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JUNE [13-15, 2024]

Roma Pain Days
HYBRID CONGRESS!



CONGRESS CENTER: Roma Eventi - Fontana di Trevi

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Proceedings of the
Roma Pain Days (#RPD24) Hybrid Congress

June 13-15, 2024

Congress Center: Roma Eventi – Fontana di Trevi
Rome, Italy

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Introduction

The fourth edition of the Roma Pain Days is becoming a reality. The enthusiasm that it has generated in the Pain Physicians interested in this event is self-explained looking at the interest they have shown in submitting several abstracts.

For the very first time, the Paolo Procacci Foundation will publish the proceedings of the congress in its new journal, *Advancements in Health Research* (<https://www.ahr-journal.org/site>), as a Supplement. This initiative will certainly stimulate new research projects on Pain Medicine, and a generally increased interest on the topic.

The Scientific Committee has selected the material of interest, and it is possible to see that most of the submissions are related to the clinical approach to pain patients. It is clear that the management of the patients represents the key point for most of the Colleagues that will actively participate to the Roma Pain Days. And this sounds like a very interesting point.

The enthusiasm of the Organizing Committees is increasing, considering the results they are observing. The congress has attracted the attention of Colleagues from an incredible quantity of countries, all over the world. For obvious reasons, over 75% of them will participate to the online event, but even so, they may take part in the discussion both of the previously organized program (<https://romapaindays.com/program/>) and of the free presentations that are included in this abstract book.

The Paolo Procacci Foundation is proud and happy to represent a driving force in the growth of Pain Medicine. It is also very grateful to all the enthusiastic Colleagues willing to participate in the discussion and the scientific growth of the topic, both as Members of the Committees, as reviewers of the submitted material, and as Faculty of the congress. They have generously offered their time and their scientific background for the benefit of the suffering patients.

Giustino Varrassi

Paolo Procacci Foundation, Rome, Italy



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DIABETIC NEUROPATHY

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Introduction: Diabetic neuropathy is a common microangiopathic complication of diabetes mellitus. Its painful form is the most frequent, increasing the risk of severe complications such as ulcers and amputation. The aim of our study is to investigate the frequency of painful diabetic neuropathy and to describe the challenges of management in physical medicine.

Materials: We conducted a cross-sectional study during the period from January 1, 2023 to January 1, 2024, including diabetic patients consulting the physical medicine and functional rehabilitation department of CHU Sahloul for peripheral neuropathic pain. Neuropathic pain was clinically assessed using the DN4 scale and the visual analog scale. We included 90 patients from 340 diabetic subjects. The mean age was 60 years. A predominance of women was noted. Only 16 patients had social security coverage. The majority had unbalanced diabetes with a mean Hb1AC of 8.5. Carpal tunnel syndrome was the most important cause of neuropathic pain, with a mean DN4 of 6/10 and a mean pain VAS of 6/10. Neuropathic sock pain in both lower limbs was discovered incidentally on clinical examination. Given the difficulty of accessing neurophysiological investigations in hospital, only 30 patients had an electroneuromyogram (ENMG) confirming peripheral nervous system involvement. Four patients benefited privately from an ENMG showing ulnar syndrome. Severe median nerve damage requiring neurolysis was noted in 6 patients. Because of social security coverage problems, only 40 patients received appropriate treatment.

Conclusions: Diabetic neuropathy remains largely under-diagnosed and under-treated. A clinical as well as a psychosocial approach is necessary for good disease management.

MIGRAINE BY MITOCHONDRIAL DYSFUNCTION: MIND A STROKE-LIKE EPISODE. A CASE REPORT

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Background: Migraine is the second among the world's causes of disability. Cortical spreading depression and fluctuations in the cerebral blood flow are one part of the puzzle. Recent research now shows that mitochondrial dysfunction may have a role to play. We present a case of hemiplegic migraine due to mitochondrial dysfunction.

Case presentation: A 31-year-old patient with history of head trauma and migraine consulted for dyspnea with asthenia and myalgia of abrupt onset, followed by a 2-minutes loss of contact with muscle twitching, then onset of intense headache and vomiting. The patient had been in sleep debt for 48 hours. Examination revealed a right hemiplegia, central facial paralysis and

vascular algia of the face. Morphine titration and treatment with acetylsalicylic acid (1g), an antivertiginous, magnesium, corticosteroid therapy, metoclopramide and rehydration were instituted as a matter of urgency. A cerebral MRI was performed with no abnormalities. Immunological investigation was negative. A pyruvate kinase and lactate assay were requested. Hypomagnesemia, hypovitamin D and iron-deficiency anemia were observed. For 3 days, there was an improvement in the motor deficit and facial algia, with a reduction in headaches. The patient was put on full-dose topiramate, magnesium, Riboflavin, vitamin D, iron and antivertigo drugs. She benefited from rehabilitation and acupuncture sessions, with a clear regression in terms of seizure frequency and motor deficit.

Conclusions: Migraine by mitochondrial dysfunction is a serious central nervous system disease. Its pathogenesis is highly complex, making clinical treatment extremely difficult. Riboflavin, magnesium and topiramate have shown to prevent recurrent headaches. Therefore, interventions to enhance function like acupuncture may reduce its risk and frequency.

IMPACT OF PERIOPERATIVE OPIOID USE ON POSTOPERATIVE OUTCOMES: A COMPREHENSIVE STUDY OF 1270 HIP FRACTURE PATIENTS

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Background and aims: Hip fractures are common in the elderly and lead to serious health issues. Effective pain management during this period is vital for recovery and preventing complications like deep vein thrombosis and muscle atrophy. While opioids are key for pain relief during the perioperative phase, they carry risks like respiratory depression, and constipation. In this study, we aim to investigate the impact of perioperative opioid use on postoperative outcomes in hip fracture repair patients.

Methods: This is a retrospective observational study analyzing data from 1,270 patients who underwent hip fracture surgery between 2019 and 2021. The study used anonymized patient data from hospital databases, focusing on demographic characteristics, perioperative opioid use, hospital stay, ICU readmission, thromboembolic complications, and revision surgeries. We employed descriptive statistics, independent samples t-test, and Chi-square Test to compare postoperative outcomes, particularly examining the impact of perioperative opioid use. A multivariate analysis was also conducted to adjust for various covariates and reduce bias. The study was approved by the Ethical Committee and adhered to confidentiality guidelines.

Results: Of the independent samples t-test revealed signifi-

cantly less hospital stay duration in patients with perioperative opioid use ($p < 0.05$). Additionally, perioperative opioid use was independently associated with reduced hospital stay (coefficient estimate = -0.656 (95%CI -1.217 – -0.096, $p = 0.022$). Moreover, patients with perioperative opioids also had significantly less frequent ICU readmissions within a month after surgery ($p = 0.024$). On the other hand, the chi-square tests did not show any significant difference between perioperative opioid use and thromboembolic complications ($p = 0.759$), death within a year after surgery ($p = 0.089$), or the need for revision surgery ($p = 0.336$). Having a cardiovascular disease is an independent risk factor for hospital readmission within a month (OR = 1.509 95%CI 1.026-2.220, $p = 0.037$).

Conclusions: Overall, this study contributes to the growing body of literature on perioperative opioid use and its implications on surgical recovery, offering valuable insights for health-care practitioners to optimize patient care and enhance surgical outcomes.

ULTRASOUND-GUIDED REGENERATIVE INTERVENTION FOR LARGE GASTROCNEMIUS TEAR: A NOVEL APPROACH

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Background: Tears of medial head of gastrocnemius are common clinical condition (tennis leg) and can compromise lower limb function and pose a challenge for non-surgical recovery. This case report describes a novel approach using ultrasound-guided regenerative intervention to treat such an injury.

Case presentation: A 45-year-old police officer presented with a large tear in the medial head of the gastrocnemius, confirmed by ultrasound examination (Figure 1). Conventional treatments had failed to yield satisfactory results.

Intervention: after obtaining written informed consent: 1. Hydro-dissection of sural nerve; 2. Hydro-dissection of tibial nerve; 3. Ultrasound guided aspiration of the intralesional hematoma; 4. Ultrasound guided intralesional “growth factors and hyaluronic acid combo injection” into upper, middle, dis-

tal parts of the tear.; 5. Bandage. Patient received 2nd injection after 21 days.

Outcomes: Significant improvement was noted within 7 weeks post-procedure, with the patient returning to full activities of daily living without pain or limitation (Figure 2).

Discussion: This case highlights the potential of our novel approach as an effective treatment for significant muscular tears, offering a viable alternative to surgical intervention.

Conclusions: The successful outcome of this case suggests that ultrasound-guided regenerative injections may provide a promising solution for athletes with similar injuries, warranting further research and consideration in clinical practice.

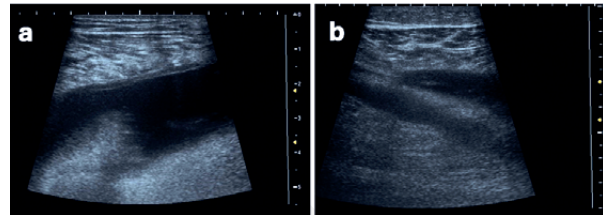


Figure 1. Long (a) and short (b) axis scans of large tear of medial head of left gastrocnemius muscle.

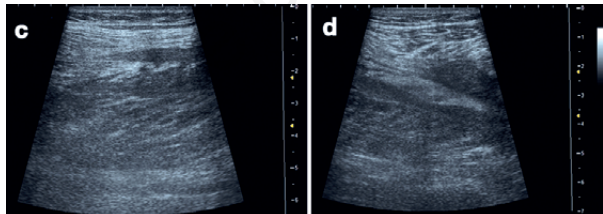


Figure 2. Long (c) and short (d) axis scans of medial head of left gastrocnemius muscle seven weeks post procedure with healing of the tear.

PAIN NURSING MANAGEMENT IN PSYCHIATRIC SETTINGS: A SCOPING REVIEW

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Background: Pain is a widespread symptom that critically impacts patient care, requiring appropriate management. Although nurses are instrumental in managing pain across various clinical settings, their roles in psychiatric contexts remain unclear. This study aims to explore the role of mental health nurses in pain assessment and management in psychiatric settings and to identify existing knowledge gaps.

Methods: A scoping review followed Joanna Briggs Institute’s methodology. Literature searches were performed in PubMed, CINAHL, Scopus, and Web of Science. Independent article screening performed using Rayyan software.

Results: Out of the 1033 articles initially retrieved, only eight met the stringent eligibility criteria and were included in this study. These studies, spanning from 1995 to 2021, predominantly employed qualitative research designs (62.5%). The findings are significant, revealing that mental health nurses employ a tailored nursing process to measure and manage pain, taking into account the unique challenges of psychiatric patients, such



as their tendency to overestimate pain. However, the assessment and management of pain by mental health nurses are potentially influenced by various factors, including stigma, beliefs about pain tolerance, concerns about drug addiction, and the imperative of maintaining ward safety. Importantly, nurses emerge as key players in managing the emotional pain of psychiatric patients through their empathetic and compassionate relationships. **Conclusions:** Research is needed concerning nurses' assessment and management of pain in psychiatric settings. These procedures seem influenced by several factors, including professional attitudes. Future research is needed to improve nursing practice in pain assessment and management in psychiatric settings.

