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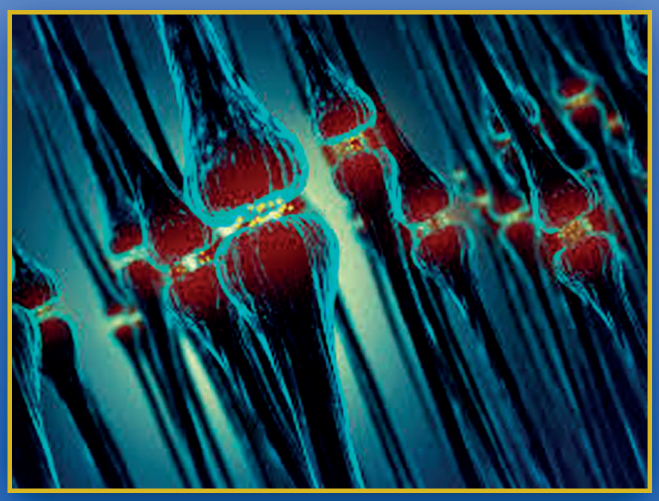

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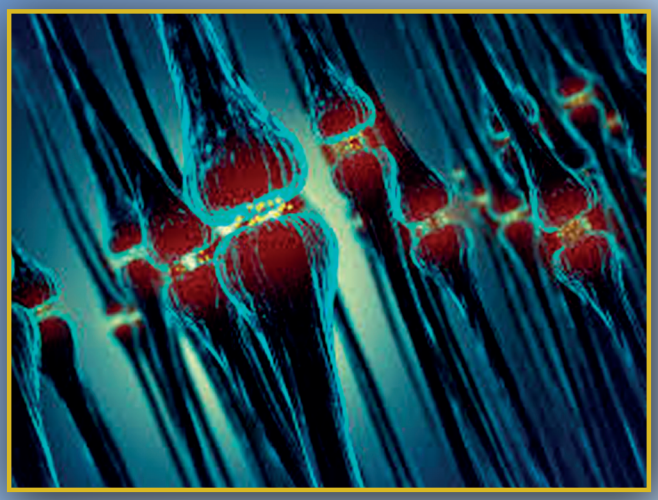

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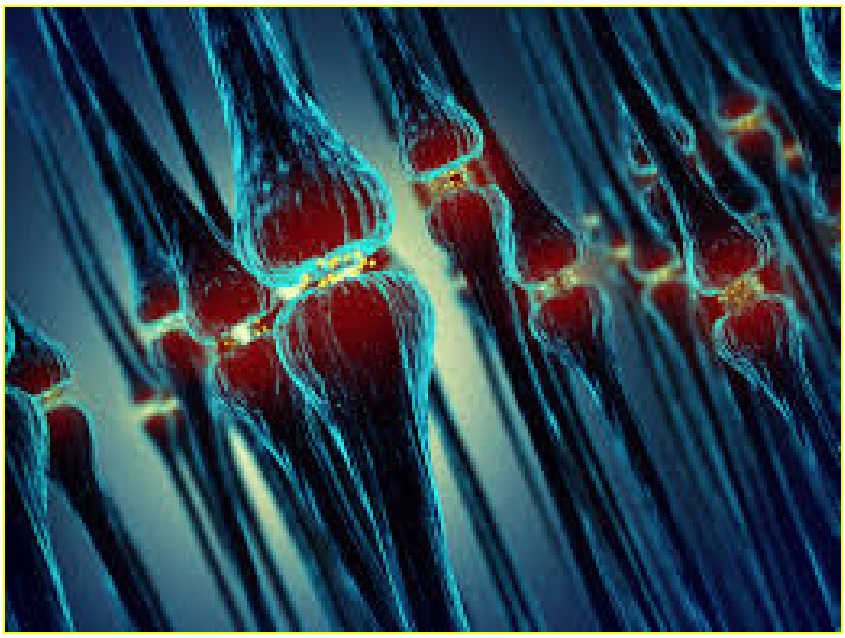

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Tatjana Nožica Radulović[1], Jelena Stanković[1], Vedran Milojević[1], Tamara Popović[1], Maja Vučković[1], Sandra Trivunović[1], Dragana Kožul[1], Milan Jovanović[1]

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Osteoarthritis is chronic degenerative joint disease which is a leading cause of locomotor disability in the world. Most common clinical manifestation is knee osteoarthritis. Pain, stiffness, reduced physical function and disablement are the key determinants in the treatment of osteoarthritis, therefore pharmacological treatment is symptomatic and physical therapy is practically permanent and the most important part of the therapeutic strategy. Early detection of dysfunction enables more efficient implementation of all physical interventions. Questionnaires of daily life activities are used to asses functional status of patients, they can be used as guides for rehabilitation program planning and indicators of the effectiveness of therapeutic intervention. When conservative treatment fails, therapy is surgery. Surgery goals are reduction of pain and function improvement. Arthroplasty involves surgical removal of joint surfaces and their replacement with endoprosthesis and they are gold standard in OA treatment. Through all these processes and planning , its important not to loose sight of psychological aspects of patients, for most their expectations regarding pain and physical functioning. If those expectations are unrealistic, the results of overall treatement may be unsatisfactory. Physical and rehabilitation medicine are indispensable due to the biopsychosocial approach, which respects the different dimensions of health at the biological, individual and social levels through the teamwork of different profiles of experts.

Keywords: knee osteoarthritis, knee arthroplasty, rehabilitation.

TAJMING FIZIJATRIJSKE INTERVENCIJE KOD PACIJENATA SA OSTEOARTRITISOM I ARTROPLASTIKOM KOLJENA-"DA HRONIČNO NE BUDE AKUTNO"

Tatjana Nožica Radulović[1], Jelena Stanković[1], Vedran Milojević[1], Tamara Popović[1], Maja Vučković[1], Sandra Trivunović[1], Dragana Kožul[1], Milan Jovanović[1]

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Osteoartritis je hronična degenerativna bolest zglobova koja je vodeći uzrok lokomotorne onesposobljenosti u svijetu. Osteoarthritis koljena je klinički najčešći oblik osteoartritisa. Bol, ukočenost, smanjeno fizičko funkcionisanje su ključne odrednice u liječenju osteoartritisa pa je farmakološko liječenje simptomatsko, a fizijatrijsko praktično trajni i najvažniji dio terapijske strategije. Rano otkrivanje disfunkcije omogućava efikasniju primjenu svih mjera fizijatrijske intervencije. Upitnici aktivnosti svakodnevnog života ocjenjuju funkcionalni status pacijenata, mogu biti vodiči za planiranje rehabilitacionog programa i pokazatelji djelotvornosti terapijske intervencije. Kod neuspjeha konzervativnog liječenja pristupa se artroplastici koljena koja je danas zlatni standard u liječenju osteoartritisa. Ciljevi hirurškog liječenja su smanjenje bolova i poboljšanje fizičke funkcije. Kroz sve te procese ne smije se izgubiti iz vida psihološki aspekt pacijenta, prije svega njegova očekivanja po pitanju smanjenja bola i fizičkog funkcionisanja. Ukoliko su ta očekivanja nerealna, rezultati sveukupnog liječenja mogu biti nezadovoljavajući. Fizikalna i rehabilitaciona medicina su nezaobilazne zbog biopsihosocijalnog pristupa koji uvažava različite dimenzije zdravlja na biološkom , individualnom i socijalnom nivou kroz timski rad različitih profila stručnjaka

Ključne riječi: osteoartritis koljena , artroplastika koljena, rehabilitacija

PAIN AND OSTEOPOROSIS

Snežana Tomašević Todorović[1]*, Damjan Savić[1], Jelena Starčev[1], Saša Milićević[2], Sindi Mitrović[3], Olivera Ilić Stojanović[4]

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Pain in patients with osteoporosis leads to decreased mobility, loss of walking ability and balance, restricts physical activity, and increases the risk of falls in older patients. Higher intensity pain and increased frequency of bone fractures are serious causes of morbidity and mortality in patients with osteoporosis. Pain prevention is important for an appropriate treatment of osteoporosis, and managing painful conditions in patients with osteoporosis requires a multidimensional approach. Aging, high bone turnover, obesity, spinal global sagittal malalignment and a high number of previous vertebral fractures were potential independent risk factors of pain-related disorders or gait disturbance in patients with osteoporosis. Osteoporosis causes certain types of pain, which can be divided into two types: traumatic pain due to fragility fractures and pain arising from osteoporotic pathology without evidence of fracture. There is insufficient data regarding whether osteoporosis without fractures causes pain. Pain is associated with bodily changes that occur in patients with osteoporosis. Increased back pain as a result of bone resorption occurs in patients with osteoporosis. Research findings indicate that obesity may affect pain intensity in the older population with osteoporosis. Pain in osteoporosis is primarily nociceptive, and if it becomes persistent, it can lead to sensitization of the peripheral and central nervous systems, thereby highlighting the transition to a chronic pain syndrome. The mechanisms of central sensitization are complex. Nontraumatic osteoporotic pain may arise from undetectable microfractures or structural changes, such as muscle fatigue in patients with kyphosis. Traditional treatment for osteoporotic pain potentially prevents possible pain induced by fractures by increasing bone mineral density and affecting related mediators such as osteoclasts and osteoblasts. Conclusions: Osteoporotic pain has traumatic and non-traumatic factors, as well as a very complex pathophysiology. Anti-osteoporotic therapies are effective in treating osteoporotic pain as they improve bone structure and the condition of the pain-related sensory nervous system. *Keywords: pain, osteoporosis, fractures, drugs, side effects*

BOL I OSTEOPOROZA

Snežana Tomašević Todorović[1]*, Damjan Savić[1], Jelena Starčev[1], Saša Milićević[2], Sindi Mitrović[3], Olivera Ilić Stojanović[4]

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Bol kod pacijenata sa osteoporozom dovodi do smanjenja mobilnosti, gubitka sposobnosti hodanja i ravnoteže, ograničava fizičku aktivnost i povećava rizik od pada kod pacijenata starije životne dobi. Bol višeg intenziteta i povećana učestalost preloma kostiju predstavljaju ozbiljne uzroke morbiditeta i mortaliteta kod pacijenata sa osteoporozom. Prevencija bola povezana je sa odgovarajućim lečenjem osteoporoze, a lečenje bolnih stanja kod pacijenata sa osteoporozom zahteva multidimenzionalni pristup.
Starenje, visoka metabolička aktivnost kostiju, gojaznost, deformiteti kičmenog stuba i visok broj prethodnih vertebralnih preloma bili su potencijalni nezavisni faktori rizika za poremećaje povezane s bolom ili poremećaje hoda kod pacijenata sa osteoporozom. Osteoporoza uzrokuje određene vrste bola, koje se mogu podeliti na dva tipa: traumatski bol nakon preloma usled fragilnosti i bol proizašao iz osteoporotske patologije bez dokaza o prelomu. Ne postoji dovoljno podataka u literaturi o tome da li osteoporoza bez preloma uzrokuje bol. Bol se dovodi u vezu sa telesnim promenama koje se javljaju kod pacijenata sa osteoporozom. Povećani bol u leđima kao rezultat resorpcije kostiju javlja se kod pacijenata sa osteoporozom. Rezultati istraživanja ukazuju na činjenicu da gojaznost može uticati na intenzitet bola kod starije populacije sa osteoporozom. Bol kod osteoporoze je uglavnom nociceptivan, a ako postane perzistentan, može dovesti do senzitizacije perifernog i centralnog nervnog sistema, čime se naglašava prelazak u sindrom hroničnog bola. Mehanizmi centralne senzitizacije su složeni. Netraumatski osteoporotski bol može poticati iz nedetektabilne mikrofrakture ili strukturne promene, kao što je zamor mišića kod pacijenata s kifozom. Tradicionalno lečenje osteoporotskog bola potencijalno sprečava mogući bol koji je izazvan prelomima time što utiče na povećanje mineralne gustine kostiju i deluje na povezane medijatore kao što su osteoklasti i osteoblasti. Zaključci: Osteoporotski bol ima traumatske i netraumatske faktore, kao i veoma složenu patofiziologiju. Antiosteoporotske terapije su efikasne u lečenju osteoporotskog bol, jer poboljšavaju strukturu kostiju i stanje senzornog nervnog sistema povezanog s bolom.

Ključne reči: bol, osteoporoza, prelomi, lekovi, nuspojave

PAIN IN SYSTEMIC AUTOIMMUNE RHEUMATIC DISEASES

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Chronic pain is a serious health condition that dramatically reduces quality of life. Reciprocal interactions between the nervous and immune systems are complex and crucial in initiating and maintaining pain. Peripheral and central sensitization through neuroimmune signaling can promote chronic pain via various autoimmune mechanisms. These pathogenic autoimmune mechanisms include the production and release of autoreactive antibodies from B cells. Pain is mainly mediated through cytokines, reactive oxygen and nitrogen species, growth factors, and bioactive lipids. Active, high-grade, chronic inflammation and/or tissue damage can lead to autoimmune responses, characterized by the activation of T-cell clones that recognize self-antigens. Although autoimmune diseases differ in disease-specific immune responses, pathological chronic pain is a common symptom in most systemic autoimmune diseases. In autoimmune rheumatic diseases, pain, predominantly musculoskeletal, is caused by inflammatory pathways and responds to medications such as glucocorticoids, disease-modifying agents, and biologic drugs. However, pain is always a subjective experience influenced by biological, psychological, and social factors. Clinicians often face the challenge of persistent pain despite inflammation control, which requires the use of pharmacological and non-pharmacological strategies for pain management. Persistent chronic pain associated with rheumatoid arthritis (RA) and spondyloarthritis (SpA) has a multifactorial origin, both central and peripheral, and may result from active inflammation, joint damage, or tissue destruction caused by previous inflammatory conditions. Symptoms of inflammatory pain can be partially alleviated by nonsteroidal anti-inflammatory drugs (NSAIDs) or biologic and non-biologic disease-modifying antirheumatic drugs (DMARDs), but many patients still experience moderate pain due to changes in central pain regulation mechanisms or in cases of chronic widespread pain, characteristic of fibromyalgia (FM). Pain treatment requires a combined approach, including pharmacological analgesia, biological and standard disease-modifying drugs, and, as a last resort, joint replacement surgery. Nevertheless, although joint replacement surgery can significantly reduce pain associated with RA, it should only be an option for patients with the most advanced stage of the disease.

Keywords: pain, systemic autoimmune rheumatic diseases

BOL U SISTEMSKIM AUTOIMUNSKIM REUMATSKIM BOLESTIMA

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Hronični bol je ozbiljno zdravstveno stanje koje dramatično smanjuje kvalitet života. Recipročne interakcije između nervnog sistema i imunog sistema su kompleksne i odlučujuće u pokretanju i održavanju bola. Periferna i centralna senzibilizacija preko neuroimune signalizacije može promovisati hronični bol kroz različite autoimune mehanizme. Ovi patogeni autoimuni mehanizmi uključuju proizvodnju i oslobađanje autoreaktivnih antitela iz B ćelija. Promocija bola uglavnom je posredovana preko citokina, reaktivnih partikula kiseonika i azota, faktora rasta i bioaktivnih lipida. Aktivna, visokostepena, hronična inflamacija i/ili oštećenje tkiva mogu dovesti do autoimunih odgovora, koje karakteriše aktivacija klonova T-ćelija koji prepoznaju sopstvene antigene Iako se autoimune bolesti razlikuju prema imunim odgovorima specifičnim za bolest, patološki, hronični bol je zajednički simptom većine autoimunskih sistemskih bolesti. Kod autoimunskih reumatskih bolesti, bol, pretežno mišićno-skeletni, izazvan je inflamatornim putevima i reaguje na lekove kao što su glukokortikoidi, agensi koji modifikuju bolest i biološki lekovi. Međutim, bol je uvek subjektivno iskustvo na koje utiču biološki, psihološki i socijalni faktori. Kliničari se u praksi često suočavaju sa izazovom upornog bola uprkos kontroli upale što zahteva upotrebu farmakoloških i nefarmakoloških strategija za upravljanje bolom. Uporan hroničan bol povezan sa reumatoidnim artritisom (RA) i spondiloartritisom (SpA) ima multifaktorijalno poreklo, istovremeno centralno i periferno, i može biti posledica aktivnog zapaljenja, ili oštećenja zgloba i destrukcije tkiva, uzrokovano prethodnim inflamatornim stanjem. Simptomi inflamatornog bola mogu se delimično ublažiti nesteroidnim antiinflamatornim lekovima (NSAIL) ili biološkim i nebiološkim antireumatskim lekovima koji modifikuju bolest BML), ali mnogi pacijenti i dalje osećaju umereni bol zbog promena u mehanizmima centralne regulacije bola. ili u slučaju hroničnog rasprostranjenog bola koji karakteriše fibromijalgiju (FM). Lečenje bola zahteva kombinovani pristup koji uključuje farmakološku analgeziju, biološke i standardne bolest modifikujuće lekove, i, u krajnjem slučaju, implantaciju endoproteze. Ipak, iako operacija zamene zglobova može značajno da smanji bol povezan sa RA, može biti dostupna samo pacijentima sa najtežom uznapredovalom bolešću.

Ključne reči: bol, sitemske autoimunske reumatske bolesti

SELECTION OF THERAPEUTIC INTERVENTIONS IN DIFFERENT CLINICAL FORMS OF LUMBAR PAIN

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The approach of selecting therapeutic interventions according to the clinical form of lumbar pain promises answers to the questions of therapeutic efficiency and the influence of contextual factors in the rehabilitation of patients with lumbar pain. Identifying subgroups of patients with low back pain (LB) has attracted the attention of clinical researchers for decades to facilitate diagnosis, prognosis, and treatment. The dynamics of diagnosis, prognosis, and focus of therapy best fit into the psycho-social model of the disease. Within this model, emphasis was often placed on the role of psycho-social factors and their impact on recovery. However, despite the undeniable impact on the treatment outcome, focusing the therapeutic goal on these factors did not produce the expected results. Focusing the treatment on the patho-anatomical substrate and understanding the motor behavior that potentiates the further development of structural changes seems to be a good basis for creating a therapeutic approach and rehabilitation. The pathoanatomical substrate includes diseases and injuries of the intervertebral disc, displacement of the disc with pressure on the nerve, the existence of spinal stenosis, changes in the facet joints, sacroiliac pathology, vertebral fractures, and spondylolisthesis of the vertebral bodies. It is of primary importance to establish the structural pathoanatomical substrate and supplement it with other additional clinical classifications in terms of the dynamics of disorders about the substrate, motor behavior, and the psycho-social characteristics of the individual patient. The most well-known classification system that establishes a connection between motor behavior and clinical forms is the system based on treatment (Treatment Based Classification-TBC), which can be established from the examination of the patient; that is, the patient is classified into subgroups of LB with the need for mobilization, for specific exercises, for immobilization and for stretching. Another important classification system is based on the ICF system, which distinguishes low back pain with lack of mobility, low back pain with impaired coordination of movements, low back pain with associated pain in the lower extremities, low back pain with disorder movement coordination, and pain associated with generalized pain. A key aspect of the selection is the identification of subgroups, that is, the assessment of the patient.

Keywords: Lumbar pain, Classification, Selection of therapeutic interventions

SELEKCIJA TERAPIJSKIH INTERVENCIJA U RAZLIČITIM KLINIČKIM OBLICIMA LUMBALNOG BOLA

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Pristup selekcije terapijskih intervencija prema kliničkom obliku lumbalnog bola obećava odgovore na pitanja terapijske efikasnosti i uticaja kontekstualnih faktora u rehabilitaciji pacijenata sa lumbalnim bolom.

Identifikacija podgrupa pacijenata sa lumbalnim bolom (LB) zaokuplja pažnju kliničkih istraživača decenijama unazad, sa idejom da se olakša dijagnoza prognoza i lečenje. Dinamika dijagnoze, prognoze i fokusa terapije najbolje se uklapa u psiho-socijalni model bolesti. Unutar ovog modela stavljan je često naglasak na ulozi psiho-socijalnih faktora i njihovog uticaja na oporavak, ali i pored neospornog uticaja na ishod lečenja, fokusiranje terapijskog cilja na ove faktore nije dalo očekivane rezultate u smislu ishoda. Fokusiranje tretmana na pato-anatomski supstrat i razumevanje motornog ponašanja koje potencira dalji razvoj strukturalnih promena čini se kao dobra osnova za kreiranje terapijskog pristupa i rehabilitacije. Patoanatomski substrat podrazumeva bolesti i povrede intevertebralnog diskusa, pomeranja diskusa sa pritiskom na nerv, postojanje spinalne stenoze, promene na faset zglobovima, sakroilijačnu patologiju, frakture pršljenja i spondilolisteze pršljenskih tela. Od primarnoj je značaja ustanoviti strukturalni patoanatomski supstrat i dopuniti ga drugim dodatnim kliničkim razvrstavanjem u smislu dinamike poremećaja na relaciji supstrat motorno ponašanje, kao i psiho-socijalnim osobinama kod individualnog pacijenta. Najpoznatili klasifikacioni sistem koji uspostavlja vezu izmedju motornog ponašanja i kliničkih oblika je sistem zasnovan na lečenju (engl. *Treatment Based Clasiffication-TBC*), što se može ustanoviti iz pregleda pacijenta, odnosno pacijent se razvrstavaju u podgrupe LB sa potrebom za mobilizacijom, za specifičnim vežbama, za imobilizacijom i za istezanjem. Drugi važan sistem klasifikacije bazira se na ICF sistemu, koji razlikuje bol u donjem delu leđa sa nedostatkom pokretljivosti, bol u donjem delu leđa sa oštećenjem koordinacije pokreta, bol u donjem delu leđa sa povezanim bolom u donjim ekstremitetima, bol u donjem delu leđa sa poremećajem koordinacije pokreta i bol asociran sa generalizovanim bolom. Ključan aspekt selekcije je identifikaciji podgrupa odnosno procena pacijenta.

Ključne reči: lumbalni bol, klasifikacija, selekcija terapijskih intervencija

MULTIMODAL PAIN THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Pain in patients with rheumatoid arthritis is a chronic unpleasant sensory and emotional experience, which is associated with existing or potential tissue damage. It is accompanied by fatigue, mood swings, insomnia, physical incapacity, impaired quality of life. According to the mechanism of origin, the chronic pain of autoimmune inflammatory rheumatic disease is primarily of nociceptive character, and with long-term duration it can have both neuropathic and neuroplastic components. There is evidence that the proinflammatory cytokine TNF alpha, through its action on the CNS, causes pain independent of inflammation. The therapy of chronic rheumatic inflammatory pain seen in this way implies a multimodal approach, integrating pharmacological and non-pharmacological therapy. Modern pharmacological treatment of pain in patients with rheumatoid arthritis involves the use of analgesics and anti-inflammatory drugs as symptomatic therapy in addition to primarily used disease-modifying drugs, conventional and biological disease-modifying drugs and even more modern drugs that inhibit Janus kinase. A personalized approach is also necessary in order to ensure the best therapeutic efficiency. When choosing pharmacological therapy, one should be guided by the recommended guidelines based on the intensity of pain, but the quality of the pain should also be taken into account. It is necessary to take into account the existence of comorbidities, concomitant therapy, as well as the patient's psychological state. Non-pharmacological treatment of chronic pain syndrome includes physical therapy, psychotherapy (cognitive behavioral therapy, relaxation techniques and meditation), acupuncture and physical activity (aerobic exercises, stretching exercises, hydrokinesitherapy). Patient education about the nature of chronic pain and therapeutic possibilities is very important and is a basic prerequisite for good compliance. Multimodal personalized therapeutic programs are recommended for the most efficient achievement of the set goals in the treatment of pain in patients with rheumatoid arthritis.

An adequately managed pain relief program implies a good knowledge of the nature of the pain in patients with rheumatoid arthritis, a proper assessment of the patient's condition, a good knowledge of the pharmacotherapeutic properties of the selected drug, monitoring the patient and changing the therapeutic plan in case of poor effectiveness or the appearance of signs of toxicity and unwanted side effects.

