBAL HEALTH

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Background: Despite the fact that vaccination against serious illnesses is among the greatest successes in public health history, many parents today choose not to vaccinate their children. There has been an increase in vaccine-preventable diseases (VPD) as a consequence of the recent trend of parents choosing to either postpone or completely refuse to vaccinate their children according to the recommended guidelines. The purpose of this study was to identify potential causes of parental immunization reluctance as well as potential solutions to this issue.

Material and methods: An online questionnaire was used in this study to gather data from parents or persons who have legal guardianship over minors. We included both open-ended and multiple-choice question in the survey. The demographic distribution of the participants, their educational level, the reasoning behind their reluctance to vaccinate their children, their prior vaccination experience, and their views on the implementation of legislation requiring childhood vaccination. **Results:** 106 parents have responded to the questionnaire. The poll indicates that 67% of the participants are afraid of the vaccine's negative effects. About 20% indicated that they are relatively uninformed about the effects and benefits of vaccination. Approximately 30% of parents answered that their child or children have not received all the vaccination as recommended for their age. 44% said that their views have been influenced by the previous pandemic. When asked if the parents would support a legislation which would require childhood immunization, the majority of parents said that only parents should be the ones to decide whether or not their child should be immunized and such laws would only increase the mistrust between parents, government officials and medical professionals. **Conclusions:** It is evident that parents' lack of knowledge, mistrust of the government and medical professionals and fear of the adverse effects of a vaccine are among the primary explanation why they refuse or delay immunization. Building a relationship with parents is something that we as a collective should aim in order to erase outdated beliefs. Further data will be available in the future as this research progresses.

Keywords: Vaccine hesitancy, vaccination, vaccination refusal, childhood vaccination, global health

VISUAL ACUITY AND SPECTACLE INDEPENDENCE AFTER UNILATERAL DIFFRACTIVE TRIFOCAL INTRAOCULAR LENS IMPLANTATION, SECOND EYE EDOF LENS - STUDY DESIGN

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Background: Multifocal intraocular lenses (MIOL) enable a high level of patient satisfaction and independence from visual aids in the case of cataract surgery (Mester et al., 2007). However, MIOL are associated with a higher rate of visual side effects, such as halo and glare, compared to monofocal intraocular lenses (IOL) (de Silva et al., 2016). Recently the Extended Depth of Focus (EDoF) IOL were introduced to address this issue. The EDoF IOL offer a good uncorrected vision in the far and intermediate distance, which is nowadays crucial for working on tablet and on the computer, and induce less visual side effects compared to MIOL (Knorz et al. 2020, Kohnen et al. 2022). On the other hand, EDoF IOL show worse function in the near range compared to MIOL (Bohm et al. 2019). The objective of the study is to investigate whether a combination of different IOLs in the same patient: a trifocal MIOL in one eye and an EDoF IOL in the second eye, offer a high rate of spectacle independence and a

low rate of visual side effects (halo, glare). **Material and methods:** Our aim is to conduct a retrospective controlled nonrandomized case control study. Two patient groups will be formed: the study group includes patients who received on one eye a trifocal PanOptix® MIOL and in the second eye a LuxSmart® EDoF IOL, while the control group received on both eyes a trifocal PanOptix® MIOL. The visual acuity in three distances (far in 5m, intermediate in 70cm and near in 33cm) using ETDRS vision charts, spectacle usage, visual side effects and patient satisfaction, using a questionnaire, will be compared between the two groups. Inclusion criteria: - Patients with cataract on both eyes, who underwent a cataract surgery- Patients without any other ocular disease or previous eye surgery- Patients who have voluntarily agreed to participate in the study and signed a written consent. Exclusion criteria:- Endothelial cells < 2000 cells/mm² präoperatively. - Best corrected near visual \geq Niden 5 (20/40) - Best corrected far-distance visual acuity preoperatively > 20/200 - No severe postoperative complications that affect the visual acuity or need for reoperation. **Results:** The received data will be compared between the two groups, to investigate if statistically significant results occurred. To the best of our knowledge there is no other study in the literature, that compared a bilateral PanOptix® implantation with a combination of PanOptix® and LuxSmart® IOL. **Conclusions:** Not applicable because it's a study design

Keywords: Cataract, Multifokal intraocular lenses, Extended depth of vision intraocular lenses, Patient satisfaction, Visual side effects

A POST COVID MULTI SYSTEMIC INFLAMMATORY SYNDROME VERSUS AN ATYPICAL KAWASAKI DISEASE – A CASE REPORT

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Background: Multi-systemic inflammatory syndrome (MIS-C) is a rare complication of COVID-19 in children. It is a hyper-inflammation state marking a severe illness and involvement of multiple organ systems. Kawasaki disease (KD), is an acute medium-sized vasculitis. It is a rare disease of an unknown etiology but is mostly preceded by an infectious disease. Both conditions usually present with fever, rash, cervical lymphadenopathy, neurological symptoms, and extremity changes. But Kawasaki usually involves conjunctivitis and oral mucosal changes while MIS-C has mostly presented GI symptoms, myocarditis, and coagulopathy. **Material and methods:** This paper is a case report of a 2.10-year-old boy with a COVID infection history, suspected with MIS-C later to be diagnosed with an atypical Kawasaki disease. It is a rare case involving both complications, highlighting the differences between the 2 conditions. **Results:** A 2.10-year-old presented to the emergency department after several days with rhinorrhea, dysphagia, and fever unresponsive to antipyretics. The labs came back with a marked elevation of inflammatory markers, D-dimers, and increased anti-SARSCOV2 antibodies. For this reason, it was concluded to be a multi-systemic inflammatory syndrome of COVID. The treatment began with corticosteroids, anticoagulants, diuretics, rehydration, and symptomatic infusions. A day after, a right peripheral facial paresis was detected during the physical examination, and a treatment with group B vitamins and Piracetam was initiated. In the next 2 days, the fever has subsided and the inflammatory markers have decreased. Until he suddenly developed a fever again but this time accompanied by a rash, pancytopenia, and an increase in LDH, transaminases, ferritin, and d-dimers. Treatment with IV IG has begun and a cardiology exam revealed coronary dilations. An anticoagulant and an antiaggregant were added to the treatment and even though not all criteria were filled, a Kawasaki diagnosis was made – an atypical form. The administration of IVIG has shown a favorable evolution and the remission of fever, rash, and inflammatory markers, in a couple of days. A relapse with fever and returning rash occurred a week later but with reinstating IV IG and CS the patient's state was evolving well again. **Conclusions:** This case was interpreted in the end as an MIS-C evolving later into an atypical KD. This case is a good example of the overlapping in the clinical presentation of MIS-C and KD. The first phase of the disease, with neurological manifestations and SARSCOV2 antibodies, pointed at MIS-C. In a later phase, coronary dilations were indicative of KD since MIS-C is more commonly manifested with myocardial changes.

Keywords: Kawasaki, Covid, Multisystemic Inflammatory Syndrome

UNDERSTANDING THE INTERPLAY BETWEEN NICOTINE AND MOOD DISORDERS: A SCHOLAR REVIEW

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Background: Background: Smoking has been linked to depression and anxiety problems for a long time, and it is a known health risk. The precise nature of the varied and intricate association between smoking and mental health illnesses is still unknown, though. Three studies have been carried out to look at this intriguing subject. **Material and methods:** Materials and Method: The first study primarily focused on nicotine dependence in patients already diagnosed with depression or anxiety. It looked into how these people's experiences of sadness and anxiety developed in relation to their smoking and nicotine dependence. The third study looked at the relationship between adolescent depression and smoking initiation, while the second study focused on smoking and depression in particular in teenagers. **Results:** Results: Patients with anxiety or depression who had previously been treated were monitored over time in the first research. The most severe symptoms and the slowest recovery were seen in smokers who were also nicotine dependent. If nicotine dependency remained, people's symptoms did not always get better even after they stopped smoking. This implies that the intensity and progression of anxiety and depressive disorders may be made worse by nicotine dependency. Teenagers were observed for a full year in the second trial. The results showed that whereas depressed teens were not necessarily more likely to start smoking heavily, smoking adolescents were more likely to experience depression. Additionally, the best indicator of becoming a heavy smoker was trying cigarettes before going through depression. This suggests that depression may not always be the main cause of a teen's decision to start smoking. The idea that smoking may cause depression in teenagers was further supported by the third study, which evaluated previous data. **Conclusions:** Conclusion: When considered collectively, these studies point to a complicated reciprocal relationship between smoking and anxiety or depression. Depression and anxiety disorders can worsen in intensity and course, even though smoking—especially when it leads to nicotine dependence—may not always precede the onset of depression, especially in teenagers. For those who are battling these disorders, understanding this complex interplay is essential to creating interventions and treatment plans that work. To clarify the underlying mechanisms and guide comprehensive preventative and intervention efforts, more study is necessary. Healthcare professionals can provide their patients with more comprehensive care if they simultaneously address mental health and smoking-related disorders. For those who are battling melancholy or anxiety in addition to smoking, this strategy might provide greater results and enhance general wellbeing.

