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PHYSIATRIST'S APPROACH TO NEUROPATHIC PAIN IN ONCOLOGICAL PATIENTS

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Summary

Neuropathic pain is relatively common, often poorly treated, and associated with impaired quality of life. Neuropathic pain therapy is carried out with a multidisciplinary approach, and rehabilitation as an integral part of therapy must be included early because it can significantly affect the patient's functioning and improve the quality of life. In oncology patients, there is limited experience in the application of physical therapy methods for the treatment of neuropathic pain. The most significant evidence exists for kinesitherapy methods, and the evidence for the effectiveness of transcutaneous electrical nerve stimulation (TENS) is inconsistent due to the low quality of evidence from the included studies.

KEY WORDS: *neuropathic pain, oncological patients, quality of life, rehabilitation, kinesitherapy*

Neuropathic pain, as defined by the International Association for the Study of Pain (IASP), is chronic pain caused by a lesion or disease of the somatosensory nervous system. In the general population, 7-8% of adults have neuropathic pain(1). Depending on the localization of the lesion, neuropathic pain can be central or peripheral, and it represents an important problem due to its complexity, often unclear etiology, or poor response to physical therapy modalities(2). Such pain significantly reduces the quality of life, causes disability, and increases healthcare costs. Various mechanisms are involved in developing neuropathic pain, such as central sensitization, presynaptic or postsynaptic mechanisms, disinhibition, descending pathways alterations, and supraspinal changes in the cortical brain structures(3).

To distinguish it from other types of pain, it is necessary to take a careful medical history and assess the intensity of the pain (e.g. with a visual analog scale). This will provide information on the character of neuropathic pain: paresthesias, dysesthesias, hyper– and hypoalgesia, analgesia, and hyperpathia. In addition to physical examination and diagnostic workup (electromyoneurography, magnetic resonance, and possibly skin biopsy), specialized evaluation scales are also used: Leeds Assessment of Neuropathic Symptoms and Signs (LANSS), Neuropathic Pain Questionnaire (NPQ) and Douleur Neuropathique en 4 questions (DN4) (4). Neuropathic pain requires a multidisciplinary approach and multimodal treatment that includes pharmacotherapy, physical therapy, psychotherapy, acupuncture, and various relaxation techniques. Pharmacotherapy can include the use of antidepressants (tricyclic antidepressants, serotonin, and noradrenaline reuptake inhibitors), antiepileptics (pregabalin, gabapentin), opioids (tramadol), and topical anesthetics (capsaicin, lidocaine). Rehabilitation is an important part of neuropathic pain treatment and should be initiated as early as possible for it can significantly im-

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prove patient's functionality, independence, and quality of life.

Neuropathic pain can occur in patients with spinal cord injury, stroke, diabetic neuropathy, brachial plexus lesions, and radiculopathy. In patients with cancer, neuropathic pain can be caused by tumor compression, radiation plexopathy, or chemotherapy-induced polyneuropathy.

Physical medicine and rehabilitation specialists usually have a wide variety of physical therapy modalities at their disposal for the treatment of pain. Unfortunately, as mentioned earlier, neuropathic pain often responds poorly to physical modalities. Also, there have been very few studies evaluating the efficacy and safety of these modalities in patients with cancer, so traditionally caution was exercised in their use. However, there has been a paradigm shift in recent years concerning contraindications for modalities in cancer patients. Application of physical agents directly over an area of active tumor is still contraindicated, but malignancy as an underlying disease is no longer considered a contraindication. With this understanding, the clinician must decide if the potential benefit for the patient outweighs the risk of increasing tumor growth. Each patient must be considered on an individual basis, with careful consideration of oncologic treatment history, presence of active disease, and placement of the modality. The clinician should maintain awareness of all signs and symptoms of new cancer occurrence or recurrence(5,6).

Despite this new approach, there is a paucity of comparative data to guide the selection of specific modalities for pain treatment, and everyday clinical decision-making is still mostly empirical. In the remainder of this paper, we will describe physical modalities and exercises supported by the most robust evidence for the treatment of neuropathic pain.