Keywords: rheumatoid arthritis, inflammatory pain, multimodal treatment, disease modifying drugs, biological drugs, janus kinase inhibitor

MULTIMODALNA TERAPIJA BOLA KOD PACIJENATA SA REUMATOIDNIM ARTRITISOM

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Bol kod pacijenata sa reumatoidnim artritisom je hronični neprijatan senzorni i emotivni doživljaj, koji je povezan sa postojećim ili potencijalnim oštećenjem tkiva. Praćen je pojavom zamora, promenama raspoloženja, nesanicom, fizičkom nesposobnošću, narušenim kvalitet života. Prema mehanizmu nastanka hronični bol autoimunog zapaljenskog reumatskog oboljenja je prvenstveno nociceptivnog karaktera a sa dugotrajnošću može imati i neuropatsku i neuroplastičnu komponentu. Postoje dokazi da proinflamatorni citokin TNF alfa, svojim delovanjem na CNS, izaziva bol nezavisno od inflamacije. Terapija na ovaj način sagledanog hroničnog reumatskog zapaljenskog bola podrazumeva multimodalni pristup, integrišući farmakološku i nefarmakološku terapiju. Savremena farmakološka terapija bola kod pacijenata sa reumatoidnim artritisom podrazumeva primenu analgetika i antiinflamatornih lekova kao simptomatsku terapiju uz primarno primenjene bolest modifikujuče lekove, konvencionalne i biološke bolest modifikujuće lekove i još savremenije lekove koji inhibiraju janus kinazu. Takodje je neophodan personalizovan pristup kako bi se osigurala najbolja terapijska efikasnost Pri izboru farmakološke terapije treba se voditi preporučenim smernicama baziranim na intenzitetu bola, ali treba uzeti u obzir i kvalitet bola. Neophodno je voditi računa o postojanju komorbiditeta, konkomitantne terapije kao i psihičkog stanja pacijenta. Nefarmakološka terapija hroničnog bolnog sindroma uključuje fizikalnu terapiju, psihoterapiju (kognitivno bihejvioralna terapija, tehnike relaksacije i meditacija), akupunkturu i fizičku aktivnost (aerobne vežbe, vežbe istezanja, hidrokineziterapija). Edukacija pacijenta o prirodi hroničnog bola i terapijskim mogućnostima je veoma značajna i osnovni je preduslov za dobru komplijansu. Multimodalni personalizovani terapijski programi su preporučeni radi najefikasnijeg ostvarenja postavljenih ciljeva u lečenju bola kod pacijenata sa reumatoidnim artritisom.

Adekvatno vodjen program uklanjanja bola kod pacijenata sa reumatoidnim artritisom podrazumeva dobro poznavanje prirode bola, pravilnu procenu stanja pacijenta, dobro poznavanje farmakoterapijskih osobina izabranog leka, praćenje pacijenta i izmenu terapijskog plana u slučaju slabe efikasnosti ili pojave znakova toksičnosti i neželjenih nuspojava.

Ključne reči: reumatoidni artritis, zapaljenski bol, multimodalno lečenje, bolest modifikujući lekovi, biološki lekovi, inhibitor janus kinaze

CHALLENGES OF TREATING CHRONIC PAIN IN PEOPLE WITH KNEE OSTEOARTHRITIS

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The treatment of knee osteoarthritis pain in daily clinical practice most often does not include the optimal application of evidence-based guidelines. Namely, despite international guidelines that undoubtedly recommend exercise as a non-pharmacological form of treatment for knee OA pain, as evidenced by the results of randomized, controlled studies, the guidelines are not optimally implemented in clinical practice. According to research, the successful implementation of guidelines in clinical practice requires a comprehensive approach adapted to the specific environment and an adequately designed program that includes a set of strategies and measures to resolve obstacles in their implementation. The Osteoarthritis School at the Department of Physical and Rehabilitation Medicine with Rheumatology of the Dubrava Clinical Hospital was established in 2013 with the aim of implementing guidelines for the treatment of knee OA in daily clinical practice. The OA school includes an individualized program implemented by the rehabilitation team with an emphasis on medical exercises prescribed by specialists in physical and rehabilitation medicine, including manual techniques such as myofascial relaxation and manual lymphatic drainage, application of a stabilometric platform, analgesic electrotherapy and electrostimulation, education about the disease and advice from a clinical nutritionist. After the OA school conducted at the Institute, significant effectiveness in reducing pain intensity, regulating body weight, improving the quality of life of OA patients and reducing the need for chronic use of analgesic medication therapy was demonstrated. During the COVID-19 pandemic, when physical therapy was not available to the majority of OA patients, a survey was conducted that confirmed the long-term effectiveness of the OA school implemented before the COVID-19 pandemic in comparison to classical physical therapy. In conclusion, according to the experiences of the Department of Physical and Rehabilitation Medicine with Rheumatology KB Dubrava, both classical physical therapy and the OA school lead to a reduction in pain intensity, improvement in knee joint function, and improvement in the quality of life of patients with knee OA, but the effect of the OA school is more significant and long-lasting.

Keywords: knee osteoarthritis, OA school

IZAZOVI LIJEČENJA KRONIČNE BOLI U OSOBA OBOLJELIH OD OSTEOARTRITISA KOLJENA

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Liječenje boli osteoartritisa koljena u svakodnevnoj kliničkoj praksi najčešće ne uključuje optimalnu primjenu smjernica utemeljenih na dokazima. Naime, unatoč međunarodnim smjernicama koje nedvojbeno preporučuju tjelovježbu kao nefarmakološki oblik liječenja boli OA koljena što dokazuju i rezultati randomiziranih, kontroliranih studija smjernice nisu optimalno implementirane u kliničkoj praksi. Prema istraživanjima, uspješna implementacija smjernica u kliničku praksu zahtijeva sveobuhvatan pristup prilagođen specifičnoj okolini te adekvatno dizajniran program koji obuhvaća skup strategija i mjera za rješavanje prepreka u implementaciji istih. Osteoartritis škola u Zavodu za fizikalnu i rehabilitacijsku medicinu s reumatologijom Kliničke bolnice Dubrava uspostavljena je 2013. godine s ciljem provedbe smjernica za liječenje OA koljena u svakodnevnoj kliničkoj praksi. OA škola uključuje individualizirani program kojeg provodi rehabilitacijski tim s naglaskom na medicinske vježbe propisane od specijalista fizikalne i rehabilitacijske medicine uključujući manualne tehnike primjerice miofascijalnu relaksaciju i manualnu limfnu drenažu, primjenu stabilometrijske platforme, analgetsku elektroterapiju i elektrostimulaciju, edukaciju o bolesti te savjete kliničkog nutricionista. Nakon provedene OA škole u Zavodu dokazana je značajna učinkovitost na smanjenje intenziteta boli, regulaciju tjelesne mase, poboljšanje kvalitete života OA bolesnika te smanjenu potrebu za kroničnom upotrebom analgetske medikamentozne terapije. Tijekom COVID-19 pandemije, kada fizikalna terapija nije bila dostupna većini bolesnika s OA, provedena je anketa kojom je potvrđena dugoročna učinkovitost OA škole provedene prije COVID-19 pandemije usporedno s klasičnom fizikalnom terapijom. Zaključno, prema iskustvima Zavoda za fizikalnu i rehabilitacijsku medicinu s reumatologijom KB Dubrava obje i klasična fizikalna terapija i OA škola dovode do smanjenja intenziteta boli, poboljšanja funkcije koljenskog zgloba te poboljšanja kvalitete života bolesnika s OA koljena, ali je učinak OA škole značajniji i dugotrajniji.

Ključne riječI: osteoartritis kolejna, OA škola

MULTIMODAL PAIN MANAGEMENT, WHAT WE LEARNED FROM ANIMAL PAIN MODELS

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There are a huge number of different pain models in animals. For almost every human disease, there is an animal model of that same disease. The various pain models that have been developed in animals can be divided in various ways. There is no classification that is unique and comprehensive. One of the classifications is according to the duration of the pain. Thus, there are acute models of pain (implying pain that lasts while a painful stimulus is present) and chronic models of pain (long-term pain lasting several days and weeks). Anatomical classification is made according to the part of the body where the pain occurs, so there are: skin models, muscular models, models with joint inflammation, ocular models, visceral models. There is also a classification according to the type of noxious stimulation used to cause pain, so there are: chemical models, thermal models, mechanical models. The most acceptable and most common division is according to the mechanism of pain, namely: nociceptive pain models (caused by nociceptor irritation - inflammatory pain, traumatic pain, surgical pain) and neuropathic pain models (pain caused by nerve damage). Inflammatory models of pain are used to study the mechanisms of pain at the molecular, cellular, electrophysiological and anatomical levels. They serve to study the pathophysiological mechanism underlying acute and chronic pain. These models enable preclinical evaluation of potential analgesics and other therapeutic procedures (use of viral vectors, RNA modulation, cognitive treatments, surgical treatments) aimed at pain relief. The main limiting factor is that pain cannot be directly measured in animals. In animals, pain is assessed by observing the response to the application of nociceptive stimuli. Thus, the animal's response to thermal, mechanical or chemical stimulation is measured. Animal behavior can also be evaluated in terms of evaluating the animal's desire to avoid pain, evaluating the animal's vocalizations, etc. There is no best pain model. When choosing a pain model, it must be ensured that the model is specific to the disease or organ that causes a specific type of pain. Models are indispensable in the research of new therapeutic methods for the treatment of chronic or acute pain. The model is chosen based on the disease being examined - skin disease, muscle disease, joint disease, nerve disease, visceral disease. The advantage is given to the pain model, which is cheaper and easier to perform.

Keywords: animal models, multimodal models, reflex nociceptive tests, pain models performed on the skin

MULTIMODALNO ZBRINJAVANJE BOLA ŠTO SMO NAUČILI NA OSNOVU ANIMALNIH MODELA BOLA

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Postoji ogroman broj različitih modela bola kod životinja. Gotovo za svaku ljudsku bolest postoji model te bolesti kod životinja. Različiti modeli bola koji su razvijeni kod životinja se mogu podeliti na razne načine. Ne postoji klasifikacija koja je jedinstvena i sveobuhvatna. Jedna od klasifikacija je prema dužini trajanja bola. Tako postoje akutni modeli bola (podraazumevaju bol koji traje dok je i prisutan bolni stimulus) i hronični modeli bola (dugotrajni bol u trajanju od nekoliko dana i nedelja). Anatomska klasifikacija je izvršena prema delu tela gde se javlja bol, pa tako postoje: kutani modeli, muskularni modeli, modeli sa zapaljenjem zglobova, okularni modeli, visceralni modeli. Postoji i klasifikacija prema vrsti nokse koja se koristi da izazove bol, pa tako imamo: hemijske modele, termičke modele, mehaničke modele.

Najprihvatljivija i najčešća podela je prema mehanizmu nastanka bola, to su: nociceptivni modeli bola (izazivaju se draženjem nociceptora - inflamatorni bol, traumatski bol, hirurški bol) i neuropatski modeli bola (bol se izazaiva povredom nerava). Inflamatorni modeli bola se koriste kako bi se izučili mehanizmi nastanka bola na molekularnom, ćelijskom, elektrofiziiološkom i anatomskom nivou. Služe izučavanju patofiziološkog mehanizma koji leži u osnovi akutnog i hroničnog bola. Ovi modeli omogućavaju predkliničku evaluaciju potencijalnih analgetika i drugih terapeutskih postupaka (korišćenje virusnih vektora, RNK modulacija, kognitivni tretmani, hirurški tretmani) koji imaju za cilj nestanak bola. Glavni ograničavajući faktor je što bol kod životinja ne može direktno da se meri. Kod životinja se bol procenjuje i to posmatranjem odgovora pri aplikaciji nociceptivnih stimulusa. Dakle, meri se odgovor životinje na termičku, mehaničku ili hemijsku draž. Može se procenjivati i ponašanje životinja u smilu procene želje životinje da izbegne bol, procene vokalizacije životinje, itd. Ne postoji najbolji model bola. Pri izboru modela bola mora se voditi računa da model bude specifičan za bolest ili organ ida izaziva specifičnu vrstu bola. Modeli su nezamenjivi u istraživanjima novih terapeutskih metoda za lečenje hroničnog ili akutnog bola. Model se bira na osnovu bolesti koju ispitujemo – kožna bolest, bolest mišića, zglobova, nerava, visceralna bolest. Prednost ima model bola koji je jeftiniji i koji se lakše izvodi.

Ključne reči: animalni modeli, multimodelni modeli, refleksni nociceptivni testovi, modeli bola koji se sprovode na koži

THE INFLUENCE OF PERSONALITY TYPE AND EMOTIONAL STATUS ON THE EXPERIENCE OF PAIN

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Pain is defined as „unpleasant sensory and emotional expeirence associated with, or resembling that associated with, actual or potential tissue damage“. Pain is personal, subjective category, prone to significant individual variations, and therefore difficult to measure by objective methods. Emotional status, exposure to stress and also personality traits could have significant influence on pain experience. Person with depression, anxiety and stress problems has lower threshold and pain tolerance. They are more prone to regression of pain in future, and generally have more difficulties in fighting pain. Person high on scale of neuroticism are vulnerable and iritable. They are prone to catastrophising actual situation, which could have main impact in transition to a chronic pain. It could also have significant impact on the course and outcome of disease. Due to a wide range of potential individual factor on pain experience, further study and medical practice should be more based on individual aproach and multidisciplinarity, in order to find best solution for every patient, and to improve quality of their life, which is the main goal of medicine.

Keywords: emotional status, personality, pain tolerance, chronic pain

UTICAJ TIPA LIČNOSTI I EMOCIONALNOG STATUSA NA DOŽIVLJAJ BOLA

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Bol se definiše kao ″neprijatno čulno ili emocionalno iskustvo, povezano sa aktuelnim ili potencijalnim oštećenjem tkiva″. Bol je subjektivna kategorija, podložna velikim individualnim varijacijama, te je stoga, teško merljiva objektivnim metodama. Različiti parametri, počevši od trenutnog emocionalnog stanja, raspoloženja ali i tipa ličnosti, mogu imati značajan uticaj na percepciju bola i ponašanje u hroničnim bolnim stanjima. Depresivnost, anksioznost i stres u velikoj meri utiču na doživljaj bola. Osobe sklone depresivosti, anksioznom afektu i osobe izložene stresu u dužem vremenskom periodu, imaju niži prag bola, manju toleranciju, sklonije su regresiji bolnog stanja i teže se bore sa bolom kao neprijatnom senzacijom. Osobe označene kao neurotične, lako iritabilne i vulnerabilne, sklone su katastrofiziranju trenutne situacije i težoj racionalizacji. Usled psihološkog distresa, percepcija bola se menja, što sve zajedno može imati značajne reperkusije na tok same bolesti i ishod lečenja. Usled širokog spektra subjektivnih faktora na doživljaj bola, proučavanje ovog fenomena zahteva individualni pristup svakom pojedincu i multidisciplinarno angažovanje, sve u cilju pronalaska najboljeg terapijskog rešenja, oporavka pacijenta i poboljšanja kvaliteta njegovog života.

Ključne reči: emocionalno stanje, tip ličnosti, doživljaj bola, hronični bol

PAIN AND SLEEP: HOW TO HEGOTIATE?

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The relationship between sleep and pain is reciprocal and complex, pain interfering with sleep stability and poor sleep exacerbating pain. A better understanding of the physiological mechanisms linking sleep and pain would be essential to improve the management of patients with chronic pain syndromes. The mechanisms involved in hyperalgesia linked to sleep deprivation will be discussed, as will those that do or do not lead to pain-induced sleep interruption. During sleep, we remain able of filtering sensory information according to its relevance to bodily integrity and, of course, to sleep depth. The factors that lead to sleep disruption, whether perceptual or influenced by memory and emotion, remain to be determined, but certainly involve high-level brain processing. The relationship between pain and sleep alone cannot explain sleep disorders in chronic pain patients, since for 20-30% of them, pain has little impact on their sleep. Direct evidence of a common vulnerability factor in relation to that of depression is still lacking to confirm the existence of a predilection terrain, but indirect clinical evidence points in this direction. Sleep disorders in different clinical pain situations will be presented, as well as the different ways of documenting them, to search for specific disorders such as sleep apnea and restless legs syndrome. These elements will help guide the therapeutic management of these patients, whether behavioural or drug-based, bearing in mind the adverse effect of certain analgesic treatments on sleep.

Keywords: sleep, pain, hyperalgesia

DIFFERENCES IN PAIN PERCEPTION BETWEEN THE SEXES

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Data on the differences in pain perception between men and women are still not convincing. Populationbased research demonstrate higher pain prevalence among women relative to men, with women being more likely to report chronic widespread pain.The issue of whether the intensity of pain varies between the sexes is difficult to answer, however the majority of studies indicated that women rated their pain greater on average. The precise mechanisms that cause these differences remain unclear. These variations are probably caused by a combination of biological, psychological and social factors, among which biological have the greatest influence on pain perception. Namely, it has been shown that there are variations based on sex in the brain processing of pain signals, especially in the descending modulatory system of pain, as well as in cerebral blood flow. There is an ongoing debate about the influence of sex hormones, especially the influence of estrogen on pain perception, while the role of androgens seems to be clearer. Methodologies in this field mostly include quantitative sensory testing modalities where pressure, temperature and ischemia are used as stimuli. The results based on sex varied depending on the type of stimulus and research methodology. From previous studies emerges the fact that men have higher pain threshold and tolerance than woman, except when cold stimulus is applied, where the results are contradictory and depend on the site of the stimulus application. It was found that age and gender influenced pressure pain threshold in healthy people. More precisely, female gender and older age are associated with lower pressure pain thresholds, but these sex differences seem to attenuate with aging.

Keywords: pain perception, pain assessment, pain thresholds

RAZLIKE U PERCEPCIJI BOLA IZMEĐU POLOVA

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Dosadašnji podaci iz literature o razlikama u percepciji bola između muškaraca i žena nisu ubedljivi. Populaciona istraživanja pokazuju veću prevalencu bola među ženama u odnosu na muškarce, pri čemu je i veća verovatnoća da će žene prijaviti hronični široko rasprostranjeni bol. Teško je odgovoriti na pitanje da li intenzitet bola varira u zavisnosti od pola, ali većina studija je pokazala da su žene u proseku rangirale intenzitet bola na višem nivou u odnosu na muškarce. Precizni mehanizmi koji uzrokuju ove razlike ostaju nejasni. Ove varijacije su verovatno uzrokovane kombinacijom bioloških, psiholoških i društvenih faktora, od kojih na percepciju bola u najvećoj meri utiču biološki faktori. Naime, pokazano je da postoje polne varijacije u moždanoj obradi signala bola, posebno u silaznom modulatornom sistemu bola, kao i u cerebralnom krvotoku. Aktuelna je debata o uticaju polnih hormona, posebno o uticaju estrogena na percepciju bola, dok se čini da je uloga androgena u percepciji bola jasnija. Metodologije istraživanja iz ove oblasti mahom obuhvataju modalitete kvantitativnog senzornog testiranja gde se kao stimulus koriste pritisak, temperatura i ishemija. Dobijeni rezultati zasnovani na polu iz preglednih istraživanja su varirali u zavisnosti od vrste stimulusa i metodologije istraživanja. Iz dosadašnjih studija proizilazi činjenica da muškarci imaju značajno viši prag bola i toleranciju na bol od žena, osim kada je kao stimulus primenjena hladnoća, gde su rezultati oprečni i zavise od mesta primene stimulusa. Pokazano je da starost i pol utiču na prag bola na pritisak kod zdravih ljudi. Tačnije, ženski pol i starija životna dob povezani su sa nižim pragom bola na pritisak, ali deluje da se razlike u vrednostima pragova bola na pritisak među polovima smanjuju sa starenjem.

Ključne reči: percepcija bola, procena bola, pragovi bola

SEX AND GENDER DIMORPHISM IN PAINFUL CONDITIONS

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Painful conditions have a significant impact on the quality of life of the patient, family, society and the health system. Numerous studies have shown that there are gender differences in painful conditions, which must be respected in the planning of therapeutic treatment. Sexual dimorphism refers to a set of morphological and physiological characteristics of female and male individuals, which are determined by genetic, anatomical, endocrine, immunological and neurological factors. Gender differences refer to the "socially constructed roles, behavior, expressions and identity" associated with male or female gender. Genetically, women have an increased sensitivity to pain, with a lower efficiency of endogenous pain inhibitory mechanisms, while men have a higher threshold for pain. Sex hormones can modulate signaling pathways of pain and inflammation. Sex differences also cause different functional mapping of the brain. So, in women there is atypically greater functional involvement of the cingulate cortex (affective elaboration of pain), with a weaker connection with the prefrontal cortex (cognitive processing and descending modulation of pain), while men showed stronger connections with the sensorimotor cortex and greater volume and thickness of the prefrontal cortex. There is also a significant sex difference in the mechanism of neuropathic pain: in men disinhibition of dorsal horn neurons is caused by proliferated microglia, while in women by immune cells, i.e. probably T lymphocytes.

Gender differences can alter the actual individual experience of pain often as a result of tradition, education, certain social rules and expectations.

Conclusion: During the clinical assessment of pain and the planning of therapeutic treatment, the sex and gender characteristics of patients should be respected. Future research should provide a more detailed analysis of sex and gender differences in the basic mechanisms of pain and analgesia, in order to achieve an adequate and effective algorithm of therapeutic pain treatment.

Key words: pain, sexual dimorphism, gender dimorphism

POLNI I RODNI DIMORFIZAM U BOLNIM STANJIMA

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Bolna stanja imaju značajan uticaj na kvalitet života pojedinca, porodice, društva i zdravstvenog sistema. Mnogobrojna istraživanja su pokazala da u bolnim stanjima postoje polne i rodne razlike, koje je potrebno respektovati u planiranju terapijskog tretmana. Polni dimorfizam se odnosi na skup morfoloških i fiziloških karakteristika ženskih i muških jedinki, koje su determinisane genetskim, anatomskim, endokrinim, imunološkim i neurološkim faktorima. Rodne razlike se odnose na "društveno konstruisane uloge, ponašanje, izraze i identitet" koji su povezani za muški ili ženski pol.

Genetski je kod žena povećana senzitivnost na bol, uz slabiju efikasnost endogenih inhibitornih mehanizama za bol, dok muškarci imaju viši prag za bol. Polni hormoni mogu da moduliraju signalne puteve bola i inflamacije. Polne razlike uslovljavaju i promene funkcionalnog mapiranja mozga, pa je kod žena atipično veće funkcionalno uključivanje cingularne kore (afektivna elaboracija bola), uz slabiju povezanost sa prefrontalnom korom (kognitivna obrada i descedentna modulacija bola), dok su muškarci pokazali jače veze sa senzomotornom korom i veći volumen i debljinu prefrontalne kore.

Značajna je polna razlika i u mehanizmu nastanka neuropatskog bola: kod muškaraca dezinhibiciju neurona dorzalnih rogova prouzrokuje proliferisana mikroglija, a kod žena imune ćelije, tj. verovatno T-limfociti. Rodne razlike mogu da izmene realan individualni doživljaj bola često kao rezultat tradicije, vaspitanja, određenih društvenih pravila i očekivanja.

Zaključak: pri kliničkoj proceni bola i planiranju terapijskog tretmana treba respektovati polne i rodne karakteristike pacijenata.