Keywords: Depression, Anxiety, Nicotine, smoking, dependence

HEALTH IN A CUP.EXPLORING COFFEE'S INFLUENCE ON MEDICAL STUDENTS

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Background: Coffee, with its stimulative properties, plays a significant role in supporting the cognitive functions of students. Caffeine, the main active ingredient in coffee, is known for its ability to enhance concentration and memory. In the academic environment, where cognitive demands are intense, moderate coffee consumption can provide efficient stimulation, contributing to improved academic performance. Students generally recognize the benefits of this beverage in managing stress, enhancing alertness, and increasing the ability to focus on academic tasks. **Material and methods:** The research hypothesis is formulated to address the investigation into the potential impact of coffee consumption on the academic and health aspects of medical students. The study aims to explore the association between coffee consumption and academic performance, considering factors such as concentration, memory retention, and collaborative dynamics. Additionally, the research aims to discover potential adverse health effects associated with coffee consumption in medical students. Questionnaire survey was performed among 100 medical students ,aged between 20-30 years. Questionnaire was totally anonymous .The questionnaire designed for this research comprised a total of 22 questions, focusing on the impact of coffee

consumption among medical students. This research centered around the analysis of three distinct domains: evaluating the impact of coffee on academic performance, investigating adverse health effects related to coffee consumption, and examining the influence of coffee consumption on collaboration and teamwork. **Results:** This study involving 41 male and 59 female participants with a median age of 25, investigated the patterns and perceived effects of coffee consumption in relation to academic performance, health outcomes, and collaborative dynamics. Notably, a majority (65.3%) demonstrated an increased coffee intake during periods of academic stress, attributing this behaviour to a perceived positive impact on concentration and memory enhancement. While a significant portion (45.7%) reported no adverse health effects associated with coffee consumption, a noteworthy minority experienced physiological reactions, including heightened heart palpitations and restlessness (19.1%). A smaller subset (8.5%) acknowledged a discernible dependency, characterized by headaches and irritability upon abstaining from regular coffee intake, with 21.3% noting digestive issues when exceeding a threshold of 3 cups. Interestingly, 42.6% of participants identified a positive influence of coffee consumption on collaboration and teamwork. This was particularly evident during coffee breaks, which served as informal settings fostering case discussions and idea sharing, contributing to a collaborative atmosphere. Furthermore, a notable proportion of female participants (37.9%) reported a reduction in coffee consumption during menstrual periods. **Conclusions:** In conclusion, we observe that the majority of students confidently acknowledge the significant role of coffee in the context of their daily studies, deeming it an essential element for improving academic performance. The consumption of coffee among medical students exerts beneficial effects on concentration and memory, making these individuals aware of the positive contribution of this beverage in successfully managing daily academic challenges. The steadfast belief in the utility of coffee has evolved into an intrinsic component of their student routines, thereby underscoring the importance of this beverage as a reliable ally in navigating the complexity of the learning process and meeting academic demands.

Keywords: coffee, memory, concentration

THE SCALE AND STETHOSCOPE

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Background: Obesity is becoming an alarming problem in contemporary society, affecting both adults and children, with roots deep in an unhealthy lifestyle. Medical students and future medical professionals face a lack of educational resources on healthy lifestyle in a hectic and demanding context. Limited time for exercise and healthy eating leads to fatigue and the adoption of unhealthy habits. Solving this problem requires an educational approach and finding a balance. This research investigates the relationship between student life, eating habits and sedentary lifestyle among medical students. Focusing on understanding the reasons behind obesity trends and identifying strategies to motivate students towards a balanced lifestyle, the paper also explores psychosocial issues related to nutrition and physical activity, tailored to the pressures specific to the medical field. This research has wide-ranging implications, highlighting the need for effective strategies to promote health among medical students and prevent long-term health problems. **Material and methods:** We conducted a study of 100 medical students, aged 19-24+ years, from diverse backgrounds. The extensive questionnaire, completed by participants from general medicine, military medicine, dental medicine, and pharmacy programs, addressed issues such as demographics, weight trends, eating habits, exercise, and access to obesity information. These findings represent a valuable resource for the development of future health education interventions and programs, providing an in-depth understanding of the implications of obesity in this population. **Results:** In the study, 100 medical students, evenly distributed between men (42%) and women (58%), revealed significant obesity and healthy lifestyle concerns. An impressive 86.5% perceive obesity as a serious problem, and 33.3% have had obesity-related problems before college. Looking at eating habits, 67.4% adopt a moderately healthy diet, while 10.1% have unhealthy eating habits. Regarding physical activity, 34.8% exercise occasionally, 21.3% rarely, and 5.6% not at all. Interestingly, 33.3% adopted unhealthy eating habits after starting college. Perceptions related to obesity and academic performance indicate that 48.3% believe that obesity negatively affects academic performance, 31.5% see the problem as complex and influenced by individual factors, and 46.7% believe that academic stress contributes to the development of obesity. In conclusion, 48.9% support the need for an education programme to promote a balanced lifestyle in the academic environment. These results highlight the importance of a comprehensive approach to health promotion and awareness among medical students. **Conclusions:** The results of this research reveal a significant concern among medical students regarding obesity and healthy lifestyle. The

high percentage of those who perceive obesity as a serious problem, as well as the frequency of obesity-related problems among this group, highlights the need for educational and preventive interventions. In light of these findings, the implementation of education and financial support programmes, together with the promotion of healthy eating habits and physical activity, could significantly contribute to improving the health and well-being of future health professionals.

Keywords: obesity, medical student, lifestyle, nutrition, balance

LUNG POCUS: IS IT POSSIBLE FOR AN UNDERGRADUATE STUDENT TO ACQUIRE SKILL AND KNOWLEDGE?

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Background: Point of care ultrasound (POCUS) examination has noticed significant growth in its implementation across various medical areas. As a safe and efficient diagnostic instrument, it has been incorporated in the undergraduate medicine curricula. The key objective of this research aimed to evaluate the progress of a medical undergraduate student in his development of knowledge and proficiency in basic lung ultrasonography (LUS) in healthy subjects. **Material and methods:** While the subject lay supine, the probes were placed to the intercostal spaces of the anterior thorax, apical and basal (linear probe) and posterior-lateral thorax (convex probe). The LUS evaluation focused on the following aspects: bat sign, lung sliding, A lines and B lines, and diaphragm. Different findings and the duration, for both the student and a medical doctor to detect predefined LUS landmarks, were recorded. In order to keep bias of the main investigation as low as possible, the student had to attain a certain accuracy, meaning that he needed to be able to independently spot the same characteristics as the medical doctor. The assessment was conducted to compare the outcomes achieved by the student and a medical doctor in Anesthesia and Intensive Care. **Results:** In total, 20 young, healthy, male subjects were assessed. The preliminary comparison of student and medical doctor performance with the LUS yielded a complete accordance of findings for all the evaluated elements (bat sign, lung sliding, A and B lines, diaphragm) on both right and left hemithorax. In terms of time of the investigation, the student required on average 4 minutes and 27 seconds time to complete the procedure, while the doctor needed on average 3 minutes and 17 seconds. Furthermore, practicing LUS showed an improvement in the student's time management (minimum time was 2 minutes and 45 seconds). The major differences were noticed when the student performed alone the ultrasound (maximum time was 9 minutes and 55 seconds) or when the doctor provided LUS explanations to other students (maximum time was about 5 minutes). **Conclusions:** Medical student can achieve the ability to directly visualize structures and analyze artifacts through LUS training. For the main investigations and relevant images on LUS less than 5 minutes are needed.

Keywords: point of care ultrasound, lung, medical student

THE INCIDENCE OF CORONARY ARTERY ANOMALIES AND ITS CLASSIFICATION – A CORONARY COMPUTED TOMOGRAPHY ANGIOGRAPHY STUDY

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Background: Coronary artery anomalies (CAAs) are rarely found pathologies, occurring in less than 1 % of the population. They are mostly described as benign, nevertheless, there are malignant types, that are associated with potentially fatal events, like myocardial ischemia and sudden cardiac death, which makes it a non-negligible pathology. Coronary computed tomography angiography (cCTA) is the golden standard for the diagnosis, and therefore essential in distinguishing benign from malignant anomalies. The study's purpose is to outline definitions and the classification of CAAs, using cCTA, to determine the most important CAAs, those with suspected malignant characteristics. **Material and methods:** All investigations have been performed using a GE Revolution CT and one of the current available contrast media. Among all patients who underwent CTA between 2015 and 2023, those associated with aberrant vessels were identified from the entire radiological CTA-related database. From this data, all patients' files related to any type of CAAs were extracted and categorized in an Excel

table, according to anomalies of origin, course and termination, following the current guideline-based classification criteria. **Results:** From the database, 193 patients were determined with any kind of vascular anomaly, of which in turn 42 revealed a CAA (22 %), with a male proportion of 52 %. Eleven were found with a malignant type, out of which two showed an anomalous origin from the pulmonary trunk, while nine presented an interarterial or intraseptal course. Both anomalies are considered malignant according to their anomalous anatomy itself and are associated with myocardial ischemia and sudden cardiac death. The diagnosis of a CAA by CTA in the patient group is mostly an incidental finding as part of the work-up for possible coronary artery diseases, only three patients were already suspected with CAA. **Conclusions:** Considering the period that includes the patients' database, a minor number presented with a vascular anomaly, out of which a significant amount of the patients presented CAAs, which raises suspicion that CAAs are more common compared to other vascular anomalies. The occurrence of malignant CAAs only based on the two above-mentioned types includes every fourth case of a CAA and represents, therefore, a non-negligible proportion. In terms of the total number of patients these malignant types are rare entities but overall carry a certain life-threatening risk and should be considered as differential diagnosis. The diagnosing and categorization of CAAs by CTA is therefore mandatory and plays an important role in minimizing the risk and might improve the patient's outcome. It is worth mentioning that the study is limited, as it is a single-center study, that only includes patients who underwent CTA in that hospital.

