Neuropathic Pain and Lumbar Spinal Column Injuries: A Chronic Perspective

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ABSTRACT

Background: Neuropathic pain commonly occurs as a consequence of spinal cord injuries, manifesting as persistent and often debilitating pain sensations resulting from damage or dysfunction of the nervous system within the spinal column. This systematic review aimed to analyze existing guidelines on rehabilitation interventions for neuropathic pain and clarify their significance.

Methodology: A comprehensive search of literature was performed using the databases Google Scholar, Microsoft Academic, and PubMed. The inclusion criteria encompassed research articles written in Greek, English, and French languages, while articles that were not directly relevant to the subject of investigation were excluded.

Results: A systematic review of published guidelines on rehabilitation interventions for neuropathic pain to elucidate their significance. While some interventions, such as TENS therapy, physiotherapy, and psychological interventions, have been proposed, the core approach to managing neuropathic pain lies in the implementation of comprehensive multidisciplinary interventions that address all the various aspects affected by this chronic and highly disabling condition. It is worth noting the limited literature examining the role of rehabilitation specifically in patients with neuropathic pain, with a focus on individual interventions solely targeting the treatment of neuropathic pain.

Conclusions: Neuropathic pain has significant effects not only on the injuries of the lumbar spine, but also on subsequent functions. Therefore, the involvement of a specialist focused on managing and restoring functional impairments is necessary. This role can be fulfilled by a physical therapist who specializes in addressing the functional issues associated with the patient’s condition. Physiotherapists should employ a multiprofessional and multidisciplinary approach, collaborating closely with various healthcare professionals involved in the patient’s management to ensure optimal pain management.

Keywords: Chronic pain, Lumbar spine, Neuropathic pain, Spine injuries.

1. Introduction

Neuropathic pain is predominantly spontaneous in nature, but it can also manifest as intense pain accompanied by an extremely unpleasant sensation (hyperalgesia) and pain in response to non-painful stimuli. The International Association for the Study of Pain (IASP) defines neuropathic pain as pain that originates or is caused by a primary lesion or dysfunction of the nervous system [1]. Central neuropathic pain is characterized by its persistent nature and variable intensity, typically becoming more intense during physical activity and exposure to cold. Patients often report a worsening of pain over time, both in terms of intensity and the affected area [2]. Chronic neuropathic pain is more prevalent in women (8% compared to 5.7% in men) and individuals over 50 years of age (8.9% compared to 5.6% in a sample of 12,000 patients with chronic pain referred to pain specialists in Germany). Among these patients, 40% exhibit some characteristics of
neuropathic pain, such as a burning sensation, numbness, and tingling. Those with chronic back pain and radiculopathy are particularly affected [3].

Pain is widely acknowledged as the most common medical consequence of traumatic spinal cord injury (SCI), with estimated prevalence rates of approximately 60% [4], [5]. Each year, around 40 million individuals worldwide experience SCI [6]. The majority of these cases involve young men between the ages of 20 and 35, although children account for 1% of this population [7]. Many individuals with SCI consistently experience pain severity over time [8]. Data from the NIH SCI Model Systems database show that pain severity scores, rated on a scale of 0 to 10 (where 0 represents no pain and 10 indicates the worst pain), averaged 4.2 at year 1, 4.5 at year 10, 4.3 at year 20, and 4.2 at year 40 [9]. The treatment and rehabilitation process for SCI-related trauma is extensive, costly, and physically and mentally draining, resulting in various biophysical, psychosocial, and economic challenges [10]. Treatment for spinal cord injury patients is an ongoing, multi-year endeavor that begins shortly after the injury with acute care and early surgical interventions, followed by the management of sensory, motor, and autonomic dysfunction in the chronic phase, and finally, lifelong treatment in the home environment [6].