Buduća istraživanja treba da obezbede podobniju analizu polnih i rodnih razlika u bazičnim mehanizmima bola i analgezije, da bi se postigao adekvatan i efikasan algoritam terapijskog tretmana bola. *Ključne reči: bol, polni dimorfizam, rodni dimorfizam*

DIFFERENTIAL DIAGNOSTIC ASPECTS OF PAIN IN MENOPAUSE

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Estrogens are a regulatory metabolism factor in many connective tissues; bones, muscles, cartilages, ligaments, and tendons. However, the connection between various musculoskeletal pain syndromes and menopause was only recently established, because the expression of estrogen receptors (ER) in tendon and ligament tissue was proven for ERα in 1996 and ER-β in 2010. The frequency of hot flashes and musculoskeletal pain in menopause is very similar. A progressive decrease in estradiol in the connective tissue is associated with diffuse pain and a feeling of stiffness in the spine and joints, which reduces the quality of life by about 40%, and for women who already had pain, the complaints increase by about 50%. Multiple brain areas are involved in transmitting and modulating pain, and they contain receptors for sex hormones. Estrogen modulates spinal and central processing of nociception by neurons in the spinal cord and brain that contain opioids and express estrogen receptors. Hypoestrogenemia increases pain perception. VitD receptor expression is stimulated by 17b-estradiol. The VitD receptor is present in neurons, oligodendrocytes, astrocytes within the limbic system, in the basal ganglia, spinal cord, cerebellum, and cerebral cortex. The signaling pathways and mechanisms of VITD on pain transmission are primarily nociceptive. Estrogens can increase the concentration of 1.25(OH)2 D3 (calcitriol), and the brain can regulate the local concentration of calcitriol. However, the exact mechanism by which VIT D and ovarian hormones alter pain perception is unrecognized. The findings indicate a differential, dose-dependent effect of estrogen on bone and tendon in combination with mechanical loading. Low levels of estrogen metabolites: endogenous E2 and 2 hydroxyestrone are associated with the incidence of knee OA even after adjustment for age, BMI, and injury. The menopausal transition is a turning point for the prevalence of numerous tenosynovitis, tendinitis, as well as compressive tunnel syndromes, positively associating the expression of ERb in tenosynovial tissue with the clinical degree of the disease. The protective effect of hormonal therapy in the presentation of OA has been proven in several publications. However, current knowledge is not sufficient for conclusions in this area.

Keywords: hypoestrogenemia, tenosynovitis, osteoarthritis, musculoskeletal pain.

DIFERENCIJALNO DIJAGNOSTIČKI ASPEKTI BOLA U MENOPAUZI

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Estrogeni su poznati kao regulacioni faktor metabolizma u mnogim vezivnim tkivima; kostima, mišićima, hrskavicama, ligamentima i tetivama. Međutim, povezanost izmedju različitih muskuloskeletnih bolnih sindroma i menopauze je tek nedavno ustanovljena, jer je I ekspresija estrogenskih receptora (ER) u tkivu tetiva i ligamenta dokazana za ERα 1996. a za ER-β, 2010. godine. Još manje se zna da je učestalost valunga I muskuloskeletnog bola u menopauzi veoma slična. Progresivno sniženje estradiola u vezivnom tkivu je povezano sa difuznim bolom i osećajem ukočenosti u kičmenom stubu i zglobovima, što smanjuje kvalitet života za oko 40 %, a ženama koje su već imale bol, tegobe se povećavaju za oko 50%. Mnoge oblasti mozga su uključene u prenos I modulaciju bola I sadrže receptore za polne hormone. Estrogen moduliše spinalno i centralno procesuiranje nocicepcije neuronima u kičmenoj moždini i mozgu koji sadrže opioide i eksprimiraju estrogenske receptore, a hipoestrogenemia povećava osećaj za bol. I ekspresija VitD receptora je stimulisana 17b-estradiolom. VitD receptor se prezentuje u neuronima, oligodendrocitima, astrocitima u okviru limbičkog sistem, u bazalnim ganglijama, kičmenoj moždini, cerebelumu i kori mozga. Signalni putevi i mehanizmi VITD na prenos bola su prevashodno nociceptivni. Estrogeni mogu da povećaju koncentraciju $1.25(OH)_2$ D3 (kalcitriola), a mozak može da reguliše lokalnu koncentraciju kalcitriola. Međutim tačan mehanizam kojim VIT D i hormoni jajnika menjaju osećaj bola nije poznat. Nalazi ukazuju na diferencijalno, dozno zavisno dejstvo estrogena na kosti i tetive u kombinaciji sa mehaničkim opterećenjem. Niski nivoi metabolita estrogena: endogenog E2 i 2 hydroxyestrona povezani su sa incidencom OA kolena i posle korekcije za starost, BMI i povrede. Menopauzna tranzicija je prekretnica za prevalenciju mnogobrojnih tenosinovitisa, tendinitisa kao i kompresivnih tunelnih sindroma pozitivno povezujući ekspresiju ERb u tenosinovijalnom tkivu sa kliničkim stepenom bolesti. Protektivni efekat hormonske terapije u prezentaciji OA je dokazana u nizu radova. Ipak, sadašnja saznanja nisu dovoljna za zaključke u ovoj oblasti.

Ključne reči: hipoestrogenija, tenosinovitisi, osteoartritisi, muskuloskeletna bol.

MINIMALLY INVASIVE TREATMENT OF VISCERAL PAIN

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While the treatment of musculoskeletal pain is widespread and the patients themselves are well sensitized to its treatment, the treatment of visceral pain carries many questions, especially since both NSAIDs and opioids are sometimes contraindicated in the treatment of visceral pain. In particularly refractory, chronic or cancerous visceral pain, minimally invasive procedures are sometimes the best treatment option. Blockade of the splachnicus, ganglia celiacus, superior and inferior hypogastric ganglia as well as blockade of the ganglia impar are the most common procedures for the treatment of visceral pain. The celiac plexus supplies sympathetic, parasympathetic and visceral sensory fibers to the upper abdominal organs such as the distal esophagus, pancreas, liver, biliary tract, spleen, kidneys, adrenal glands, stomach, small intestine, colon to the transverse colon and mesentery. A splanchnic nerve block is preferred in patients in whom it is not possible to perform a celiac plexus block due to altered anatomy by a tumor mass or due to lymphadenopathy. The superior hypogastric plexus block is used in patients who have pain in the area of the pelvic viscera. In patients with non-malignant pain, a temporary block can help better define the cause of the pain. Much more often, superior hypogastric neurolysis is used for very strong visceral pelvic pain of malignant origin. Patients with local invasion of cancer into the vagina, uterus, ovaries, prostate, and rectum associated with pelvic pain often have a significant reduction in pain after blockade or neurolysis of the superior hypogastric block. Specific painful conditions that can be treated with an inferior hypogastric block are pelvic pain, pain due to endometriosis, malignant pelvic pain, vulvodynia, tenesmus caused by radiation, enteritis of the rectum and sigmoid colon, proctalgia fugax and postherpetic neuralgia of the sacral dermatomes. Blockade of the ganglia impar can lead to a reduction of pain in the lower part of the rectum, anal region, lower part of the urethra, vagina, vulva and scrotum.

Keywords: visceral pain, celiac ganglion, hypogastric ganglion, ganglion impar

MINIMALNO INVAZIVNI LIJEČENJE VISCERALNE BOLI

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Dok je liječenje mišićno koštane boli široko rasprostranjeno i sami bolesnici u dobro senzibilizirani za njeno liječenje, liječenje visceralne boli nosi sa sobom puno pitanja, osobito jer su i NSAID i opioidi ponekad kontraindicirani u liječenju visceralne boli. Kod osobito refrakterne bilo kronične bilo karcinomske visceralne boli minimalno invazivni zahvati su ponekad najbolja opcija u liječenju. Blokada splahnikusa, ganglia celiacusa, superiornog i inferiornog hipogastričnog ganglia kao i blokada ganglia impar najrasprostranjenije su procedure za liječenje visceralne boli. Celijačni pleksus opskrbljuje simpatičkim, parasimpatičkim i visceralnim senzornim vlaknima gornje abdominalne organa kao što su distalni jednjak, pankreas, jetra, bilijarni trakt, slezena, bubrezi, nadbubrežne žlijezde, želudac, tanko crijevo, debelo crijevo do transverzalnog kolona i mezenterija. Blok splanhničkih živaca ima prednost kod bolesnika kod kojih nije moguće napraviti blok pleksusa celijakije uslijed izmijenjene anatomije tumorskom masom ili zbog limfadenopatije. Superiorni hipogastrični pleksus blok koristi se u bolesnika koji imaju bol u području zdjelične viscere. . U bolesnika s nemalignom boli privremeni blok može pomoći u boljem definiranju uzroka boli. Mnogo češće superiorna hipogastrična neuroliza rabi se kod vrlo jake visceralne zdjelične boli zloćudnog porijekla. Bolesnici s lokalnom invazijom karcinoma u vaginu, uterus, ovarije, prostatu i rektum koji su povezani s pelvičnom boli često imaju značajno smanjenje boli nakon blokade ili neurolize superiornoga hipogastričnog bloka. Specifična bolna stanja koja se mogu liječiti inferiornim hipogastričnim blokom su bol u zdjelici, bol zbog endometrioze, maligna bol zdjelice, vulvodinija, tenezmi uzrokovani zračenjem, enteritis rektuma i sigmoidnog kolona, proktalgija fugax te postherpetična neuralgija sakralnih dermatoma. Blokada ganglia impar može dovesti do smanjenja bolova u Lower part of the rectum, Anal region, Lower part of the urethra, Vagina, vulva i skrotuma.

Ključne riječi: visceralna bol, ganglij celiacus, hipogastrični ganglij, ganglij impar

POSTOPERATIVE PAIN MANAGEMENT – LOOK BEYOND THE HORIZON

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Perioperative pain management or analgesia (POPM) denotes preoperative, intraoperative, and postoperative analgesia. In recent years, the complexity of POMP is better understood, as well as the consequences of improperly treated pain. Despite this, moderate to severe pain and chronic pain (CPSP) are still frequent. Novel recommendations suggest medical staff education, construction and implementation of pain guidelines, patient education, and medical documentation. Opioid-sparing analgesia techniques, including regional anesthesia, non-opioids (paracetamol, metamizol, and NSAIDs), coanalgesics (alpha-2 adrenergic agonists, dexamethasone, NMDA antagonists), and non-pharmacological techniques are implemented in multimodal pain management. POPM should be based on multidimensional pain monitoring, functionality, sleep quality, and patient satisfaction. Step 1 includes preoperative screening of potentially modifiable risk factors (e.g., smoking status and psychological well-being) and nonmodifiable factors (demographic and surgical factors) for severe acute pain and CPSP. Step 2, which is of paramount importance, includes preventive measures with a multidisciplinary approach (e.g., psychologist or clinical pharmacologist consultation). This approach ensures that all aspects of the patient's well-being are considered, providing comprehensive care. Step 3 is the information presentation to the patients, which is the activity of all team members. Step 4 includes implementing procedure-specific recommendations (e.g., PROSPECT) adjusted to hospital and medical staff capacity and individualized toward patient's characteristics. Opioids present a golden standard for POMP and should be used in the lowest possible effective dose and immediate release forms. Novel data shows that if intraoperative sparingly given opioids casing unsatisfactory analgesia might lead to increased pain and opioid demand during postoperative period. Oral analgesia use should be implemented whenever the surgery type enables it. Step 5 includes continuity of perioperative analgesia to discharge and hospital post-discharge period. The guidelines about post-discharge analgesics (predominantly non-opioids), pain therapy, and the possibility for consultation. Different procedures necessities patient follow-up if opioids are prescribed, and a de-escalation plan should be prepared. This individualized approach ensures that each patient's unique needs are met, enhancing their comfort and recovery. Perioperative pain management is complex and includes the biological, psychological, social, and spiritual dimensions of the pain experience. Each should be acknowledged in providing optimum pain management in the postoperative setting. The continuity of care is a crucial part of analgesia process, ensuring that the patient's needs are met at every stage of their recovery.

Keywords: acute pain, postoperative, surgery; analgesia, multimodal

ERIOPERATIVNA TERAPIJA BOLA-POGLED IZA HORIZONTA

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Perioperativna terapija bola (PTB) podrazumeva preoperativnu, intraoperativnu i postoperativnu analgeziju. Kompleksnost PTB se danas bolje poznaje kao i posledice neadekavne PTB. Uprkos tome, osrednji do snažan postoperativni akutni i hronični postoperativni bol (HPOB) su česti. Nove preporuke podrazumevaju edukaciju medicinskog osoblja, formiranje i primenu vodiča za terapiju bola, edukaciju pacijenata i vođenje medicinske dokumentacije. Opioid poštedna analgezija (*opioid-sparing analgesia*) uključuje regionalnu anesteziju, neopioide (paracetamol, metamizol, NSAIL), koanalgetike (alfa-2 adrenergičke agoniste, deksametazon, NMDA antagoniste) i nefarmakološke tehnike koje se primenjuju u sklopu multimodalne terapije bola. PTB se bazira na multidimenzionalnom monitoringu bola, funkcionalnosti, kvalitetu sna i zadovoljstvu pacijenta.

Prvi korak podrazumeva preoperativni skrining potencijalno korektabilnih faktora rizika (na pr. pušački status i psihološki boljitak) i nekorektabilni faktori (demografski i hirurški faktori) za snažan akutni bol i HPOB. Drugi korak je izuzetnog značaja i podrazumeva primenu preventivnih mera i najčešće podrazumeva multidisciplinarni pristup (na pr. konsultacija psihologa ili kliničkog farmakologa). Ovakav pristup omogućava pokrivanje svih aspekata i sveobuhvatnost pristupa. Treći korak je informisanje pacijenata, što je aktivnost svih članova hirurškog tima. Četvrti korak uključuje primenu preporuka koje su specifične za hiruršku proceduru (PROSPECT) prilagođeno obučenosti osoblja, resursima bolnice i pacijentu. Opioidi predstavljaju zlatni standard PTB. Opioide treba primeniti u minimalnoj delotvornoj dozi i u formi trenutno oslobađajućih opioida, a novi podaci ukazuju da redukovana intraoperativna primena opioida može dovesti do porasta intenziteta postoperativnog bola i upotrebe opioida. Oralni analgetici se primenjuju ukoliko ne postoje hirurške kontraindikacije. Peti korak podrazumeva kontinuitet perioperativne analgezije na celokupan period hospitalizacije i nakon otpuštanja iz bolnice.

Pacijenta treba edukovati za terapiju bola nakon izlaska iz bolnice i prepisati analgetike (dominantno neopioidi) i omogućiti kontakt za konsultaciju. Neophodno je isplanirati procedure praćenja pacijenta ukoliko su prepisani opioidi i de-eskalacioni plan. Individualizovani pristup pacijentu obezbeđuje komfor i oporavak. Perioperativna terapija bola je kompleksna i uključuje biološke, psihološke, socijalne, i spiritualne aspekte doživljaja bola. Svaki od ovih elemenata obezbeđuju optimalnu terapiju PTB. Kontinuitet analgezije je krucijalni elemenat pacijentovog postoperativnog oporavka.

Ključne reči: akutni bol, postoperativni, hirurgija; analgezija, multimodalna

RADIOSYNOVECTOMY IN THE TREATMENT OF PAINFUL ARTHROPATIES

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Radiosynoviectomy (RS), or intra-articular injection of radioactive yttrium (90Y) silicate or citrate, is one of the therapy options for refractory arthropathies. The procedure has been carried out throughout Europe for over 20 years in compliance with the 2002 and 2021 standards that were updated by the European Association for Nuclear Medicine. The committee, in collaboration with a multidisciplinary team, determines the indications for RS, which include painful arthropathies that do not respond to traditional treatment (medication or surgery). Patients who suffer from rheumatoid arthritis, seronegative spondyloarthropathy (e.g. reactive arthritis, psoriatic arthritis, ankylosing spondylitis), arthritis in hemophilia, persistent effusions in the joint after a prosthesis, inflammatory joint diseases - Behcet disease, intra-articular giant cell tumor of the diffuse type/ pigmented villonodular synovitis can all benefit from RS.

In preparation for the therapeutic procedure, bone scintigraphy and knee ultrasound are performed. The therapy has a low risk of negative repercussions (joint infection and beta radiation burns). RS involves injecting radioactively labeled particles (0.05-2 πm) into the joint cavity and evenly distributing them. Also, radioactive particles move deep into the synovium and are phagocytosed by macrophages. The average amount of radioactivity applied to the knee is 185-222 MBq. In terms of the physical properties of the radioisotope yttrium 90Y, a beta emitter with a maximum energy of 2.27 MeV, a mean energy of 0.935 MeV, and an average range in soft tissue of 3.6 mm and a physical half-life of 2.7 days, and in relation to the specific accumulation of radionuclide particles in the synovial space, radiation exposure outside the joint is very low. In the time after the application of radionuclides for 3 months, there is a reduction of effusion, radioactivity leading to fibrosis, and reduction of pain.

RS can be repeated at an interval of 3-6 months, if a sufficient therapy success has not been achieved after the first application. Contraindications for this method are pregnancy and lactation, local infection, massive hemartosis and ruptured Baker's cyst.

Keywords: radioactive yttrium, arthropathies, scintigraphy

RADIJACIONA SINOVIEKTOMIJA U LEČENJU BOLNIH ARTROPATIJA

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Jedan od modaliteta lečenja bolnih refraktornih artopatija je i nuklearno medicinska terapijska procedura, radijaciona sinoviektomija (RS) - intraartikularna aplikacija radionuklida itrijuma (90Y) silikat ili citrat. U Evropi se izvodi unazad više od 20 godina prema standarima koji su usvojeni 2002. godine., a nadograđeni 2021. od strane Evropskog udruženja za nuklearnu medicinu. Indikacije za radiosinevijektomiju obuhvataju bolne artropatije refraktorne na klasično lečenje (medikamentozno ili hirurško) i postavljaju se komisijski, u saradnji sa multidisciplinarnim timom. RS je moguće sprovesti kod pacijenata sa reumatoidnim artritisom, seronegativnom spondiloartropatijom (npr. reaktivni artritis, psorijatični artritis, ankilozni spondilitis), artritisima u hemofiliji, perzistentne efuzije u zglobu nakon proteze, upalne bolesti zglobova - Behčetova bolest, intraartikularni tumor džinovskih ćelija difuznog tipa/pigmentirani vilonodularni synovitis. U pripremi za terapijsku proceduru izvode se scintigrafski pregledi kostiju i ultrazvučni pregled kolena. Terapija ima nisku stopu komplikacija (infekcija zgloba i lokalne opekotine od beta zračenja). Tokom radijacione sinoviektomije radioaktivno obeležene partikule veličine od 0.05-2 πm se aplikuju direktno u artikularnu šupljinu, a potom homogeno distribuiraju u zglobnom prosturu. Dalje se radioaktivne partikule transportuju u dubinu sinovije i fagocituju od strane makrofaga. Uobičajena količina radioaktivnosti koja se aplikuje u koleno je 185–222 MBq. U odnosu na fizičke karakteristike radionuklida itrijuma 90Y, beta emitera, sa maksimalnom energijom 2,27 MeV, srednjom energijom od 0,935 MeV i prosečnim dometom u mekom tkivu od 3,6 mm i fizičkim poluživotom od 2,7 dana, a u odnosu na specifično nakupljanje radionuklidnih partikula u sinovijalnom prostoru, ekspozicija zračenju van zgloba je veoma niska. U vremenu nakon aplikacije radionuklida tokom 3 meseca dolazi do smanjenja efuzije, radiocionog zapanjelja koje vodi ka fibrozi i smanjenju bola. Radijaciona sinoviektomija se može ponavljati u intervalu od 3-6 meseci, ukoliko prvi tretman nije pokazao uspešan efekat. Kontraindikacije za ovu metodu su trudnoća i laktacija, lokalna infekcija, masivna hemartoza i rupturirana Bakerova cista.

Ključne reči: intraartikularna aplikacija radionuklida itrijuma, artopatija, scintigrafija

THERAPEUTIC MODALITIES FOCUSED ON THE INDIVIDUAL (NOT ON THE PAIN) CONTRIBUTE TO THE SUCCESSFUL MANAGEMENT OF CHRONIC PAIN

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Conventional medicine uses a uniform approach to the patient. It mainly focuses on the patient's disease, diagnosing diseases, followed by the therapy prescription. It has its advantages in the fields of emergency medicine and surgery. It is a model of medical care in acute situations, but it has not proven sufficient for chronic health problems. With this model, only two-thirds of patients benefit from their therapy, and one in three currently used drugs does not achieve the desired result. The reason is simple: diseases and treatments must be different, just as people are different. The latest medical research points to the disadvantages of the usual "one size fits all" approach, which ignores the individual characteristics of each patient. For this reason, a new medical approach called personalised medicine has been developed, which uses the patient's unique genetic profile.[1,2] Consider specific differences in an individual's genes, environment, and lifestyle. The goal is to tailor medical treatment to the specific characteristics of each patient, allowing for more precise and effective treatment of the individual. “The right medicine at the right time in the correct dose for the right patient."[4] A person's unique genetic makeup is studied using genomic diagnostic testing, including variations in their DNA sequences. Advances in genomic technology have made it possible to identify genetic markers (biomarkers) that are measurable indicators of a biological state or process that can help in diagnosis and prognosis, as well as in predicting therapeutic response and monitoring outcomes. Genomic analysis makes it possible to predict the disease risk and is vital in selecting prevention plans that suit the individual.[3.5] Of course, this concept does not mean that there is a specific cure for each patient but that a treatment exerts its maximum effectiveness precisely in some subgroups that have certain similarities, either at the genetic or molecular level of the disease. It is used in various diseases: malignancy, asthma, diabetes, cardiac arrhythmias, arthritis, migraine, depression, epilepsy, anxiety, coagulation disorders, and pain. This approach has also found a place in mental health, nutrition, and sleep. It is recommended for people who want to know their reactions to medications even before the onset of health problems, in patients who frequently change medications, have frequent occurrences of side effects and in cases where it is necessary to combine drugs to achieve an adequate therapeutic response. “It's more important to know what sort of person has a disease than to know what sort of disease a person has.” Hypocrites

Keywords: conventional medicine, personalised medicine, biomarkers, pharmacogenomics

TERAPIJSKI MODALITETI FOKUSIRANI NA POJEDINCA /NE NA BOL/ DOPRINOSE USPEŠNOJ KONTROLI HRONIČNOG BOLA

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Konvencionalna medicina koristi uniformni pristup pacijentu. Uglavnom se fokusira na bolest koju ima pacijent, dijagnostikovanje bolesti, nakon čega sledi propisivanje terapije. Ima svoje prednosti u oblastima urgentne medicine i hirurgije. To je model medicinskog zbrinjavanja u akutnim situacijama, ali za hronične zdravstvene probleme nije se pokazao kao dovoljan. Njenom primenom samo dve trećine pacijenata ima korist od svoje terapije, jedan od tri leka koji se trenutno primenjuje ne postiže željeni rezultat. Razlog je jednostavan, bolesti su različite, terapije treba da su različite kao što se i ljudi razlikuju. Najnovija medicinska istraživanja ukazuju na mane uobičajenog "one size fits all" pristupa koji zanemaruje individualne karakteristike svakog pacijenta. Upravo iz ovog razloga razvijen je novi medicinski pristup pod nazivom personalizovana medicina koji se koristi jedinstvenim genetskim profilom pacijenta.(1,2)

Uzima u obzir specifične razlike u genima, okruženju i načinu života pojedinca.Cilj je da se medicinski tretman prilagodi specifičnim karakteristikama svakog pacijenta, omogućavajući precizniji i efikasniji tretman pojedinca."Pravi lek u parvo vreme u pravoj dozi za pravog pacijenta"(4) Korišćenjem genomskog dijagnostičkog testiranja proučava se jedinstveni genetski sastav osobe, uključujući varijacije u njihovim

DNK sekvencama. Napredak genomske tehnologije omogućio je identifikaciju genetskih markera (biomarkera) koji su merljivi pokazatelji biološkog stanja ili procesa koji mogu pomoći u postavljanju dijagnoze, prognoze kao i u predvidjanju terapijskog odgovora i praćenje ishoda. Genomska analiza omogućava da se predvidi rizik od bolesti, igra ključnu ulogu u odabiru preventivnih planova koji odgovaraju pojedincu.(3,5) Naravno, ovaj koncept ne znači da postoji specifičan lek za svakog pacijenta, već da postoji tretman koji svoju maksimalnu efikasnost ispoljava upravo na nekim podgrupama koje imaju određene sličnosti, bilo na genetskom ili molekularnom nivou bolesti. Primenjuje se kod raznih bolesti: malignitet, astma, dijabetes, srčane aritmije, artritis, migrena, depresija, epilepsija, anksioznost, koagulacioni poremećaji, bol. Ovakav pristup našao je mesto I kod mentalnog zdravlja, ishrane, sna. Preporučije se osobama i pre pojave zdravstvenih problema koje žele saznati svoje reakcije na lekove, kod pacijenata koji često menjaju lekove, imaju učestale pojave neželjenih efekata i u slučajevima gde je potrebno kombinovanje lekova za postizanje adekvatnog terapijskog odgovora. "Vaznije je znati kakva je osoba koja je bolesna od toga kakva je bolest od cega se neko razboleo " /Hippocrates/

Ključne reči: konvencionalna medicina, personalizovana medicina, biomarkeri farmakogenomika

ADJUVANT PHARMACOTHERAPY AS AN ESSENTIAL ELEMENT OF MIXED CANCER PAIN THERAPY

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Mixed cancer pain is a combination of nociceptive and neuropathic pain components, which is very common in cancer patients. Classical opioid therapy, thanks to its mechanism of action, only suppresses the nociceptive component, while the neuropathic component of pain is still inadequately suppressed. Therefore, it is necessary to apply adjuvant pharmacotherapy along with opioid therapy in this painful syndrome.