Keywords: malignant coronary artery anomalies, myocardial ischemia, computed tomography angiography

MEDICAL STUDENT'S ASSESSMENT OF FLOW VELOCITIES AND PULSATILE INDEX USING TRANSCRANIAL DOPPLER ON HEALTHY SUBJECTS: CASE SERIES

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Background: Transcranial Doppler (TCD) ultrasound enables fast, safe, and continuous evaluations of brain function, proving to be helpful for the clinical diagnosis of various cerebrovascular diseases. Moreover, nowadays ultrasonography education for medical students has become a significant component of their education. The main aim was to assess a medical student's understanding of the anatomical position of the middle cerebral artery in relation to the transtemporal window, as well as the knowledge of blood flow velocities and the pulsatile index.

Material and methods: This presentation consisted of a case series with 9 healthy subjects. They underwent TCD measurements using a 2 MHz impulse probe. The probe was set up above the zygomatic arch, along a horizontal line that intersects with the external ear canal. The focus of the investigation was the middle cerebral artery, which enables analysis of cerebral blood flow. The measurements were made for the peak-systolic (PSV), end-diastolic (EDV), mean blood velocities (MDV), and pulsatile index (PI) of the mean cerebral artery. The measurements were performed by an Anesthesia and Intensive Care specialist and an undergraduate medical student. All data was assessed for normality and the Pearson correlation coefficient was calculated. **Results:** The outcomes of the medical doctor's TCD were as follows: for the right middle cerebral artery: PSV= 107.74±18.20 cm/s, EDV= 43.88±8.15 cm/s, MDV= 42.94±7.83 cm/s, PI= 0.99±0.20; for the left middle cerebral artery: PSV= 91.35±10.50 cm/s, EDV= 42.94±8.80 cm/s, MDV= 39.84±9.33 cm/s, PI= 0.88±0.20. The outcomes of the medical student's TCD were as follows: for the right middle cerebral artery: PSV= 103.32±17.95 cm/s, EDV= 47.28±11.97 cm/s, MDV= 42.94±9.94, PI=0.90±0.18; for the left middle cerebral artery: PSV= 93.81±27.49 cm/s, EDV= 53.42±20.73 cm/s, MDV= 42.66±13.05 cm/s, PI= 0.91±0.21. Positive Pearson correlation coefficient was obtained, with r=0.68 for left PSV, r=0.55 for right PI and r=0.90 for right PI. **Conclusions:** Medical student can acquire real-time information on cerebral hemodynamics through TCD training.

Keywords: transcranial Doppler, cerebrovascular function, flow velocities, pulsatile index

CRP LEVELS IN NEONATES: A COMPREHENSIVE ANALYSIS OF DIAGNOSTIC ACCURACY AND CLINICAL IMPLICATIONS

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Background: Neonatal sepsis is the third-leading cause of death and disability in the first month following delivery.

Due to non-specific and inconclusive symptoms in early neonatal sepsis and bacterial culture (that is used as the gold standard) taking time, the diagnosis of early-onset sepsis (EOS) is challenging. Serum C-reactive protein (CRP) increase is a frequent inflammatory measure being studied for its diagnostic accuracy in neonatal sepsis. But challenges still exist, driven by various sensitivities and specificities determined by the kind of pathogen, reference values, and patient gestational and chronological age. **Material and methods:** Relevant retrospective clinical studies were carefully reviewed, and comprehensive analysis aimed to discern common ground and supporting ideas between them. The sequential CRP levels (each infant had at least 3 measurements) were recorded at different intervals after birth within the first 72 hours of age. The methodology and objectives of these studies were similar **Results:** The dynamics of C-reactive protein (CRP) levels were investigated in one of the studies involving 145 infants who met the inclusion criteria, 25% of whom were preterm. Particularly, at 12–24–36 and 48 hours, term babies had higher CRP levels than preterm babies. These levels peaked at 24 hours, then declined at 36 hours and settled by 48 hours. There was a substantial increase in the median CRP readings in the term group at all time points when compared to the preterm infants. Another study included 863 newborns, of which 179 term and 353 preterm babies met the inclusion criteria. In this study, preterm newborns had lower median CRP values in the group of EOS-positive (9 vs. 18.5 mg/L) and EOS negative infants (0.5 vs. 2 mg/L). Furthermore, it was noted that CRP levels were also increased in neonates with meconium aspiration syndrome (MAS) in term, severe respiratory distress syndrome, and the administration of surfactant in preterm newborns. We included another study to reiterate the above findings. In a retrospective cross-sectional study of 872 neonates, CRP levels higher than 8 mg/L were recorded when neonates were exposed to premature rupture of membrane (PROM), maternal autoimmune diseases, and MAS, and significantly lower when newborns were exposed to antenatal steroids, placenta previa, Intrahepatic cholestasis of pregnancy (ICP), and caesarean delivery. **Conclusions:** When comparing the median CRP values at different time intervals within the 72-hour period, we found that the median CRP values recorded in EOS-diagnosed preterm newborns were lower than those of EOS-diagnosed term newborns. Other non-infectious factors that contribute to elevated CRP levels include the administration of surfactant, MAS, PROM, and maternal autoimmune diseases. We now also know that, for instance, a caesarean delivery may show a lower-than-expected CRP level. This temporal profile reveals a unique CRP response in term and pre-term newborns, emphasizing the significance of taking these differences to heart while making clinical judgments. Ongoing efforts to refine gestational age-specific reference values for CRP are pivotal for enhancing its reliability in neonatal care.

Keywords: C-Reactive Protein, Neonatal sepsis, Diagnostic tools, Neonatology

A COMPARATIVE ANALYSIS OF STUDENT'S LEARNING: SIMULATION TRAINING VS. VIRTUAL REALITY TRAINING IN THE ANESTHESIA AND INTENSIVE CARE DEPARTMENT

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Background: Medical simulation and virtual reality (VR) provide a specific educational environment that can fit various learning approaches, formats that traditional learning cannot replicate. A further advantage of both of these learning experiences is that they may be standardized to encourage the development of trainees' skills while providing with the opportunity to practice clinical scenarios multiple times. Both medical simulation and VR strive to create safe settings where the students can address any gaps in their knowledge. **Objective:** The main purpose was to conduct a comparative examination of student learning with simulation training and VR training in the field of anesthesia and intensive care. **Material and methods:** General medicine students in their 6th year of study participated in this observational and descriptive research. A 25 items questionnaire was developed and pretested for language and clarity previously of its online distribution. The questions included binary responses, a 5-point Likert scale, and open-ended responses. It required approximately 15 minutes completing the questionnaire. **Results:** Out of 45 students that answered, 82.2% participated in medical simulation stations and 48.9% in VR. When comparing the results, over one-third of the participants believed that simulation is an effective method for improving understanding of anesthesia and intensive care concepts. Additionally, 64.4% of the participants agreed that simulation increases confidence in their skills and contributes to knowledge acquisition. Similarly, more than half of the participants expressed a positive attitude towards VR in these regards. Over 50% of the students expressed that their entire experience with medical simulation was either very good or excellent, whereas 40% had the same positive opinion of VR. Out of the total respondents, 57.85% indicated a preference for simulation as a training alternative, whereas only 15.6% expressed interest in VR. **Conclusions:** Medical students have

recognized the advantages of using simulation and VR for medical training. The numerous applications in the field of anesthesia and intensive care contribute to their enhancement.

Keywords: simulation training, virtual reality, anesthesia, intensive care

LIVER CIRRHOSIS - ASSOCIATED COMPLICATIONS REGARDING TO ITS AETIOLOGY

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Background: Liver cirrhosis is a result of chronic damage to the liver which will cause scarring and fibrosis, ultimately leading to irreversible damage if it is not resolved or treated in the early stages, where it is still reversible if the harming agent factor is eliminated. Due to the ability of the liver to compensate even when damaged, the diagnosis of the disease is often late, leading to difficulty in treating. Therefore, the treatment consists in preventing cirrhosis and death. The only curable treatment option for patients remains with liver transplant. **Material and methods:** This study tries to focus on different aetiologies of liver cirrhosis and the associated complications they carry with them and whether there is any exclusivity to an aetiology when it comes to complications. This retrospective study includes 60 patients admitted to the Gastroenterology department of Mures county clinical hospital of Targu Mures, Romania, between the 01.01.2023 and 01.01.2024. The inclusion criteria consist in patients being above 18 years and diagnosed with liver cirrhosis, including all aetiologies presented to the clinic.