Many studies have confirmed the effectiveness of transcutaneous electrical nerve stimulation (TENS) in reducing neuropathic pain(7-9), and numerous international guidelines recommend it for this indication(10-13). However, systematic reviews concluded that there was insufficient evidence to judge whether TENS should be used in adults with cancer-related pain(14,15). Cochrane systematic review published in 2017 could also not reliably confirm the effectiveness of TENS on neuropathic pain due to the very low quality of evidence of the included studies(16).

When considering electrotherapy we should also mention Scrambler therapy, a novel, non-invasive pain-modifying technique that utilizes transcutaneous electrical stimulation of pain fibers with the intent of re-organizing maladaptive signaling pathways(17). The technique was invented by Giuseppe Marineo, who co-authored and published a paper on the topic in 2000(18). Scrambler therapy was developed to treat resistant chronic neuropathic and cancer pain. It has been evaluated in patients with chronic cancer and non-cancer neuropathic pain(19-21), including chemotherapy-induced polyneuropathy(22-24), with mainly positive results. The available data support the Scrambler therapy as a safe(25) and useful option for cancer and non-cancer patients with refractory pain syndromes(26,17).

A systematic review from 2016 confirmed the effectiveness of low-level laser therapy (LLLT) in reducing neuropathic pain, although without a clear conclusion regarding parameters and application protocols (energy, power density, length and frequency of application differed significantly in the included studies)(27).

In a systematic review from 2021, the effectiveness of exercises on neuropathic pain was studied, and expert recommendation was given(28). Spinal cord injury and radiculopathy were included, among other causes of neuropathic pain. In patients with spinal cord injury, stretching and strengthening exercises were effective in reducing neuropathic pain, and their implementation is recommended (level of evidence II, A). In patients with cervical radiculopathy, stretching and strengthening exercises of the neck muscles are recommended (level of evidence II, B). In patients with sciatica, static and dynamic stabilization exercises, hydrotherapy, and static strengthening exercises for the trunk and lower extremities were effective in reducing leg pain, and their implementation is recommended (level of evidence I, A).

When prescribing kinesitherapy in patients with a spinal tumor the potential instability of the spine should be taken into account. Spinal Instability Neoplastic Score (SINS) can be used as a helpful tool(29). SINS includes six parameters (location, presence of pain, type of bone lesion, spinal align-

ment, vertebral body collapse, and posterolateral involvement of spinal elements). If the result indicates an unstable or potentially unstable spine (score 7 and above), a surgical consultation is recommended before commencing with exercises.

CONCLUSION

Neuropathic pain therapy is complex and multidisciplinary. Rehabilitation and physical therapy can relieve symptoms and improve functioning and quality of life. Given that the traditional paradigm in the application of certain modalities of physical therapy in oncology patients is changing(30), further research is needed to determine the safety and effectiveness of other treatment modalities in oncology patients with neuropathic pain.