Of the adjuvant drugs, drugs from the following groups are most often prescribed: gabapentinoids - pregabalin and gabapentin, selective serotonin and noradrenaline reuptake inhibitors (SNRIs) - duloxetine and venlafaxine, tricyclic antidepressants - amitriptyline, long-acting corticosteroids - dexamethasone, bisphosphonates - zolendronic acid, skeletal muscle relaxants - tizanidine, tolperisone, baclofen, local anesthetics - topical lidocaine, supplements - capsaicin, vitamin B complex, palmitoylethanolamine. The adjuvant pharmacotherapy of this painful syndrome includes groups of drugs that are not direct analgesics or coanalgesics, but represent drugs that patients take as needed due to possible side effects of analgesia and possible interactions in the form of so-called supportive therapy for oncology patients. These include: central antiemetics - granisetron, ondansetron, drugs from the laxative group - macrogols (recommended for opioid-induced constipation), lactulose, proton pump inhibitors - pantoprazole, rabeprazole, esomeprazole, antipsychotics - chlorpromazine, benzodiazepines - lorazepam, alprazolam. Each patient with mixed cancer pain should be evaluated and his adjuvant pharmacotherapy should be individually adjusted against prescribed opioid therapy and pharmacotherapy that the patient may already be taking due to other associated diseases. This ensures adequate management of possible side effects and possible drug-drug interactions.

Conclusion: Adjuvant pharmacotherapy of mixed cancer pain is an equally important element of pharmacotherapy of this pain syndrome as basal opioid therapy. By not prescribing adjuvant drugs, patients' adherence to opioid therapy is reduced due to the possible and frequently occurring side effects of opioid therapy and possible interactions with other drugs.

Keywords: pharmacotherapy, mixed cancer pain, adjuvants, interactions, side effects.

ADJUVANTNA FARMAKOTERAPIJA KAO BITAN ELEMENT TERAPIJE MEŠOVITOG KANCERSKOG BOLA

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Mešoviti kancerski bol predstavlja kombinaciju nociceptivne i neuropatske komponente bola koja je veoma zastupljena kod onkoloških pacijenata. Klasična opioidoterapija, zahvaljući mehanizmu delovanja, kupira samo nociceptivnu dok je neuropatska komponenta bola i dalje neadekvatno kupirana. Zbog toga, neophodno je primeniti adjuvantnu farmakoterapiju uporedo sa opiodoterapijom kod ovog bolnog sindroma.

Od adjuvantnih lekova najčešće se propisuju lekovi iz sledećih grupa: gabapentinoidi – pregabalin i gabapentin, selektivni inhibitori preuzimanja serotonina i noradrenalina (SNRI) – duloksetin i venlafaksin, triciklični antidepresivi – amitriptilin, dugodelujući kortikosteroidi – deksametazon, bisfosfonati – zolendronična kiselina, skeletni mišićni relaksanti – tizanidin, tolperison, baklofen, lokalni anestetici – topikalni lidokain, suplementi – kapsaicin, kompleks vitamina B, palmitoiletanolamin.

U adjuvantnu farmaoterapiju ovog bolnog sindroma ubrajamo i grupe lekova koji nisu diretktni analgetici niti koanalgetici već predstavljaju lekove koje pacijenti uzimaju po potrebi usled mogućeih neželjenih efekata analgezije i eventualnih interakcija u vidu takozvane suportivne terapije onkoloških pacijenata. Tu spadaju: centralni antiemetici – granisetron, ondansetron, lekovi iz grupe laksativa – makrogoli (preporučeni za opioidima indukovanu opstipaciju), laktuloza, inhibitori protonske pumpe – pantoprazol, rabeprazol, esomeprazol, antipsihotici – hlorpromazin, benzodiazepini – lorazepam, alprazolam. Svakog pacijenta sa mešovitim kancerskim bolom treba sagledalati i individualno prilagoditi njegovu adjuvantnu farmakoterapiju naspram propisane opioidoterapije i farmakoterapije koju pacijent eventualno već uzima usled drugih pridruženih bolesti. Time se obezbedjuje adekvatno zbrinjavanje mogućih neželjenih efekata i nastanak mogućih lek-lek interakcija.

Zaključak: Adjuvantna farmakoterapija mešovitog kancerskog bola je podjednako bitan element farmakoterapije ovog bolnog sindroma kao i bazalna opioidoterapija. Nepropisivanjem adjuvantnih lekova, smanjuje se adherenca pacijenata na opioidoterapiju usled mogućih i često zastupljenih neželjenih efekata opioidoterapije i eventualnih interakcija sa drugim lekovima.

Ključne reči: farmakoterapija, mešoviti kancerski bol, adjuvansi, interakcije, neželjeni efekti.

GENDER DIFFERENCES IN ADEQUACY OF CHRONIC CANCER PAIN MANAGEMENT

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Pain occurs in approximately 50-70% of cancer patients. Studies on gender differences in perceived pain generally show lower pain thresholds and an increased prevalence of pain in women, which may be attributed to gender-specific behaviors, stereotypes, and unknown etiologic factors. Clinical studies show that women report pain more often than men and report greater pain intensity. Moreover, the risk of chronic pain and experimental pain sensitivity are higher among women. Gender differences in clinical and experimental pain appear to occur across the lifespan and are associated with differences in central sensitization. Interactions between sex hormones and the opioid system likely contribute to gender differences in pain. For example, women may show a greater analgesic response to morphine. There is also a growing body of literature showing gender differences in neuroimmune interactions associated with pain hypersensitivity and the development of chronic pain. Currently, no clear central mechanism underlying gender differences in pain perception across the lifespan has been identified. Chronic cancer pain occurs in as many as 80–90% of patients with metastatic cancer. Because pain management is the primary goal of palliative care patients, research into sex-specific pain differences in patients with advanced cancer is of great importance. In previous trials in the advanced cancer subgroup, mean differences in pain perception scores did not differ significantly between genders, so the administration of analgesics should not be modified based on gender. Male and female patients should be treated equally for the treatment of chronic cancer pain, without assuming that women are more sensitive to pain. However, given that only four studies have been published in this setting, future research should investigate gender differences in pain perception among advanced cancer patients. This would facilitate and give greater confidence in the validity of these observations.

Key words: chronic cancer pain, morphine, neuroimmunity, gender

POLNE RAZLIKE U ADEKVATNOSTI UPRAVLJANJA HRONIČNOG KANCERSKOG BOLA

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Bol se javlja kod otprilike 50-70% pacijenata sa karcinomom. Studije o polnim razlikama u percipiranom bolu generalno pokazuju niže pragove bola i povećanu prevalenciju bola kod žena, što se može pripisati rodno specifičnom ponašanju, stereotipima i nepoznatim etiološkim faktorima. Kliničke studije pokazuju da žene češće prijavljuju bol od muškaraca i prijavljuju veći intenzitet bola. Štaviše, rizik od hroničnog bola i eksperimentalna osetljivost na bol veći su među ženama. Čini se da se rodne razlike u kliničkom i eksperimentalnom bolu javljaju tokom životnog veka i povezane su sa razlikama u centralnoj senzibilizaciji. Interakcije između polnih hormona i opioidnog sistema verovatno doprinose rodnim razlikama u bolu. Na primer, žene mogu pokazati veći analgetički odgovor na morfijum. Takođe postoji sve više literaturnih podataka koji pokazuju polne razlike u neuroimunim interakcijama koje su povezane sa preosetljivošću na bol i razvojem hroničnog bola. Trenutno nije identifikovan jasan centralni mehanizam koji leži u osnovi polnih razlika u percepiji bola tokom životnog veka. Hronični kancerski bol se javlja kod čak 80–90% pacijenata sa metastatskim karcinomom. Pošto je upravljanje bolom primarni cilj pacijenata sa palijativnim zbrinjavanjem, istraživanje polno specifičnih razlika bola kod pacijenata sa uznapredovalim karcinomom je od velike važnosti. U dosadašnjim ispitivanjima u podgrupi uznapredovalog karcinoma, srednje razlike u rezultatu percepije bolova nisu se značajno razlikovale između polova, tako da administraciju analgetika ne treba modifikovati na osnovu pola. Muške i ženske pacijente treba tretirati podjednako za lečenje hroničnog kancerskog bola, bez pretpostavke da žene imaju veću osetljivost na bol. Međutim, s obzirom na to da su samo četiri studije objavljene u ovoj postavci, buduća istraživanja trebalo bi da istraže polne razlike u percepiji bola među uznapredovalim pacijentima sa karcinomom. Ovo bi olakšalo i dalo veće poverenje u validnost ovih zapažanja.

Ključne reči: hronični kancerski bol, morfin, neuroimunitet, pol

RHEUMATOLOGICAL SIDE EFFECTS OF IMMUNOTHERAPY IN THE TREATMENT OF LUNG CANCER PATIENTS

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Immunotherapy has become a key component of modern lung cancer treatment, especially in patients with metastatic non-small cell lung cancer (NSCLC), though it also has a role in treating early-stage NSCLC as well as small cell lung cancer (SCLC). This therapeutic approach, which utilizes the immune system to recognize and destroy tumor cells, has shown significant results in terms of survival and quality of life for lung cancer patients. However, the application of immunotherapy is not without risks, as it can cause a range of immune-mediated side effects known as immune-related adverse events (irAEs), including rheumatologic manifestations. These rheumatologic side effects have become a subject of intense research in recent years due to their complexity, unpredictability, and significant impact on the quality of life of cancer patients. Rheumatologic side effects associated with immunotherapy include a wide range of conditions, from autoimmune joint diseases, such as rheumatoid arthritis, to inflammatory muscle disorders, vasculitis, and similar inflammatory rheumatic diseases. Other complications may include polymyositis, dermatomyositis, spondyloarthritis, and the development of systemic lupus erythematosus. Although the incidence of rheumatologic side effects from immunotherapy is relatively low, their clinical significance is high as they can severely compromise the functional status of patients and limit the ability to continue cancer treatment.

Multidisciplinary collaboration between oncologists, rheumatologists, and immunologists is essential to achieve a balance between the effectiveness of cancer treatment and the minimization of adverse effects. As immunotherapy is increasingly used in the treatment of various types of cancer, including lung cancer, it is expected that the incidence of rheumatologic side effects will rise. Therefore, it is important to develop standardized protocols for managing these side effects and continue research to address the long-term consequences of immunotherapy on the musculoskeletal system. Understanding the risks and benefits of immunotherapy in the context of rheumatologic complications enables the medical team to provide patients with better-informed treatment decisions and ensure optimal outcomes through tailored therapeutic strategies.

*Keywords**:** lung cancer, immunotherapy, side effects*

REUMATOLOŠKE MANIFESTACIJE-NEŽELJENI EFEKTI IMUNOTERAPIJE U LEČENJU KARCINOMA BRONHA

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Imunoterapija je postala ključna komponenta savremenog tretmana karcinoma bronha, posebno kod pacijenata sa metastatskim nemikrocelularnim karcinomom pluća (NSCLC) mada ima svoje mesto i lečenju ranog stadijuma NSCLC kao i u lečenju mikrocelularnog karcinoma bronha. Ovaj terapijski pristup, koji koristi imunološki sistem za prepoznavanje i uništavanje tumorskih ćelija, pokazao je značajne rezultate u pogledu preživljavanja i kvaliteta života bolesnika sa karcinomom bronha. Međutim, primena imunoterapije nije bez rizika, jer može izazvati niz imunološki posredovanih neželjenih efekata poznatih kao imunološki povezani neželjeni događaji (irAEs), koji uključuju i reumatološke manifestacije. Ove reumatološke nuspojave postale su predmet intenzivnog istraživanja u poslednjih nekoliko godina zbog njihove složenosti, nepredvidljivosti i značajnog uticaja na kvalitet života bolesnika. Reumatološke nuspojave povezane sa imunoterapijom uključuju širok spektar stanja, od autoimunskih bolesti zglobova, poput reumatoidnog artritisa, do inflamatornih mišićnih poremećaja, vaskulitisa, i sličnih inflamatornih reumatskih bolesti. Slične komplikacije mogu uključivati polimiozitis, dermatomiozitis, spondiloartritis, kao i razvoj sistemskog lupusa eritematozusa. Iako je incidenca reumatoloških nuspojava imunoterapije relativno niska, njihov klinički značaj je visok jer mogu znatno kompromitovati funkcionalni status bolesnika i ograničiti mogućnost nastavka onkološkog tretmana.
Multidisciplinarna saradnja između onkologa, reumatologa i imunologa je ključna kako bi se postigao balans između efikasnosti lečenja karcinoma i minimiziranja neželjenih efekata. S obzirom na to da se imunoterapija sve češće koristi u lečenju različitih vrsta karcinoma, uključujući i karcinom bronha, očekuje se da će učestalost reumatoloških nuspojava rasti. Stoga je važno razviti standardizovane protokole za upravljanje ovim nuspojavama, kao i nastaviti sa istraživanjima koja bi obuhvatila dugoročne posledice imunoterapije na mišićno-skeletni sistem. Razumevanje rizika i koristi imunoterapije u kontekstu reumatoloških komplikacija omogućava lekarskom timu da bolesnicima pruži bolje informisane odluke o lečenju i da osigura optimalne ishode kroz prilagođene terapijske strategije.

Ključne reči: karcinom bronha, imunoterapija, nuspojave

THE PLACE AND IMPORTANCE OF PALLIATIVE MEDICINE IN THE TREATMENT OF CHRONIC PAIN

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"Palliative care is an approach that improves the quality of life of patients and their families who are facing problems associated with life-threatening illnesses" (WHO). It. is estimated that the number of people requiring palliative care (PC) will increase by 14%-20% by 2040, and in 2060 50% of the population will need PC at the end of life. But, only 14-35% of people with needs are receiving the necessary palliative care. (WHO, EAPC – European Association for Palliative Care). Pain is one of the most common, complex, and multidimensional symptoms that affects patients with diagnosed terminal illness. Despite the improved healthcare technologies, assessment, and pain management techniques, patients with cancer report pain as the most common symptom at any stage of disease, at diagnosis, during and after treatment, end-of-life, and before death. Pain, even treated or untreated, impairs patients' quality of life and functionality on a large scale. The goal of palliative care is to "improve the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain, illnesses including other problems whether physical, psychosocial, and spiritual". (WHO). Therefore, integration of palliative care along with all other disciplines with curative intent must be included since the diagnosis of incurable disease. Its holistic, "total pain" approach is not only necessity but covers all unmet needs in the disease management including all aspects of patient's life (physical, psychological, social and spiritual) improving not only the pain management but also the quality of their and their family's life.

Keywords: Total pain, Palliative Care, Holistic medicine

MESTO I ZNAČAJ PALIJATIVNE MEDICINE U ZBRINJAVANJU HRONIČNOG BOLA

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„Palijativno zbrinjavanje je pristup kojim se poboljšava kvalitet života pacijenata i njihovih porodica koji se suočavaju sa problemima povezanim sa neizlečivim bolestima". (SZO) Procenjeno je da će se do 2040. godine broj ljudi kojima je potrebno palijativno zbrinjavanje (PZ) povećati za najmanje 14%-20%, a do 2060. godine 50% stanovništva će imati potrebu trebati za nekim vidom PZ na kraju života. Ipak, samo 1435% ljudi ovaj vid zbrinjavanja i dobija. (SZO; Evropska asocijacija za palijativno zbrinjavanje - EAPC). Hronični bol je jedan od najčešćih, složenih i višedimenzionalnih simptoma koji pogađaju pacijente sa dijagnostikovanom terminalnom bolešću. Uprkos poboljšanim zdravstvenim tehnologijama, procenjivanju i tehnikama upravljanja, pacijenti sa dijagnozom carcinoma i dalje prijavljuju bol kao najčešći simptom u bilo kojoj fazi bolesti, pri samom postavljanju dijagnoze, tokom i nakon lečenja, na kraju života i pre smrti.

Bol, ako se ne leči pa i čak i dad se leči narušava kvalitet života i funkcionalnost pacijenata. Cilj palijativnog zbrinjavanja je "*prevencija i ublažavanje patnje, što zahteva ranu identifikaciju, ispravnu procenu i lečenje bola zajedno sa drugim simptomima, koji obuhvataju fizičke, psihosocijalne ili duhovne aspekte*" (SZO). Integracija palijativnog zbrinjavanja uporedo sa svim drugim disciplinama koje imaju nameru izlečenja mora biti uključena već od dijagnoze neizlečive bolesti. Ovaj holistički pristup nije samo neophodan, već ključan za zbrinjavanje svih nezadovoljene potrebe u lečenju bolesti, uključujući sve aspekte života pacijenata: fizički, psihološki, socijalni i duhovni, poboljšavajući ne samo upravljanje bolom, već i kvalitet života pacijenata kao i života njihovih porodica.

Ključne reči: totalni bol, palijativno zbrinjavanje, holistička medicina

SAFETY CONSIDERATIONS OF THE PRESCRIPTION OF NON-STEROIDAL ANTI-INFLAMMATORY DRUGS AND OPIOIDS IN THE TREATMENT OF CHRONIC NONCANCER PAIN

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Analgesic medication of CNCP implies effective therapy and minimization of risk potential. The liberal prescription of opioids contributed to the use of opioids reaching epidemic proportions in some countries of the world and leading to the phenomenon of medicalization, iatrogenesis, and fatal outcomes, i.e. the opioid crisis. The opioid crisis has renewed interest in non-steroidal anti-inflammatory drugs (NSAIDs) as alternatives to opioids. The safe practice of NSAID prescribing in CNCP (most commonly musculoskeletal) is followed by many evidence-based guidelines. Long-term use of NSAIDs is associated with adverse CV and GI events, so some current guidelines recommend only short-term use in people with these comorbidities. The balance between thromboxane (TXA2) and prostacyclin (PGI2) synthesis is associated with CV events. COX-1 inhibitors inhibit the synthesis of TXA2, and COX-2 inhibitors inhibit the synthesis of PGI2. The predominant effects of TXA2 increase the risk of thrombosis (coronary, cerebral). Numerous randomized studies and meta-analyses prove that coxibs have a higher CV risk and a safer GI profile. Celecoxib is the only coxib with the lowest CV and GI risks. Naproxen is the safest NSAID in people at CV risk. All NSAIDs, in proportion to the dose and duration of therapy, increase the CV risk, and due to greater safety, they are recommended as a component of multimodal analgesia.

Opioids are essential analgesics for cancer pain, and their use in HNKB is controversial. Opioid side effects are well known and increase with dose and duration of therapy. Short-term opioid therapy compared with placebo (musculoskeletal pain) shows little clinical improvement in pain and physical functioning. It increases the risk of GI (RR 1.86) and central (RR 2.91) side effects and discontinuation. Long-term opioid therapy is not superior to NSAID medication in improving pain and functioning and shows more adverse events, discontinuation, abuse, dependence, and mortality. Opioid analgesics in CNCP are a choice only when non-opioid pharmacological and non-pharmacological therapy is ineffective, tolerable, or contraindicated and if a clinically significant improvement in pain and functionality is expected, which outweighs the risks to patient safety.

There is no ideal analgesic medication for CNCP, so opioids and NSAIDs can be effective and safe components in a multimodal analgesic approach.

*Keywords: Chronic non-cancer pain (*CNCP*), non-steroidal anti-inflammatory drugs (NSAIDs), opioids, safety*

RAZMATRANJA BEZBEDNOSTI PRESKRIPCIJE NESTEROIDNIH ANTIINFLAMATORNIH LEKOVA I OPIOIDA U TRETMANU HRONIČNOG NEKANCERSKOG BOLA

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Analgetička medikacija HNKB podrazumeva efektivnu terapiju i minimizaciju potencijala za rizik. Liberalna preskripcija opioida, doprinela je da upotreba opioida zauzme epidemijske razmere u nekim zemljama sveta i dovede do fenomena medikalizacije, jatrogeneze i smrtnih ishoda, tj. *opioidne krize.* Opioidna kriza obnovila je interesovanje za nesteroidne antinflamatorne lekove (NSAIL) kao alternative opioidima. Bezbedna praksa propisivanja NSAIL kod HNKB (najčešće mišićnoskeletnog) praćena je brojnim vodičima zasnovanim na dokazima. Dugoročna upotreba NSAIL povezana je sa neželjenim CV i GI događajima, pa neki aktuelni vodiči preporučuju samo kratkoročnu upotrebu kod osoba sa ovim komorbiditetima. Balans između sinteze tromboksana (TXA2) i prostaciklina (PGI2) povezan je sa CV događajima. COX-1 inhibitori inhibiraju sintezu TXA2, a COX-2, inhibiraju sintezu PGI2. Prevladavajući efekti TXA2 povećavaju rizik od tromboze (koronarne, cerebralne). Brojne randomizovane studije i metaanalize dokazuju da koksibi imaju veći CV rizik, a bezbedniji GI profil. Celecoxib je jedini koksib sa najmanjim CV i GI rizicima. Naproxen je najbezbedniji NSAIL kod osoba sa CV rizikom. Svi NSAIL, proporcionalno dozi i dužini trajanja terapije povećavaju CV rizik, te se zbog veće bezbednosti preporučuju kao komponenta multimodalne analgezije. Opioid su esencijalni analgetici za kancerski bol, a njihova upotreba kod HNKB je kontroverzna. Opioidni neželjeni efekti su dobro poznati i povećavaju se sa dozom i dužinom trajanja terapije. Kratkoročna opioidna terapija u poređenju sa placebom (mišićnoskeletni bol) pokazuje malo kliničko poboljšanje bola i fizičkog funkcionisanja, a povećava rizik od GI (RR 1.86) i centralnih (RR 2.91) neželjenih efekata i odustajanja od terapije. Dugoročna opioidna terapija nije superiornija od NSAIL medikacije u poboljšanju bola i funkcionisanju i pokazuje više neželjenih događaja, odustajanja od terapije, zloupotrebe, zavisnosti i mortaliteta. Opioidni analgetici kod HNKB su izbor samo onda kada neopioidna farmakološka i/ili nefarmakološka terapija nisu efikasne, tolerabilne ili su kontraindikovane i ako se očekuje klinički značajno poboljšanje bola i funkcionalnosti, koji prevazilaze rizike za bezbednost pacijenta. Idealne analgetičke medikacije za HNKB nema, pa opioidi i NSAIL mogu biti efektivne i bezbedne komponente u multimodalnom analgetičkom pristupu.

Ključne reči: Hronični nekancerski bol (HNKB), nesteroidni antiinflamatorni lekovi (NSAIL), opioidi, bezbednost.