Results: Most of the patient's diagnosis are caused solely by chronic alcoholic intoxication (44/60), whereas some patients suffer from viral Hepatitis B and C, also combinations of the mentioned aetiologies are present, which present with a significant increase in abnormal blood values. From the included patients, 3 patients died during their stay, where toxic liver cirrhosis caused by alcohol seemed to be the causing factor among other comorbidities. Worth mentioning is that 2/3 of the deceased patients were males and 2/3 below 60 years of age. Most of the patients are male (49/60) and above 60 years of age (35/60). **Conclusions:** Most of the patient diagnosed with liver cirrhosis in our clinic where due to chronic alcohol consumption, with comorbidities such as chronic cardiac and pulmonary diseases as well as diabetes and obesity. Patients' death was associated with chronic alcohol consumption.

Keywords: Cirrhosis, Complication, Aetiology, Alcohol

TEST EVALUATING THE IMPACT OF ALCOHOL CONSUMPTION IN WOMEN ON MENSTRUAL BLEEDING PATTERN

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Background: Every month 1.8 billion women menstruate; this means over 800 million girls and women menstruate every day. Taking up quite an important and dominant role in a woman's life, menstrual complaints may greatly influence their quality-of-life. The menstrual cycle is greatly dependent on hormonal homeostasis, anything that causes a change in hormonal level might lead to a state of imbalance, cycle irregularities, and disturbances. The aim of this study is the evaluation of lifestyle factors, such as alcohol consumption, that might influence the menstrual cycle. Alcohol is known for its impact on health, hormone balance, and body function. According to the WHO, harmful use of alcohol is a causal factor for over 200 diseases and injury conditions. This part of the study aimed to show a relationship between times of alcohol consumption per week and the amount of blood loss per menstrual cycle. **Material and methods:** The data were collected by an online questionnaire, comprising single and multiple-choice questions between 15/01/2024 and 17/02/2024. The questionnaire was distributed among women in their reproductive years in Germany, Romania, and Italy. Distribution was achieved through WhatsApp groups and social media. The participation was voluntary and anonymous. A total of 234 women participated in the study during this period. Inclusion criteria in this evaluation consisted of being female, of reproductive age, and of no alcohol consumption at all up to 5 times per week. Normal bleeding was defined as 40-80 ml per cycle, whereas anything >80 ml, < 40 ml or only spotting was considered abnormal. Women on contraception were excluded from the data analysis since it influences the menstrual cycle and the amount of bleeding. The collected data were statistically analyzed using GraphPad InStat software, and a p-value < 0.05 was

considered significant. **Results:** Since the study is still ongoing, the collected data are preliminary. Out of the 234 women 177 met the inclusion criteria and were included in the statistics. The evaluation showed that 17 women stated to consume alcohol 2-5 times per week, 41.17% of them having abnormal bleeding. 98 women consume alcohol ≤ 1 time per week, with abnormal bleeding occurring in 34.69%. Claiming to consume no alcohol at all were 62 women of whom only 24.19% experienced abnormal bleeding during menstruation. The statistical analysis showed a significant difference ($p= 0.0153$) between alcohol consumption of 2-5 times per week and no alcohol consumption at all and the occurrence of abnormal bleeding. Alcohol consumption of ≤ 1 time per week showed no statistically significant difference when compared with 2-5 times per week or no alcohol intake. **Conclusions:** The occurrence of abnormal menstrual bleeding seems to correlate with an increase in alcohol consumption, showing a significant difference between the absence of alcohol and an intake exceeding once a week. While alcohol intake of ≤ 1 time per week does not make a significant difference statistically, the percentile of abnormal bleeding is still higher compared to abstinent women.

Keywords: menstrual bleeding pattern, alcohol consumption, questionnaire

A CONTROVERSIAL STANCE ON KETOGENIC DIET AND INTERMITTENT FASTING

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Background: Ketogenic diet (KD) and intermittent fasting (IF) are becoming more and more popular among health and fitness seekers. Both diets promote weight loss by causing a metabolic switch between the use of carbohydrates to ketone bodies as a primary energy source but over a different time span. Important literature data regarding changes in parameters like BMI, cortisol, fat-free mass (FFM), aspartate aminotransferase (AST), alanine aminotransferase (ALT), maximal aerobic capacity (VO_2) and muscle mass will be assessed to establish whether these diets are suitable for athletes seeking enhanced physical abilities or looking to maintain/increase their muscle mass. **Material and methods:** Data from Pub Med was used to analyse the effects of IF and KD on athletic performance by using keywords including 'ketogenic diet' or 'intermittent fasting', 'athletic performance' and 'biochemical parameters'. **Results:** In the case of both KD and IF lower body weight, lower muscle mass, lower FFM was observed, while serum levels of free fatty acids, β -hydroxybutyric acid, cortisol, and epinephrine levels were higher in both KD and IF. Regarding physical performance and VO_2 literature results are contradictory and depend a lot on the number of fasting days / hours per day and the type of effort. For example, in sports relying on anaerobic metabolism like sprinting, low available glycogen limits the execution and speed of repeated, intense efforts while in power sports like weightlifting results are still controversial, some report that there was no significant difference in muscle power in diet groups in comparison to the control group while other studies suggest the contrary, that fasting has no benefit to athletic performance. **Conclusions:** Several beneficial effects have been correlated to KD and IF: control of body weight, improving insulin sensitivity, reducing systemic inflammation (decrease of interleukin-6 or C-reactive protein levels), and strengthening the immune system. Still, the effects on sports performance are controversial as there is no gold standard when it comes to athletes nutrition and it still depends on a multitude of confounding external factors.

Keywords: ketogenic diet, intermittent fasting, ketone bodies, athletic performance, biochemical parameters'

MONOMERIC C-REACTIVE PROTEIN – A KEY FACTOR IN CHRONIC INFLAMMATION AND NEURODEGENERATIVE PATHWAYS

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Background: Chronic inflammation is a hallmark of type 2 diabetes mellitus (T2DM), characterized by elevated levels of systemic C-reactive protein (CRP), originating from hepatic synthesis and visceral adipose tissue. In diabetic individuals, persistent inflammation is exacerbated by non-healing wounds and ulcers, further increasing CRP levels. Monomeric CRP (mCRP), its biologically active form, impairs diabetic wound healing by activating immuno-vascular responses. Moreover, recent evidence suggests the involvement of mCRP in neuroinflammation and subsequent neurodegeneration. **Objectives :** This perspective aims to analyze the association between mCRP, aberrant diabetic wound healing, and neurodegeneration, exploring mechanisms and implications for potential therapeutic interventions. **Material and methods:** A comprehensive literature search was conducted using PubMed to elucidate the role of mCRP in immuno-vascular activation, its vascular effects, and its influence on macrophage polarization. Keywords including C-reactive protein, monomeric C-reactive protein, chronic inflammation, type 2 diabetes mellitus, diabetic wound, macrophage polarization, and Alzheimer's disease (AD) were utilized to identify relevant studies, published in the last 10 years, and investigating CRP and mCRP's impact on diabetic wound healing and neurodegeneration. **Results:** Studies demonstrated several mechanisms through which mCRP influences diabetic wound healing and neurodegeneration. mCRP activates endothelial cells and inflammatory responses, contributing to vascular dysfunction. It induces monocyte chemoattractant protein-1 (MCP-1) and interleukin (IL)-8 expression, amplifying micro-environmental inflammation; stimulates the gene expression and production of receptor for advanced glycation end-products (RAGE) and phosphorylates the insulin receptor substrate-1 (IRS-1), hindering wound healing. Elevated mCRP correlates with systemic glycation, worsening

diabetic complications. mCRP-treated monocytes polarize into pro-inflammatory M1 macrophages, perpetuating chronic inflammation in diabetic wounds. Additionally, mCRP promotes neuroinflammation, increases the risk of cognitive decline, by penetrating the blood-brain barrier, activating microglia, disrupting the neurovascular unit, and promoting the hyperphosphorylation of Tau proteins, contributing to the pathogenesis of conditions like AD.

Conclusions: These findings highlight mCRP's pivotal role in impairing wound healing and exacerbating neurodegeneration in diabetes, via its numerous pro-inflammatory and vascular effects. Targeting these pathways, including mCRP membrane attachment and signaling, could be a promising therapeutic approach for improving wound healing and preventing cognitive decline in elderly people with T2DM.