REFERENCES

1. Murnion BP. Neuropathic pain: current definition and review of drug treatment. Aust Prescr. 2018 Jun;41(3):60-63. doi: 10.18773/austprescr.2018.022.
2. Akyuz G, Kenis O. Physical therapy modalities and rehabilitation techniques in the management of neuropathic pain. Am J Phys Med Rehabil. 2014 Mar;93(3):253-9. doi: 10.1097/PHM.0000000000000037.
3. Campbell JN, Meyer RA. Mechanisms of neuropathic pain. Neuron. 2006 Oct 5;52(1):77-92. doi: 10.1016/j.neuron.2006.09.021.
4. Bernetti A, Agostini F, de Sire A, Mangone M, Tognolo L, Di Cesare A, et al. Neuropathic pain and rehabilitation: a systematic review of international guidelines. Diagnostics (Basel). 2021 Jan 5;11(1):74. doi: 10.3390/diagnostics11010074.
5. O'Dell M, Stubblefield M. Cancer rehabilitation: Principles and practice [Internet]. Springer Publishing Company; 2009. Available from: https://books.google.hr/books?id=ST875-2C93kC
6. Goodman CC, Boissonnault WG, Fuller KS. Pathology: implications for the physical therapist, 2nd ed. Philadelphia, PA: Saunders; 2003
7. Bi X, Lv H, Chen B, Li X, Wang X. Effects of transcutaneous electrical nerve stimulation on pain in patients with spinal cord injury: a randomized controlled trial. Journal of Physical Therapy Science 2015;27:23-5. doi: 10.1589/jpts.27.23. Epub 2015 Jan 9.
8. Buchmuller A, Navez M, Milletre-Bernardin M, Pouplin S, Presles E, Lantéri-Minet M, et al. Value of TENS for relief of chronic low back pain with or without radicular pain. European Journal of Pain 2012;16:656-65. doi: 10.1002/j.1532-2149.2011.00061.x.
9. Barbarisi M, Pace MC, Passavanti MB, Maisto M, Mazzariello L, Pota V, et al. Pregabalin and transcutaneous electrical nerve stimulation for postherpetic neuralgia treatment. Clinical Journal of Pain 2010;26(7):567-72. doi: 10.1097/AJP.0b013e3181dda1ac.
10. Cruccu G, Aziz TZ, Garcia-Larrea L, Hansson P, Jensen TS, Lefaucheur JP, et al. EFNS guidelines on neurostimulation therapy for neuropathic pain. Eur J Neurol. 2007;14(9):952–70.
11. Demarin V, Basić-Kes V, Zavoreo I, Bosnar-Puretić M, Rotim K, Lupret V, et al. Recommendations for neuropathic pain treatment. Acta Clin Croat. 2008;47(3):181–91.
12. Martinez V, Attal N, Bouhassira D, Lantéri-Minet M. Les douleurs neuropathiques chroniques : diagnostic, évaluation et traitement en médecine ambulatoire. Recommandations pour la pratique clinique de la Société française d'étude et de traitement de la douleur. Douleurs : Evaluation – Diagnostic – Traitement. 2010;11(1):3–21.
13. Chetty S, Baalbergen E, Bhigjee AI, Kamerman P, Ouma J, Raath R, et al. Clinical practice guidelines for management of neuropathic pain: expert panel recommendations for South Africa. S Afr Med J. 2012; 102(5):312–25.
14. Hurlow A, Bennett MI, Robb KA, Johnson MI, Simpson KH, Oxberry SG. Transcutaneous electric nerve stimulation (TENS) for cancer pain in adults. Cochrane Database Syst Rev. 2012;2012(3):CD006276. doi:10.1002/14651858.CD006276.pub3.
15. Robb K, Oxberry SG, Bennett MI, Johnson MI, Simpson KH, Searle RD. A cochrane systematic review of transcutaneous electrical nerve stimulation for cancer pain. J Pain Symptom Manage. 2009;37(4):746-53. doi:10.1016/j.jpainsymman.2008.03.022.
16. Gibson W, Wand BM, O'Connell NE. Transcutaneous electrical nerve stimulation (TENS) for neuropathic pain in adults. Cochrane Pain, Palliative and Supportive Care Group, editor. Cochrane Database of Systematic Reviews [Internet]. 2017 Sep 14 [cited 2024 Jul 11];2021(3). Available from: http://doi.wiley.com/10.1002/14651858.CD011976.pub2
17. Majithia N, Smith TJ, Coyne PJ, Abdi S, Pachman DR, Lachance D, et al. Scrambler therapy for the management of chronic pain. Support Care Cancer. 2016;24(6):2807-14. doi:10.1007/s00520-016-3177-3.
18. Serafini G, Marineo G, Sabato AF. 'Scrambler therapy': a new option in neuropathic pain treatment? The Pain Clinic. 2000;12(4):287–98. doi:10.1163/156856900750233785.
19. Marineo G, Iorno V, Gandini C, Moschini V, Smith TJ. Scrambler therapy may relieve chronic neuropathic pain more effectively than guideline-based drug management: results of a pilot, randomized, controlled trial. J Pain Symptom Manage. 2012;43(1):87-95. doi:10.1016/j.jpainsymman.2011.03.015.
20. Coyne PJ, Wan W, Dodson P, Swainey C, Smith TJ. A trial of Scrambler therapy in the treatment of cancer pain syndromes and chronic chemotherapy-induced