PAIN IN THE 21st CENTURY, A NEW APPROACH IN TREATMENT

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The paradigm that pain is an exclusively physical and physiological experience has through time and experience been proven to be completely incorrect, because how someone will experience pain depends on neurophysiological factors, as well as the age and gender of the patient. Pain is a biopsychosocial phenomenon and when treating a patient with pain, all these factors, which determine how someone will experience pain must be taken into account equally. Trends in medicine in the 21st century emphasize the biopsychosocial model of health care. It implies a holistic approach to the patient that takes into account not only biological, but also psychological, social and spiritual factors, as well as the individual's behavior when defining his pain. Therefore, when applying the biopsychosocial model in the treatment of pain, it is necessary to integrate biological factors with social and psychological factors that shape the patient experience. In other words, a treatment plan is created that focuses on the patient as a whole ("both soul and body"), in order to achieve the best results.The experience of pain is not universal but very individual, and therefore it is necessary to approach each patient with empathy, taking into account all possible social and cultural factors that may influence the patient's experience of pain. The patient may be burdened by the attitudes imposed on him by the cultural norms of the community or family, so it is possible to either underestimate or overestimate the pain, and also what and how much information the patient wants to share about himself and his pain. Pain behavior or "behavior in pain", verbal and/or non-verbal, is of key importance in assessing the quantity and quality of pain felt by an individual and without proper assessment it is impossible to determine adequate therapy.

In this sense, it is extremely important that the doctor has the necessary communication skills, which will help him get a more precise insight into the pain the patient feels.
These skills require the establishment of a certain doctor-patient relationship, which implies empathy, patience, professionalism and self-confidence of the doctor. These skills can also contribute to the placebo effect and thus reduce the need for analgesics. Empathy is key to developing a trusting patient-doctor relationship. It is necessary to avoid all ethnic, social or religious stereotypes that could affect this relationship. Analgesics are the cornerstone of pain treatment, but given the possible side effects of these drugs, it is important to properly assess the patient's reasons for needing analgesics, which is achieved through communication skills. A patient should never be deprived of analgesic therapy, especially one with documented chronic pain, but in some cases there is a risk of a patient asking for analgesic drugs in cases when it is not medically justified. Also, there are other, increasingly common cases, where chronic pain and its cause have been confirmed, but the patient refuses analgesics. Fear of the side effects of

analgesic drugs, feeling shame because of the disease, feelings of guilt, expectations from the patient's family and community about how to deal with pain are potential reasons for refusing analgesia. A conversation is necessary with both of these groups of patients. These reasons can also be religious and must be respected. In addition, it is necessary to keep in mind that certain patients need, first of all, psychological support in order to suppress pain, which is in accordance with the biopsychosocial model of treatment. Certain patients take analgesic drugs, so that "they are not a burden to their children or their family", for the same reason, but also for financial reasons, it is possible to reduce the pain, which is extremely important to recognize. In the case of chronic pain, the role of the doctor as an "ally" in the fight against pain has proven to be crucial and indispensable in the process of treating chronic pain. In addition to the "alliance" regarding the prescription of adequate analgesics and their dosage, the doctor, with this approach, provides the patient's "emotional and psychological refuge" and becomes his "advisor", almost a friend. This approach is in accordance with the biopsychosocial model of chronic pain treatment and the practice of "patient-centered care", where the patient himself is placed in the center.

Keywords: pain treatment, biopsychosocial model, pain behaviour, patient-centered care

BOL U 21. VEKU, NOVI PRISTUP LEČENJU

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Paradigma da je bol isključivo telesno, fiziološko, iskustvo se kroz vreme i iskustvo pokazala kao potpuno netačna jer to kako će neko doživeti bol zavisi od neurofizioloških faktora, kao i od starosti i pola pacijenta. Bol je biopsihosocijalni fenomen i prilikom tretmana pacijenta sa bolom, svi ovi faktori, koji određuju kako će neko doživeti bol, se moraju uzeti podjednako u obzir. Trendovi u medicini 21. veka stavljaju akcenat upravo na biopsihosocijalni model zdravstvene zaštite. On podrazumeva holistički, odnosno pristup pacijentu koji uzima u obzir ne samo biološke, već i psihološke, socijalne i duhovne faktore, kao i ponašanje pojedinca pri definisanju svoga bola. Stoga, pri primeni biopsihosocijalnog modela u tretmanu bola, potrebno je integrisati biološke faktore sa socijalnim i psihološkim faktorima koji oblikuju pacijentovo iskustvo. Drugim rečima, stvara se plan lečenja koji stavlja fokus na pacijenta u celini („i duša i telo“), kako bi se postigli najbolji rezultati. Iskustvo o bolu nije univerzalno već vrlo individualno i zbog toga je neophodno svakom pacijentu pristupiti sa empatijom, uzevši u obzir sve moguće društvene i kulturološke faktore koji mogu uticati na njegov doživljaj bola. Pacijent može biti opterećen stavovima koje mu nameće kulturološki obrazac zajednice ili porodica, pa je moguće ili preterano potcenjivanje ili precenjivanje bola, a takođe i koje i koliko informacija želi da podeli o sebi i svom bolu.

Pain behaviour ili „ponašanje u bolu“, verbalno i/ili neverbalno, je od ključnog značaja u proceni kvantiteta i kvaliteta bola koju pojedinac oseća i bez pravilne procene je nemoguće odrediti adekvatnu terapiju. U tom smislu, od izuzetne je važnosti da lekar poseduje potrebne komunikacione veštine pomoću kojih će dobiti precizniji uvid u bol koji pacijent oseća.

Ove veštine zahtevaju uspostavljanje određenog odnosa lekar- pacijent, koje podrazumeva empatiju, strpljenje, profesionalizam i samouverenost lekara. Ove veštine mogu doprineti i placebo učinku i time smanjiti potrebu za potrošnjom analgetika. Empatija je ključna za razvijanje poverljivog odnosa pacijent lekar. Neophodno je izbegavati sve etničke, društvene ili religiozne stereotipe koji bi mogli uticati na ovaj odnos. Analgetici predstavljaju kamen temeljac tretmana bola ali obzirom na moguća neželjena dejstva lekova važno je dobro proceniti pacijentove razloge potrebe za analgeticima što se postiže komunikacionim veštinama.

Pacijent nikad ne bi smeo biti uskraćen za analgetsku terapiju, pogotovo onaj sa dokumentovanom hroničnim bolom, ali u nekim slučajevima postoji opasnost od medicinski neopravdanog traženja analgetika. Takođe, postoje i drugi, sve češći slučajevi, gde je potvrđen hronični bol i njegov uzrok ali pacijent odbija analgetik. Strah od nuspojava analgetika, stid zbog bolesti, osećaj krivice, očekivanja od pacijentove porodice i zajednice kako se treba nositi sa bolom su potencijalni razlozi odbijanja analgezije. I sa jednom i sa drugom grupom pacijenata je neophodan razgovor. Ovi razlozi mogu biti i religijski i moraju se poštovati. Uz to, potrebno je imati na umu da je određenim pacijentima potrebna, pre svega, psihološka podrška u cilju suzbijanja bola, što je u skladu sa biopsihosocijalnom modelom tretmana. Određeni pacijenti uzimaju analgetike, da „ne budu na teretu deci ili porodici " , iz istog razloga, ali i iz finansijskih razloga, je moguća pojava umanjivanja bol, koju je izuzetno važno prepoznati.

U slučaju hroničnog bola uloga lekara kao „saveznika" u borbi protiv bola se pokazala ključnom i neizostavnom u procesu tretmana hroničnog bola. Osim „savezništva" u vezi propisivanja adekvatnih analgetika i njihovog doziranja, lekar, ovim pristupom, pruža pacijentu „emocionalno i psihološko utočište" i postaje njegov" savetnik", gotovo prijatelj. Ovakav pristup je u skladu s biopsihosocijalnim modelom tretmana hroničnog bola i praktikovanja „patient-centered care", gde se u centar stavlja sam pacijent.

Ključne reči: tretman bola, biopsihosocijalni model, pain behaviour, patient-centered care

THE ROLE OF PSYCHOLOGIST IN THE MULTIDISCIPLINARY PROGRAM OF THE TREATMENT OF CHRONIC PAIN

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The multidisciplinary pain management program is based on an approach that educates and involves the patient as an equal and active participant in the treatment of chronic pain. An experts from different profiles are part of the multydisciplinary team: anesthesiologist educated for pain management, nurse, psychiatrist, psychologist, physiotherapist, nutritionist and work therapist. The aim of this paper is to show the role of psychologist in the work of a team for the treatment of chronic pain. During group and individual work with patients, the psychologist uses various psychological procedures that are part of a complete therapy of pain. Numerous cognitive-behavioral techniques are used, from which the most commonly used are: psychoeducation on different factors that can affect pain experience, cognitive restructuring, distraction techniques and attention refocusing, relaxation techniques, behavioral activation, behavioral experiment and time management. The goal of the multidisciplinary program is to acquire knowledge and skills so that patients can cope with chronic pain more successfully, all with the desire to improve their quality of life.

Keywords: chronic pain, pain management, patient care team, cognitive behavioral therapies

ULOGA PSIHOLOGAU MULTIDISCIPLINARNOM PROGRAMU ZA LIJEČENJE HRONIČNE BOLI

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Multidisciplinarni program za liječenje kronične boli temelji se na pristupu koji educira i uključuje pacijenta kao ravnopravnog i aktivnog sudionika u liječenju kronične boli. Članovi multidisciplinarnog tima su stručnjaci različitih profila: anesteziolog educiran za liječenje boli, medicinska sestra, psihijatar, psiholog, fizioterapeut, nutricionist i radni terapeut. Cilj ovog rada je prikazati ulogu psihologa u radu tima za liječenje kronične boli. U grupnom i individualnom radu s pacijentima psiholog koristi različite psihološke postupke koji su dio cjelovite terapije boli. Koriste se brojne kognitivno-bihevioralne tehnike od kojih su najčešće korištene: psihoedukacija o različitim čimbenicima koji mogu utjecati na doživljaj boli, kognitivno restrukturiranje, tehnike distrakcije i refokusiranja pažnje, tehnike opuštanja, bihevioralna aktivacija, bihevioralni eksperiment i upravljanje vremenom. Cilj multidisciplinarnog programa je stjecanje znanja i vještina kako bi se pacijenti uspješnije nosili s kroničnom boli, a sve sa željom poboljšanja njihove kvalitete života.

Ključne riječi: kronična bol, liječenje boli, tim za liječenje, kognitivno-bihevioralna terapija

KNOWLEDGE AND ATTITUDES ABOUT PAIN, HOW DO WE KNOW WE HAVE MADE A DIFFERENCE?

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Introduction: Nurses in the majority of cases represent the first step in the pain treatment in the hospital settings. Knowledge and attitudes of nurses can influence the interpretation of the patient's pain experience, as well as the decision to initiate additional therapeutic interventions. Today, the majority of research related to pain is focused on various modalities of pain treatment, while a smaller part recognizes the need to examine the impact of knowledge and attitudes of nurses regarding pain. The aim of this research was to examine the knowledge and attitudes related to pain of nurses employed in a tertiary health care institution.

Material and methods: The research was conducted in the Clinical Center of Vojvodina in January 2024. Nurses with more than 6 months of work experience (N = 223) were included in the research. Structured questionnaire called "Knowledge and Attitudes Survey Regarding Pain" (NKSARP) was used as an assessment instrument. Each correct answer is scored as "one" and each incorrect as "zero" (total score from 0 to 41). The total score is expressed as a percentage of correct answers. A result less than 50% is classified as "unacceptable knowledge and attitudes", and a result greater than 50% is classified as "acceptable knowledge and attitudes".

Results: The average number of correct answers was 51.3% ± 7.3% (21 ± 3), the lowest achieved result was 31.7% (13 correct answers), and the best achieved result was 78% (32 correct answers). A score value greater than 50% was achieved by 55.2% (123) of respondents.

Conclusion: Half of the respondents presented acceptable knowledge and attitudes regarding pain. This result indicates the need to improve the education of nurses/technicians in the field of pain treatment, which indicates the need to improve education in the field of pain treatment in hospital conditions.

Keywords: knowledge; attitudes; nurses; pain

ZNANJA I STAVOVI O BOLU KAKO ZNAMO DA SMO NAPRAVILI RAZLIKU?

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Uvod: Medicinske sestre/tehničari u najvećem broju slučajeva predstavljau prvi stepenik u tretmanu bola u bolničkoj sredini. Njihovo znanje i stavovi mogu uticati na interpretaciju pacijentovog doživljaja bola, ali i na odluku za inicijacijom dodatnih terapijskih intervencija. Danas, je najveći broj istraživanja u vezi sa bolom usmerena na različite modalitete tretmana bola, dok manji deo perepoznaje potrebu ispitivanja uticaja znanja i stavova medicinskihsestara/tehničara u vezi sa bolom. Cilj rada bio je da se ispitaju znanja i stavovi u vezi sa bolom medicinskih sestara zaposlenih u tercijernoj zdravstvenoj ustanovi.

Materijal i metode: Istraživanje je sprovedeno u Kliničkom centru Vojvodine u januaru 2024. godine. U istraživanje su uključene medicinske sestre/tehničari sa najmanje 6 meseci radnog iskustva (N = 223), a kao instrument za procenu korišćen je struktuirani upitnik pod nazivom „Znanja i stavovi u vezi sa bolom“(Knowldge and Attitudes Survey Regarding Pain – NKSARP). Svaki tačan odgovor bodovan je kao „jedan“, a svaki netačan kao „nula“ (ukupni skor od 0 do 41). Ukupni skor je iskazan kao procenat tačnih odgovora. Rezultata manji od 50% klasifikovan je kao „neprihvatljivo znanje i stavovi“, a rezultat veći od 50% klasifikovan je kao „prihvatljivo znanje i stavovi“.

Rezultati: Prosečan broj tačnh odgovora iznosio je 51,3% ± 7,3% (21 ± 3), najmanji ostvareni rezultat iznosio je 31,7% (13 tačnih odgovora), a najbolji ostvareni rezultat iznosio je 78% (32 tačna odgovora). Vrednot skora veću od 50% ostvarilo je 55,2% (123) ispitanika.

Zaključak: Polovina ispitanika prikazala je prihvatljivo znanje i stavove u vezi sa bolom. Ovakav rezultat ukazuje na potrebu za unapređenjem edukacije medicinskih sestara/tehničara iu oblasti tretmana bola što ukazuje na potrebu za unapređenjem edukacije iz oblasti tretamana bola u bolničkim uslovima

Ključne reči: znanja medicinskih sestara/tehničara; stavovi medicinskih sestara/tehničara; bol

PREVALENCE OF CHRONIC NON-CANCER PAIN IN VOJVODINA

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Introduction: In Serbia, chronic pain prevalence data were first collected in 2013 and 2019, not focusing on life-long prevalence. In 2023, the Institute for Public Health of Vojvodina initiated annual surveillance of behavioral risk factors for chronic non-communicable diseases, leading to the first standard indicator data collection on chronic non-cancer pain in 2024.
Objective**:** This study aimed to determine the prevalence of chronic low back pain (CLBP)—the leading cause of chronic non-cancer pain—among adults in the Autonomous Province of Vojvodina/APV and identify associated socioeconomic predictors.
Methods**:** A cross-sectional study was conducted with a representative sample of healthcare users from 46 health centers in APV, with data collected between May 20 and October 10, 2024. A multivariate binary logistic regression model assessed the relationship between CLBP and five sociodemographic factors related to self-reported health.
Results**:** Among 3.910 surveyed (52.3% female and 47.7% male), an average age of 49.27 years, the lifelong prevalence of CLBP is 48.3%. A higher likelihood of CLBP was found in the: aged 66 and older compared to younger than 30 (CI=5.45; p<0.001) and aged 31-50 (CI=1.64; p=0.002), or 50-65 years (CI=1.39; p=0.026); respondents with a primary school education or lower compared to those with a secondary (CI=1,50; p=0.001) and university degree (CI=1.77; p<0.001); those with inactive work status (CI=1,48; p=0.008) compared to active; those who assess their material status as poor compared to average (CI=1.31; p=0.048) and good (CI=1.56; p=0.02), and respondents who assess their health as poor compared to those who rate it as average (CI=1.55; p<0.001) or very good/excellent health (CI=3.09; p<0.001). Gender and marital status did not prove to be predictors of CLBP.
Conclusion**:** Key predictors of high life-long prevalence of CLBP (48.3%) in Vojvodina include older age, lower education level, poor self-assessment of material conditions and health, and inactive work status.
Keywords: Pain, Back Pain, Low Back Pain, Cross-Sectional Studies.

PREVALENCIJA HRONIČNOG NEKANCERSKOG BOLA U VOJVODINI

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Uvod: U Srbiji, prvi podaci o prevalenciji hroničnog bola prikupljeni u okviru nacionalnih studija istraživanja zdravlja 2013. i 2019. godine, nisu procenili celoživotnu prevalenciju. U 2023. godini Institut za javno zdravlje Vojvodine pokrenuo je godišnji nadzor nad bihevioralnim faktorima rizika za hronične nezarazne bolesti u Autonomnoj pokrajini Vojvodini/APV, a u 2024. godini po prvi put prikupio podatke o celoživotnoj prevalenciji hroničnog nekancerskog bola kroz standardni indikator.

Cilj: Utvrditi prevalenciju hroničnog bola u donjem delu leđa (engl. *CLBP*), kao najčešćeg uzročnika hroničnog nekancerskog bola, na reprezentativnom uzorku odraslog ustanovništva APV i socioekonomske prediktore veće prevalencije *CLBP*.

Metode: Studijom preseka obuhvaćen je reprezentativan uzorak odraslih korisnika zdravstvene zaštite, intervjuisanih 20.05-10.10.2024. godine, u 46 domova zdravlja u APV. Multivarijantni binarni logistički regresioni model analizirao je povezanost između *CLBP* i 5 sociodemografskih faktora u relaciji sa samoprocenom zdravlja.

Rezultati: Kod 3910 anketiranih (52,3% ženskog i 47,7% muškog pola), prosečne starosti 49,27 godina, celoživotna prevalencija *CLBP* iznosi 48,3%. Utvrđena je veća verovatnoća javljanja *CLBP* kod: uzrasne grupe 66 i više godina u odnosu na mlađe od 30 godina (CI=5,45; p<0.001) i osobe 31-50 godina (CI=1,64; p=0,002), odnosno 50-65 godina (CI=1,39; p=0,026); osoba sa završenom osnovnom školom ili manje u odnosu na ispitanike za završenom srednjom školom (CI=1,50; p=0,001) i višom školom/fakultetom (CI=1,77; p<0,001); neaktivnog radnog statusa (CI=1,48; p=0,008) u odnosu na aktivni; onih koji materijalno stanje samoprocenjuju kao loše u odnosu na prosečno (CI=1,31; p=0,048) i dobro (CI=1,56; p=0,02), kao i ispitanici koji svoje zdravlje procenjuju kao loše u odnosu na one koji ga procenjuju kao prosečno (CI=1,55; p<0,001) ili vema dobro/odlično (CI=3,09; p<0,001). Pol i bračnost se nisu pokazali kao prediktori *CLBP*.

Zaključak:

Značajni prediktori visoke celoživotne prevalencije *CLBP* kod odraslog stanovništva Vojvodine (48,3%) su starija životna dob, niži nivo obrazovanja i samoprocene materijalnog stanja, neaktivni radni status i loša smoprocena sopstvenog zdravlja.

Ključne reči: bol, bol u leđima, bol u donjem delu leđa, studije poprečnog preseka

PREEMPTIVE ANALGESIA AS CRUCIAL FACTOR FOR LOWERING ACUTE PAIN

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The concept of preemptive analgesia was postulated by George Washington Creel during the early 1900s. Creel found that the trauma caused by surgery leads to "shock and exhaustion" of the CNS. He continued to advocate for preincisional and intraoperative infiltrations of local anesthesia in addition to general anesthesia. In this way, noxious stimuli could be prevented from reaching the brain, thus establishing "shockless surgery." The protocol process of introducing this idea was established in the 1980s. Preemptive analgesia is an antinociceptive treatment that prevents the establishment of altered processing of afferent input, which increases postoperative pain. Preemptive analgesia is defined as treatment that: 1. begins before surgery; 2. prevents the establishment of central sensitization caused by an incisional injury (includes only the period of surgery); and 3. prevents the establishment of central sensitization caused by incisional and inflammatory injuries (includes the period of surgery and the initial postoperative period).

Two conditions are particularly important for a clinical study: ensuring effective suppression of afferent input with sufficient duration of such treatment (which includes the initial postoperative period) and combined approaches to treatment aimed at: preventive treatment, maintenance of the obtained effect and cancellation of central sensitization (in case of incomplete preventive actions).

Keywords. Preemptive analgesia, postoperative pain, acute pain.

PREEMPTIVNA ANALGEZIJA KAO KRUCIJALNI FAKTOR SMANJENOG POSTOPERATIVNOG AKUTNOG BOLA

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Koncept preventivne analgezije je postulirao Džordž Vašington Kril tokom ranih 1900-ih. Kril je utvrdio da trauma izazvana operacijom, dovodi do „šoka i iscrpljenosti" CNS-a. Nastavio je da se zalaže za preincizione i intraoperativne infiltracije lokalne anestezije I pored opšte anestezije. Na ovaj način bi se štetni stimulansi mogli sprečiti da dođu do mozga, čime bi se uspostavila „operacija bez šoka". Protokolarni process uvodjenja ove ideje je osnovan 1980-ih. Preemptivna analgezija je antinociceptivni tretman koji sprečava uspostavljanje izmenjene obrade aferentnog inputa, što povećava postoperativni bol. Preemptivna analgezija se definiše kao tretman koji: 1.počinje pre operacije; 2. sprečava uspostavljanje centralne senzibilizacije izazvane incizionom povredom (obuhvata samo period operacije); i 3. sprečava uspostavljanje centralne senzibilizacije izazvane incizionim i inflamatornim povredama (obuhvata period operacije i početni postoperativni period). Posebno su važna dva uslova za kliničku studiju: obezbeđivanje efikasne supresije aferentnog inputa sa dovoljnim trajanjem takvog lečenja (koji obuhvata početni postoperativni period) i kombinovani pristupi lečenju koji imaju za cilj: preventivno lečenje, održavanje dobijenog efekta i otkazivanje centralne senzibilizacije (u slučaju nepotpunog preventivnog dejstva).

Ključne reči: Preemptivna analgezija, postoperativni bol, akutni bol.

DILLEMAS IN POSTOPERATIVE PAIN THERAPY

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Postoperative pain is a widespread and underestimated problem in Serbia and globally. Numerous studies conducted in countries with advanced healthcare systems have shown that even in the 21st century, postoperative pain is not adequately managed. Postoperative recovery depends on patient characteristics and factors that facilitate postoperative recovery, including the presence or absence of postoperative complications. The pharmacology of postoperative pain targets pathophysiological mechanisms such as nociception, peripheral sensitization, ectopic activity, and central sensitization. Modern pharmacological management of postoperative pain involves balanced multimodal analgesia. The principle of multimodal analgesia is based on the multifactorial nature and complexity of pain transmission pathways and is defined as the use of various medications or techniques with different mechanisms of action on the peripheral or central nervous system, which can have additive or synergistic effects. Several drug groups are involved in the multimodal approach, each with a specific pathophysiological mechanism of action. The effectiveness of opioid analgesics in treating moderate to severe postoperative pain is achieved due to the lack of a ceiling effect. However, increasing dosage leads to increased side effects. Nonsteroidal anti-inflammatory drugs (NSAIDs), cyclooxygenase-2 inhibitors (COX-2), and systemic steroids reduce the inflammatory component of surgical pain. Systemic and local anesthetics reduce the release of inflammatory mediators,interleukin-(IL-6, IL-1β, and IL-1 receptor antagonist (-1RA)). Gabapentinoids, by binding to the α-2-δ-1 subunit of voltage-gated Ca^{2+} channels in the central nervous system (CNS), reduce the release of important excitatory neurotransmitters involved in nociception. α-2-agonists, such as clonidine and dexmedetomidine, modulate pain impulse transmission by activating the spinal cord's presynaptic and postsynaptic α2 receptors. Local anesthetics (e.g. lidocaine) block neural transmission by inhibiting voltage-gated Na^{+} channels, thus preventing the transmission of pain stimuli from the periphery to the central nervous system. N-methyl-D-aspartate receptor (NMDA receptor) antagonists, ketamine and magnesium, reduce central sensitization mechanisms.