RED WINE CONSUMPTION AND PAIN: A NARRATIVE REVIEW OF THE BIOMARKERS, THE MECHANISMS, AND THE CLINICAL TRIALS

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Background and aims: Red wine is a polyphenol-rich alcoholic beverage with numerous purported health benefits, including pain relief. Pain is a complex healthcare problem due to the individuality of the experience and the risks of pharmaceutical analgesics. Therefore, this review sought to identify the possible mechanisms behind red wine for pain relief and the clinical data supporting its use.

Methods: Nineteen searches were conducted across PubMed, ScienceDirect, Medline, the Cochrane Trials, and the Centers for Disease Control and Prevention, yielding 147 unique entries. Relevant information was extracted from these entries to assess for clinical trial data and possible mechanisms.

Results: The possible mechanisms for red wine resulting in analgesia are mostly derived from the pharmacologic effects of the polyphenols in the wine. There are over 8,000 polyphenols identified, with resveratrol and quercetin being two of the more commonly studied polyphenols. Mechanisms for pain relief are vast and include cyclooxygenase (COX) inhibition, prostaglandin-2 (PGE-2) inhibition, serotonin receptor subtype-3 (5HT-3) facilitation, transient receptor potential (TRP) blockade, increased nitric oxide production, inhibition of tumor necrosis factor-alpha (TNF-alpha), N-methyl-D-aspartate (NMDA) inhibition, interleukin-1B (IL-1B) inhibition, glycine modulation, promotion of specific pro-resolving mediators of inflammation (SPMs), activation of sirtuin, reduction of chemokine proteins, reduction of reactive oxygen species (ROS), and decreased nuclear factor-kappa beta (NF-kB). Many of the flavonoids in red wine are anti-inflammatory, anti-catabolic, and antioxidative in nature. Naloxone reverses the effects of resveratrol in preclinical trials. There is a U-shaped relationship between red wine consumption and markers of inflammation, where excess consumption of red wine promotes inflammation and pain largely due to the proinflammatory effects of alcohol binge. Two clinical trials directly assessed the effects of red wine consumption on pain scores and found a positive correlation between moderate red wine consumption and pain relief. Red wine consumption was associated with increased migraine prevalence and worsening of intestinal conditions, like Crohn's Disease.

Discussion: There are many mechanisms behind how red wine

could improve pain, but much of this data is either preclinical or does not directly assess the effects on pain scores. Positive effects were not found in every study. Many of the preclinical mechanisms of flavonoids like resveratrol were found at concentrated doses not found in red wine. Red wine contains low concentrations of resveratrol.

Conclusions: Red wine has promising potential for pain relief, but much of the data is preclinical. More clinical data is needed to ascertain the benefits of red wine for pain.

EXCESSIVE PAIN MEDICATION AND REDUCED COGNITIVE FUNCTIONING IN A PROBATE CASE

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Background and aims: To describe pain clinicians' experience with providing expert witness testimony based on medical record review of a hospitalized patient who received escalating doses of multiple pain medications prior to signing a last will and testament. Documents and records were analyzed to compile evidence which supported the assertion that compromised cognitive functioning deprived subject of testamentary capacity to understand the full nature and extent of a will, which was signed shortly after certain pain medication doses were doubled and tripled to treat excruciating pain from metastatic cancer.

Methods: Consultant clinicians were provided complete medical records for a hospitalized patient during a six-week period that suffered from multiple co-morbidities, including severe pain from metastatic cancer. This was a retrospective analysis of an in-patient chart, which included various documentation and assessments by clinical staff, along with pain medication dosing schedules. The data was correlated with physiologic parameters and cognitive function assessments (BIMS) to identify changes during escalating doses of pain medications. Fentanyl patch and Oxycontin-SR were the main pain agents used and oral morphine equivalent doses were doubled and tripled respectively, prior to subject signing last will. Other factors noted that were evidentiary of cognitive decline, and associated with CNS side effects, included chemotherapy (rituximab), radiation therapy (cervical spine), other medications used to treat pain (gabapentin and lidocaine patch), and age-related changes in function (mobility, auditory, visual, etc.).

Results: Analysis of subject records indicated that multiple factors likely contributed to reduced cognition, and an evidence-based strategy was utilized. Referenced clinical citations were provided to support each assessment or indication of reduced mental functioning as described in the medical record. Escalating oral morphine equivalent pain doses of a Fentanyl patch (doubling) and sustained-release oxycodone (tripling) that occurred two weeks prior to subject's will signing were highly suspect, and these were correlated with a sixty-seven percent cognitive decline based on BIMS (Brief Interview of Mental Status) score comparisons, which were performed one month before, and five days prior to signing of the will. An additional factor strongly indicative of reduced cognitive functioning was comparison of subject's handwriting (*i.e.*, significant changes in signature) two months prior and at will signing. This was barely recognizable from previously and it was noted the subject expired eleven days after the will signing.

Conclusions: Pain clinicians working in a consultative capacity can provide valuable expertise for attorneys involved with legal cases who seek discovery in probate matters, enabling them to present valid arguments to hypothesize whether or not pain

medication may be a probable cause for reduced cognitive functioning. It is crucial to thoroughly analyze medical records to identify if clinical evidence of mental status changes is commensurate with increases in pain medication doses, and how pharmacological properties of these agents impact physiologic functioning, especially with respect to effects on the central nervous system and abnormalities of brain function.

AN EGREGIOUS CASE OF EXCESSIVE OPIATE PRESCRIBING AND DISPENSING IN A 48-YEAR-OLD WOMAN

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Background: As the opioid epidemic continues to spiral out of control one need not look further from questionable decisions on the part of frontline clinicians to properly treat various pain conditions. In the case of an unfortunate 48-year-old subject, the excessive opiate prescribing and dispensing that resulted in death should have been avoided. The subject's pain might have been initially addressed with non-pharmacologic or safer pharmacologic treatment options and/or adherence to generally regarded safety protocols. This case illustrates how a patient's safety was compromised due to negligence on the part of physician and pharmacy for not recognizing that the subject's addiction and dependence had resulted from excessive opiate use. The pharmacy took no action to halt their excessive opiate dispensing and the physician made no attempt at opiate dose reduction and/or transition to safer agents. These deficiencies in clinical judgement and deviations from professional practice standards caused an unnecessary death.

Methods: A grid was developed based on forty-seven months of opiate prescription data prior to subjects death. This listed sequential prescription dating for each month in columnar fashion, along with drug dispensed (M=morphine, F=fentanyl, H=hydromorphone), milligram amount (for morphine and hydromorphone) or microgram amount (for fentanyl), and quantity dispensed. Cumulative prescriptions dispensed for each month were represented from two to seven rows in the grid (*i.e.*, subject had anywhere from 2 to 7 opiate prescriptions filled each month at the Pharmacy). MME (morphine milligram equivalent) calculations for each prescription are depicted in blue columns of the grid and assumes subject is taking the entire opiate prescription as written for the month. It was assumed the quantity dispensed was for a one-month supply, and this allows a cumulative daily MME calculation to be made for each month (represented in the yellow column in the grid), which totals the MME calculation of each blue column in the grid across the monthly rows. Evidence from the medical record review confirmed that the MME calculations were accurate.

Results: It was calculated that subject received an average of 536 MME daily during the forty seven months prior to death, assuming that she exhausted the entire opioid prescriptions as written. The excessive daily MME dispensing during this period is both tragic and horrific, and no doubt was the direct and proximal cause of subject's demise. In response to the opioid epidemic raging throughout the United States, the CDC issued opioid prescribing and dispensing guidelines in March of 2016 that stated that the risk of overdose is increased significantly when 50 MME's daily was exceeded. The pharmacy obviously ignored this practice standard and their dispensing clearly exposed subject to a serious risk of harm and death. The data

points on a graph, compiled from the MME data grid, shows an alarming pattern of daily MME values way above the highest CDC threshold of 90 MME. These data points ranged anywhere from 150 MME/daily up to 1,060 MME/daily.

Conclusions: As the opioid epidemic in the United States continues to spiral out of control, physicians and other prescribers have been held criminally liable to overdose-related deaths. Pharmacists are not exempt from liability in this setting and have been held legally and criminally liable for patients overdose deaths. State Boards of Pharmacy have been increasing the number of investigations against pharmacies, pharmacists, pharmacy technicians, interns, and associate staff members for not carrying out "corresponding responsibility" or addressing "Red Flags". There is an urgent need for appropriate opiate prescribing and dispensing that fall within regulatory guidelines. This case illustrates the actions of both physician and pharmacy proximately caused subject's misuse of opiates, which ultimately caused suffering from an overdose and death. Both physician and pharmacy blatantly failed to adhere to appropriate professional practice standards and protocols that caused subject great harm, suffering and ultimate death.

OSTEOPATHY: HOW IT MAY HELP TO MANAGE CHRONIC PAIN

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After the USA, United Kingdom, Canada, Australia, France, the Netherlands, Switzerland, and a few others, Italy has finally recognised osteopathy as a healthcare profession with Law No. 3 of 2018, known as the Lorenzin's Law.¹ Subsequently, the healthcare profession of osteopath was established with the law of July 7-2021, No. 131.² Last year, with ministerial decree No. 1563,³ the didactic organization and training criteria preparing the subjects to entry into universities have been defined. Osteopathy is a complementary discipline to conventional medicine and is oriented towards identifying the origin of pain and resolving its causes. It originated in 1874 when Dr. Andrew Taylor Still articulated its principles. The four key principles of osteopathic philosophy are as follows: 1. The human body is a dynamic unit of function. 2. The body possesses self-regulatory mechanisms that are healing in nature. 3. Structure and function are interrelated at all levels. 4. Rational treatment is based on these principles. Dr. Still advocated for the restoration of bodily structure and function through palpatory assessment and manipulative treatment. He also embraced a holistic view that included physical, mental, and spiritual health, a perspective recognized by the World Health Organization (WHO) in 2006.⁴ The WHO recognizes and promotes the acknowledgment of osteopathy worldwide, adhering to basic principles, as a primary healthcare profession with skills in diagnosis, management, and treatment of patients, exclusively manual, addressing all citizens from newborns to the elderly. The limitations of osteopathy are certainly related to the palpation and manual skills of the practitioner. However, osteopathy cannot address all medical conditions and issues. For instance, it cannot cure degenerative diseases, genetic disorders, infectious and/or inflammatory diseases, fractures, severe anatomical injuries, or medical emergencies. Nonetheless, OMT can alleviate symptoms associated with these conditions. This holistic and global approach ensures that osteopathy offers a unique perspective and therapeutic interventions for managing chronic pain. The most common issues that osteopathy addresses in pain therapy include: 1.