The purpose of this review is to examine published guidelines regarding rehabilitation interventions for patients experiencing neuropathic pain. Specifically, it aims to investigate the guidelines provided to both male and female patients of all ages who have mild to severe neuropathic pain resulting from various causes, primarily related to nervous system lesions or dysfunctions. Furthermore, the review seeks to explore the effects of rehabilitation therapy on pain and functional outcomes. The rehabilitation therapies under examination include therapeutic exercise, braces, massage, physiotherapy, behavioral therapy, interdisciplinary approaches, and physical therapy. The recommendations derived from the analysis are compared and extended to highlight areas of agreement and discrepancy among them. The primary outcomes assessed in this review are pain levels and functional improvement.

2. Methods

A systematic search of the literature was conducted using Google Scholar, Microsoft Academic, and PubMed databases. The inclusion criteria considered research articles written in Greek, English, and French languages, while articles not directly relevant to the research topic were excluded. Keywords such as “neuropathic pain,” “spine,” “lumbar spine,” “injuries,” “intervertebral disc,” and “physiotherapy” were used to facilitate the search.

The selection of papers for this study followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) approach [11]. The PRISMA framework provides a transparent and structured methodology for conducting systematic reviews. Adhering to the PRISMA guidelines, a step-by-step process was followed to identify, screen, and include relevant research articles (Fig. 1). Initially, the search strategy yielded a total of 100 articles, and duplicates (n = 20) were removed. Subsequently, the titles and abstracts of the remaining articles were screened to determine their relevance to the research question. Finally, the full-text articles that met the inclusion criteria (n = 13) were thoroughly evaluated for eligibility and included in the study. This systematic approach ensures a comprehensive and rigorous selection process, minimizing bias and ensuring the inclusion of high-quality studies in the review.

3. Results

Various symptoms, including sensory deficits, motor weakness, and particularly pain, can be associated with different pathological processes in the spinal column. These symptoms can arise from mechanical compression of the nerve root (mechanical radicular pain), pain caused by tissue changes within the degenerated disc (local radicular pain), or the action of inflammatory mediators such as chemokines and cytokines, which can originate from disc degeneration even without mechanical stress (inflammatory radicular pain). Several studies have explored the biochemical interactions between the affected tissue and the nerve roots, demonstrating that mediators can reach nerve fibers in the same or adjacent lumbar segments. Consequently, nerve fibers not involved in mechanical compression can also be affected [12]-[15].

Miyamoto et al. [16] conducted a study that showed the effect of cyclic mechanical stress on the production of inflammatory factors and supported the idea of a possible synergistic effect of simultaneous mechanical and chemical stimulation of annulus fibrosus cells in the production of reactive mediators (e.g., prostaglandin E2). Consequently, sensitization processes of peripheral nerves or roots lead to secondary central sensitization of spinal neurons, which contributes to these abnormal neuropathic pain states.

An analysis based on a US health insurance database revealed that neuropathic pain in the lumbar and cervical regions is likely the most common neuropathic disorder [17]. Recent research from Germany, which modeled the prevalence and cost of neuropathic pain in patients with lumbago in the general population, demonstrated that nearly one in five individuals with lumbago exhibits symptoms indicative of neuropathic pain. Considering that approximately one-third of the general population experiences lumbar pain, the number of individuals with some form of neuropathic pain in the lumbar region corresponds to approximately 6% of the general population, amounting to almost 5 million patients in Germany alone [18]. Furthermore, neuropathic pain has a significant economic impact. The cost associated with a patient suffering from neuropathic lumbago is typically around 50% higher than that of an average patient, and even 70% higher than the cost of a patient with non-neuropathic lumbago. Based on German data, it has been estimated that the total cost of lumbago for German society is $65 billion, with the population with neuropathic etiology bearing a total cost (direct plus indirect) of $22.6 billion.

However, the diagnosis of neuropathic elements in the lumbar region remains challenging primarily due to the

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absence of a gold standard. The diagnostic value of physical examination has not been adequately documented, and there are inherent limitations in the accuracy of most diagnostic tests. Although widely used, self-assessment questionnaires, which have been shown to be reliable and valid, still remain a topic of discussion [19]. Therefore, in the 21st century, diagnosis continues to rely on a thorough history taking and sound clinical judgment.