Keywords: postoperative pain, pharmacological management, drugs

DILEME U TERAPIJI POSTOPERATIVNOG BOLA

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Postoperativni bol je i dalje veoma rasprostranjen i još uvek potcenjen problem kako u našoj zemlji, tako i u svetu. Brojne studije koje su sprovedene u zemljama s razvijenim sistemom zdravstvene zaštite pokazale su da čak ni u 21. veku postoperativni bol nije adekvatno tretiran. Više od 80% pacijenata koji se podvrgavaju hirurškim procedurama iskuse akutni postoperativni bol, a 75% pacijenata opisuju akutni bol kao srednje težak, težak ili ekstreman. Postoperativni oporavak zavisi od karakteristika pacijenta, ali i od faktora koji omogućavaju postoperativni oporavak, odnosno od prisustva ili odsustva komplikacija posle operacije. Farmakologija postoperativnog bola je usmerena prema patofiziološkim mehanizmima kao što su: nocicepcija, periferna senzitizacija, ektopična aktivnost, centralna senzitizacija. Savremeno medikamentno lečenje postoperativnog bola podrazumeva balansiranu multimodalnu analgeziju. Princip multimodalne analgezije je baziran na multifaktorijalnoj prirodi i kompleksnosti puteva prenošenja bola, a definiše se kao upotreba različitih lekova ili tehnika sa različitim mehanizmom dejstva na perifernom ili centralnom nervnom sistemu, koje mogu imati aditivan ili sinergistički efekat. Nekoliko grupa lekova je uključeno u multimodalni princip, i svaki od njih ima specifičan patofiziološki mehanizam dejstva. Efikasnost opioidnih analgetika u terapiji umerenog do teškog postoperativnog bola se ostvaruje zbog nedostatka plato efekta. Međutim, povećanjem doze dolazi do povećanja neželjenih efekata. Nesteroidni anti-inflamatorni lekovi (NSAIL), ciklooksigenaza-2 inhibitori (COX-2) i sistemski steroidi smanjuju inflamatornu komponentu hirurškog bola. Sistemski i lokalni anestetici redukuju oslobađanje inflamatornih medijatora (IL-6, Il-1β, i IL-1RA). Gabapentinoidi, vezujući se za alfa-2-delta-1 subjedinicu voltažnih kalcijumskih kanala u centralnom nervnom sistemu, redukuju oslobađanje važnih ekscitatornih neurotransmitera uključenih u nocicepciju. Alfa-2-agonisti, kao što su klonidin i deksmedetomidin, aktiviranjem presinaptičkih i postsinaptičkih α2 receptora u kičmenoj moždini modulišu transmisiju bolnih impulsa. Lokalni anestetici (lidokain) blokiraju neuralnu transmisiju blokirajući natrijumske kanale, pa preveniraju transmisiju bolnih stimulusa sa periferije u centralni nervni sistem. NMDA antagonisti, ketamin i magnezijum, smanjuju mehanizam cetralne senzitizacije.

Ključne reči: postoperativni bol, farmakološko lečenje, lekovi

INTERVENTIONAL PROCEDURES FOR THE TREATMENT OF CHRONIC MIGRAINE

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Migraines are a complex disorder with a strong genetic component, characterized by episodes of moderateto-severe headaches that can last from hours to days. They typically present unilaterally and are often associated with nausea, along with increased sensitivity to light and sound. Migraines are highly prevalent, affecting 12% of the population, including up to 17% of women and 6% of men annually. Chronic migraine is defined as experiencing headaches on at least 15 days per month, with migraine symptoms present on at least eight days, for a duration of three months. When chronic migraines prove refractory to standard pharmacological treatments, interventional procedures should be considered.

In this lecture, we will review studies testing various non-invasive interventional procedures, including transcutaneous electrical nerve stimulation devices, remote electrical stimulation, external trigeminal nerve stimulators, and transcranial magnetic stimulation. We will also examine different injection techniques for treating chronic migraine, such as greater occipital nerve blocks, supraorbital nerve blocks, and sphenopalatine ganglion blocks. Additionally, the effects of radiofrequency techniques (pulses and ablation), and more invasive interventional procedures like peripheral nerve stimulation and primary occipital nerve neuromodulation, will be discussed for their role in treating refractory chronic migraines.

We will also address the types of studies needed, including appropriate control groups, when evaluating the efficacy of different interventional modalities for treating refractory migraines. Interventional treatment options targeting the inhibition of painful nerves offer a promising avenue for chronic headache sufferers, though large, randomized trials are necessary to confirm their effectiveness.

Keywords: chronic migraine, migraine refractory to pharmacological treatments, interventional procedures

INTERVENCIONALNE PROCEDURE ZA LEČENJE HRONIČNE MIGRENE

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Migrenski napadi predstavljaju složen poremećaj sa jakom genetskom komponentom, karakterisan epizodama umerenih do jakih glavobolja koje mogu trajati satima ili danima. Migrena se obično manifestuje na jednoj strani glave i često je praćena mučninom i povećanom osetljivošću na svetlost i zvuk. Migrene su vrlo rasprostranjene, pogađajući 12% populacije, uključujući do 17% žena i 6% muškaraca godišnje. Hronična migrena se definiše kao prisustvo glavobolje najmanje 15 dana mesečno, sa simptomima migrene prisutnim najmanje osam dana, u periodu od najmanje tri meseca. Kada je hronična migrena otporna na standardne farmakološke tretmane, treba razmotriti intervencione procedure.

U ovom predavanju, razmotrićemo rezultate studija koje testiraju različite neinvazivne intervencione procedure, kao što su transkutana električna stimulacija nerava, daljinska električna stimulacija nerava, spoljni trigeminalni nervni stimulatori i transkranijalna magnetna stimulacija. Takođe ćemo analizirati različite tehnike injekcija za lečenje hroničnih migrena, uključujući blokade velikog okcipitalnog nerva, supraorbitalnog nerva i sfenopalatalnog gangliona. Pored toga, biće razmotreni efekti radiofrekventnih tehnika (puls i ablacija) i invazivnijih intervencionih procedura, kao što su stimulacija perifernih nerava i neuromodulacija primarnog okcipitalnog nerva, u tretmanu otpornih hroničnih migrena.

Diskutovaćemo koje vrste studija su potrebne, kao i koje kontrolne grupe treba koristiti pri testiranju efekata različitih intervencionih modaliteta u lečenju otpornih migrena. Intervencione opcije lečenja koje ciljaju inhibiciju bolnih nerava predstavljaju obećavajući pravac za pacijente sa hroničnim glavoboljama, a velika randomizovana klinička ispitivanja su potrebna da bi se dokazala njihova efikasnost.

Ključne reči: hronična migrena, migrena otporna na farmakološke tretmane, intervencione procedure

HEADACHES IN WOMEN

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Population-based research demonstrates greater pain prevalence among women relative to men. Multiple biopsychosocial mechanisms contribute to these sex differences in related to pain, including sex hormones, endogenous opioid function, genetic factors, gender roles, pain coping and catastrophizing. Sex and gender differences are present in both acute and chronic pain. About half of chronic pain conditions are more common in women, with only 20% having a higher prevalence in men. Migraine and tension type headache are three times more common in women than in men. Women who suffer from headache usually experience a greater burden of disease, longer-lasting attacks, and higher rates of relapse. The relationship between headaches and hormones is complex. Migraine is significantly affected by fluctuating sex hormone levels in women during menses and across the perimenopause. Menstrual-related headaches are related mainly to estrogen, which has actions involved in the serotonergic and glutamatergic systems of the central nervous system. The monitoring established that: the prevalence of migraine increases during menarche, oscillation of estrogen levels during menstruation is often a migraine trigger, prescribing estrogen via oral contraceptives or hormone replacement therapy can be a trigger for migraines, during the second and third trimesters of pregnancy, when estrogen levels are high, migraine typically has a reduced prevalence, migraine is common in the postpartum period, which is caused by a sudden drop in estrogen levels, migraine usually improves in physiological menopause. Cluster headache is more common in men. Both male and female cluster patients show low testosterone levels and testosterone supplementation could have a positive effect on headache attacksSex-related differences do not only regard epidemiology but also comorbidities, treatment responses, and disease-modifying factors.To date, no pharmacological options for the management of chronic pain have been specifically developed for women, and the treatment of chronic pain is largely managed using drugs that were initially developed for other diseases and have limited effectiveness and tolerability. Hormonal therapy can be used for hormone-related headaches. *Keywords: headache, migraine, sex, gender, hormones*

GLAVOBOLJE KOD ŽENA

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Populacione studije pokazuje veću prevalenciju bola kod žena u odnosu na muškarce. Višestruki biopsihosocijalni mehanizmi doprinose polnim razlikama u vezi sa bolom, uključujući polne hormone, endogenu opioidnu funkciju, genetske faktore, rodnu ulogu, suočavanje sa bolom i katastrofizam. Polne i rodne razlike prisutne su i u akutnom i u hroničnom bolu. Otprilike polovina hroničnih bolnih stanja je češća kod žena, a samo 20% ima veću prevalenciju kod muškaraca. Migrena i glavobolja tenzionog tipa su tri puta češće kod žena nego kod muškaraca. Žene koje pate od glavobolje obično doživljavaju veći teret bolesti, dugotrajnije napade i veće stope relapsa. Odnos između glavobolje i hormona je složen. Na migrenu značajno utiču fluktuacije nivoa polnih hormona kod žena tokom menstruacije i tokom perimenopauze.

Glavobolje povezane sa menstruacijom uglavnom su povezane sa estrogenom, koji deluje na serotonergičke i glutaminergične sisteme centralnog nervnog sistema. Praćenjem je utvrđeno da: prevalenca migrene raste tokom menarhe, oscilacija nivoa estrogena tokom menstruacije je često okidač migrene, ordiniranje estrogena putem oralnih kontraceptiva ili terapije nadoknade hormona može biti okidač migrene, tokom drugog i trećeg trimestra trudnoće, kada je nivo estrogena visok, migrena tipično ima smanjenu prevalencu, migrena je česta u postpartalnom periodu što je uzrokovano naglim padom nivoa estrogena, migrena se obično poboljšava u fiziološkoj menopauzi. Klaster glavobolja je češća kod muškaraca. I muški i ženski pacijenti sa klaster glavoboljom pokazuju nizak nivo testosterona i suplementacija testosteronom može imati pozitivan efekat na napade glavobolje. Razlike u vezi sa polom ne odnose se samo na epidemiologiju već i na komorbiditete, odgovore na lečenje i faktore koji modifikuju bolest. Do danas, nijedna farmakološka opcija za lečenje hroničnog bola nije posebno razvijena za žene, a lečenje hroničnog bola se uglavnom rukovodi upotrebom lekova koji su prvobitno razvijeni za druge bolesti i imaju ograničenu efikasnost i podnošljivost. Kod hormonski povezanih glavobolja može se primeniti hormonska terapija. *Ključne reči: glavobolja, migrena, pol, rod, hormoni*

DIAGNOSTIC AND THERAPEUTIC CHALLENGES IN TRIGEMINAL NEURALGIA IN THE EMERGENCY CENTRE

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Introduction: Pain is among the most common reasons for emergency department (ED) visits. Neuralgias are the most frequent type of neuropathic pain caused by dysfunction or injury of these neural structures. Despite precise definitions in the International Classification of Headache Disorders 3rd edition (ICHD-3) and the subsequent International Classification of Orofacial Pain (ICOP), trigeminal neuralgia (TN) also represents a significant clinical challenge. Objectiv: The aim was to determine characteristics and management of TN and painful trigeminal neuropathy (TNp) in the neurological emergency department. Methods: A cross-sectional study of adult TN and TNp patients referred to the ED for the last fourteen years. Demographic, clinical, and treatment characteristics were collected from electronic medical records, and patients were classified according to their discharge diagnosis. Results: 156 patients were included in the study, 122 (91.7%) with TN (average age 58) and 11 (8.3%) with TNp (average age 66). TN was etiologically defined in 24.6%. There were no significant differences in CFP incidence and characteristics before and after the COVID-19 outbreak. The pain was usually unilateral right-sided (59.9%) and severe (48.4%) while in TNp it was moderate (54.5%). Carbamazepine (71.3%) was the most frequently prescribed. The results are presented by methods of descriptive statistics: frequencies and percentages; median and interquartile range for non-normally distributed data. Data normality was assessed by histogram visual inspection and the Shapiro-Wilk test with Fisher's exact test was used to analyze differences in the frequency of sensory disturbans in TN, SPSS, version 23.0. Conclusion: Management of TN is challenging in the busy clinical environment of the ED. The typical patient is an elderly female with right-sided TN affecting the V2 and V2/V3 branches. Institutional evidence-based guidelines for TN management and documentation based on ICHD3 or ICOP should be considered.

Keywords: Cranial Neuralgia; Clinical Characteristics; Pain Management; Emergency department.

DIJAGNOSTIČKI I TERAPIJSKI IZAZOVI KOD TRIGEMINALNE NEURALGIJE U URGENTNOM CENTRU

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Uvod: Bol je jedan od najčešćih razloga za dolazak u Urgentni centar (UC). Neuralgije su najčešća vrsta neuropatskog bola uzrokovane disfunkcijom ili povredom neuralnih struktura. Uprkos preciznim definicijama u Međunarodnoj klasifikaciji poremećaja glavobolje 3. izdanje (ICHD-3) i kasnijoj Međunarodnoj klasifikaciji orofacijalne boli (ICOP), trigeminalna neuralgija (TN) i dalje predstavlja značajan klinički izazov. Cilj: Utvrditi kliničke karakteristike i strategije lečenja koje se koriste u neurološkoj prijemnoj ambulanti UC, kod TN i bolne trigeminalne neuropatije (TNp). Metode: Urađena je studija preseka odraslih bolesnika sa TN i TNp koji su upućivani u UC, u posljednjih četrnaest godina. Demografske, kliničke karakteristike i primenjena terapija prikupljeni su iz elektronskih medicinskih zapisa, a pacijenti su klasifikovani prema otpusnoj dijagnozi. Rezultati: U studiju je bilo uključeno 133 bolesnika, od toga 122 (91,7%) sa TN (prosečno 58 godina) i 11 (8,3%) sa TNp (prosečno 66 godina). TN je etiološki definisana u 24,6%. Nije bilo značajnih razlika u incidenciji i karakteristikama TN i TNp pre i nakon izbijanja COVID-19. Bol je obično bila unilateralna desno (59,9%) i jakog intenziteta (48,4%), dok je kod TNp bila umerenog intenziteta (54,5%). Najčešće je propisivan karbamazepin (71,3%). Rezultati su prikazani metodama deskriptivne statistike: frekvencije i postoci; medijana i interkvartilni raspon za podatke koji nisu normalno distribuirani. Normalnost podataka procenjena je vizualnim pregledom histograma i Shapiro-Wilkovim testom uz Fisherov egzaktni test za analizu razlika u učestalosti senzornih poremećaja. Zaključak: Dijagnostički i terapijski postupci kod TN jesu izazov u užurbanom kliničkom okruženju UC. Tipični pacijent je starija žena sa desnostranom TN u distribuciji V2 i V2/V3. Neophodno je razmotriti konstitusanje institucionalnih smernica utemeljenih na dokazima za pristupne modalitete TNi kao i standardizovanje dokumentacije na temelju ICHD3 ili ICOP-a.

Ključne reči: Kranijalna neuralgija, Kliničke karakteristike, Terapija bola, Urgentni centar

PAIN IN MULTIPLE SCLEROSIS

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Multiple sclerosis (MS) is a chronic, autoimmune, inflammatory, neurodegenerative disease of the central nervous system with unknown etiology, characterized by variable clinical manifestations and progression towards severe functional disability.

Pain is not a characteristic symptom of MS, but it is an important and frequent one, significantly affecting the level of disability, mental health, and quality of life of those affected. The overall prevalence of pain symptoms among MS patients is around 63%, while the prevalence of neuropathic pain alone is approximately 50%. Gender differences have been observed, with neuropathic pain being about twice as common in female patients. Recognized risk factors for pain in MS include: older age, longer disease duration, higher scores of functional disability (EDSS), accompanying depression or mental disorders, the presence of three or more spinal cord lesions, lower levels of education, and progressive disease phenotypes.

Several classifications of pain in MS are described in the literature. Truini and colleagues proposed a contemporary classification of MS-related pain based on underlying mechanisms:

- *Neuropathic pain*: dysesthetic pain in the limbs, trigeminal neuralgia, Lhermitte's sign
- *Nociceptive pain*: pain associated with optic neuritis, musculoskeletal pain, back pain, migraines, tension headaches, therapy-related pain
- *Mixed pain*: painful tonic spasms and pain associated with spasticity
- *Other pain*: psychogenic pain and pain caused by other conditions unrelated to MS

Among MS patients experiencing pain, only 38% receive pain treatment, and of those, 61% believe their pain is adequately managed. These issues highlight the complexity of diagnosing the type of pain in MS and selecting appropriate treatments, considering factors such as efficacy, safety profile, costs, and the patient’s clinical complexity. A multimodal approach to pain management is essential, incorporating pharmacotherapy, rehabilitation, psychotherapy, neuromodulatory procedures, and lifestyle modifications to achieve the best treatment outcomes and improve the quality of life for both patients and their families.

Keywords: Multiple sclerosis, pain, pain clasification

BOL I MULTIPLA SKLEROZA

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Multipla skleroza (MS) je hronično, autoimuno, inflamatorno, neurodegenerativno oboljenje centralnog nervnog sistema nepoznate etiologije, sa varijabilnim kliničkim manifestacijama i progresijom ka teškoj funkcionalnoj onesposobljenosti. Bol nije karakterističan ali je važan i čest simptom MS koji značajno utiče na stepen invaliditeta, mentalno zdravlje i kvalitet života obolelih. Ukupna prevalencija simptoma bola kod pacijenata sa MS je oko 63%, a prevalencija samo neuropatskog bola je oko 50%. U odnosu na pol, zabeležena je značajna razlika u prevalenci neuropatskog bola koji je oko dva puta češći kod obolelih osoba ženskog pola. Prepoznati faktori rizika za bol kod MS su: starija životna dob, duže trajanje bolesti, viši skor stepena funkcionalne onesposobljenosti(EDSS), prateća depresija ili mentalni poremećaji, ≥3 lezije kičmene moždine, niži stepen obrazovanja, progresivni fenotipovi bolesti. U literaturi se opisuje nekoliko klasifikacija bola kod MS. Truini je sa saradnicima predložio savremenu, na mehanizmima zasnovanu, klasifikaciju bola kod MS:

- *Neuropatski bol:* distenični bol u ekstremitetu, Trigeminalna neuralgija, Lermiteov fenomen
- *Nociceptivni bol*: bol povezan sa optičkim neuritisom, muskuloskeletni bolovi, bol u leđima, migrene, tenzione glavobolje, bolovi povezani sa terapijom
- *Mešoviti bol*: bolni tonički grčevi i bol povezan sa spasticitetom
- *Bol drugog porekla*: psihogeni bol i bol indukovan od strane drugih oboljenja koji nije povezan sa MS.

Od ukupnog broja MS pacijenata sa prisutnim bolom kod samo 38% obolelih biva primenjena terapija bola, a od tretiranih 61% smatra da je bol adekvatno kupiran. Izneti problemi govore u prilog kompleksnosti pre svega dijagnostikovanja vrste bola kod MS, a potom izbora lečenja u kontekstu efikasnosti, bezbedonosnog profila, troškova i posebno kliničke složenosti pacijenta što uključuje njegovu starosnu dob, pol, prisustvo komorbiditeta i istovremenu primenu lekova. Neophodan je multimodalni pristup kupiranja bola koju uključuje farmakoterapiju, rehabilitaciju, psihoterapiju, neuromodulatorne procedure i modifikaciju načina života kako bi se postigao najbolji ishod lečenja i poboljšao kvalitet života kako obolelog tako i njegove porodice.

Ključne reči: multipla skleroza, bol, klasifikacija bola

ALGOMETRIC EXAMINATION OF PAIN IN PEOPLE WITH RADICULOPATHY

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Introduction: Algometry as a highly sensitive method provides objective insight into the degree of pain, while the use of questionnaires in a simple way can estimate the characteristics of pain and the patient's biopsychosocial status. The study was conducted in order to measure the pressure pain threshold and pressure pain tolerance threshold in patients with cervical and lumbar radiculopathy and found a possible association of pain with the biopsychosocial factors.

Methods: The study examined 60 patients with cervical radiculopathy (30 men and 30 women) and 60 patients with lumbar radiculopathy (30 men and 30 women) before starting and after finishing treatment cycle. All patients were hospitalized in the Clinic for Medical Rehabilitation, Clinical Center of Vojvodina in Novi Sad. Research was conducted using Pain Detect Test, Brief Pain Inventory, Neck Disability Index, Quebec Back Pain Disability Scale, Hospital Anxiety and Depression Scale, The Fear-Avoidance Beliefs Questionnaire and Pain Catastrophizing Scale.

Results: There was no statisticallly significant difference in algometric values between patients with cervical radiculopathy and patients with lumbar radiculopathy. It was found that females have a lower pressure pain threshold and lower tolerance to pain than males. Comparing algometric values before starting and after finishing treatment cycle can be noted that the program of rehabilitation favorable influence on patients with lumbar radiculopathy, while in patients with cervical radiculopathy occured deterioration in subjective symptoms. It was established that biopsychosocial factors greatly affect the pain.

Conclusions: Quantification and mapping the pain by algometer and determination of biopsychosocial status through questionnaires will provide the implementation of appropriate therapy for patients, which is based on individual approach. At the same time, the applied methodology would be achieved better verification of the results in rehabilitation program.

Keywords: Radiculopathy; Pain Measurement; Pain Threshold; Psychology; Surveys and Questionnaires

ALGOMETRIJSKO ISPITIVANJE BOLNOSTI KOD OSOBA SA RADIKULOPATIJOM

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Uvod: Algometrija kao visokosenzitivna metoda pruža objektivan uvid u stepen bola, dok se upotrebom upitnika na jednostavan način mogu proceniti karakteristike bola i biopsihosocijalni status pacijenta.

Cilj: Izmeriti prag bola i prag tolerancije na bol kod pacijenata sa cervikalnom i lumbalnom radikulopatijom i utvrditi moguću povezanost bola sa biopsihosocijalnim faktorima.

Metode: Studijom je pre započinjanja i posle završavanja terapijskog ciklusa ispitano 60 pacijenata sa dijagnostikovanom cervikalnom radikulopatijom (30 muškaraca i 30 žena) i 60 pacijenata sa dijagnostikovanom lumbalnom radikulopatijom (30 muškaraca i 30 žena). Svi pacijenti su bili hospitalno lečeni u okviru Klinike za medicinsku rehabilitaciju, Kliničkog centra Vojvodine u Novom Sadu. U istraživanju su korišćeni test za detekciju bola (Pain Detect Test), kratki upitnik o bolu (Brief Pain Inventory), indeks onesposobljenosti zbog bolova u vratu (Neck Disability Index), Kvebekova skala onesposobljenosti kod lumbalnog sindroma (Quebec Back Pain Disability Scale), bolnička skala za anksioznost i depresiju (Hospital Anxiety and Depression Scale), upitnik za procenu prisustva straha od fizičke aktivnosti/posla i njihovog izbegavanja (The Fear-Avoidance Beliefs Questionnaire) i skala katastrofizma bola (Pain Catastrophizing Scale). *Rezultati:* Nije uočena statistički značajna razlika algometrijskih vrednosti između pacijenata sa cervikalnom radikulopatijom i pacijenata sa lumbalnom radikulopatijom. Ustanovljeno je da osobe ženskog pola imaju niži prag bola i nižu toleranciju na bol od osoba muškog pola. Poređenjem algometrijskih vrednosti pre započinjanja i posle završavanja terapijskog ciklusa zapaža se da je program rehabilitacije povoljno uticao na pacijente sa lumbalnom radikulopatijom, dok je kod pacijenata sa cervikalnom radikulopatijom došlo do pogoršanja tegoba. Utvrđeno je da biopsihosocijalni faktori u velikoj meri utiču na bolnost.