Chronic musculoskeletal pain: This includes a wide range of conditions such as arthritis, fibromyalgia, myofascial syndrome, and other chronic musculoskeletal disorders. Studies have examined the effectiveness of osteopathy in managing pain associated with these conditions and improving patients' quality of life.⁵⁻⁸

2. Chronic migraine: Chronic migraine is characterized by recurrent and debilitating headaches. Some studies have examined the effects of osteopathy in reducing the frequency and intensity of chronic migraines, as well as improving patients' quality of life.⁸⁻¹⁰

3. Chronic neuropathic pain: This type of pain is caused by damage or dysfunction of the nervous system and may be associated with conditions such as diabetic neuropathy, post herpetic neuropathy, and carpal tunnel syndrome. Studies have examined the effectiveness of osteopathy in managing chronic neuropathic pain and improving nervous system function.^{8,11,12} It's interesting to note that recent studies have shown that patients treated by osteopathic physicians who utilize OMT for chronic low back pain report lesser pain intensity and back-related disability, while also using opioids and nonsteroidal anti-inflammatory drugs less frequently than patients treated by allopathic physicians.⁶ Therefore, not only has OMT proven effective in managing pain in patients with chronic back pain,⁶ but recent pilot studies are also examining how OMT may have a molecular-level effect, reducing specific biomarkers associated with pain and cytokine concentrations within the bloodstream post-osteopathic treatment.^{13,14} The most common techniques utilized within these studies, characteristic of osteopathy, include:

- 1. Joint manipulation:** This technique involves precise and direct movements of the joints to restore joint mobility and improve function.
- 2. Soft tissue mobilization:** This technique involves manipulation of muscles, tendons, and ligaments to reduce tension and improve flexibility.
- 3. Visceral manipulation:** This technique focuses on assessing and treating visceral dysfunctions, using manual techniques to improve organ function and blood flow.
- 4. Myofascial release technique:** This technique aims to treat trigger points and tensions in the fascial tissues to reduce pain and improve function.
- 5. Craniosacral technique:** This technique focuses on assessing and treating the craniosacral system, including the skull, spinal cord, and spinal membranes, using very gentle hand movements. OMT has been shown to reduce pain intensity, improve functional status, and enhance quality of life in patients with chronic pain conditions. In conclusion, osteopathy provides a valuable therapeutic option for managing chronic pain, addressing underlying dysfunctions and promoting holistic well-being. Further research is warranted to elucidate the mechanisms of action and long-term efficacy of osteopathic interventions in chronic pain management.

νόσων φύσεις ιητροί - vis medicatrix naturae, Hippocrates

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SACRAL NEUROMODULATION IN 47 PATIENTS SUFFERING FROM BLADDER DISORDERS AND/OR PELVIC PAIN

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Background and aims: Patients suffering from bladder disorders and/or pelvic pain, not responding to surgical and conservative options, could be successfully treated with sacral neuromodulation (SNM). The aim of the study was to demonstrate that the effectiveness of SNM may not only be based on what the patient reported in terms of pain improvement, but also on objective data. Therefore, we compared the changes in urodynamics before and after SNM.

Methods: Forty-seven patients (36 women and 11 men) were treated. This technique has also been successfully adopted for a paraplegic patient suffering from neurologic bladder. All patients were treated with two leads, placed bilaterally on sacral roots through a retrograde approach or placed through the sacral hiatus (Figures 1 to 3). All patients underwent a trial period. Urodynamic study was performed before and after the trial period in patients with functional bladder disorders. In the paraplegic patient the urodynamic study was performed also intraoperative. The patients' follow-up varies from 12 months to 11 years.

Results: Forty-two patients reported significant improvement. In all patients urodynamic study was significantly improved. All patients reported significant pain relief. Both physical and mental items of the SF-36 were substantially improved. We had no cases of infection.

Conclusions: Bilateral stimulation SNM is an effective technique used in pelvic pain syndromes and functional bladder disorders. SNM techniques, like many other electrical neurostimulation procedures, need objective data on effectiveness to have the role that these techniques deserve in treatment al-

gorithms and not only be considered as a last chance.

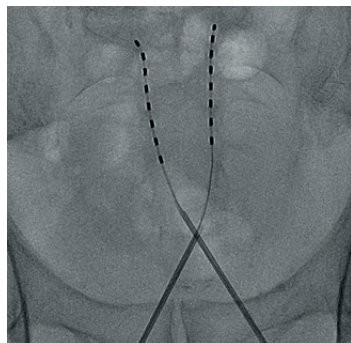


Figure 1. Sacral hiatus approach AP view.

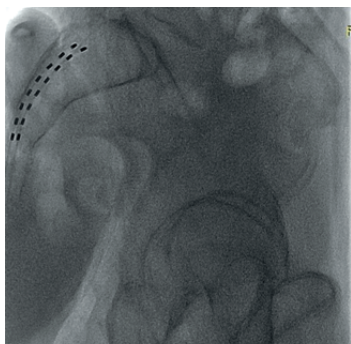


Figure 2. Sacral hiatus approach L-L view.

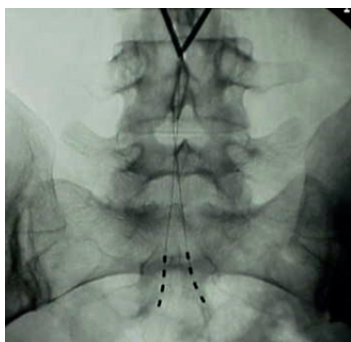


Figure 3. Upside down technique AP view.

NEURONUTRITION IN FIBROMYALGIA MANAGEMENT

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Background and aim: Fibromyalgia is a chronic disorder characterized by widespread pain, fatigue, sleep disturbances, cognitive difficulties, and other somatic symptoms. The etiology remains unclear, and nutrition has emerged as a potential modifiable factor in its management.¹ We aimed to review recent research on diet and dietary supplements in fibromyalgia management.

Methods: A search was conducted in electronic databases such as PubMed, Google Scholar, and Elsevier for original articles published over the past 10 years, using such keywords as “fibromyalgia”, “diet” and “dietary supplement”.

Results: The main neuronutritional molecular targets are neu-

roinflammation, oxidative/nitrosative stress, gut-brain axis disturbance, and neurotransmitters imbalance. Although no specific diet has been universally endorsed, certain dietary modifications may offer symptomatic relief. Vegetarian diet as well as low energy diet has shown some benefits in pain relief independent of its influence on weight.^{2,3} Dietary interventions aimed at restoring gut health, such as low FODMAP, modulate immune responses and neuroendocrine pathways involved in fibromyalgia.⁴ Certain food avoidance, such as monosodium glutamate and aspartame, and gluten-free diet may be beneficial for some patients.^{5,6} Acting on both neurotransmitters imbalance and neuroinflammation Tryptophan and Magnesium-Enriched Mediterranean Diet is showing promising results.⁷ Beneficial supplements include Vitamin D, Omega-3 fatty acids, Mg citrate, α -tocopheryl acetate + ascorbic acid as well as probiotics.⁸⁻¹²

Conclusions: While fibromyalgia remains a challenging condition to manage, nutrition offers a promising avenue for symptom management and improving overall health. Further research is needed to establish evidence-based dietary guidelines for patients with fibromyalgia.

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NEURONUTRITIONAL APPROACH TO MIGRAINE TREATMENT IN PREMENOPAUSE

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Background and aim: Both episodic and chronic migraine are assumed to happen due to energy deficit and mismatch between energy reserves and brain expenditure, which forms the basis of the neuroenergetic theory of migraine.¹ Neuronutritional approach could help increase the quality of in migraine patients, too.²

Case presentation: A 49-year-old female complains of regular migraine attacks associated with menstrual cycle, fatigue in the afternoon and nocturnal awakenings. She flies regularly and has an irregular, uncontrolled diet. Blood tests showed impaired carbohydrate metabolism: high level of glycated hemoglobin, increased levels of 2-ketoglutaric acid and malonic acid. Continuous blood monitoring was used to measure metabolic flexibility and showed postprandial hyperglycemia and nocturnal hypoglycemia. Under paradigm of neuronutrition, she got recommendations on food culture, dietary patterns, and nutrient intake: eat three regular meals a day with compulsory breakfast and one nutritious snack a day with the fasting period no more than 12 hours. Based on continuous blood monitoring the patient was recommended personalized diet to avoid glucose spikes. The following supplements were advised for 2 months: coenzyme q10, 100 mg per day, magnesium citrate 400 mg per day. Two month follow up showed reduction in the number of days with headache from 15 to 8, better flight tolerance and sleep quality.

Conclusions: Neuronutritional approach could improve the patient's quality of life and offer a personalized approach to migraine management.

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FROM MINIMALLY INVASIVE PERCUTANEOUS TECHNIQUES TO FULL ENDOSCOPIC MICRODISCECTOMY: NEW TRENDS FOR THE TREATMENT OF LUMBAR HERNIATED DISC

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Minimally invasive surgical techniques, as percutaneous laser disc decompression or gelified ethanol nucleolysis, have recently been developed as alternative treatments to open surgical interventions, especially for small or contained herniated disc. Moreover, in the last years Full-endoscopic lumbar discectomy (FELD) has been developed to decrease approach-related morbidity and provide superior visualization respect open microdiscectomy: with the use of a working channel endoscope, lumbar disc herniations can be approached via the transforaminal approach or the interlaminar approach. These minimally invasive procedures are successful surgical treatments for lumbar disc herniation. In this study, we report our surgical experience focusing also on the steep learning curve, especially for the FELD, and demonstrate the feasibility, safety, and efficacy of percutaneous techniques and full-endoscopic lumbar discectomies in the different types of herniated disc, and how the choice of the surgical approach may depend on the stage of disc herniation. Furthermore, we discuss the indications, contraindications, surgical technique, complications, and outcomes in our series of patients.

scopic lumbar discectomies in the different types of herniated disc, and how the choice of the surgical approach may depend on the stage of disc herniation. Furthermore, we discuss the indications, contraindications, surgical technique, complications, and outcomes in our series of patients.

INTERSPINOUS PROCESS DEVICE: IS IT STILL A TREATMENT OPTION FOR SPINAL STENOSIS?

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Various interspinous process devices (IPD) have been used in the last decades for the treatment of various degenerative pathologies of the lumbar spine. The main indications for the implantation of an IPD are spinal stenosis and neurogenic claudication. The function of IPD is to unload the facet joints, thus performing the enlargement of the neural foramen and the decompression of the roots forming the cauda equina in the central part of the vertebral canal, and to provide sufficient stability of the spinal segment. The interspinous devices currently in the market are classified into two main groups: motion preservation devices (static and dynamic) and fusion devices. The insertion of IPD between the spinous processes permits a distractive effect at the affected spinal level with an increase in the area of the spinal canal and foramen, while the adjacent levels are not influenced by the device. The fusion devices encourage a rigid interspinous arthrodesis of the affected spinal level through the use of a spacer body that allows a distraction of the adjacent vertebrae and performs a synthesis and fusion of the interspinous space. These devices used in stand-alone mode, but seldom they are accompanied with cages. In this study, we reviewed the biomechanical properties of the major IPD and their clinical and radiological characteristics. In the last years there was an abuse of IPDs implantation, because they became a trend; but they were extremely dangerous in wrong hands. It is extremely important to understand their appropriate use and to know in detail their effects, with a correct implantation without risk of complications.