Keywords: monomeric C-reactive protein, type 2 diabetes mellitus, chronic inflammation, diabetic wounds, neurodegeneration

LIPOXINS: POTENTIAL THERAPEUTIC STRATEGIES IN DIABETIC NEPHROPATHY

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Background: Diabetic nephropathy (DN) represents one of the chronic complications associated with diabetes mellitus (DM) type 1 and 2, a disorder characterized by chronic high levels of glucose and free fatty acids (FFAs). The pathogenesis of DM and its complications have recently been linked to underlying inflammatory processes, especially in the renal milieu, where increased expression of proinflammatory markers, consequent infiltration of M1 macrophages, and tubule-interstitial fibrosis (TIF) concerted contribute to the development of DN. Specialized pro resolving lipid mediators (SPMs) are lipid derived molecules that have a crucial role in inflammation resolution. Prime SPMs are lipoxins (LX), and specifically LXA4, which has been proven to reverse fibrosis associated with inflammatory kidney diseases. Considering the inflammatory background implicated in DN, it is reasonable to speculate utilization of these substances in blocking disease progression. **Objective:** The aim of this work is to investigate the molecular development of DN and LX biosynthesis, further examining future utilization of LXs as potential strategies in DN treatment. **Material and methods:** A comprehensive English literature review was carried out on PubMed and Google Scholar on 24.02.2024. Selection criteria included publication between 2014 and 2024, and presence of the keywords "diabetic nephropathy", "specialized pro resolving lipid mediators" and "lipoxins". **Results:** Studies conducted on ApoE ^{-/-} murine models of diabetic kidney disease demonstrated augmented creatinine clearance, evidence of renal hyperfiltration, and albuminuria in the intervention cohort as opposed to the non-diabetic group. Subsequent administration of LXA4 attenuated such manifestation at the 10 weeks intervention mark, and further protection was warranted till the end of the study period. Moreover, administration of LXA4 repressed the proinflammatory/profibrotic Tumor Necrosis Factor alpha (TNF- α) and Transforming Growth Factor beta (TGF- β) signaling networks in diabetic ApoE ^{-/-} mice. Additional research showed a direct modulation of the SPM metabolism by mesenchymal stem cells (MSCs), following their transplantation in the kidney of DN rats. Exertion of the MSCs' pro-lipid metabolism action resulted in augmented expression and accumulation of LXA4 in the renal microenvironment. A recent randomized clinical trial highlighted the differences in circulating levels of 15-epi-LXA4 between DN patients and their diabetes-free counterparts. Administration of low-dose aspirin, due to its distinctive ability to create an endogenous mimetic of LXA4, increased baseline values of 15-epi-LXA4 in the individuals affected by chronic kidney disease. **Conclusions:** High LX levels are positively associated with a reduction of DN manifestations and inflammatory sequelae. Direct administration of exogenous LX mimetics or indirect stimulation of endogenous production classify as future potential therapeutic schemes in the management of DN. **Acknowledgments:** This work was supported by the George Emil Palade University of Medicine, Pharmacy, Science and Technology of Târgu-Mureş, Junior Researcher Academy Initiation Research Grant number NR. 311/2/10.01.2024, with the title "Utilization of lipoxins and other SPMs in the prevention and treatment of diabetic nephropathy and diabetic cardiovascular disease".

Keywords: diabetic nephropathy, inflammation, specialized pro resolving lipid mediators, lipoxins

C-REACTIVE PROTEIN AND ITS MONOMERIC FORM AS EXACERBATORS OF EPITHELIAL MESENCHYMAL TRANSFORMATION IN DIABETIC NEPHROPATHY

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Background: Epithelial Mesenchymal Transformation (EMT) is a swift biological process where epithelial cells undergo alterations, adopting typical traits of mesenchymal cells. These changes include loosening of cell-to-cell adhesion molecules, and adjustments in polarity and cytoskeleton organization, leading to the expression of vimentin filaments and the downregulation of cytokeratin. EMT is promoted by C-reactive protein (CRP), an acute phase pentameric protein produced by the liver in response to inflammation. Specifically, the interaction of CRP with various signaling pathways, including FcγRII, Wnt/β-catenin, and Extracellular Signal-Regulated Kinase (ERK), has been proposed as a potential mechanism through which this protein exacerbates EMT, resulting in renal fibrosis and dysfunction, therefore playing a role in the development of a chronic complication of diabetes mellitus (DM), namely diabetic nephropathy (DN). Recent studies have been focused on analyzing the effects of the monomeric form of CRP, mCRP, as it displays more potent proinflammatory biological activities, hence its involvement in EMT aggravation and DN pathogenesis is contemplated here. **Objective :** This study aims to investigate the role of CRP and its monomeric form in the modulation of EMT pathways, particularly in the context of DN. **Material and methods:** A PubMed search was conducted in the domain of English literature including the keywords "C-reactive protein", "Epithelial Mesenchymal Transformation" and "diabetic nephropathy". An additional selection was then implemented to examine the involvement of CRP in its monomeric configuration. **Results:** In a study examining rat models of streptozocin-induced diabetic nephropathy, notable distinctions emerged between the Diabetic Kidney Disease Wild-Type Group (DKD wt) and the Diabetic Kidney Disease C-reactive protein Knockout Groups (DKD Crp^{-/-}). The latter exhibited significantly lower levels of blood glucose, serum creatinine, and blood urea nitrogen, as opposed to the DKD wt group, at the end of the 12 weeks experiment. Histological findings further demonstrated a decrease in both mesangial matrix deposition and thickness of the glomerular basement membrane, along with reduced renal fibrosis and glycogen accumulation in the DKD Crp^{-/-} group compared with the DKD wt rats. An immunohistochemical study utilizing the monoclonal mouse anti-human CRP-antibody, clone 8, revealed a specific mCRP-positive signal in the tubular cytoplasm of 17 out of 20 renal tissue samples of diabetic patients. Moreover, a notable correlation between the severity of histologic changes, namely nodular or diffuse glomerulosclerosis and interstitial fibrosis assessed by histology score, and the mCRP staining was observed. **Conclusions:** CRP acts as a molecular switch in controlling EMT thus contributing to the progression of DN. Despite promising studies assessing the role of CRP monomers in the pathogenesis of diabetic renal disease, more research efforts must be warranted in order to clarify how mCRP affects progression and exacerbation of this disorder.

Keywords: Epithelial Mesenchymal Transformation, C reactive protein, monomeric C-reactive protein, diabetic nephropathy

ACETYL-L-CARNITINE AS A BENEFICIAL SUPPLEMENT AGAINST COGNITIVE DECLINE AND NEURODEGENERATION

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Background: Cognitive decline represents a progressive neurological disorder affecting the elderly population, consisting in loss of memory, awareness, ability of problem solving, and reasoning. With increasing age, the cerebral tissue undergoes steady morphological changes, namely grey matter shrinkage and myelin sheath deterioration, with subsequent impairment of brain functionality. Acetyl-L-carnitine (ALCAR), the acetylated form of carnitine, contributes to normal fatty acid metabolism by binding and transporting long fatty acid chains into the mitochondria, resulting in improved cellular energy status. Studies carried out in the past two decades have

established ALCAR's positive effects on cognitive decline and neurodeterioration by slowing down degenerative processes, stabilizing mitochondrial function, and re-establishing normal neurotransmission. **Material and methods:** An extensive literature search was conducted on PubMed and ScienceDirect in order to retrieve English articles published between 2004 and 2024. The included articles presented the keywords "Acetyl-L-carnitine", "cognitive decline", "dementia", and/ or "neurodegeneration". **Results:** In vivo studies on rats showed that ALCAR upregulated the Heme-oxidase 1 gene responsible for the production of antioxidant agents, which in turn stabilized the mitochondrial function, protecting against lipid peroxidation and oxidative stress, and slowing down the neurodegeneration process. Furthermore, in vitro studies with double-blind controlled hippocampal cultures have shown that ALCAR administration enhanced alpha-secretase activity, which is responsible for cutting the amyloid precursor protein (beta-amyloid being a key biomarker in Alzheimer's disease (AD) contributing to amyloid plaque formation), at a specific nucleotide, hence, a reduction in amyloid beta full protein synthesis was observed. Additionally, human clinical studies involving patients with dementia associated with vascular cognitive impairment have indicated that administration of ALCAR for 28 weeks efficiently restored the normal neuronal membrane potential, thus reducing mitochondria-induced neural toxicity. **Conclusions:** Acetyl-L-carnitine prevents neural damage by reducing oxidative stress and ensuring normal mitochondrial function, which is crucial for proper neurotransmission. Considering the scarcity of clinical trials and studies, further research exploring the ALCAR treatment in neurodegenerative diseases might verify the positive effects of carnitine on the central nervous system and indicate a potential therapeutic use.