Zaključci: Kvantifikovanje i mapiranje bola uz pomoć algometra i utvrđivanje biopsihosocijalnog statusa putem upitnika će omogućiti primenu adekvatne terapije kod pacijenata, koja je zasnovana na individualnom pristupu. Istovremeno bi primenjenom metodologijom bila postignuta bolja verifikacija rezultata rehabilitacionog programa.

Ključne reči: radikulopatija; merenje bola; prag bola; psihologija; istraživanja i upitnici.

BIOTENSEGRITY AND FASCIOTENSEGRITY – AN INNOVATIVE APPROACH IN THE TREATMENT OD PAINFUL CONDITIONS

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Designer B. Fuller coined the term tensegrity, which implies tensional integrity and denotes an architectural constructive principle whereby the structure creates its own balance, maintaining its shape. Tensegrity, in 1993, was presented as a conceptual model according to the cell, emphasizing how the organization of living things can be interpreted as a tensegrity structure. According to this concept, the organization conceived in this way enables the restoration of the original shape of structures after deformation by passing mechanical tension without damaging the components that make up the shape. The key concepts of the tensegrity model are: elasticity, deformability, mechanical transmission and restoration. Biotensegrity (Levin) is a more complex view of functionality because it takes into account the musculoskeletal and fascial systems to explain the mechanics of movement. This model sheds light on how cells are able to adapt to mechanical deformations by stimulating biochemical responses and allowing the cell to adapt and survive. Biotensegrity enables: mobility, stability and function. The strength of this model is based on the presence of mechanotransduction at the cellular level and force redistribution. Deformation of cell shape is the language a cell uses in relation to its mechanometabolic environment. By fascia we mean a sheath, sheet, or any number of other dissectable aggregations of connective tissue that form beneath the skin to attach, enclose, and separate muscles and internal organs. Fascia has a superficial and a deep layer, but more and more studies talk about the existence of liquid and solid fascia. The main sensory receptors in the musculoskeletal system, which are integrated into the fascia, are mechanoreceptors and muscle spindles. Recent studies have expanded the understanding of the role of fascia in muscle force transmission and biomechanics. In addition, 70% of muscle force transmission is directed through tendons, and 30% is transmitted through myofascial connections and deep fascia. Pathological conditions of the fascia lead to increasing the number, sensitization and length of nociceptors and change in the activity of myofibrils and extracellular matrix.

Keywords: biotensegrity, fasciotensegrity, pain

BIOTENSEGRITY AND FASCIOTENSEGRITY - INOVATIVNI PRISTUP U TRETMANU BOLNIH STANJA

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Dizajner B. Fuller je osmislio termin tensegrity što podrazumeva tenzioni integritet i označava arhitektonski konstruktivni princip čime se struktura stvara sopstvenu ravnotežu, održavajući svoj oblik. Tensegrity, je 1993. godine kao konceptualni model prikazan prema ćeliji, naglašavajući kako se organizacija živih može tumačiti kao tensegrity struktura. Prema ovom konceptu ovako zamišljena organizacija omogućava vraćanje prvobitnog oblika struktura nakon deformacije prolaskom mehaničke napetosti bez oštećenja komponenti koje čine oblik. Ključni koncepti tensegrety modela su: elastičnost, deformibilnost, mehanička transmisija i restauracija.

Biotensegrity (Levin) je kompleksniji pogled na funkcionalnost jer uzima u obzir mišićno-skeletni i fascijalni sistem kako bi objasnio mehaniku pokreta. Ovaj model baca sveto na to kako su ćelije u stanju da se prilagode mehaničkim deformacijama stimulišući biohemijske odgovore i omogućavajući ćeliji da se prilagodi i preživi. Biotensegrity omogućava: mobilnost, stabilnost i funkciju. Snaga ovog modela zasniva se na prisustvu mehanotransdukcije na ćelijskom nivou i redistribuciji sile. Deformacija ćelijskog oblika je jezik koji ćelija koristi u odnosu na svoje mehanometaboličko okruženje.

Pod fascijom podarzumevamo omotač, list ili bilo koji broj drugih agregacija vezivnog tkiva koje se mogu secirati i koje se formiraju ispod kože da bi se pričvrstili, zatvorili i odvojili mišići i unutrašnji organi. Fascija ima površinski i duboki sloj, ali sve više studija govori o postojanja tečne i čvrste fascije. Glavni senzorni receptori u mišićno-skeletnom sistemu, a koji su integrisani u fasciju, su mehanoreceptori i mišićna vretena. Nedavne studije su proširile razumevanje o ulozi fascije u prenosu mišićnih sila i biomehanici. Osim toga, 70% prenosa mišićne sile usmereno kroz tetive, a da se 30% prenosi miofascijalnom konekcijama i dubokom fascijom. Kod patoloških stanja fascije dolazi do povećanja, senzibilizacije i dužine nociceptora i promena u aktivnosti miofibrila i ekstracelularnog matriksa.

Ključne reči: biotensegrity, fasciotensegrity, pain

COMPLEX REGIONAL PAIN SYNDROME AS A CONSEQUENCE OF ALTERED ORGANIZATION OF THE LOCAL AND GENERALIZED BRAIN NETWORK

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Hypothesis: Complex Regional Pain Syndrome (CRPS) is a functional pain syndrome caused by an unconscious overreaction to negative emotions, with a sense of being threatened. It can be balanced with positive thoughts and expectations, such as expecting to flush out cytokines from the painful area after dry needling (DN), acupuncture, or other methods that make a person feel safe and healthy. In the chronic stage of CRPS, normalization is less likely. Method and Subjects: A retrospective analysis of 136 patients was conducted over the last 17 years. The diagnosis of CRPS was confirmed using the Budapest Criteria. Hand/foot function, temperature, and skin sensitivity were evaluated. Pain was assessed using a visual analog scale (VAS). The therapy involved explaining the pain and dry needling (DN). Dry needling was performed at pressure-sensitive points of 2 kg or less, measured with a pressure algometer. Patients were divided into three groups. Group 1 consisted of 38 patients (31 females and 7 males), aged 21 to 82 years; the time interval from pain onset was less than 3 months. The maximum pain intensity was VAS 10 in 9 cases, VAS 8-9 in 8 cases, and VAS 3-7 in 18 cases. Group 2 consisted of 61 patients (48 females), aged 17-71 years, with pain lasting 3-11 months. The maximum pain intensity was 6-10 in 38 cases. Group 3 consisted of 37 patients (26 females), aged 25-71 years, with pain lasting 1-2 years. Maximum pain intensity was 7-10 in 30 cases. Results: In Group 1, 18 out of 38 CRPS patients achieved complete pain elimination and normalization of function. Moderate residual dysfunction and pain remained in 20 cases. In Group 2, after just one DN session, 38 of the 61 patients reported complete analgesia without residual allodynia or hypokinesia. In Group 3, following repeated DN sessions, complete analgesia was observed in 5 patients. Partial improvement (reduced pain and partial dysfunction) was seen in 19 patients after 3 to 28 DN sessions. Eighteen patients discontinued DN therapy due to worsening pain after the first attempt. Conclusion: We confirmed that for pain lasting up to one year in CRPS cases, dry needling, explaining the nature of pain, and positive treatment suggestions such as "every step I take is safe" (placebo effect) can lead to a dramatic analgesic effect. Dry needling enhances neural connectivity in adjacent regions and directs local information flow, thus contributing to the reorganization of the brain network and its plasticity process.

Keywords: cytokines, acupuncture, emotions.

KOMPLEKSNI REGIONALNI BOLNI SINDROM KAO POSLEDICA IZMENJENE ORGANIZACIJE LOKALNE I GENERALIZOVANE MREŽE MOZGA

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Hipoteza. Kompleksni regionalni bolni sindrom (KRBS) je funkcionalni bolni sindrom uzrokovan nesvesnom preteranom reakcijom na negativne emocije, da smo ugroženi. Može se uravnotežiti pozitivnim mislima i očekivanjima, na primer, očekivanju da ćemo isplaknuti citokine iz bolne regije posle suvoiglene (SI) terapije, akupunkture ili na druge načine koji učine da se osoba oseti bezbedno i zdravo. U hroničnom stadiju KRBS su manje mogućnosti za normalizaciju.

Metoda i subjekti. Retrospektivna analiza 136 pacijenata tokom zadnjih 17 godina. Dijagnoza KRBS je potvrđena po Budimpeštanskim kriterijumima. Ocenjivana je funkcija ruke/noge, temperatura i senzibilitet kože. Bol je ocenjen na vizuelno analognoj skali (VAS). Terapiju je činilo objašnjenje o bolu i suvom iglanju (SI). Suvo iglanje je izvedeno na mestima osetiljivim na pritisak 2 kg ili manje, mereno algometrom na pritisak. Pacijenti su razdeljeni u tri grupe. Grupu 1 je sačinjavalo 38 pacijenata (31 žena i 7 muških), 21 do 82 god starosti; vremenski interval od začetka bola je bio manji od 3 meseca. Maksimalni intenzitet bola je bio VAS 10 kod 9 primera, VAS 8-9 kod 8 i VAS 3-7 u 18 primera. Grupu 2 je sačinjavalo 61 pacijenata (48 ž.) 17-71 god. života, bol je trajao 3-11 meseci. Max intenzitet bola je bio 6-10 kod 38 slučajeva. Grupu 3 je sačinjavalo 37 pacijenata (26 žena), 25-71 god starosti, bol je trajao 1-2 godine. Maksimalan bol je bio 7-10 kod 30 slučajeva.

Rezultati. U grupi 1 je u 18 od 38 pacijenata sa KRBS, došlo do kompletne eliminacije bola i normalizacije funkcije. Umerena rezidualna disfunkcija i bol je preostala kod 20 slučajeva. U grupi 2, posle samo jedne SI terapije od 61 pacijenata, kompletna analgezija je opisana kod 38 pacijenata bez rezidualne alodinije ili hipokinezije. U grupi 3 je ishod posle ponavljane SI terapije: kompletna analgezija kod 5 pacijenata. 19 je imalo delimično poboljšanje - boli delimična disfunkcija su ostali posle 3 do 28 SI ponavljanja. 18 pacijenata je otklonilo SI terapiju zbog pogoršanja bola posle prvog pokušaja Sl.

Zaključak. Potvrdili smo da do godinu dana trajanja bola kod KRBS suvo iglanje, objašnjenje šta je bol i pozitivne sugestije o lečenju, kao «svaki moj korak je bezbedan<< (placebo) može dovesti do dramatičnog analgetskog učinka. Suvo iglanje pojača neuralnu povezanost susednih regija i usmerava lokalni informacijski tok. Tako učestvuje u reorganizaciiji moždane mreže i procesu njene plastičnosti.

Ključne reči: citokini, akupunktura, emocije

APPLICATION OF EXTRACORPORAL SHOCKWAVE THERAPY IN TREATING PAIN SYNDROMES

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Extracorporal shockwave therapy (ESWT) has been increasingly used for the treatment of various musculoskeletal disorders, but there are still not enough recommendations to guide its use for various diseases and patient categories. The technique is based on the generation of shock waves that are delivered to the target tissue via radial or focused probes. ESWT reduces pain, promotes angiogenesis and lokal metabolism, breaks down calcifications, and stimulates tissue regeneration. A recent meta-analysis has shown that ESWT can be successfully used for the treatment of myofascial pain syndrome, avoiding the adverse effects of various invasive procedures such as trigger point injection, dry needling, ultrasoundguided pulsed radiofrequency, etc. Recent systematic reviews and meta-analyses based on randomized controlled trials have shown that the use of ESWT is effective in alleviating pain and improving the general functional state for patients with low-back pain, including chronic low-back pain. In such patients, ESWT provided better pain relief and improved lumbar dysfunction compared with the other interventions included, without serious adverse effects. ESWT also has a significant effect on reducing pain in various tendinopathies or related conditions, such as plantar fasciitis, lateral epicondylitis, chronic Achilles tendinopathy, and rotator cuff tendinopathy. However, given the substantial heterogeneity among the studies, it is necessary to conduct more well-designed studies to provide stronger evidence for the rational use of ESWT for various pain syndromes.

Keywords: shockwave therapy, angiogenesis, calcifications

PRIMENA TERAPIJE UDARNIM TALASIMA ZA LEČENJE BOLNIH SINDROMA

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Ekstrakorporalna terapija udarnim talasima (*extracorporal shockwave therapy*, ESWT) se sve više koristi za lečenje različitih mišićno-skeletnih poremećaja, ali još uvek nema dovoljno preporuka koje bi usmerile njenu primenu za različite bolesti i kategorije pacijenata. Tehnika se zasniva na generisanju udarnih talasa koji se isporučuju u ciljno tkivo preko radijalnih ili fokusiranih sondi. ESWT smanjuje bol, pospešuje angiogenezu i lokalni metabolizam, razbija kalcifikate, podstiče regeneraciju tkiva i dr. Nedavna metaanaliza je pokazala da se ESWT može uspešno koristiti za lečenje miofascijalnog bola, izbegavajući štetne efekte različitih invazivnih procedura. Nedavni sistematizovani pregledi literature i meta-analize zasnovane na randomizovanim kontrolisanim studijama su pokazale da je upotreba ESWT efikasna u ublažavanju bolova i poboljšanju opšteg funkcionalnog stanja kod pacijenata sa bolom u donjem delu leđa, uključujući i one sa hroničnim bolom u donjem delu leđa. Kod takvih pacijenata, ESWT je pružio bolje olakšavanje bolova i poboljšanje lumbalne disfunkcije u poređenju sa drugim terapijskim intervencijama, bez ozbiljnih neželjenih efekata. ESWT takođe ima značajan uticaj na smanjenje bolova kod različitih tendinopatija i srodnih stanja, kao što su plantarni fasciitis, lateralni epikondilitis, hronična Ahilova tendinopatija i tendinopatija rotatorne manžete. Međutim, s obzirom na značajnu heterogenost među studijama, neophodno je sprovesti dodatne dobro dizajnirane studije kako bi se pružili jači dokazi za racionalnu upotrebu ESWT za različite sindrome bola.

Ključne reči: terapija udarnim talasima, angiogeneza, kalcifikati

THE IMPORTANCE OF PROPER EVALUATION IN CHILDREN IN ORDER TO PREVENT CHRONIC PAIN

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Good posture control is a complex neural task. The central nervous system engages with the interaction between continuous afferent information about body position and orientation from visual, vestibular, or somatosensory input, as well as subsequent motor commands to muscles to maintain posture. Posture cannot be considered only as a static reflex response, but is a complex competence based on the interaction of sensory-motor processes. Postural control implies automatic control of body position in space with the aim of orientation and stability against the force of gravity, the basis for achieving functional movement in all positions: lying, sitting and standing. Deviation in postural reactions or abnormal postural reactions show a disturbed function of postural reactivity, due to which there is loss of the ability to adapt to a change in body position. Postural reflexes, which represent automatic reactions for posture- muscle tone, stability, balance, coordination, are active until the end of life.

During the period of learning to walk, children show signs of reorganization of their motor behavior. However, they do not show similar signs of reorganization of their muscle postural control strategies during sitting. Instead, each infant uses its own strategy of muscular postural control during sitting, as well as during the period of verticalization and establishment of independent walking. In the course of neurological maturation, the child needs to develop adapted, almost reflex motor responses in the trunk and lower extremities in order to be able to stand upright and move. The first step for children consists of building a repertoire of postural strategies. The second step consists in learning to select the most appropriate postural strategy depending on the ability to predict the consequences of movements in order to maintain balance control and task efficiency.

Sagittal alignment of the spine can be altered by spinal deformity, causing regional imbalance and adjacent compensations (eg, Scheuermann's kyphosis or spondylolisthesis). Research indicates that there is a high prevalence of lower back pain in adolescents, who do not use ergonomic positions when sitting or standing. In girls, greater rotational instability was found, as well as a much higher incidence of scoliosis. Also, in girls, the shape of the spine shows more posterior inclination of the upper back vertebrae and vertebrae of the thoraco-lumbar junction.

Keywords: children, posture, evaluation

ZNAČAJ PRAVILNE EVALUACIJE POSTURE U DEČJEM UZRASTU U CILJU PREVENCIJE HRONIČNOG BOLA

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Dobra kontrola posture je složen neuronski zadatak. Centralni nervni sistem se bavi interakcijom između neprekidnih aferentnih informacija o položaju i orijentaciji tela od vizuelnog, vestibularnog ili somatosenzornog unosa, kao i narednih motornih komandi mišićima za održavanje držanja. Postura se ne može smatrati samo statičkim refleksnim odgovorom, već je kompleksna kompetencija zasnovana na interakciji senzorno-motornih procesa. Posturalna kontrola podrazumeva automatsku kontrolu položaja tela u prostoru sa ciljem orijentacije i stabilnosti protiv sile zemljine teže, osnovu za postizanje funkcionalnog pokreta u svim pozicijama: ležećoj, sedećoj i stojećoj. Odstupanje u posturalnim reakcijama ili abnormalne posturalne reakcije pokazuju poremećenu funkciju posturalne reaktibilnosti zbog čega dolazi do manjeg ili većeg gubitka sposobnosti prilagođavanja na promenu položaja tela. Posturalni, refleksi koji predstavljaju automatske reakcije za ujednačenu posturu, odnosno, tonus mišića, stabilnost, ravnotežu, koordinaciju aktivni su do kraja života. U periodu učenja hodanja deca pokazuju znake reorganizacije svog motoričkog ponašanja. Međutim, oni ne pokazuju slične znake reorganizacije svojih strategija mišićne posturalne kontrole tokom postavljanja u sedeći položaj. Umesto toga, svako odojče koristi sopstvenu strategiju mišićne posturalne kontrole tokom posedanja, kao i u periodu vertikalizacije i uspostavljanja samostalnog hoda. U toku neurološkog sazrevanja dete treba da razvije prilagođene, gotovo refleksne motoričke odgovore u trupu i donjim ekstremitetima kako bi bilo sposobno za uspravan položaj i kretanje. Prvi korak za decu sastoji se od izgradnje repertoara posturalnih strategija. Drugi korak se sastoji u učenju odabira najprikladnije posturalne strategije u zavisnosti od sposobnosti predviđanja posledica pokreta kako bi se održala kontrola ravnoteže i efikasnost zadatka.

Sagitalno poravnanje kičme može biti promenjeno deformitetom kičme, što izaziva regionalni poremećaj ravnoteže i susednih kompenzacija (npr. Scheuermannove kifoze ili spondilolisteze). Istraživanja ukazuju da postoji visoka prevalenca bola u donjem delu leđa kod adolescenata, koji ne koriste ergonomske položaje kada sede ili stoje. Kod devojčica pronađena je veća nestabilnost rotacije, kao i mnogo veća učestalost skolioza. Takođe, kod devojčica, oblik kičme pokazuje više posteriorne inklinacije gornjih leđnih pršljenova i pršljenova torako-lumbalnog spoja.

Ključne reči: deca, postura, evaluacija

FROM PAIN THERAPY TO PASSIVE EUTHANASIA

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Today's development of medical science, therapeutic procedures, resuscitation techniques and pharmacology has led to improvements in the treatment of a large number of chronic and so-called incurable diseases. This is accompanied by increased expectations of patients and their environment, related to the results of certain treatments and diagnostic procedures. This is especially true for patients who are lifethreatening, i.e. in the terminal phase of the disease. Recommendation 1418 of the Council of Europe of 1999 emphasizes that these procedures must not neglect the quality of life, and medical practice should not only have as its sole aim the prolongation of life, but also the alleviation of suffering.

In the case where the patient is exposed to great pain and suffering, it is possible to prolong the treatment, perform procedures that accelerate the process of dying or choose the direction of palliative care to alleviate the pain and suffering of the patient. That is why in the processes related to the education of not only the lay but also the professional public, it is necessary to work on the model of distansia, in correlation with euthanasia and the patient's right to make decisions in the procedures of "treatment" that are related to the terminal phase of the disease. Distance, or medical uselessness as a concept of bioethics, refers to medical interventions with the purpose of sustaining life, even when there is no hope of ultimate cure, where medical treatments are accompanied by suffering and pain of the patient. Some authors believe that distance is dying where the patient loses the quality of life and the possibility of dying with dignity. The question is how much the patient has to participate in such a state to make a decision.

Distancing is a very vulnerable area where there is no precisely established protocol that would appreciate the quality of life, that is, whether further continuation of treatment is useless, as well as what are the patient's rights in such situations, and he is no longer able to really participate in decision-making. In other words, the Law on Patients' Rights establishes the obligation of doctors to respect the will of the patient even when that will is aimed at refusing medical treatment necessary to sustain life, but at the same time provides for the misdemeanor liability of the doctor for treatment without the consent of the informed patient. At the present moment, we are caught between the patient's right to refuse treatment and the doctor's responsibility for the patient's death in accordance with the provisions of criminal legislation.

By resolving this discrepancy, we would eliminate the dilemmas and possible responsibility of doctors due to the conflict between the rules of the profession and science, but also the value of the right to life, which includes the right to a dignified death. In the context of the social moment, the views of professionals, i.e. members of the medical profession, lawyers, psychologists, ethicists and others, are also important. A precise position on the issue raised, and the discrepancy between the right to life and a

dignified death, the right to make decisions by the patient, the obligation of treatment, palliative care, distancing and euthanasia, must be harmonized by the profession, science and legislators.

Keywords: distance, patient's right to participate in decision-making, doctor's responsibility, views of professionals.

OD TERAPIJE BOLA DO PASIVNE EUTANAZIJE

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Današnji razvoj medicinske nauke, terapijskih postupaka, tehnika reanimacije i farmakologije je doveo do unapređenja u lečenju većeg broja hroničnih i tzv. neizlečivih bolesti. To prati i povećana očekivanja bolesnika i njihove okoline, vezanih za rezultate određenih tretmana i dijagnostičkih postupaka. Ovo se naročito odnosi na bolesnike koji su životno ugroženi, odnosno u terminalnoj fazi bolesti. U Preporuci 1418
Saveta Evrope iz 1999. naglašava se da ovi postupci ne mogu zanemarivati kvalitet života, a medicinska praksa ne bi smela da ima kao jedini cilj tek produženje života, već i ublažavanje patnje.

U slučaju gde je pacijent upravo izložen velikim bolovima i patnji moguće je produžiti lečenje, raditi postupke kojima se ubrzava proces umiranja ili izabrati pravac palijativne nege radi ublažavanja bola i patnje pacijenta. Zato je u procesima vezanim za edukaciju ne samo laičke već i stručne javnosti neophodno raditi na modelu distanazije, u korelaciji sa eutanazijom i pravom pacijenta na donošenje odluka u postupcima "lečenja" koji su povezani sa terminalnom fazom bolesti. Distanazija ili medicinska beskorisnost kao pojam bioetike, odnosi se na medicinske zahvate sa svrhom održavanja života pa i onda kada ne postoji nikakva nada za krajnjim izlečenjem, gde su medicinski tretmani praćeni i patnjom i boli pacijenta. Pojedini autori smatraju da distanazija znači umiranje gde pacijent gubi kvalitetu života i mogućnost na dostojanstveno umiranje. Pitanje je, koliko pacijent ima mogućnosti da učestvuje u takvom stanju da donese neku odluku.