CHALLENGES OF SHOULDER PAIN IN TUNISIAN HEMIPLEGIC PATIENTS

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Background: Pain is a common complication after stroke and is associated with the presence of depression, cognitive dysfunction, and impaired quality of life mainly if it occurs in a hemiplegic shoulder. Hemiplegic shoulder pain (HSP) can hamper functional recovery as well as participation in specific Neuro-rehabilitation programs and subsequently lead to disability. The aim of our study is to describe the Challenges of shoulder pain in hemiplegic patients.

Methods: It is a quantitative descriptive cross-sectional study carried out among vascular hemiplegic patient consulting the outpatient clinic of physical medicine and rehabilitation (PMR) for management of shoulder pain during the period between November 2021 and November 2023. We studied so-

ciodemographic data, clinical and functional status (as assessed by Barthel Index), pain's characteristics and management. Pain was assessed by The visual analogue scale (VAS) and the ALGOPLUS scale.

Results: We enrolled 44 children hemiplegic patients. The Mean age was 58.32 years, with a sex ratio of 1.6. Cerebrovascular accident (CVA) was ischemic in 82% of cases. Left hemiplegia accounted for 54.5% of cases. Twenty-three of patients had non-functional arm. Thirty-eight percent of patients experienced HSP. The main causes of pain were complex regional pain syndrome type 2 (85.8%), spasticity (23.8%), shoulder subluxation (11.8%) and Central post-stroke pain (18%). Hemiplegic patient with communication difficulties had an ALGOPLUS scale above 3 in 5 patients. Neuropathic pain was reported in 45%, with a mean DN4 score of 6.54 ± 1.6 . The most common treatment was the physical therapy (76.52%) followed by corticosteroid injection (58.8%), upper limb orthotics (29.4%) and botulium toxin injection (23%).

Conclusions: Health care providers who treat stroke survivors need to be knowledgeable about pathologic conditions of the shoulder and available treatments. Diagnosis of the cause of HSP can be challenging to providers because of the overlap of signs and symptoms of different pathologies and because of the frequency at which multiple pathologies coexist. Careful inquiry, use of rating scales, and physical examination may lead to improved identification and effective treatment of post-stroke shoulder pain. This may improve patient comfort, mood, rehabilitation, and quality of life.

MONONEURITIS MULTIPLEX OCCURRING IN A DIABETIC PATIENT

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Case description: We report the case of a 43-year-old woman with history of type 1 diabetes mellitus for the past 8 years who presented in the outpatient clinic of physical medicine and rehabilitation (PMR) with disabling neuropathic pain of the right upper limb. The patient described persistent numbness, particularly at night, the feeling of the fingers being useless, tingling sensation in the fingers and arm during the day, especially with as talking on the phone and reading books. She is suffering from severe pain in the upper back. There was no past history of trauma. Physical examination showed that the neck was stiff with a clear limited range of motion, particularly neck extension. The patient had poor posture with rounded shoulders and stooped head and neck. The Adson maneuver was negative however spurling, phalen and tincl tests were positive. Neurological exam revealed absence of osteotendinous reflex with. Weakness in the biceps brachii, brachioradialis, flexor digitorum, and abductor pollicis brevis. Neuropathic pain DN4 Questionnaire was 5/10 and VAS pain was 7/10. Her Functional Independence Measure (FIM) used to assess his functional status was low 100/126. Electromyography showed minimal, diffuse, sensory-motor peripheral multineuritis of all 4 limbs with a negative etiological work-up. To manage his severe neuropathic pain we prescribed gabapentin associated to tramadol and rehabilitative treatment including physical and manual therapies. Patient underwent 2 months of rehabilitation. Patient improves her neuropathic pain and functional assessment, and her VAS pain was 4/10, FIM was 112.

Discussion: Distal symmetric polyneuropathy is a well-recognized complication of diabetes mellitus. Mononeuritis multiplex is less frequent. Unlike it is seen in elderly patients but is not a feature in young diabetics.

Conclusions: This case highlights a peripheral nerve syndrome of mononeuritis multiplex secondary to type 1 DM with excellent outcome following rehabilitative and pharmacological treatment.

PAIN'S CHALLENGES IN TUNISIAN CHILDREN WITH CEREBRAL PALSY

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Background: Cerebral palsy (CP) is a common cause of physical disability in childhood. As children with CP grow, secondary comorbidities, which form underlying pain sources, evolve and change. Little is known regarding the influence of CP on childhood pain experiences, leading to a lack of targeted pain management strategies in this population. Our study is aimed to describe pain challenges and in CP patients.

Methods: It is a quantitative descriptive cross-sectional study carried out among children with CP consulting the outpatient clinic of physical medicine and rehabilitation (PMR) for management of CP secondary comorbidities during the period between November 2021 and November 2023. We studied demographic information, clinical and functional status (as assessed by the Global Motor Function Classification System (GMFCS)), pain's characteristics and management. Pain was assessed by The Faces Pain Scale Revised (FPS-R), the visual analogue scale (VAS), The Face, Legs, Activity, Cry, Consolability (FLACC) Behavioral Pain Scale and The Echelle Douleur Enfant San Salvador (DESS). Results: Forty-Five children were evaluated, 53% of whom were females. The mean age was 6.72 ± 5.4 years. Thirty-six of patients had a severe motor impairment with a GMFCS of 4 in 40% of cases. Sixty-five percent of patients experienced pain, most children with pain had orthopedic pain and 48% had pain of another origin. The main sites of pain were the hips (65%) and knee (18%). Pain was considered intense in 15% of cases, and the DESS was greater than 20 in 7 patients. The prevalence of pain was positively associated with age ($p=0.169$). Pain was reported more often in GMFCS Level V patients. The most common treatment was the physical therapy (70.37%) followed by botulinum toxin injection (34.14%) and surgical treatment (26.8%).

Conclusions: Despite frequent reports of pain in childhood CP, pain is typically under identified, under measured, and under treated by clinicians. In our study, pain is reported to be present in 65% of our children. However, obtaining representative population cohorts is difficult because of the likelihood of non-response bias and need for prospective data collection of pain measures.

A UNIQUE CASE OF CALCINOSIS IN A PATIENT WITH SYSTEMIC SCLEROSIS TREATED WITH SPINAL CORD STIMULATION

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Background: Systemic sclerosis (SSc), also called scleroderma, is a complex autoimmune disease that presents with a wide organ-manifestation. One out of three patients with SS is affected by calcinosis, *i.e.* the deposition of apatite in soft tissue. The pathogenesis of calcinosis is still under investigation, but the association between digital ulcers and calcinosis suggests a role of tissue hypoxia and inflammation. Treatment of SSc related ulcers and calcinosis includes immunosuppressive agents, autologous haematopoietic stem cell transplantation, dihydropyridine calcium channel blockers (especially nifedipine), then phosphodiesterase 5 inhibitors iloprost or bosentan. Recently, different reports provided promising results about the effect of spinal cord stimulation in the management of digital ulcers, both in terms of pain relief and an improvement in microcirculatory insufficiency. However, none of these reports describe the possibility to retrieve calcinosis even around the epidural catheter or the pulse generator.

Case presentation: The present case report describes a unique case of calcinosis distributed along the course of the extension and the pulse generator in a patient with SSc and digital ulcers. The patient was a 45-year-old woman, who was diagnosed SSc in 1994. She presented a long history of Raynaud's phenomenon, skin thickening of both hands, proximal to metacarpophalangeal joints, digital tip ulcers involving both toes and the third, fourth and fifth fingers of both hands, and a proximal involvement of trunk and legs. She presented severe osteoporosis. Moreover, she showed evolving pulmonary fibrosis and pulmonary hypertension. The patient underwent a trial of spinal cord stimulation with a single octopolar catheter, and the pulse generator was allocated in a subcutaneous pocket in the supra-gluteal right region. The patient was then referred to our Pain Unit in December 2023 since the pulse generator has expired and a replacement was deemed necessary. The patient underwent under local anesthesia to the replacement of the pulse generator. At surgical incision, calcium deposition was evident also in the subcutaneous pocket, where the pulse generator was allocated, surrounding and completely covering the generator and the extension near the generator. A careful removal of hydroxyapatite depositions was performed, in order to free the extension, and the new generator was connected. The stimulation was then reprogrammed, ensuring an adequate paresthetic coverage. The patients then returned home with no complications.

Key summary points: i) Systemic sclerosis, also called scleroderma, is a complex autoimmune disease that presents with a wide organ-manifestation; ii) one out of three patients with SSc is affected by calcinosis; iii) calcinosis could be localised even around implantable devices, such this unique case describes.

DORSAL ROOT GANGLION STIMULATION CAN IMPROVE SOCIAL AND WORKING ABILITY IN CPRS 1 OF THE KNEE. A CASE REPORT

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Background: Complex regional pain syndrome (CRPS) is a debilitating condition characterized by a continuing (spontaneous and/or evoked) regional pain that is seemingly disproportionate in time or degree to the usual course of any known trauma or other lesion, associated with abnormal sensory, motor, sudomotor, vasomotor and/or trophic findings. CRPS 1 lacks nerve injury while CRPS 2 has evidence of it. The diagnosis is clinical, basing on the Budapest Criteria. Several mechanisms have been implicated in CRPS, such as inflammation, altered cutaneous innervation, sympathetic nervous system, changes in circulating catecholamines, autoimmunity, brain plasticity, genetic effects and psychological influences. Therefore, CRPS treatment can be a very difficult challenge. Oral medications, topical treatment, intramuscular bisphosphonates, intranasal calcitonin, and recently botulinum toxin type A, with psychotherapy and functional restoration are utilized. Invasive treatment options for CRPS include spinal cord stimulation (SCS) and dorsal root ganglion stimulation (DRG). Recent evidence suggests that DRG stimulation may be more effective for lower limb CRPS in terms of pain reduction and quality of life. The aim of the present case report is to underline the beneficial impact on pain and function of DRG stimulation in a case of CPRS 1 of the knee.

Case presentation: The present case describes a 46-year-old female with CPRS 1 of the right knee for 6 years. After a motor accident with foreign bodies retention, the patient underwent seven surgical interventions, including several prosthesis implant and removal, but she still complains of burning, excruciating pain of the right knee, that gets worse by night and in the up-right position, making walking impossible without the use of double support. Tactile allodynia in the antero-medial portion of the knee and anesthesia of the inferolateral portion were retrieved on physical examination. The knee was warm and vasomotor changes were evident. The patients reported that the treatment with gabapentinoids, antidepressants, opioids, topical lidocaine, NSAIDs was ineffective. A DRG stimulation trial was performed, with a double catheter at L3 and L4 level on the right side. Immediately after the trial phase, allodynia and pain at rest completely disappeared and the patient started rehabilitation programme. The patient underwent definitive implant: soon after stopped antidepressants, started to walk for 1 km and returned to work.

Conclusions: This case report underlines the clinical value of DRG stimulation in the management of CPRS of the extremities, in terms of pain reduction, motor function, social impact and working ability.

PERCUTANEOUS ELECTRICAL NERVE STIMULATION FOR PAINFUL SURGICAL SCAR

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Background: Percutaneous electrical nerve stimulation (PENS) is one of the declinations of the neuromodulation treatments for pain management consisting in a temporary application of electrical field targeting the subcutaneous terminal fibers of sensory nerves. PENS has been proved to be effective in several cases of peripheral neuropathic pain,

nerve entrapments, CRPS. In this short series we treated patients with pain related to surgical scar and observed the effect on pain, neuropathic symptoms and quality of life.