Keywords: Acetyl-L-Carnitine, Cognitive decline, Neurodegeneration, Oxidative stress, Alzheimer's Disease

EFFICACY OF MONOCLONAL ANTIBODY GANTENERUMAB IN TARGETING AMYLOID BETA AND TAU PROTEINS IN ALZHEIMER'S DISEASE

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Background: Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by a preclinical pathological state, which involves the aggregation of Amyloid Beta-protein (A β), leading to neuroinflammation, and Tau phosphorylation. Current treatment strategies focus on the utilization of Monoclonal Antibodies (MAB) to eliminate these aberrant structures, with Gantenerumab (GAB) being a suitable candidate. **Objective :** This literature review aims to assess the effectiveness of the monoclonal antibody GAB in comparison to other promising pharmacological treatments for AD. **Material and methods:** A search of English, German and Italian literature was conducted on January 13, 2024, using the academic search engines PubMed and Google scholar. Inclusion criteria comprised articles published between 2019 and 2024, presenting the keywords "Alzheimer's disease", "amyloid beta proteins", "monoclonal antibodies", "gantenerumab". **Results:** A human randomized, placebo-controlled trial comparing GAB and Solanezumab in patients with Dominantly Inherited AD (DIAD), across asymptomatic and symptomatic disease stages, demonstrated that GAB significantly reduced amyloid plaques and tau levels in the cerebrospinal fluid (CSF). Despite cognitive deterioration being more pronounced for the participants receiving Solanezumab, no statistically significant difference in cognitive decline was observed with the utilization of GAB, as opposed to the control group. A recently conducted systematic analysis aimed to assess pharmacological characteristics, biomarkers, and clinical profiles of the only four anti-amyloid agents that successfully completed phase 3 or 2 trials and presented an acceptable safety with treatment duration ≥ 12 months, namely GAB, Aducanumab, Lecanemab, and ALZ-801. GAB was found to have remarkable inhibitory effects on both the phosphorylated and total tau expression within the CSF, despite not providing improvement in cognition, compared with the placebo. Conversely, treatment with the other agents showed considerably less benefits in biomarker reduction, yet a statistically significant cognitive amelioration. Furthermore, several studies demonstrated how the incidence of amyloid-related imaging abnormalities (ARIA), the most common adverse effect seen in MAB-treated individuals, was directly proportional to the clearance of cerebral amyloid on PET imaging, therefore indicating the importance of constant patient monitoring, and dose adjustment. **Conclusions:** GAB effectively reduces the biomarkers associated with AD pathology, without a corresponding improvement in cognitive function. Considering these trials collectively, MABs offer a foundational approach for future therapeutic options in AD, with GAB being a valid candidate, taking into account the necessity of dosage monitoring in order to minimize unwanted side effects.

Keywords: Alzheimer's disease, Amyloid beta proteins, Monoclonal antibodies, Gantenerumab

TOLL-LIKE RECEPTOR ANTAGONISTS AS A POTENTIAL THERAPEUTIC APPROACH FOR PSORIASIS

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Background: Psoriasis is a chronic inflammatory skin disorder characterized by hyperproliferation of keratinocytes and immune dysregulation, leading to plaques covered in scales. In the last decade studies have exhibited an association between autoimmune disorders, like psoriasis, and antimicrobial peptides (AMPs), which are amphipathic cytotoxic peptides, like the active form cathelicidin, LL-37. LL-37, released from damaged keratinocytes, serves an important role in immune reactions as well as in the activation of cell proliferation.

Material and methods: A comprehensive literature review was carried out, including articles retrieved from PubMed and Google Scholar between 2007 and 2024. The selected articles were published in English in peer-reviewed journals, and presented the keywords "psoriasis", "antimicrobial peptides", "cathelicidin (LL-37)", and "Toll-like receptors". **Results:** An increased concentration of AMPs, including LL-37, has been observed in psoriatic skin, linking their immune activities to the triggering of inflammation, independent of infection in the disease. LL-37's mechanism of antimicrobial activity includes priming keratinocytes for inflammation, acting on T-cells as autoantigens. Moreover, they activate dendritic cells (DCs) through endosomal Toll-like receptors (TLRs) 7, 8 and 9 leading to the release of Interferon-alpha (IFN- α), Interleukin- 12 (IL-12) and Interleukin-23 (IL-23), and the activation of T- and B-cells, promoting the immune reaction and proliferation of keratinocytes. The activation of TLRs 7, 8 and 9 can be engaged by self-nucleic acids bound to AMPs such as LL-37. In this regard, a study investigating the effect of TLR7, 8 and 9 antagonists as therapeutic agents in IL-23-induced psoriasis mouse models, demonstrated that these antagonists decreased expression of IL-23 and Th17 cytokines, inhibited epidermal hyperplasia and inflammasome activation, and blocked IL-12 expression. **Conclusions:** This review underlines the positive correlation between high levels of LL-37 in psoriatic skin lesions and disease activity, indicating endosomal TLR-antagonists as a potential therapeutic approach for psoriasis given the importance of TLR 7, 8 and 9 for LL-37 activity. Further research is needed to investigate the effectiveness as well as evaluate the advantages and disadvantages of TLR-antagonists as potential treatment options.

Keywords: antimicrobial peptides, psoriasis, cathelicidin (LL-37), Toll-like receptors

EVALUATING THE SEVERE ADVERSE EFFECTS ASSOCIATED WITH THE PRACTISE OF SELECTIVE ANDROGEN RECEPTOR MODULATORS.

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Background: Selective Androgen Receptor Modulators (SARMs) are not yet FDA approved. Their structures were synthesised to differentially bind to androgen receptors. Current studies are evaluating their effects in the treatment of breast cancer and cachexia. Off label use of the prior mentioned compounds is associated with athletes in particular body builders both professional and amateur. The World anti-doping agency, considered the anabolic effects of these compounds and voted to prohibit their use in professional sports. Adverse effects triggered by use of SARMs, and variances in comparison with AAS, associated with cardiovascular toxicity are the focus of this literature review. **Material and methods:** A search of English, German and Romanian literature was conducted on February 27, 2024, using the academic search engines PubMed and Google scholar. Inclusion criteria comprised articles published between 2019 and 2024, presenting the keywords "selective androgen receptor modulators", "androgenic anabolic steroids", "adverse effects", "binding properties" "cardiovascular toxicity". **Results:** We identified several published case studies, and below are representative examples of the findings: 1) A 32 year old (y/o) male presenting to the hospital with a history of diabetes Mellitus Type 1 and sudden onset of Shortness of

Breath (SOB) on exertion since one day. The patient discloses, self medication of the SARM testolone. Results of clinical investigations concluded: left ventricular dysfunction and elevated trop, leading to the conclusion of Acute Myocarditis. 2) A 31 y/o male following the diagnosis of Crohn's disease treated with infliximab every six weeks. The patient complains of a sudden onset of substernal chest pain with accompanying symptoms after his workout. For the past 10 years the patient underwent multiple cycles of AAS. Coronary angiography revealed a thrombus in the left descending artery, allowing for the diagnosis of an myocardial infarct and chronic AAS use as etiology. **Conclusions:** This literature review analysed the mechanism of action of SARM and concluded that the overexpression of physiological signalling pathways is the foundation of the adverse effects. The mechanism involves an increased fibrosis mediated by an increase in markers of cardiomyopathy such as β myosin heavy chain and cytotoxicity measured by lactate dehydrogenase. These effects are more pronounced in males than in females. Whilst the WADA are very strict in relation to the use by professional athletes, used as a supplementation in amateur sport, their use is not as highly regulated in terms of quality, composition and concentration etc and therefore under or overdosing is common leading to the risk of cardiovascular events. The definite pathophysiological mechanism is not fully understood and requires further investigation.

Keywords: Selective Androgen Receptor Modulators, Androgenic anabolic steroids, cardiovascular toxicity

HIGH LEVELS OF OXIDATIVE STRESS AND REACTIVE OXYGEN SPECIES IN ATHLETES UNDERGOING INTENSE EXERCISE PROGRAMMES PREDICTS THE RISK OF VENTRICULAR ARRHYTHMIA AND SUDDEN CARDIAC DEATH.

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Background: Sudden cardiac death (SCD) is often encountered in both professional athletes and in people that practice sports recreationally. Ventricular arrhythmias (ventricular tachycardia and fibrillation) are frequently blamed for such an abrupt demise. Among the mechanisms responsible for myocardium electrical instability, oxidative stress plays an important part. Reactive oxygen species (ROS) levels are demonstrated to be increased in athletes in relative proportion to the intensity not the length of the activity. The purpose of this literature search is to understand the relationship between raised ROS levels and absolute intensity of physical activity with a view to potentially utilising this process as a potential biomarker of risk stratification. **Material and methods:** An extensive examination of scientific literature was conducted using the databases PubMed, Scopus, Web of Science, and the Journal of the American Heart Association. Keywords used in this search were 'intense physical activity' and 'ROS' and 'cardiac arrhythmia' and 'oxidative stress' and 'sudden cardiac death' **Results:** Muscle contractions during activity trigger the production of reactive oxygen species (ROS) in active muscle fibers, with skeletal muscles being a key contributor. Prolonged or intense exercise can lead to oxidative damage in muscle fibers and hastened fatigue. However, the increased ROS production during exercise is necessary for skeletal muscle adaptation to endurance training. Current evidence suggests that rigorous and extended exercise can reach levels of oxidative stress detrimental to human health, in particular damaging the heart muscle leading to potentially fatal ventricular arrhythmias. In cardiac cells capable of excitation, reactive oxygen species (ROS) play a dual role in governing cellular metabolism and ion balance. Emerging research indicates that heightened ROS levels within cells can prompt modifications in the cardiac sodium channel ($\text{Na}_v 1.5$), disrupt calcium handling, impact mitochondrial function, and induce remodeling of gap junctions, ultimately contributing to the development of arrhythmias. **Conclusions:** Acute cardiovascular events may arise and progress, partially due to oxidative stress. A mounting body of evidence indicates that oxidative stress is a significant factor in the development of various cardiac diseases. Multiple treatment modalities have been broadened to address oxidative stress. While some studies have shown the positive effects of antioxidant therapy and exercise in various heart conditions, results from human clinical trials vary significantly. A more comprehensive understanding of oxidative stress resulting from intense physical activity, and associated with ventricular arrhythmia and sudden cardiac death, should inform moderated exercise regimens and possibly include novel antioxidant medications.