Distanazija je vrlo vulnerabilno područje gde nema tačno utvrđenog protokola koji bi cenio kvalitet života odnosno da li je dalji nastavak lečenja bez koristi, kao i koja su prava pacijenta u takvim situacijama, a on više nije u stanju da zaista učestvuje u odlučivanju. Drugim rečima, Zakonom o pravima pacijenata ustanovljena je obavezu lekara da poštuje volju pacijenta čak i kada je ta volja usmerena ka odbijanju medicinskog tretmana neophodnog za održavanje života, ali je istovremeno predviđena i prekršajna odgovornost lekara za lečenje bez pristanka obaveštenog pacijenta. U aktuelnom trenutku nalazimo se između prava pacijenta na odbijanje tretmana i odgovornosti lekara za smrt pacijenta u skladu sa odredbama kaznenog zakonodavstva.

Rešavanjem ove diskrepancije otklonili bi dileme i moguću odgovornost lekara zbog sukoba između pravila struke i nauke, ali i vrednosti prava na život, u čijem se sastavu nalazi i pravo na dostojanstvenu smrt. U kontekstu društvenog trenutka, važni su i stavovi profesionalaca, odnosno pripadnika medicinske struke, pravnika, psihologa, etičara i drugih. Precizan stav o postavljenom pitanju, i raskoraku između prava na život i dostojanstvenu smrt, pravu na donošenja odluka od strane pacijenta, obaveza lečenja, palijativne nege, distanazije i eutanazije, moraju i od strane struke, nauke i zakonodavca biti usklađeni.

Ključne reči: distanazija, pravo pacijenta da učestvuje u odlučivanju, odgovornost lekara, stavovi profesionalac

WHY IS IMPORTANT TO DETERMINE THE TENSION DIRECTIONS OF THE NERVE NETWORK?

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The need to explain the physical function of neural network tension arises due to the neural network's rigidity to stretch.

Thanks to the development of ultrasound elastography, today we are able to measure the tension of certain nerves in correlation with muscle tension and better understand the functioning and nature of neurophysiological processes in the body. It is also possible to explain developmental processes, as well as regenerative-protective processes in the organism in a special way, sublimating them in the "Theory of the directions of tension of the nervous network".

The focus of this theory is the Iliopsoas muscle, through which pass a large number of nerves which have a great influence on all other systems in the body.

Keywords: neural network tension, ultrasound elastography, neurophysiological processes.

ZAŠTO JE VAŽNO DEFINISATI PRAVCE TENZIJE NERVNE MREŽE?

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Potreba da se objasni fizička funkcija tenzije Nervne mreže proizilazi iz svojstva rigidnosti nervne mreže na istezanje.

Zahvaljujući razvoju ultrazvučne elastografije, danas smo u mogućnosti da izmerimo tenziju pojedinih nerava u korelaciji sa tenzijom mišića i bolje razumemo funkcionisanje i osnovu neurofizioloških procesa u telu. Takođe je moguće na poseban način objasniti razvojne procese, kao i regenerativno-protektivne procese u organizmu, sublimirajući ih u "Teoriju pravaca tenzije nervne mreže".

U fokusu ove torije je mišić Iliopsoas, kroz koji prolazi veliki broj nerava motornog, senzornog i autonomnog nervnog sistema što za posledici ima veliki uticaj na sve ostale sisteme u organizmu.

Ključne reči: tenzije nervne mreže, ultrazvučna elastografija, neurofiziološki process.

RISK FACTORS FOR THE OCCURRENCE OF PHANTOM PAIN IN PATIENTS WITH AMPUTATION OF THE LOWER EXTREMITIES

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INTRODUCTION**:** Phantom limb pain is a common complication after amputation, with its exact mechanism still not fully understood. It likely involves a mix of peripheral, central, and psychological factors, necessitating a multidisciplinary treatment approach. Since current treatments are only partially effective, further exploration of its mechanisms and contributing risk factors is essential. AIM**:** The aim of this study is to examine certain risk factors that are linked to the occurrence of phantom limb pain as a complication following lower limb amputation. METHODS**:** A cross-sectional study was conducted at the Rehabilitation Clinic of the University Clinical Center of Vojvodina in Novi Sad from April to the end of September 2024. It included participants who had undergone lower limb amputation and were evaluated during the pre-prosthetic phase of rehabilitation or admitted for the prosthetic phase within the outpatient clinic, day hospital, or inpatient services of the clinic. Based on anamnesis data, medical documentation, and clinical examination findings, the study examined the relationship between certain data and phantom pain. RESULTS**:** Out of 41 patients, 30 (73.17%) were male, and 11 (26.83%) were female. The average age of the patients was 63 years. A statistically significant association was found between the occurrence of phantom limb pain and diabetes mellitus ($p < 0.01$), the level of amputation ($p = 0.033$), and the phase of rehabilitation treatment ($p = 0.04$). CONCLUSION**:** The results of the study indicated a statistically significant correlation between phantom pain and diabetes mellitus, as well as the level of amputation and the phase of rehabilitation treatment. Further research and a better understanding of these risk factors and the mechanisms behind phantom pain are necessary for improved prevention and adequate treatment of this disorder.

*Keywords**: phantom limb pain, lower limb amputation, diabetes mellitus.*

FAKTORI RIZIKA ZA NASTANAK FANTOMSKOG BOLA KOD PACIJENATA SA AMPUTACIJOM DONJIH EKSTREMITETA

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UVOD: Fantomski bol je jedna od najčešćih komplikacija nakon amputacije ekstremiteta. Smatra se da ovaj poremećaj nastaje kao složena kombinacija perifernih, centralnih i psiholoških mehanizama te je i njegovo lečenje musltidisciplinarno. Obzirom da su sve farmakološke, psihološke i rehabilitacione procedure koje su u upotrebi prilikom lečenja fantomskog bola delimično efikasne potrebno je detaljnije istražiti mehanizam nastanka ovog poremećaja kao i faktore rizika koji dovode do njegovog nastanka. CILJ: Cilj ovog rada je ispitivanje pojedinih faktora rizika koji se u literarnim podacima vezuju za nastanak fantomskog bola kao komplikacije nakon amputacije donjih ekstremiteta. METODE: Studija preseka sprovedena je na Klinici za medicinsku rehabilitaciju Univerzitetskog kliničkog centra Vojvodine u Novom Sadu u periodu od aprila do kraja septembra 2024. godine i uključila je ispitanike kod kojih je načinjena amputacija donjih ekstremiteta koji su procenjivani u okviru pretprotetske faze rehabilitacionog tretmana, ili su primljeni radi sprovođenja protetske faze rehabilitacije u okviru ambulantno-polikliničke službe, Dnevne bolnice ili stacionarne delatnosti klinike. Na osnovu anamnestičkih podataka, podataka iz medicinske dokumentacije i podataka dobijenih kliničkim pregledom ispitana je povezanost određenih podataka sa fantomskim bolom. REZULTATI: Od ukupno 41 ispitanika 30 (73.17%) je bilo muškog, a 11 (26.83%) ženskog pola. Prosečna starost ispitanika je bila 63,46 $\pm$ 10.63 godine. Ukupno 14 pacijenata (34.15%) je imalo potkolenu amputaciju, dok je 27 pacijenata (65.85%) imalo natkolenu amputaciju.

Pokazana je statistički značajna povezanost između pojave fantomskog bola i dijabetes melitusa ($p < 0.01$), nivoa amputacije ($p=0.033$) i faze rehabilitacionog tretmana ($p=0.04$). ZAKLJUČAK: Rezultati ispitivanja ukazali su na to da postoji statistički značajna povezanost između fantomskog bola i oboljevanja od dijabetes melitusa, zatim nivoa amputacije i faze rehabilitacionog tretmana. Dalja istraživanja i bolje razumevanje ovih faktora rizika i mehanizma nastanka fantomskog bola je neophodna radi bolje prevencije i adekvatnog tretmana ovog poremećaja.

Ključne reči: fantomski bol, amputacija donjih ekstremiteta, dijabetes mellitus

CASE REPORT OF COMPLEX REGIONAL PAIN SYNDROME

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Introduction**:** Complex Regional Pain Syndrome (CRPS) is a condition that most commonly occurs after trauma, fracture, or surgery, sometimes even spontaneously, and significantly reduces functional ability. It is characterized by severe, persistent pain, often affecting one limb. Despite advancements in research and treatment, CRPS remains a challenge for diagnosis and effective treatment. The standardized Budapest criteria, which include sensory, motor, vasomotor, and sudomotor symptoms, are used to diagnose CRPS.

Case Report: A 46-year-old female patient sustained a fracture of the left lateral malleolus on June 1, 2024, after an awkward landing on her left foot while descending down the stairs. Timely diagnostics and conservative treatment, along with regular follow-ups, were conducted at the Emergency Department of the University Clinical Center of Vojvodina by an orthopedic surgery and traumatology specialist. The patient was admitted to the Day Hospital of the Clinic for Medical Rehabilitation UCCV for a multi-day rehabilitation treatment that began on September 5, 2024, and ended on October 14, 2024, aimed at further diagnostics and evaluation of the patient's condition, alleviating subjective symptoms, and improving functional outcomes. It was established that the patient met the Budapest diagnostic criteria for CRPS, and testing was conducted using the PainDETECT questionnaire (16/38 - the result is ambiguous, but a neuropathic pain component may be present). The main symptoms at the start of treatment were pain in the area of the left ankle joint (pain intensity 8/10 according to the NRS - numerical rating scale) when bearing weight on the left foot and during certain movements. By the end of the treatment the symptoms had reduced, and the pain intensity was 3/10 according to the NRS. The Bath CRPS body perception disturbance scale was administered (11/57). A Color Doppler ultrasound of the arteries and veins of the lower extremities, an X-ray of the left ankle joint and foot, and laboratory tests for bone metabolism markers were performed, along with DXA diagnostics. Medication therapy was introduced, and the patient underwent a combined, individually tailored rehabilitation treatment (kinesiotherapy, hydrotherapy program, and underwater massage, as well as occupational therapy, including mirror therapy, along with physical modalities).Conclusions**:** Timely diagnosis and a multimodal approach based on evidence-based recommendations are essential for the effective treatment of CRPS.

*Keywords**:** Complex Regional Pain Syndrome; pharmacological treatment; physical therapy; mirror therapy.*

PRIKAZ SLUČAJA KOMPLEKSNOG REGIONALNOG BOLNOG SINDROMA

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Uvod: Kompleksni regionalni bolni sindrom (eng. Complex Regional Pain Syndrome - CRPS) je oboljenjekoje se najčešće javlja nakon traume, preloma ili operacije, nekada i spontano, aznačajno redukuje funkcionalnu sposobnost i karakteriše ga izražen, perzistentan bol, koji često zahvata jedan ekstremitet. Uprkos napretku u istraživanju i lečenju, CRPS ostaje izazov za postavljanje dijagnoze i efikasno lečenje**.** Za postavljanje dijagnoze CRPS-a se koriste standardizovani Budimpeštanski kriterijumi koji obuhvataju senzorne, motorne, vazomotorne i sudomotorne simptome.

Prikaz slučaja: Pacijentkinja, 46 godina starosti, prelom levog lateralnog maleolusa zadobila je 01.06.2024. godine nakon nezgodnog oslonca na levu nogu pri silaženju niz stepenice. Pravovremena dijagnostika i konzervativno lečenje, te redovne kontrole su sprovedene u Urgentnom centru Univerzitetskog kliničkog centra Vojvodine od strane specijaliste ortopedske hirurgije i traumatologije. Pacijentkinja je primljena u
Dnevnu bolnicu Klinike za medicinsku rehabilitaciju UKCV radi sprovođenja višednevnog rehabilitacionog tretmana započetog 05.09.2024. i završenog 14.10.2024., u cilju sprovođenja dopunske dijagnostike i evaluacije stanja pacijentkinje, kupiranja subjektivnih tegoba i poboljšanja funkcionalnog nalaza. Ustanovljeno je da pacijentkinja ispunjava Budimpeštanske CRPS dijagnostičke kriterijume i sprovedeno je testiranje sa Paindetect upitnikom (16/38- rezultat je neodređen, međutim komponenta neuropatskog bola može biti prisutna). Glavne tegobe pacijentkinje na početku tretmana su bili bolovi u predelu levog skočnog zgloba (intenzitet bola 8/10 prema NRS (eng. numerical rating scale)) pri osloncu na levo stopalo i pri određenim pokretima. Na kraju tretmana su tegobe redukovane i intenzitet je iznosi 3/10 prema NRS. Određena je Bath-ova CRPS skala poremećaja percepcije tela (11/57). Načinjen je Color doppler ultrazvuk arterija i vena donjih ekstremiteta, RTG levog skočnog zgloba i stopala.Takođe je urađena laboratorijska analiza markera koštanog metabolizma i načinjena DXA dijagnostika. Uvedena je medikamentna terapija i pacijentkinja je sprovodila kombinovani individualno koncipiran rehabilitacioni tretman (kineziterapija, program hidroterapije i podvodne masaže, sprovodila je radnu terapiju, uključujući i mirror terapiju, uz fizikalne modalitete).

Zaključci**:** Za efikasno lečenje CRPS-a potrebno je blagovremeno postavljanje dijagnoze uz multimodalni pristup zasnovan na evidence-based preporukama.

Ključne reči:Kompleksi regionalni bolni sindrom; farmakološko lečenje; fizikalna terapija, mirror terapija.

PREDNOSTI PERIFERNIH BLOKOVA TRUPA QLB -QUADRATUS LUMBORUM BLOCK I TRANSVERSUS ABDOMINIS BLOCK- TAB U TERAPIJI POSTOPERATIVNOG BOLA

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Sažetak

Uvod. Korišćenje perifernih nervnih blokada trupa unazad više decenija u akušerstvu i abdominalnoj hirurgiji dalo je doprinos značajno bržem oporavku pacijenatana konoperativnih zahvata i implementaciji ERAS (Enchanced recovery after surgery) protokola. Optimalan tretman bola utiče na njegov san i raspoloženje, smanjuje izlučivanje hormona stresa i aktivaciju autonomnog nervnog sistema koji može dovesti do promena kardio vaskualrnog sistema. Tahikardija I hipertenzija koje se mogu javiti dovode do povećanog zahteva miokarda za kiseonik te rizika od infarkta miokarda, malignih poremaćaja ritma, hipertenzije. Postoperativna povećana koagulabilnost krvi uz imobilizaciju bolesnika je dodatni faktor koji povećava rizik od tromboza i plućne embolije. Brže se vraća funkcija gastrointenstinalnog trakta i ranije se počinje sa perosunosom. Takođe pod uticajem hormona stresa pokreću se metabolički procesi koji vode u katabolizam organizam pacijenta te na taj način dodatno kompromituje oporavak pacijenta .

Diskusija. Preporuka ACOG iz 2019. godine za postpartalnu analgeziju podrazumeva primenu multimodalne analgezije. Koncept multimodalne analgezije kod carskog reza počinje pre ili neposredno nakon završetka operacije u zavisnosti od korišćenih medikamenata. Postoperativna analgezija kod pacijenata koji su podvrgnuti carskom rezu je najčešće parenteralna, gde se primenjuje kombinacija analgetika i to: jakog analgetika iz grupe opioida (morfin, tramadol) inesteroidnih antiinflamatornih lekova (ketorolak), uz mogućnost dodatne intravenske primene paracetamola. Dobra multimodalna analgezija nakon carskog reza obezbeđuje se i pomoću perifernih nervnih blokova trupa koji su sve češće u upotrebi. Blokovi se mogu izvoditi dok je pacijentkinja još u opštoj anesteziji, ili dok traje dejstvo spinalne ili epiduralne anestezije. Blokovi koji se najčešće izvode su obostrani: ili oingvinalni - ili ohipogastrični, blok pravog abdominalnog mišića (rectus abdominis sheath block), TAP (transversus abdominis plane) blok, a poslednjih par godinai QLB (quadratus lumborum block).

Zaključak. Intenzitet bola nakon carskog reza je značajno niži u grupi pacijentkinja kod kojih se uz uobičajenu analgetsku terapiju primeni QLB tip I u prva 24 h .Primena QLB tip I doprinosi značajno manjom upotrebom neopiodnih analgetika i opioida u prva 24h posle carskog reza. Neželjeni efekti (mučnina, povraćanje i sedacije) uzrokovanih upotrebom opiodnih analgetika 24h nakon carskog reza se ređe ispoljavaju nakon primene uobičajene analgetske terapije i QLB tip I .

Ključne reči. *QLB -Quadratus lumborum block, Transversus abdominis block-TAP, terapija postoperativnog bola.*

ADVANTAGES OF PERIPHERAL TRUNK BLOCKS QLB-QUADRATUS LUMBORUM BLOCK AND TRANSVERSUS ABDOMINIS BLOCK -TAP IN THE TREATMENT OFPOSTOPERATIVE PAIN

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Summary

Introduction. The use of peripheral nerve blockades of the trunk for several decades in obstetrics and abdominal surgery has contributed to a significantly faster recovery of patients after surgery and the implementation of the ERAS (Enhanced recovery after surgery) protocol. Optimal treatment of pain affects his sleep and mood, reduces the secretion of stress hormones and the activation of the autonomic nervous system, which can lead to changes in the cardiovascular system. Tachycardia and hypertension that may occur lead to an increased demand of the myocardium for oxygen and the risk of myocardial infarction, malignant rhythm disorders, hypertension. Postoperative increased blood coagulability with immobilization of the patient is an additional factor that increases the risk of thrombosis and pulmonary embolism. The function of the gastrointestinal tract is restored faster and per os intake is started earlier. Also, under the influence of stress hormones, metabolic processes are triggered that lead to catabolism in the patient's body, thereby further compromising the patient's recovery.

Discussion. The 2019 ACOG recommendation for postpartum analgesia involves the use of multimodal analgesia. The concept of multimodal analgesia in caesarean section begins before or immediately after the end of the operation, depending on the drugs used. Postoperative analgesia in patients who have undergone caesarean section is most often parenteral, where a combination of analgesics is used, namely: a strong analgesic from the opioid group (morphine, tramadol) and non-steroidal anti-inflammatory drugs (ketorolac), with the possibility of additional intravenous administration of paracetamol. Good multimodal analgesia after caesarean section is also provided by peripheral nerve blocks of the trunk, which are increasingly being used. Blocks can be performed while the patient is still under general anesthesia, or while the effect of spinal or epidural anesthesia lasts. The most commonly performed blocks are bilateral: ilioinguinal-iliohypogastric, rectus abdominis sheath block, TAP (transversus abdominis plane) block, and in the last few years, QLB (quadratus lumborum block).

Conclusion. The intensity of pain after caesarean section is significantly lower in the group of patients in whom QLB type I is administered in the first 24 hours along with usual analgesic therapy. The use of QLB type I contributes to a significantly lower use of non-opioid analgesics and opioids in the first 24 hours after caesarean section. Adverse effects (nausea, vomiting and sedation) caused by the use of opioid analgesics 24 hours after caesarean section are manifested less often after the application of usual analgesic therapy and QLB type I.

Keywords.*QLB -Quadratus lumborum block, Transversus abdominis block-TAP, postoperative pain therapy.*

Introduction

The use of peripheral nerve blockades of the trunk for several decades in obstetrics and abdominal surgery has contributed to a significantly faster recovery of patients after surgery and the implementation of the ERAS (Enhanced recovery after surgery) protocol. Optimal treatment of pain affects his sleep and mood, reduces the secretion of stress hormones and the activation of the autonomic nervous system, which can lead to changes in the cardiovascular system. Tachycardia and hypertension that may occur lead to an increased demand of the myocardium for oxygen and the risk of myocardial infarction, malignant rhythm disorders, hypertension. Postoperative increased blood coagulability with immobilization of the patient is an additional factor that increases the risk of thrombosis and pulmonary embolism. The function of the gastrointestinal tract is restored faster and per os intake is started earlier. Also, under the influence of stress hormones, metabolic processes are triggered that lead to catabolism in the patient's body, thereby further compromising the patient's recovery (1-5).

The role of the TAP block as part of the ERAS protocol significantly reduces the use of opioids. Compared to thoracic epidural analgesia, it is not less valuable and gives less postoperative pain. Application of peripheral nerve blocks of the trunk allows implementation of the ERAS protocol, which leads to less use of opioids and less occurrence of postoperative sedation. Nausea and vomiting are less common. The urinary catheter is removed earlier. All in all, it leads to an earlier discharge of the patient to home (3-5).

A few years ago, the implementation of the ERAS protocol after caesarean section began, where better treatment of pain after surgery using QLB gives this block the possibility for more and more frequent use. Application of TAP block after abdominal surgery including caesarean section reduces the use of morphine. Nausea and vomiting, sedation, urinary retention, OIVI, confusion and agitation are significantly less common after various types of surgery where QLB is applied. Pain intensity of operated patients is significantly lower, earlier patient mobilization is possible (5-7).

Discussion

Caesarean section is the most frequently performed operation in the world. The multiple global increase in the incidence of caesarean section is conditioned by a number of reasons: increased safety of surgery, reduction of perinatal morbidity and mortality, avoidance of damage to the pelvic floor, application of assisted reproduction methods, doctors' fear of lawsuits. Also, the obstetric population has changed, the age of women when they decide to give birth is older, the occurrence of obese pregnant women is more frequent and the body weight of newborns has increased. In Serbia, the caesarean section rate has also been increasing over the last two decades. However, although the caesarean section rate is increasing, it is known that maternal mortality is 2-7 times higher in caesarean section compared to vaginal delivery, and that the patient's recovery after caesarean section is longer and more demanding. Sometimes long-term consequences remain, such as chronic pain, which significantly reduces the patient's quality of life. In recent years, studies have focused on investigating the development of chronic neuropathic pain at the abdominal incision site after caesarean section surgery. Retrospective studies related to chronic pain after caesarean section indicate an incidence of 1% - 18.3%. Effective treatment of postoperative pain according to the recommendations of the ASA and ACOG (American College of Obstetricians and Gynecologists) minimizes the development of chronic pain after cesarean section 8).

The 2019 ACOG recommendation for postpartum analgesia involves the use of multimodal analgesia. The concept of multimodal analgesia in caesarean section begins before or immediately after the end of

the operation, depending on the drugs used. Postoperative analgesia in patients who have undergone caesarean section is most often parenteral, where a combination of analgesics is used, namely: a strong analgesic from the opioid group (morphine, tramadol) and non-steroidal anti-inflammatory drugs (ketorolac), with the possibility of additional intravenous administration of paracetamol. Good multimodal analgesia after caesarean section is also provided by peripheral nerve blocks of the trunk, which are increasingly being used. Blocks can be performed while the patient is still under general anesthesia, or while the effect of spinal or epidural anesthesia lasts. The most commonly performed blocks are bilateral: ilioinguinal-iliohypogastric, rectus abdominis sheath block, TAP (transversus abdominis plane) block, and in the last few years, QLB (quadratus lumborum block) (9).

QLB is a new method. In Serbia, it was applied for the first time in 2017, which initiated the idea to conduct this study. Research by foreign authors indicates that QLB is effective, simple to apply, that it quickly reduces the intensity of pain and that it provides postoperative analgesia for 24 to 48 hours. Consequently, the consumption of opioids is lower and there are fewer unwanted effects of their use, such as sedation, nausea and vomiting. However, the success of the block reported in previous research is not the same. It differed depending on the type of QLB, training of the anesthesiologist, etc(4-10).

Conclusion

The intensity of pain after caesarean section is significantly lower in the group of patients in whom QLB type I is administered in the first 24 hours along with usual analgesic therapy. The use of QLB type I contributes to a significantly lower use of non-opioid analgesics and opioids in the first 24 hours after caesarean section. Adverse effects (nausea, vomiting and sedation) caused by the use of opioid analgesics 24 hours after caesarean section are manifested less often after the application of usual analgesic therapy and QLB type I.

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