Methods: We treated five patients with post-surgical painful scar, with pain symptoms lasting for more than one year after the surgery, with no improvement after pharmacological treatments with NSAIDs, gabapentinoids, and opioids (Table 1). We used a monopolar PENS (AlfaMed, Porto San Giorgio, Italy) with the application of a micro-needle passing through the outer layers of the skin. The 200 mm needle and the plate were positioned parallel with the aim of keeping the scar inside the electrical field. We collected NRS, DN4 test, BPI (pain) and BPI (quality of life) at baseline and at 6 months follow-up after the procedure.

Results: The results obtained are shown in Figure 1. The variables at baseline and at 6 months were compared with *t*-test assuming paired data. We observed statistical significance in the variation of DN4 and BPI (quality of life) at 6 months follow-up (Table 2).

Conclusions: PENS treatment for painful surgical scar was effective in reducing the pain, with a significant reduction in the neuropathic symptoms and improvement of the quality of life at 6 months after the procedure.

Table 1. Population.

Male /Female	4 / 1
Age	57,4 years
Patient 1	Shoulder scar
Patient 2	Occipital scar
Patient 3	Trochanteric scar
Patient 4	Shoulder scar
Patient 5	Shoulder scar

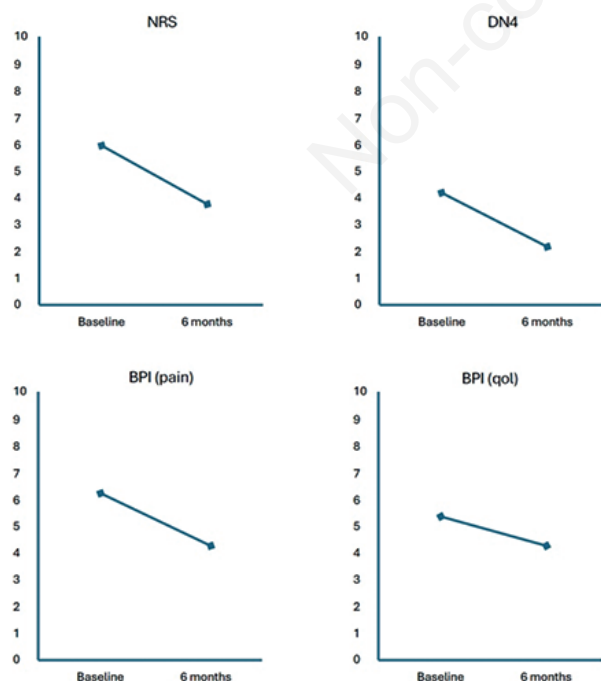


Figure 1.

Table 2. Results.

	Baseline (mean)	6 months (mean)	<i>p</i>
NRS	6	3,8	0.1475
DN4	4,2	2,2	0.0171*
BPI (pain)	6,2	4,4	0.1352
BPI (quality of life)	5,3	4,5	0.0444*

* Statistical significance $p < 0.05$. *P* is the *p*-value for HA: mean (diff 6m-Baseline) <0 .

SPINAL ACCESSORY NERVE ENTRAPMENT AS A CAUSE OF MYOFASCIAL PAIN SYNDROME INTEGRATED NERVE CONDUCTION STUDY AND NEUROMUSCULAR ULTRASOUND STUDY

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Background and aims: Cervical myofascial pain syndrome (MPS) is a common clinical condition in the daily practice of musculoskeletal physicians. Its prevalence of 21% in the general population. About 85% to 93% of MPS commonly occur in females. MPS is the leading cause of chronic and persistent regional pain, including shoulder pain, chronic back pain, tension type headaches and facial pain. The aim of this study was to assess spinal accessory neuropathy in MPS patients by integrated nerve conduction studies and using US guided hydrodissection of the SAN as an intervention treatment.

Methods: This prospective study included 60 patients with unilateral chronic MPS diagnosed according to Travell and Simon, 2011 criteria. All patients included in this study were subjected to full history taking, clinical examination (general and local), assessment of the pain severity by Numerical rating scale (NRS), Nerve conduction study (NCS) and ultrasonographic measurement of the cross sectional area (CSA) of the spinal accessory nerve (SAN) in both symptomatic side and asymptomatic healthy side. Ultrasound guided hydrodissection of the SAN on the symptomatic side with 5ml lidocaine and 5 ml glucose was done. Follow up one month after hydrodissection to assess its effect on the clinical status, NCS parameters and ultrasonographic CSA of the SAN.

Results: NCS revealed the presence of SAN neuropathy in 23.3% of MPS side, all of them (100%) showed demyelinating lesion manifested as prolonged mean motor latency, while 4 patients (28.5%) showed mixed type of neuropathy manifested as prolonged mean motor latency and reduced mean amplitude compared with the healthy asymptomatic side. Also, there was increased mean ultrasonographic CSA of the SAN on the affected side compared with the mean CSA of the SAN on the healthy asymptomatic side. One month after hydrodissection, there was significant lower mean value of the (NRS), significant lower mean value of the SAN distal latency, and significant higher mean value of CMAP amplitude of the SAN compared with their initial values. Also, ultrasonographic measurement of CSA of the SAN revealed a highly significant lower mean value of CSA of the SAN compared with its value at presentation.



Conclusions: Spinal accessory neuropathy is significantly increased in MPS patients, nerve conduction study and neuromuscular ultrasonography could lead to more reliable diagnosis. US guided hydrodissection of the SAN is good intervention for management of pain in MPS which could lead to better management.

THE RELATIONSHIP OF PERSISTENT POST-SURGERY PAIN AFTER CARDIAC SURGERY AND ANXIETY, DEPRESSION, AND ATTACHMENT STYLE: A SINGLE CENTER LONGITUDINAL STUDY IN CZECH UNIVERSITY HOSPITAL

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Background: The development of persistent post-surgical pain (PPSP) is an important issue in cardiac surgery, as it can both predict and result from psychological phenomena such as depression or anxiety. This study aimed to identify differences between cardiac surgery patients with and without PPSP at 3- and 12-months post-surgery in various psychological domains.

Methods: This is a single-center prospective longitudinal study. 125 patients who underwent cardiac surgery in the years 2018-2020 at the Department of Cardiac Surgery of the 3rd Faculty of Medicine, Charles University and University Hospital Kralovske Vinohrady, Prague, Czech Republic, were psychologically examined before the operation and by surface mail 3 and 12 months after the operation. Postoperative pain intensity was measured using a visual analog scale (VAS), Pain Map localization, BDI-II to measure depression, and GAD-7 to measure anxiety, to assess the relationship The Relationship Questionnaire (RQ). Patients were divided into two groups: the first, which met the criteria for persistent postoperative pain (PPSP), and the second, which had no PPSP; 94 patients responded 3 months after surgery and 72 patients 12 months after surgery.

Results: 3 months after surgery there were 67 (71.28%) patients with PPSP and 27 (28.72%) without PPSP, 12 months after surgery there were 44 (61.11%) patients with PPSP and 28 (38.89%) patients without PPSP. The results showed that patients with PPSP in both measurements had a significantly higher level of intensity of pain and discomfort ($p < 0.001$), depression ($p < 0.001$, $p < 0.001$) and anxiety ($p < 0.001$, $p < 0.001$) as well as a higher probability of insecure attachment ($p = 0.011$), were more often female ($p = 0.020$, $p = 0.005$) and older than those without PPSP ($p = 0.031$).

Conclusions: This study is the first to prospectively examine the psychological factors associated with PPSP in Czech cardiac surgery patients over a 12-month period. Such studies could help provide valuable information for preventive interventions in individuals with postsurgical persistent pain targeting anxiety, depression, and adult attachment styles.

OPTIMIZING PAIN MANAGEMENT IN PATIENTS WITH SEVERE L4-L5, L5-S1 DISC HERNIATION: SYNERGISTIC EFFECTS OF COMMON PERONEAL NERVE BLOCKADE AND TRANSFORAMINAL STEROID INJECTIONS

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Background: Extreme and stabbing pain deriving from a herniated disc at L4-L5, L5-S1 levels poses a significant clinical challenge. Some patients diagnosed with lumbar disc herniation experience not only typical pain but also hyperalgesia that extends over the sensory territory of the common peroneal nerve: posterior thigh, lateral and posterior leg, back, and sole of the foot. Therefore, exhaustive approaches are emerging for effective pain management. Among these emerging techniques are transforaminal steroid injections associated with common peroneal nerve blockade. The combination of these two holds promises in addressing both central and peripheral components of pain pathways. Consequently, the study aims to investigate the potential synergistic effects of integrating these two interventions to improve pain relief in patients with lumbar radiculopathy.

Methods: This is a prospective, single-center study conducted from September 2022 to September 2023. Included patients were aged 25 to 65 years, presenting to the clinic with L4-L5, L5-S1 radicular pain, and reporting discomfort throughout the common peroneal nerve's sensory territory. Participants were blindly assigned to two groups: the first receiving ultrasound-guided common peroneal nerve blockade in addition to transforaminal steroid epidural injection, while the second group received only the standard transforaminal injection method. Pain intensity was assessed using a visual analog scale (VAS) for all participants before and after interventions at regular intervals to evaluate changes in scores and duration of pain relief.

Results: 180 patients were included in the study, with 60% of the population being female and 40% male. Preliminary results showed a remarkable depletion in pain scores after combining both interventions in 100% of participants. The multimodal approach, targeting peripheral nerve involvement and central inflammation at the same time, led to a more comprehensive pain management strategy.

Conclusions: The combined approach of common peroneal nerve blockade and transforaminal steroid injections appears promising for managing severe radiculopathy correlated to lumbar disc herniation. Further investigations through larger-scale studies with long-term follow-up are crucial to confirm these findings and establish the role of this combined intervention in the management of lumbar radiculopathies.

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BUILDING AND VALIDATING A USEFUL TOOL FOR MEASURING PAIN IN THE PAEDIATRIC POPULATION WITH DOWN SYNDROME (ANDREAS)

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Background: Down's syndrome (DS) is the most common congenital anomaly, and approximately 6,000 children with DS are born each year in Italy, or about 1 in 700 births. Pediatric subjects with DS are exposed to countless pathological conditions, and frequent medical, surgical and hospitalisation services are required, which expose them to pain. The peculiarity of SD young patients is a lower pain threshold, verbal expressions, and crying, often reduced or absent and associated with freezing. Although the self-report is the gold standard in pain assessment, assessing pain in these tiny patients is not always easy. The aim of this study is to build a mixed, self-report and hetero-evaluative tool determining pain intensity in the SD paediatric population.

Methods: Mixed methods are used, and the Wong-Baker Faces Pain Rating Scale on DS is being adopted. Using qualitative methods, we have determined pain-related behaviours by literature and determination of pain-related behaviours through a focus group conducted by researchers and parents. Validation of the instrument, which we will call Assessment of Pain in Down Syndrome, by integrating bEhAviors-Self-report (ANDREAS) in terms of validity and reliability we will conduct.