Keywords: intense physical activity', ROS, cardiac arrhythmia, sudden cardiac death, oxidative stress'

PERIODONTITIS AND DIABETES, THE ROLE OF THE INFLAMMATORY MILIEU IN AFFECTING INSULIN RESISTANCE.

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Background: Diabetes type 2 is a disease associated with insulin resistance (IR), i.e. an unresponsiveness of cells to Insulin. The consequent hyperglycaemia is associated with different complications. Since treatment of diabetes is not effective at preventing these complications, it is important to reduce the prevalence of the disease, as well as avoiding factors that could favour the appearance of complications. Periodontitis is an oral disease caused by bacterial proliferation on plaques. These bacteria induce an inflammatory reaction which often becomes chronic. Periodontitis and diabetes type 2 are highly interconnected, i.e. diabetes can worsen periodontitis and periodontitis can worsen glycaemic control. The objective of this study is to better define how periodontitis can affect diabetes. **Material and methods:** On the 02.03.2024 different articles associated with diabetes and periodontal disease were searched. To get an overall understanding, scientific articles were first searched on Google, whilst afterwards details were searched on PubMed and Google Scholar. Articles that appeared relevant were chosen as sources for the abstract. It was tried to choose articles written in the last 5 years, but any article could be used, as long as the team deemed them as relevant. Key words used in the search were "periodontitis", "insulin resistance" and "diabetes". **Results:** Diabetes and periodontitis can influence each other. It was noted that diabetic patients without periodontitis have a better glycaemic control than patients with periodontitis. In addition, healing periodontitis in diabetic patients appears to reduce glycated haemoglobin by 0.4%. The increase of IR caused by periodontitis could explain why periodontitis is associated with a worse glycaemic control. The mechanism responsible for increasing IR, is being studied and it appears to be inflammation mediated. Periodontitis elicits an inflammatory reaction that not only increases inflammatory cytokines systemically but also modulates T cell activation. It was noted that in rats with induced periodontitis, the T helper 1 phenotype, which enhances IR development, was stimulated, whilst the T helper 2 and the T regulatory phenotype, which attenuates IR, was inhibited. Another mechanism by which the local periodontitis environment might favour IR involves macrophages and enhancement of obesity associated inflammation. Periodontal pathogens and inflammatory cytokines might increase monocyte activation and subsequent transformation into macrophages. Once this happens these cells will migrate to adipose tissue and enhance obesity associated inflammation. Because of these effects, treating this proinflammatory status by treating periodontitis might be a potential measure to treat IR. It is however important to mention that in case of a body mass index (BMI) > 30 kg/m² the treatment of periodontitis did not seem effective in reducing systemic inflammation. **Conclusions:** As different studies have shown, diabetes and periodontitis are highly interconnected. Periodontitis can favour IR by leading to a systemic proinflammatory status which will worsen glycaemic control and lead to chronic complications of diabetes. Therefore, treating periodontitis might be a potential new way to reduce the development of chronic complications of diabetes in individuals with a moderately increased BMI (BMI < 30 kg/m²).

Keywords: periodontitis, insulin resistance, diabetes, inflammation

EXPLORING THE POTENTIAL OF PDE5 INHIBITORS IN ALZHEIMER'S DISEASE

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Background: Alzheimer's disease (AD) is a neurodegenerative disorder characterized by progressive cognitive decline and neuropathological changes, including the accumulation of β -amyloid plaques. Phosphodiesterase 5 inhibitors (PDE5I), -the active ingredient in Viagra, exert their effects by inhibiting Phosphodiesterase 5-mediated hydrolysis of cyclic guanosine monophosphate (cGMP). Sildenafil, which is a PDE5I acts mainly on smooth muscle cells, but it also impacts upon brain tissue where it helps in the modulation of neuronal function. The aim of this abstract is to consolidate findings from studies which highlight the relationship between PDE5I and Alzheimer's disease and to point out possible benefits. **Material and methods:** A systematic search of PubMed

database with MESH terms: "Phosphodiesterase 5 inhibitors" and "Alzheimer's disease" for open access research articles was conducted. Articles from the years 2009-2024 were included. **Results:** The levels of PDE5 in patients with AD were significantly increased, whilst the inhibition of PDE5 caused a rise in cGMP and resulting in impairment of cognitive function in AD mice. Tadalafil, another PDE5I, improved spatial memory by reducing Tau protein expression in an AD mouse model. Sildenafil taken orally raised cerebral oxygen metabolism and cerebral blood flow in Alzheimer patients, indicating PDE5I as a treatment for AD linked vascular dysfunction. A systematic review analysed studies where β -amyloid levels were assessed in AD rodents in the hippocampus. With one exception (a study using only female rodents), PDE5I was effective in lowering β -amyloid levels and furthermore it blocked cognitive decline in every study. A large cohort study analysed data from over 260,000 men demonstrating that PDE5I in men with erectile dysfunction was linked with a lower risk of AD. The prescription frequency was indirectly proportional to the risk of AD. A computational analysis over six years from 2021 also revealed that sildenafil users had a 69% lower risk of developing AD indicating potential protective properties. **Conclusions:** Although the biological interactions between Alzheimer's and Sildenafil are not fully understood, a promising number of studies support the hypothesis that PDE5I can actually decrease the risk and/or slow down the development of AD. To increase the applicability in general, studies are needed which include both sexes because in most studies, only male populations were investigated. The findings suggest that there are potential implications for creating new drugs aimed at treating the underlying causes of AD and addressing cognitive decline.

Keywords: Phosphodiesterase 5 inhibitors, Alzheimer's disease, Neuroprotection, Cognitive decline

TRIMETAZIDINE, THE HEALTHIER DOPING AGENT FOR ATHLETES?

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Background: Doping for athletes has various facets, one of the most important is the abuse of drugs which enhance their performance and can lead them to have an advantage in comparison to their opponents. Trimetazidine (TMZ) belongs to the drugs usually used for its antianginal properties belonging to the partial inhibitors of fatty acid oxidation. TMZ shifts the use of lipids in physical activity towards the use of glucose and glycolysis by activating the Krebs cycle, which reduces the use of oxygen within the myocardium. **Material and methods:** The research material was retrieved from published articles. The research was conducted in a way that information was gathered using search terms about TMZ in relation with performance athletes. Then articles were selected by pre-defined inclusion and exclusion criteria. **Results:** TMZ increases glucose uptake by the cells by reducing insulin resistance. The mechanism behind this is the externalization of GLUT-4 receptors and favoring their expression. The drug inhibits 3-ketoacyl-CoA thiolase (KAT) which decreases the fatty acid beta-oxidation and activates pyruvate dehydrogenase (PDH). This in turn transforms pyruvate into Acetyl-CoA initiating the Krebs cycle, thus demanding less oxygen for Adenosine triphosphate (ATP) production. Furthermore, TMZ activates the protein kinase (AMPK) by phosphorylation leading to the externalization of GLUT-4 receptor. TMZ reduces oxidative stress which limits the degeneration of myocytes happening in very intense muscular effort. Therefore, for example metalloproteinases are downregulated which are regarded as markers for oxidative stress. Another example is that TMZ also changes the levels of expression of caspase-3 and Bcl-2 which are partly responsible for the apoptosis of myocytes. Thus, TMZ prevents the remodeling and the injury of myocardium, meaning it has a cardioprotective effect. Additionally, TMZ exhibits an increase in coronary blood flow and anti-ischemic effects. It improves the quality of mitochondria in muscles and therefore can improve the performance of athletes. Additionally, they tend to adopt for example a high-fat diet to increase the insulin sensitivity which is also supported by TMZ and therefore helps the athletes to reduce their serum glucose levels and increase their protection of coronary diseases and metabolic syndrome. **Conclusions:** To conclude, this abstract highlights that TMZ improves the performance of athletes by switching the energy use from fatty acid catabolism to glucose use which reduces the oxygen consumption and also the release of oxidative stressors. Thus, leading to a decrease in remodeling and myocyte injury or apoptosis increasing the performance capacity.