Crucucci et al. [20] conducted a study focused on neurostimulation therapy for neuropathic pain and provided guidelines on various available techniques. Transcutaneous electrical nerve stimulation (TENS) may be more effective than sham treatment and is suitable as a preliminary or adjunct therapy for managing neuropathic pain. Demarin et al. [21] emphasized the importance of an interdisciplinary approach to neuropathic pain treatment, which encompasses both invasive and non-invasive therapies (pharmacological, psychological, and physical therapy). They highlighted the critical role of physical therapy in the overall management of this complex condition. It is worth noting that among non-pharmacological interventions, only TENS for painful diabetic neuropathy was superior to sham treatment. Martinez et al. [22] recommended transcutaneous electrical nerve stimulation, spinal cord stimulation, and cognitive-behavioral therapy as effective non-pharmacological interventions for neuropathic pain treatment. They also proposed the use of acupuncture for postherpetic neuralgia and recommended TENS for localized peripheral neuropathic pain and spinal cord stimulation for chronic postoperative lumbar pain with dominant radiculopathy.

Chetty et al. [23] emphasized the critical role of an interdisciplinary approach in managing neuropathic pain. Among non-pharmacological therapies, the authors recommended a combination of psychotherapy and TENS along with adequate physical therapy. Furthermore, they suggested deep brain stimulation for neuropathic pain that is resistant to other pharmacological and non-pharmacological interventions. The guidelines provided by Acevedo et al. [24] highlighted how non-pharmacological management and polypharmacological therapy, targeting different mechanisms, could offer better therapeutic success compared to isolated interventions. They also advocated for an interdisciplinary approach to neuropathic pain management, which includes rehabilitation interventions.

4. Discussion

This systematic review aimed to examine existing guidelines on rehabilitation interventions for neuropathic pain and elucidate their significance (Table I). While certain interventions such as transcutaneous electrical nerve stimulation (TENS), physical therapy, and psychological interventions have been proposed, the fundamental approach to managing neuropathic pain lies in the application of interdisciplinary comprehensive interventions that address all the various aspects impacted by this chronic and debilitating condition. It is important to note that
there is limited literature specifically exploring the role of rehabilitation in patients with neuropathic pain, with a focus on individual interventions solely targeting the treatment of neuropathic pain.

Among rehabilitation interventions, physical therapies play a crucial role in reducing pain. Martinez et al. [22] recommend TENS for localized peripheral neuropathic pain, and Cruccu et al. [20] provide a Level C recommendation for TENS, stating that it may be superior to placebo and can be considered as a preliminary or adjunctive therapy. Furthermore, TENS can be combined with physical therapy and psychotherapy for managing neuropathic pain.

In addition, spinal cord stimulation has been proposed as a treatment for chronic postoperative lumbalgia with predominant radicular pain, as suggested by Cruccu et al. [20] and Martinez et al. [22]. Cruccu et al. [20] also propose this procedure for complex regional pain syndrome. Furthermore, Chetty et al. [23] suggest deep brain