Results: We will achieve a mixed instrument, taking into account self-report, despite the degree of cognitive impairment, and using hetero-assessment through the behaviours deemed idiosyncratic by parents and practitioners with experience with children with DS.

Conclusions: ANDREAS is a mixed instrument, adapted to the paediatric population with DS, that could be valid, reliable and specific for measuring pain in children with DS.

IMPACT OF MULTIFOCAL REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION NEUROMODULATION ON PAIN INTENSITY AND PAIN FREE INTERVALS IN EPISODIC MIGRAINE PATIENTS

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Background: Migraine is a prevalent neurological disorder which poses significant challenges to individuals worldwide due to its profound impact on daily life. Despite the availability of various prophylactic treatments, the optimal management of migraine remains elusive. Repetitive transcranial magnetic stimulation (rTMS) has presented as promising non-invasive neuromodulation modality, demonstrating eff-

ficacy in improving clinical symptoms associated with migraine. However, its efficacy may be highly dependent on the stimulation elements covered by the protocol. Our research aimed to evaluate the ability of a multifocal rTMS protocol to improve clinical outcomes in episodic migraine patients by addressing peripheral and central sensitization mechanisms and modulate the intensity of the attacks and pain free intervals.

Methods: A longitudinal, double-blinded, rTMS-intervention study including subjects with episodic migraine (with and without aura, 2-14 attacks per month) was performed. After a baseline 1 month follow up, subjects had 6 sessions of rTMS on alternative days receiving multifocal rTMS or sham stimulation. The multifocal rTMS protocol included two components; first, a series of swipe stimulations followed by spot burst stimulation. All subjects underwent assessment of pain intensity, duration of migraine attack, pain free intervals at 4 weeks.

Results: Among 72 randomized patients, sixty-seven (age 39.7±11.3; 61 females; real rTMS n=36 and sham rTMS n=31) completed the trial. After stimulation, there was a significant reduction in the intensity of attacks at 4 weeks after the treatment in the real rTMS group (6.9±1.4 at baseline; 5.5±2.4 at 4 weeks (p<0.05). The mean increase of pain free interval in real vs sham groups was + 3.5 days (p<0.05). No significant adverse events were recorded.

Conclusions: Our research provides evidence that novel multifocal rTMS approaches are able to reduce the intensity of migraine attacks and increase the pain free intervals compared to placebo treatment with no serious adverse events.

TRENDS IN MIXED-PAIN RESEARCH OVER THREE DECADES (1993-2024): A BIBLIOMETRIC ANALYSIS

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Background: The term "mixed-pain" is used and abused in different clinical settings to describe the simultaneous presence of a combination of nociceptive, neuropathic and nociplastic pain mechanisms.¹ However, due to a lack of a formal definition and ambiguous usage, this topic would benefit from an in-depth analysis. This bibliometric analysis aims to comprehensively examine the existing literature on mixed-pain, to reveal publication trends and to improve research networks.

Methods: A comprehensive review of the existing literature on mixed-pain was conducted using the Web of Science (WoS) core collection online database. The search was performed in February 2024 and Journal Citation Reports™ 2022 (Clarivate Analytics) was used as the data source for journal rankings. All the relevant information and publication data were extracted to implement a bibliometric analysis.

Results: A dataset with 229 documents was extracted. A relevant upward trend of both publications and citations number was observed over time. A linear regression model revealed an ongoing rise in the number of future publications on this topic ($y=0.57*x - 1135$; $p<0.0001$), (Figure 1). Most documents were published in highly ranked Q1 journals as research articles (77%) or review articles (19%). USA (21%),



Italy (15%) and Germany (12%) accounted for most of the published papers on this topic while the time-based analysis of co-authorship showed no strong connection nor organized structure among countries (Figure 2). The bibliometric analysis of keywords underlined 3 main clusters (“neuropathic pain”, “chronic pain”, “management”) with different sized nodes and different connection strengths. These findings highlight the gap between other crucial aspects of chronic pain management such as “quality of life” and “disability” (Figure 3).

Conclusions: Despite the progressive increase in mixed pain articles in highly ranked journals, this bibliometric analysis showed the absence of a well-structured collaborative network between authors and an absence of clear connections between keywords. Given the extremely important clinical implications of mixed-pain, further high-quality studies on this topic and international collaborations would be recommended.

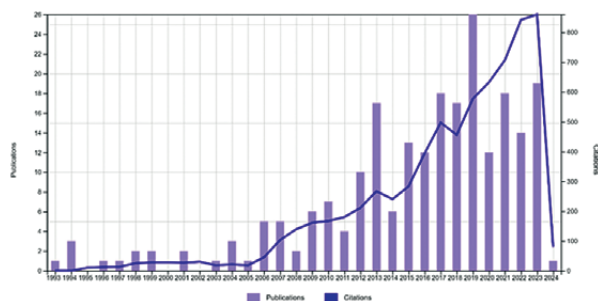


Figure 1. Annual publications and citations distribution.

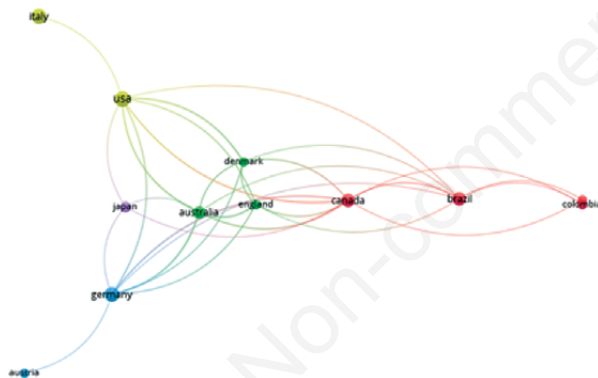


Figure 2. Co-authorship for country.

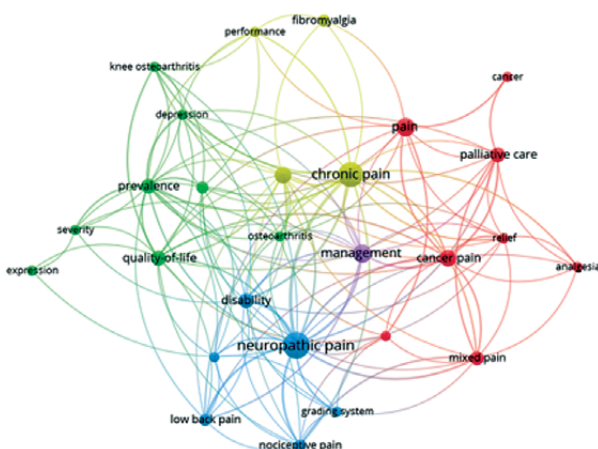


Figure 3. Keywords analysis.

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CLINICAL EVIDENCE OF OPIOID-FREE ANESTHESIA: A LITERATURE REVIEW

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Background: The escalating repercussions of opioid use in anesthesia have catalyzed the exploration of opioid-free anesthesia as a means to mitigate related adverse effects. This review seeks to amalgamate clinical evidence from studies comparing opioid-free anesthesia (OFA) to opioid-based anesthesia, assessing its efficacy and safety.

Methods: Data encompasses randomized controlled trials spanning January 2000 to February 2021, distilled through rigorous database searches. In total, 26 RCTs were included, with a cumulative patient population of 1934 participants. These trials covered surgical procedures ranging from laparoscopic gynecological and upper gastrointestinal surgeries to breast surgery. The studies varied in their OFA approaches, often including alternatives such as dexmedetomidine, ketamine, esmolol, and lidocaine.

Results: OFA demonstrated a comparable efficacy to opioid-based anesthesia in postoperative pain management. A significant reduction in postoperative opioid consumption and lesser instances of nausea and vomiting were highlighted as the key benefits. Moreover, the quality of recovery was deemed superior in OFA groups. Notwithstanding, certain RCTs noted an increase in bradycardia with OFA, suggesting careful consideration of adjunctive medications' dosing. Though robust evidence for the reduction of acute postoperative pain is indicated, data on the effect of OFA on chronic pain remains scant and inconclusive.

Conclusions: The clinical evidence advocates for the viability of OFA in reducing opioid consumption and improving postoperative outcomes in terms of nausea, vomiting, and recovery quality. Nonetheless, the data underlines the necessity for further high-quality, adequately powered studies to elaborate on the long-term effects of OFA, particularly concerning chronic pain and optimization of alternative analgesic dosing for maximal patient safety.

EVALUATING DEFENSE MECHANISMS, ALEXITHYMIA, AND CHILDHOOD TRAUMA IN WOMEN WITH FIBROMYALGIA AND CHRONIC PAIN: A COMPARATIVE STUDY OF ISOLATE AND COMORBID CONDITIONS

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Background: The central role of psychological factors in fibromyalgia (FM) and in other chronic pain (CP) syndromes is recognized in the literature. However, these factors' specific role in each chronic condition is unclear. This study aims to

compare the impact of selected psychological factors (such as defense mechanisms, alexithymia, and childhood trauma) between FM and four other groups such as chronic headache (CM), vulvodynia (VU), mixed diagnoses (MX; consisting of FM in comorbidity with CM and/or VU), and a control group. **Methods:** 1081 women (201 with FM, 220 with CM, 222 with VU, 327 MX, and 111 controls) completed a self-administered online protocol between June and November 2023.

Results: Significant differences were found among the five groups in the variables examined: neurotic defenses ($R^2=0.064$; $F=10.835$; $p<0.001$), alexithymia ($R^2=0.085$; $F=13.243$; $p<0.001$), and childhood trauma ($R^2=0.055$; $F=9.209$; $p<0.001$). The comparison shows that MX, compared with FM and the other conditions, is more characterized by a childhood history of trauma (particularly physical threats). On the other hand, FM differs from the other groups in that it scored significantly higher in both the inability to identify feelings and the use of neurotic defensive strategies.

Conclusions: Psychological factors play a significant role in CP syndromes, particularly among women with FM alone and FM mixed diagnoses. To enable improvement in the quality of life of these women, all clinicians should consider the impact of psychological variables.

PHYSICAL AND PSYCHOLOGICAL QUALITY OF LIFE IN FIBROMYALGIA: A PATH DIAGRAM ON THE EFFECTS OF PSYCHOLOGICAL PREDICTORS OF CENTRAL SENSITIVITY

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Background: Central sensitivity (CS) is an increased responsiveness of nociceptive neurons in the central nervous system to normal or subthreshold inputs. It has recently proposed as an indicator of the psychological burden associated with chronic pain, such as fibromyalgia (FM). It remains unclear which psychological factors may be more associated with CS and how. This study aims to investigate the impact of selected psychological factors on CS in women with FM. The first aim explores the influence of temperament, personality, childhood trauma, defense mechanisms, and mental pain on CS. The second aim tests the most significant predictors of CS in affecting quality of life (QoL) through a path analysis.

Methods: 510 women with FM completed a self-administered protocol online between April and June of 2023.