peripheral neuropathy. J Pain Palliat Care Pharmacother. 2013;27(4):359-64. doi:10.3109/15360288.2013.847519. Epub 2013 Oct 21.
21. Ricci M, Fabbri L, Pirotti S, Ruffilli N, Foca F, Maltoni M. Scrambler therapy: what's new after 15 years? The results from 219 patients treated for chronic pain. Medicine (Baltimore). 2019;98(2):e13895. doi:10.1097/MD.0000000000013895.
22. Pachman DR, Weisbrod BL, Seisler DK, Barton DL, Fee-Schroeder KC, Smith TJ, et al. Pilot evaluation of Scrambler therapy for the treatment of chemotherapy-induced peripheral neuropathy. Support Care Cancer. 2015;23(4):943-51. doi:10.1007/s00520-014-2424-8.
23. Loprinzi C, Le-Rademacher JG, Majithia N, McMurray RP, O'Neill CR, Bendel MA, et al. Scrambler therapy for chemotherapy neuropathy: a randomized phase II pilot trial. Support Care Cancer. 2020;28(3):1183-1197. doi:10.1007/s00520-019-04881-3.
24. Smith TJ, Razzak AR, Blackford AL, Ensminger J, Saiki C, Longo-Schoberlein D, Loprinzi CL. A Pilot randomized sham-controlled trial of MC5-A Scrambler therapy in the treatment of chronic chemotherapy-induced peripheral neuropathy (CIPN). J Palliat Care. 2020;35(1):53-58. doi:10.1177/0825859719827589.
25. Wang EJ, Limerick G, D'Souza RS, Lobner K, Williams KA, Cohen SP, et al. Safety of Scrambler therapy: a systematic review of complications and adverse effects. Pain Med. 2023;24(3):325-340. doi:10.1093/pm/pnac137.
26. Kashyap K, Bhatnagar S. Evidence for the efficacy of Scrambler therapy for cancer pain: a systematic review. Pain Physician. 2020 Jul;23(4):349-364.
27. De Andrade ALM, Bossini PS, Parizotto NA. Use of low level laser therapy to control neuropathic pain: A systematic review. Journal of Photochemistry and Photobiology B: Biology. 2016;164:36–42.
28. Zhang YH, Hu HY, Xiong YC, Peng C, Hu L, Kong YZ, et al. Exercise for neuropathic pain: a systematic review and expert consensus. Front Med. 2021;8:756940.
29. Fisher CG, DiPaola CP, Ryken TC, Bilsky MH, Shaffrey CI, Berven SH, et al. A novel classification system for spinal instability in neoplastic disease: an evidence-based approach and expert consensus from the Spine Oncology Study Group. Spine (Phila Pa 1976). 2010;35(22):E1221-1229.
30. Crevenna R, Kainberger F, Wiltschke C, Marosi C, Wolzt M, Cenik F, et al. Cancer rehabilitation: current trends and practices within an Austrian University Hospital Center. Disabil Rehabil. 2020;42(1):2-7. doi:10.1080/09638288.2018.1514665.

Sažetak

FIZIJATRIJSKI PRISTUP NEUROPATSKOJ BOLI U ONKOLOŠKIH BOLESNIKA

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Neuropatska bol je relativno česta, često se loše liječi i povezana je s narušenom kvalitetom života.

Terapija neuropatske boli provodi se mutidisciplinarnim pristupom, a rehabilitacija kao sastavni dio terapije mora biti uključena rano jer može značajno utjecati na funkcioniranje bolesnika i poboljšati kvalitetu života. Kod onkoloških bolesnika postoje ograničena iskustva u primjeni metoda fizikalne terapije za terapiju neuropatske boli. Najznačajniji dokazi postoje za metode kineziterapije, a dokazi za učinkovitost TENS-a su nekonzistentni zbog niske kvalitete dokaza uključenih studija.

KLJUČNE RIJEČI: *neuropatska bol, onkološki bolesnici, kvaliteta života, rehabilitacija, kineziterapija*