### TABLE I: STUDIES INCLUDED IN THE REVIEW

<table>
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<tr>
<th>Authors (year)</th>
<th>Results</th>
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<tr>
<td>[12]</td>
<td>Inflammatory cellular response varied in herniated intervertebral discs, with a predominant presence of macrophages during intervention, suggesting an active inflammatory process in the tissue. Inflammation may play a significant role in the pathophysiology of herniated discs and contribute to the mechanisms of pain associated with these conditions.</td>
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<td>[13]</td>
<td>The examination of samples revealed the presence of nerve fibers in the anterior longitudinal ligament and the outer region of the disc in all cases. In 8 out of 10 degenerated discs, fibers were also found in the inner parts of the disc. This indicates a more extensive innervation in severely degenerated lumbar discs compared to normal discs, supporting the existence of a morphological sublayer of discogenic pain.</td>
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<td>[14]</td>
<td>In herniated discs, a distinct histological feature was the formation of a zone of vascularized fibrous tissue along the edges of fissures, extending from the inner nucleus pulposus to the outer annulus fibrosus. Nerve fibers, including SP-, NF-, and VIP-immunoreactive fibers, were more extensive in herniated discs compared to control discs. The development of nerves within the annulus fibrosus and fibrous nucleus was primarily observed along the zone of tissue fibrosis in herniated discs. This suggests that the zone of fibrous tissue with extensive innervation in the posterior region of the painful disc may be responsible for the pain associated with herniated discs and discogenic lumbalgia.</td>
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<td>[15]</td>
<td>A study involving 52 patients and 142 discograms found that 17 discs with high-intensity zones (HIZ) showed painful reproduction and abnormal morphology, with radial tears extending through the outer third of the annulus fibrosus. Histological analysis revealed vascularized fibrous tissue formation in the outer region of the annulus fibrosus within the high-intensity zone. This suggests that the presence of a high-intensity zone on magnetic resonance imaging of the lumbar disc could indicate painful disruption of the outer annulus.</td>
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<td>[16]</td>
<td>Application of cyclic mechanical stress to the fibrous nucleus and annulus fibrosus cells increased the synthesis of PGE2. The combination of cyclic mechanical stress and inflammatory stimuli further enhanced the synthesis of PGE2 by these cells. The expression of COX-2 mRNA tended to correlate with the quantity of PGE2, with different roles observed between the fibrous nucleus and annulus fibrous cells. These findings suggest that cyclic mechanical stress may contribute to the generation of pain in intervertebral disc disorders.</td>
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<td>[17]</td>
<td>A study on painful neuropathic disorders found that pain in the lumbar and cervical regions with neuropathic involvement was the most commonly encountered condition, followed by caudalgia and diabetic neuropathy. Patients with painful neuropathic disorders were more likely to have other pain-related conditions, such as fibromyalgia and osteoarthritis, as well as chronic comorbidities like coronary artery disease and depression. Healthcare charges were significantly higher for patients with painful neuropathic disorders compared to matched control individuals. These results indicate that patients with painful neuropathic disorders generally have worse health conditions and higher healthcare costs.</td>
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<td>[18]</td>
<td>Approximately 4% of the general adult population presented with lumbosacral neuralgia, and the cost associated with neuropathic pain in the lumbar region was found to be disproportionately higher compared to nociceptive pain. The presence of neuropathic pain accounted for around 16% of the total cost associated with lumbosacral neuralgia.</td>
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<td>[19]</td>
<td>Verbal descriptions and properties of pain are valuable in distinguishing neuropathic pain from other chronic pain conditions, as pain is a subjective phenomenon. Therefore, understanding the characteristics and verbal expressions of pain can provide insights into the differentiation of neuropathic pain.</td>
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<td>[20]</td>
<td>Regarding the management of neuropathic pain, spinal cord stimulation (SCS) is recommended for the treatment of failed back surgery syndrome (FBSS) and complex regional pain syndrome (CRPS) type I. High-frequency transcutaneous electrical nerve stimulation (TENS) may be superior to sham treatment but inferior to acupuncture. Repetitive transcranial magnetic stimulation (rTMS) has temporary efficacy in central and peripheral neuropathic pains. Motor cortex stimulation (MCS) is effective for central pain after stroke and facial pain. Deep brain stimulation (DBS) should be performed by experienced centers.</td>
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<td>[21]</td>
<td>Rational polypharmacy is often used, as complete relief from neuropathic pain is unlikely with monotherapy. Antidepressants, antispasmodics, and opioid analgesics are commonly used, but their effectiveness varies. Local medications and lidocaine patches can be effective for peripheral syndromes. Sympathetic blockade is generally ineffective except for certain cases of complex regional pain syndrome.</td>
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<td>[22]</td>
<td>The goal of these recommendations is endorsed by all healthcare professionals who treat neuropathic pain in outpatient settings (general practitioners, neurologists, rheumatologists, geriatricians, physiotherapists, and nurses). Therefore, these recommendations do not concern the care provided in pain assessment and treatment facilities.</td>
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<td>[23]</td>
<td>For central neuropathic pain, pregabalin or amitriptyline are recommended as first-line agents. Adjunctive therapies, including cognitive-behavioral therapy and physical therapy, should be included as part of an interdisciplinary approach. Research on the management of HIV-associated painful neuropathy (HIV-SN) in South Africa is needed, as there is a large population of patients with HIV/AIDS and limited positive efficacy data for its treatment.</td>
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<td>[24]</td>
<td>Non-pharmacological management and multimodal pharmacological therapy that target different mechanisms can provide better therapeutic outcomes than isolated interventions. Interdisciplinary management, including rehabilitation interventions, is proposed for the treatment of neuropathic pain.</td>
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stimulation as a therapeutic approach for neuropathic pain that is unresponsive to pharmacological and adjunctive therapies. However, it is recommended that these procedures be performed only in experienced centers.