Results: Elevated levels of low sensory threshold ($\beta=0.210$), experiences of physical threat ($\beta=0.141$), neurotic defenses ($\beta=0.124$), and mental pain ($\beta=0.241$) were identified as the most significant predictors of increased CS in FM. A graphical path model was utilized to elucidate the relationship between psychological variables, CS, and QoL. This model demonstrated a satisfactory fit ($\chi^2=27.200$; $df=10$; $p=0.002$; $GFI=0.984$; $NFI=0.949$; $CFI=0.967$; $RMSEA=0.061$ [95% CI 0.034-0.090]), with substantial and moderate impacts on physical (-0.576) and psychological (-0.190) QoL, respectively.

Conclusions: The study highlights the pivotal role of psychological dimensions in influencing CS levels and their connections to QoL in FM patients. CS evaluation is suggested to improve the reference of eligible FM patients to psychological care.

SEXUAL FUNCTIONING AND SATISFACTION IN WOMEN WITH CHRONIC PAIN CONDITIONS: ADDRESSING CHRONIC HEADACHE, FIBROMYALGIA, VULVODYNIA, AND MIXED DIAGNOSES

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Background: Chronic pain (CP) is a common condition in women with disruptive effects on various aspects of daily life, including sexual activity. Sexual health has been consistently overlooked by both patients and clinicians, with a lack of cross-evidence between different CP conditions. This study aims to compare sexual functioning and satisfaction in women with different diagnoses under CP such as chronic headache (CH), fibromyalgia (FM), and vulvodynia (VU), compared to women with mixed diagnoses (MX; having two or more CP conditions selected for this study) and a control group without CP.

Methods: A total of 1006 women, divided into five groups (CH, FM, VU, MX, and controls), completed a self-administered online protocol on sexual functioning and satisfaction between April and January 2023. A one-way ANCOVA having age as covariate was used to test differences among groups.

Results: All groups (except for controls) reported a mean FSFI total score below 26.55. ANCOVAs indicated lower sexual functioning scores for FM, VU, and MIX compared to HC and CH. VU and MIX reported lower satisfaction scores than other groups. Genital pain emerged as the primary predictor of central sensitization across all groups except controls. Regarding mental QoL, sexual satisfaction was significant for CH and MIX, while genital pain and sexual satisfaction were significant for VU.

Conclusions: CP significantly impairs the sexual experience, particularly in FM, VU, and MIX. Clinicians are encouraged to disclose about sexual health during routine consultations, to better take care of the general quality of life of these patients.

NEW METHODS OF MIGRAINE DIAGNOSTICS: CGRP LEVEL IN TEAR FLUID

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Backgrounds and aims: Migraine is the most common primary headache, manifested by throbbing pain. The prevalence of migraines in the world has increased by 1.7% over the past 20 years, and in 2019 the number of common cases was estimated at 1.1 billion.¹ To effectively manage this headache, it is necessary to objectify the diagnosis by identifying diagnostic, prognostic and predictive biomarkers. Before conducting an ex-



perimental test of a new screening method for CGRP diagnosis, it is necessary to analyze information about previously conducted experiments and summarize all the data found. Tear liquid is a complex biological mixture containing electrolytes, proteins, lipids, mucins, some small organic molecules and metabolites.² The high concentration of protein in this liquid (8-10 micrograms/ml)³ in its aqueous layer, as well as the simplicity of non-invasive sample collection and understanding of physiological and pathological processes make tears an attractive source for diagnostic and prognostic purposes.⁴

Methods: We conducted a literature review in the PubMed library of articles on CGRP, migraine, biomarkers in lacrimal fluid, and methodologies for their determination. We included systematic reviews, meta-analyses, and prospective randomized controlled clinical trials from Q1-Q2 journals from the past 5 years. Keywords used in the original review: CGRP, migraine, tear biomarker, immunochromatographic test strip. Exclusion criteria included seminal papers and lack of full-text articles. Statistical aspects of the prevalence of migraine in CIS countries and the world over the last few years were also included. We propose to investigate a new method of screening patients with migraine, which is a noninvasive rapid test to detect a prognostically significant level of CGRP in tears, which can be based on immunochromatography using strip test with antibodies to CGRP.⁵⁻⁷

Results: We compare data from 46 clinical trials from the main journals of neurology, biomolecular medicine and ophthalmology. Ophthalmological method of tear fluid collection, study performed by our scientific specialists within the current research showed the following results. It is reasonable to consider tear fluid as a promising biomarker in the treatment and prognosis of several diseases, including migraine.⁸

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PULSED RADIOFREQUENCY OF THE GREAT OCCIPITAL NERVE: A RETROSPECTIVE STUDY

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Background: Pulsed radiofrequency (PRF) is a well-known minimally invasive technique for the treatment of several peripheral neuralgias. The procedure involves the delivering of

alternating electrical currents through a generator in a needle-electrode to elevate the temperature about 42 degrees on the needle tip. When placed close to nerve structures, this needle produces a non-lesional neuromodulation that reversibly alters nerve function. The current applied is generally 50.000 Hz in 20 milliseconds with a frequency of 2 Hz. The mechanism of action of PRF in pain is probably due to neuromodulation of nociceptive fibers involving noradrenergic and serotonergic pathways leading to a sustained reduction of the pain sensation, while the exact mechanism is still debatable. To date, indication for PRF were different neuralgias refractory from conventional treatments, where a non-lesional treatment is mandatory to avoid deafferentative sequelae.

Methods: In this retrospective observation, we collected data from patients treated with PRF performed at the Greater Occipital Nerve (GON) level for Arnold's Neuralgia, occipital pain from cervical arthritis, postherpetic cervical neuralgia and chronic unresponsive cervicogenic headache. The PRF procedure was performed by an ultrasound-guided (US) technique for the GON identification between the lower and oblique semispinalis capitis muscle. PRF was delivered at 42 °C for 300 sec after a sensitivity test at 50 Hz and motor at 2Hz. Data regarding pain and disability (VAS 0-100 and ODI 0-100%) were collected at baseline and at 1 (T1) and 3 months (T3) after the procedure. Adverse Events (AEs) related to the procedure were also registered.

Results: We collected data on 12 patients (11 F, 1 M) of mean age of 67.4 years, treated with PRF at our center from March 2021 to August 2022 for Arnold's Neuralgia (3 patients), occipital pain from cervical arthritis (4 patients), postherpetic cervical neuralgia (1 patient) and refractory chronic cervicogenic headache (4 patients). Mean baseline VAS was 8.25, mean baseline ODI 55.83. At T1, there was a statistically significant reduction in VAS score in the treated population (VAS 5.08 at T3, $p < 0.01$). At T1, the mean ODI value recorded was lower than baseline (ODI 46.6), although the decrease was not statistically significant. At T3, the values of VAS and ODI showed a substantial stability compared to values at T1. No AEs during procedure and at follow-up were registered. Regarding the underlying pathology, patients with Arnold's Neuralgia showed the most significant pain relief in all follow-up time-points.

Conclusions: This preliminary experience on the use of PRF targeted on GON has shown encouraging results in terms of VAS and ODI at both T1 and T3 time-points. The US guidance allow an easy and safe needle positioning, without complications. These results have been confirmed by the available literature, although the number of treated patients does not allow for conclusive inferences. The safety of the procedure and its repeatability make it a promising and interesting tool available to the pain therapist.

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THERAPEUTIC PROPERTIES OF AUTOLOGOUS MESENCHYMAL CELLS IN THE TREATMENT OF OSTEOARTHRITIS: AN OBSERVATIONAL PROSPECTIVE STUDY

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Background: Thanks to their regenerative potential, the mesenchymal cells (MSCs) might constitute a viable and effective tool in the treatment of articular damage secondary to osteoarthritis (OA). The MSCs can differentiate into different cell lines both *in vitro* and *in vivo*, thanks to their high plasticity and residual multipotency. MSCs immunosuppressive and anti-inflammatory properties also have demonstrated to impact positively on the degenerative and inflammatory component of OA pathophysiology. Furthermore, the paracrine secretion of MSCs derived growth factors, cytokines, bioactive lipids and microvesicles exerts its beneficial effects through angiopoietic and anti-apoptotic mechanisms. Previous studies have revealed the presence of MSCs in several tissue types, being particularly abundant and easily disposable in the adipose tissue which is the main source of MSCs destined to intra-articular administration.

Methods: From December 2022 to September 2023, we conducted a prospective observational study on 22 patients (13 F, 9 M), with a mean age of 68 years (± 14), affected by hip or knee pain due to OA refractory to conventional medical therapy. At admission, basal VAS (Visual Analogue Scale, 0-100), ODI (Oswestry Disability Index, 0-100%) and QoL (Quality of Life, 0-100%) scores were registered. MSCs intrarticular injection was performed according the standard manufacturers guidelines at hip level in 9 patients (4 F, 5 M) and at knee level in 13 patients (8 F, 5 M). The procedure was bilateral in half of patients. MSCs intraarticular injection was performed with three different adipose cells purification devices available on market (Milligraft[®], Dual Trend Srl, Optyfat[®], Horizon Lab Company and Sefficare[®], Seffiline Srl.). After the procedure, patients were scheduled for follow-up clinical evaluation at 3 months (T3). The evaluated endpoints were the difference in VAS, ODI and QoL scores from baseline. Tolerability and safety of the procedure in terms of incidence of Adverse Events (AEs), were also registered.

Results: Data analysis revealed a significant improvement in all considered scores from baseline to T3. In particular, VAS score decreases from 80 to 30 with Milligraft[®], from 80 to 40 with Optyfat[®] and from 80 to 45 with Sefficare[®]. Regarding ODI scores, values decrease from 70 to 40% with Milligraft[®], from 70 to 30% with Optyfat[®], and from 75 to 40% with Sefficare[®]. Finally, QoL increases from 20 to 65% with Milligraft[®], from 40 to 60% with Optyfat[®] and from 50 to 60% with Sefficare[®]. No AEs were reported both during the procedure and over the 3 months of follow-up. The tolerability of the procedure was reported as fairly satisfying by the majority of patients.

Discussion: The intra-articular administration of autologous MSCs has shown in our OA patients the ability to improve pain, disability and QoL during the evaluation period. Due to the small sample of patients, it was therefore impossible to compare the effectiveness of the different purification devices. According to the available literature, our study showed promising results for the use of MSCs as a therapeutic option in knee and hip OA. The procedure showed a satisfying overall tolerability and safety profile, consistently with the current evidence. However, the small number of enrolled patients did not allow us to make any further considerations.

Conclusions: Our study supports the use of intra-articular infiltration of MSCs as a viable, safe, effective tool for treatment of refractory pain from OA. Future studies will need to corroborate our observation.

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PERCUTANEOUS ELECTRICAL NERVE STIMULATION IN THE TREATMENT OF CHRONIC PAIN OF DIFFERENT ETIOLOGIES: A PROSPECTIVE OBSERVATION

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Background: The percutaneous electrical nerve stimulation (PENS) is a minimally invasive pain treatment aimed to deliver alternating low-frequency electric currents through a subcutaneous needle in the painful area for about 30 minutes. The actual indications for PENS treatment are painful surgical scars, postherpetic neuralgia, localized neuropathic pain, myofascial pain and refractory joint pain. The supposed PENS mechanism of action is the modulation of small nerve endings activity (including A-delta and C fibers) and the interruption of the nociceptive signal to the central nervous system. The low invasiveness, rapid execution and reproducibility make the PENS treatment an easy and safe procedure. PENS is contraindicated in patients with epilepsy, pregnancy, coagulopathy or ongoing anticoagulant therapy, in patients with pacemaker or other implanted cardiac devices and in case of infections in the pain site.