Keywords: Trimetazidine, doping, oxygen consumption, glucose metabolism

SGLT2 INHIBITORS AS THERAPEUTIC AGENTS IN ERECTILE DYSFUNCTION AS A COMPLICATION OF DIABETES MELLITUS

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Background: Diabetes mellitus (DM) is a chronic condition characterized by elevated blood sugar levels due to an autoimmune process, manifested as a lack of insulin production in type 1 (T1DM) and insulin resistance in type 2 diabetes mellitus (T2DM). DM patients, due to impaired glycemic homeostasis, face an elevated risk of complications, including neuropathy, vascular limitations and erectile dysfunction (ED). The latter is considered as a multifactorial condition which involves the delicate balance of vascular endothelium. A pivotal role in the process of penile erection is played by nitric oxide (NO), which acts as a vasodilator, thus relaxing smooth muscles. From a pharmacological perspective, sodium-glucose co-transporter type 2 inhibitors (SGLT2i) represent a class of antidiabetic agents used in the treatment of T2DM. They inhibit the channels located in the proximal renal tubules responsible for reabsorption of glucose, increasing its urinary excretion. Unlike the other antidiabetic drugs, they enhance glycemic control without interfering with insulin secretion. **Objective:** The aim of this literature review is to provide a perspective on the use of SGLT2i as therapeutic agents in the management of ED, a possible complication of T2DM. **Material and methods:** The literature review was performed on PubMed and Google Scholar, including the key words SGLT2 inhibitors, erectile dysfunction and diabetes mellitus. It included peer reviewed articles in English, and excluded ED of surgical etiology or injuries involving the pelvic area, such as prostatectomy or pelvic fractures. **Results:** Pharmacological studies aimed at evaluating the impact of SGLT2i on ED face various challenges. These challenges stem from the insufficiency of experimental studies to adequately demonstrate the efficacy of the drug in fulfilling this role. It was described that SGLT2i may exert a potentially positive influence on endothelial cells. In particular, Dapagliflozin and Empagliflozin were observed to be involved in therapeutic modulation, improving the bioavailability of NO released by endothelial cells. This positive effect is attributed to the capacity of SGLT2i to suppress Reactive Oxygen Species (ROS), which are involved in the consumption of intracellular NO. Consequently, the inhibition leads to significant NO levels elevation, enhancing endothelial function and vasodilation. Furthermore, Dapagliflozin suggested a potential involvement in the attenuation of platelet activation by inhibiting NADPH oxidase 2 (NOX2), a critical enzyme in this process. **Conclusions:** Considering the key role of endothelial dysfunction in ED, SGLT2i are favorable to have a therapeutic role. However, further studies will have to be conducted to define whether the therapeutic effects of SGLT2i in ED in patients with DM is only related to the glycemic control or whether it is additionally related to their function on endothelial cells. Given that SGLT2i are not included within current ED treatment guidelines, the study primarily focused on understanding and illustrating their underlying mechanism.

Keywords: SGLT2 inhibitors, diabetes mellitus, erectile dysfunction

SINGLE CENTER EXPERIENCE WITH THE EKOS SYSTEM IN 100 CONSECUTIVE PATIENTS WITH ACUTE PULMONARY EMBOLISM WITH INTERMEDIATE HIGH RISK

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Background: Pulmonary embolisms present a growing challenge in healthcare, with traditional treatments often carrying significant risks such as severe bleeding, blood pressure fluctuations, arrhythmias, and clot recurrences, despite the effectiveness of traditional systemic clot-dissolving therapy. This study analyzes the efficacy and safety of the novel minimally invasive EKOS-Lysis procedure as an innovative solution to mitigate risks and enhance treatment success for pulmonary embolisms, particularly in intermediate high-risk patients. The procedure entails ultrasound-guided catheter lysis intervention, which utilizes ultrasound waves to reduce the clot and involves the localized injection of the lysis drug. The objective of this study is to improve the effectiveness, safety, and comprehension of pulmonary embolism management, providing valuable insights that may redesign approaches to this life-threatening condition, while simultaneously aiming to evaluate the efficacy and safety of this novel procedure in treating pulmonary embolisms across various patient subgroups, focusing on its benefits and risks.

The study seeks to identify the subgroup of patients exhibiting the most favorable short-term outcomes. With the pharmacological therapeutic analysis, potential interactions will be highlighted between the thrombolytic therapy used in EKOS-Lysis and chronic therapy routinely taken by patients, focusing on their impact on the overall outcomes. The objective is to assess the overall effectiveness and safety of the procedure by comparing it to existing data on standardized thrombolytic management. **Material and methods:** A retrospective study is conducted using a substantial dataset extracted from 100 patient files, categorized as intermediate high-risk for pulmonary embolism. Patient eligibility is assessed through a protocol-based review of individual medical records. Comprehensive inclusion criteria are established to evaluate each patient's clinical characteristics and history. The collected data are organized into a structured Excel database to facilitate systematic analysis. Biostatistical analysis is employed to assess the significance of differences and relationships within the dataset. Results are systematically compared between stratified groups and international data reported by literature. **Results:** The expected results based on the hypothesis are anticipated to suggest several promising outcomes. It is anticipated that improved short-term outcomes will be observed, characterized by various parameters such as decreased duration of hospitalization and reduced incidence, or absence, of post-treatment complications. Additionally, the analysis aims to determine the most and least effective anticoagulation and lysis drug for specific patient subgroups, providing valuable insights into optimized treatment strategies tailored to individual needs. It is expected that the findings will indicate a superior overall outcome in comparison to standardized systematically injected lysis therapy. This comparative analysis will shed light on the potential advantages of the EKOS-Lysis procedure over traditional treatment approaches. **Conclusions:** In conclusion, this study will investigate the efficacy and safety of the EKOS-Lysis procedure as an alternative to traditional systemic thrombolytic therapy for managing pulmonary embolism, in intermediate high-risk patients. Anticipated results suggest that EKOS-Lysis may offer superior short-term outcomes, optimal anticoagulant choices for specific patient subgroups, and overall improved efficacy compared to standardized thrombolytic therapy. These findings have the potential to reshape current treatment paradigms and enhance the management of pulmonary embolism.

Keywords: Pulmonary Embolism, EKOS-Lysis, Thrombolytic therapy, Anticoagulation, Minimally-invasive treatment

EFFICACY OF PRAZOSIN IN MITIGATING PTSD-ASSOCIATED SLEEP DISRUPTIONS AND SYMPTOMS IN PATIENTS.

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Background: Post Traumatic Stress Disorder (PTSD) is an enfeebling condition marked by severe symptoms such as nightmares, flashbacks, hypervigilance, intrusive thoughts etc. While Selective Serotonin Reuptake Inhibitors (SSRIs) such as Paroxetine, Fluoxetine, or Sertraline are the first-line treatment for many PTSD symptoms, these interventions often fall short of fully addressing persistent nightmares and sleep disturbances as well as daytime symptoms of hyperarousal and flashbacks. Prazosin has been reported to be of significant effectiveness and substantial benefit as an adjuvant and an alternative pharmacotherapy. This study aims to evaluate the effectiveness of Prazosin in improving sleep quality, reducing nightmares, and enhancing overall well-being in patients with PTSD. The primary hypothesis is that prazosin administration will greatly improve sleep quality and reduce the frequency and intensity of nightmares in PTSD patients. The secondary hypothesis suggests that these improvements will correlate with enriched psychological well-being. **Material and methods:** A literature review was conducted using the Cochrane Sleep Quality Assessment tool across databases including PubMed and PMC, with search terms such as "PTSD," "prazosin," "sleep quality," and "nightmares" to find RCTs and open-label trials. Tools like the Profile of Mood States (POMS) and the Clinician-Administered PTSD Scale (CAPS) measured symptom changes post-prazosin treatment. **Results:** Prazosin, a "Zosin" class of alpha 1 antagonists, has FDA approval for hypertension and Off-Label use in treating benign prostatic hypertrophy, PTSD, Raynaud's phenomenon, and pheochromocytoma. PTSD patients have an overstimulation at the level of postsynaptic alpha-1 receptors, resulting in CNS hyperadrenergic response. During the REM sleep cycle phase, alpha-1 adrenergic receptors' hyperarousal causes nightmares. Daytime Symptoms like flashbacks and visual hallucinations associated with an individual's trauma share symptomatology with Nightmares. Prazosin crosses the Blood Brain Barrier, facilitating adrenergic downregulation. Daytime hyperarousal symptoms suggest a shared pathophysiology between flashbacks and nightmares allowing for a similar treatment approach. However, the limited literature on Prazosin's daytime dosing indicates the need for further research. Prazosin's night-time dosing

has been shown to benefit diverse groups such as military veterans and civilians. Despite the minor side effects, Prazosin is generally well-tolerated. Pavin et al. note that civilian dosages start at 1mg and can increase to 6mg nightly, whereas veterans need 10-16mg for similar benefits. Symptoms resume on cessation. Notable Statistical values from Singh, Balwinder et al.'s study compared to placebo are PTSD Score ($P < .001$); Nightmares ($P < .001$); Hyperarousal ($p=0.1$) with an increased 60.98 minutes in Total Sleep Time and comparable adverse effects ($P > .05$). **Conclusions:** The review shows Prazosin as a well-tolerated treatment for PTSD-related sleep disturbances, effective alongside psychological interventions. Despite it aligning with the known side effect profile, including nausea and orthostatic hypotension, nightmares may resurface upon cessation. The review encountered limitations such as a small number of RCTs, potential bias in study designs, and a limited scope regarding the diversity of the study populations. Most explored studies were followed for less than a year and had minimal diversity. These findings highlight the need for additional research to ascertain Prazosin's effectiveness across daytime and nighttime symptoms to develop tailored dosing strategies for varied patient demographics.

Keywords: PTSD, Prazosin, Sleep Quality, Nightmares, PTSD Daytime Symptoms

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