Methods: We conducted a prospective observation to assess the efficacy and safety of PENS in the treatment of chronic pain of different etiologies. We included patients of both sexes, aged ≥ 18 years old, affected by chronic non-malignant pain refractory to conventional treatments, that were submitted to a single PENS procedure. The technique was performed by means of the ultrasound-guided needle percutaneous positioning near the peripheral nerve or in the subcutaneous tissue directly in the area affected by pain, at a variable depth. The needle was then connected to the neurostimulation device. Stimulation was performed over a period of time of about 25-30 minutes, with a pulse frequency of 2-100 Hz at constant low voltage. The intensity of the stimulation was changed according to the patient's perception, avoiding pain or local discomfort. The endpoints were the difference of Numerical Rating Scale (NRS 0-10), Oswestry Disability Index (ODI 0-100%), Quality of Life Score (QoL 0-100%) and the cumulative consumption of analgesic drugs (CACs) from baseline (T0) and at 1 month after the procedure (T1). Short and long-term adverse events (AEs) related to the procedure were registered.

Results: We included in the observation 70 patients (43 female, 27 male) with an average age of 65 years (± 15). Among these, 16 patients (22.8%) suffered from postherpetic neuralgia, 28 patients (40%) from Low Back Pain, 16 patients (22.86%) from joint pain and 20 patients (14.29%) from post-surgical painful scars. In the whole population, the NRS values did not show a significant reduction at T1 observation. Nevertheless, we noted a significant reduction in ODI (from 55 to 37%) and a slight improvement in QoL (from 40 to 50%). Preliminary data showed better results in disability and QoL in patient suffering from refractory postherpetic neuralgia compared to other pain etiologies. No statistically significant differences in the CACS scores over time were recorded. No significant AEs during and after the procedure were registered.

Conclusions: Our preliminary observation evidenced a reduction in disability and improvement in QoL while pain scores remain unmodified 1 month after the procedure in the whole



population. The PENS procedure appears to be safe without any Adverse Events during the treatment and at follow-up. However, longer follow-up periods and repeated treatment sessions in a larger sample size are needed for better evaluate the cost-effectiveness of this procedure.

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EXTERNAL LOCUS OF PAIN CONTROL AND PERCEPTION OF HEALTH IN PATIENTS WITH CHRONIC LOW BACK PAIN

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Background: External Locus of Control (Rotter, 1954) is a belief that life is controlled by outside factors which the person cannot influence. The aim of the research was to verify whether there is a relationship between the External Pain Locus of control (EPLOC) and the perception of health.

Methods: Pain Locus of Control was measured using a 10 cm long Visual Analogue Scale (VAS 0 Internal – 10 External), God Locus of Health Control was measured by the GLHC questionnaire, degree of religiosity was measured by Duke University Religiosity Index (Durel), pain intensity was measured by VAS, fear of pain by FPQ-III, depression by BDI-II and health perception via LSQ-H.

Results: 43 patients from the Department of Rehabilitation Medicine, 2nd Medical Faculty, with chronic low back pain (69.76% of women) were psychologically examined, the average age was $M=57.62$ ($SD=16.21$). External Locus of Pain control (EPLOC) was significantly positively correlated with God Locus of Control, with instinctive religiosity (Durell), with fear of minor pain and fear of medical procedures, with depression and negatively with perception of health ($r_s=0.23-0.43$, $p<0.05$). Correlations with pain intensity were negative but non-significant. Based on linear regression, 40.49% (R^2) of EPLOC can be explained by depression and health perception variables.

Conclusions: External locus of pain control is related to a reduced perception of health. Psychotherapeutic interventions should be focused on self-efficacy in pain management of chronic low back pain. The research was approved by the ethics committee.

EFFECT OF CLOWN THERAPY ON ANXIETY OF CANCER CHILDREN: A SYSTEMATIC REVIEW WITH META-ANALYSIS

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Background: Clown therapy is widely used distraction technique for nonpharmacological management of anxiety in pediatric settings. There are some studies evaluating effect of intervention on anxiety in cancer children, but a systematic review summarizing the overall effect is lacking. Objective of this study is to summarize the available evidence on the effectiveness of clown therapy for anxiety in children with cancer.

Methods: Searching for parallel group controlled, quasi-controlled or no controlled trials was carried out on biomedical databases, trial registries, web resources and gray literature sources from each database or resource setup date to 31 January 2024. Primary outcome was anxiety. RoB 2 and ROBINS-I were used to assess risk of bias of included studies.

Results: Three quasi-randomized trials with high risk of bias that included a total of 181 children (mean age: 6.9-9.6 years, male: 40.3-68.9%) were included in this review. Children receiving clown therapy show a statistically significant reduction in anxiety ($SMD=-2.17$; 95% CI: -4.20, -0.14) compared with children receiving standard care. The GRADE method shows very low certainty/quality of evidence.

Conclusions: Clown therapy is more effective than standard care in reducing anxiety in children with cancer. Further studies are needed to confirm this finding as currently limited evidence of effectiveness does not allow routine implementation of intervention in pediatric oncology wards.

LITERATURE REVIEW OF CURRENT ALZHEIMER DISEASE PIPELINE FOR DISEASE PROGRESSION

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Background and aims: Alzheimer's disease (AD) is an irreversible progressive neurologic disorder characterized by brain atrophy, neuronal degeneration, and potentially fatal complications resulting from a continuous reduction in brain functioning. AD is the most common cause of dementia in the elderly and the fifth most common cause of death in Americans 65 years of age or older. One of the main issues in treating AD is that most of the existing drug therapies are used to control symptoms, namely behavioral, psychological, and sleep changes, but they do not affect disease progression. This review seeks to explore potential pharmacological treatments in the drug development pipeline that are currently being studied for their use in improving morbidity associated with AD, primarily with the intent to slow or reverse progression of the disease. The review highlights the most prevalent drug types being developed according to their mechanism of action.

Methods: PubMed searches were performed over the timeframe of July 2021 to December 2023 with MeSH headings to determine the most commonly studied etiologies and treatment types being investigated for AD since 2011. The MeSH headings narrowed the search results to studies specifically investigating potential treatment modalities for late-onset AD. Final search results were evaluated by hand to assess the most commonly studied disease-modifying treatment type being investigated for AD. The most frequent treatment type identified from this search was the study of compounds targeting the amyloid beta peptide. Ten studies were chosen from the results of this assessment and summarized to high-

light the varying mechanisms of action being investigated for this specific treatment modality.

Results: This review identified several drug candidates with various mechanisms of action surrounding the amyloid-beta protein. These drug candidates included a beta-amyloid anti-oligomer and aggregation inhibitor, an amyloid-beta targeting monoclonal antibody, beta-secretase enzyme (BACE) inhibitors, gamma-secretase modulators (GSMs), and an amyloid-beta receptor partial agonist. The efficacy data and study results produced for many of these drug candidates were variable and conflicting in some cases. Two studies were reviewed for ALZ-801, the beta-amyloid anti-oligomer and aggregation inhibitor. Three studies investigated the efficacy of bapineuzumab, the amyloid-beta targeting monoclonal antibody. Additionally, three studies investigated the BACE1 inhibitors, verubecestat, atabecestat, and lanabecestat. The GSM, known as BMS-932481, and the amyloid-beta receptor partial agonist blarcamesine were both reviewed in single studies.

Conclusions: The current drug development pipeline for the treatment of AD is still experimental. Despite a handful of investigational drugs showing promise, there is still substantial research to be done in this area. While more studies are needed to refine the efficacy of these drugs, the development of drug candidates targeting amyloid-beta protein is likely a step in the right direction towards optimizing treatment outcomes. Further exploration of drug mechanisms focused on this early target of AD can hopefully serve as a template for even better AD treatments to come.

DIABETIC NEUROPATHY IN TYPE 1 DIABETES PATIENTS ADMITTED TO REPUBLICAN HOSPITAL, CHISINAU, MOLDOVA

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Background: Peripheral neuropathy is a common complication in type 1 diabetes patients and can be accompanied by neuropathic pain.

Methods: This study was conducted in the endocrinology department of "Timofei Mosneaga" Republican Hospital, Chisinau, Republic of Moldova. The study included 43 participants, patients with type 1 diabetes. Diabetes control was determined by measuring HbA1c levels. Symptoms of diabetic neuropathy were assessed with the Toronto Clinical Neuropathy Score (TCNS).

Results: The subject lot included 43 patients with type 1 diabetes, mostly men, with a mean age of 36 (± 9) years, and with a mean duration of diabetes of 8.33 (± 8.06) years. All patients had poor diabetes control, evaluated through HbA1c testing, which revealed a mean of 8.99% (± 1.81). Diabetic peripheral neuropathy was present in 70% of cases, almost half of the

cases included pain as a symptom, sometimes as the only manifestation. The average TCNS score in the lot was 6 points (± 3.77), and scores varied greatly with duration and compensation of diabetes. All patients received alpha-lipoic acid during their hospitalization, and 35% of all patients were started on GABA analogs with mild improvement of symptoms and no adverse effects.

Conclusions: Diabetic neuropathy is a common complication of diabetes mellitus that has a great impact on the life of the patient, with high rates of morbidity and mortality. Practical clinical strategies for the identification and management of neuropathic pain are needed.

A RARE CASE OF VASTUS INTERMEDIUS TEAR IN A MIDDLE-AGED GENTLEMAN: A CASE REPORT

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Background: Quadriceps strains are fairly common injuries but reported cases of isolated vastus intermedius (VI) tears are scarce. We present a rare case of ultrasound-confirmed VI tear in a middle-aged patient.

Case presentation: A 57-year-old gentleman slipped while bending down and lunged forwards to prevent the fall. His left knee was flexed in 90 degrees while his hip was in extension when he heard a 'pop' sound over his anterior thigh. Post trauma, he sustained pain, swelling over his distal aspect of anterior thigh, difficulty in weight-bearing and limited knee flexion. However, extensor mechanism was intact in this patient. Plain radiograph of his injured extremity revealed an undisplaced chip avulsion fracture of patella which was treated with above-knee back-slab. A sports ultrasound was performed which revealed grade 2 VI tear. Two weeks later, the back-slab was removed and a repeat ultrasound was done which shows new fibre continuity and he was subsequently subjected to physiotherapy to aid in his rehabilitation.

Discussion: Ultrasound has enabled us to provide rapid, point of care diagnostic imaging with a high degree of clinical accuracy in determining partial or complete quadriceps tears, particularly in identifying grade 2 muscle tears in the acute phase. For this case, we treated him conservatively with POLICE principle in the acute stage and subsequently progressed with physiotherapy. However, other interventional regenerative treatment modalities such as platelet-rich plasma (PRP) can be considered as one study has shown significantly favourable outcome in treating acute grade 2 muscle tears.

Conclusions: Depending on the degree of the strain, the injury may be successfully treated with conservative treatment and adequate physiotherapy as practiced in our case. PRP however can be considered as an adjuvant to augment healing process.