Psychological aspects should not be underestimated in the management of neuropathic pain. Psychological issues are often encountered, highlighting the impact on the psychosocial sphere and quality of life in a condition that is chronic, disabling, and challenging to manage. Several authors recommend psychological intervention in the management of neuropathic pain. Acevedo et al. [24] also recommend conducting psychosocial assessments at the primary care level for these patients. Martinez et al. [22] and Chetty et al. [23] support psychotherapy, particularly cognitive-behavioral therapy.

There is a broad consensus on the importance of interdisciplinary interventions that target different aspects of neuropathic pain treatment. This includes pharmacological therapy combined with non-pharmacological approaches such as psychotherapy, physical therapies, and physiotherapy [21], [22], [26].

Overall, TENS is widely recommended in the management of neuropathic pain, and both TENS and the aforementioned interventions are typically used as preliminary treatments or in combination with other interventions as part of a multimodal approach. TENS is a non-invasive and safe technique with relatively few contraindications. It is also cost-effective, which is important considering the significant costs associated with neuropathic pain for both the healthcare system and patients. Physiotherapy, either as a standalone therapy or in combination with other interventions, is widely supported by recent scientific literature for the management of neuropathic pain. It plays a crucial role in preventing or reversing changes in nutrition, muscle atrophy, spasms, and deformities, thus preventing overall rigidity. Psychological evaluation, followed by appropriate psychotherapy, is also recommended, as neuropathic pain often leads to various psychological consequences that further impact the patient’s quality of life.

Neuropathic pain has significant consequences not only related to central nervous system injuries but also to subsequent functional impairments. Therefore, the involvement of a specialist focused on managing and restoring functional impairments is necessary. Physiotherapists, who specialize in addressing functional issues associated with the patient’s condition, play a crucial role in meeting this need.

Severe neuropathic pain is challenging to manage effectively, with only a minority of individuals experiencing clinically significant benefits from isolated interventions. Physiotherapists should establish and implement a multidisciplinary intervention, working closely with other healthcare professionals involved in the patient’s management to ensure optimal pain management. Additionally, a comprehensive and holistic approach that addresses the different dimensions affected by neuropathic pain (physical, functional, emotional, social, relational, and work-related) is essential. This approach should be implemented through a personalized intervention that actively involves and engages the patient, aiming to maximize the impact on their health-related quality of life.

5. Conclusion

The present study underscores the importance of adopting an interdisciplinary approach, incorporating both pharmacological and non-pharmacological interventions, in the management of neuropathic pain. Within this interdisciplinary framework, rehabilitation plays a crucial role as a non-pharmacological intervention and should be initiated early in the management of neuropathic pain, working in conjunction with other interventions to achieve optimal outcomes. A comprehensive treatment plan for patients with neuropathic pain should encompass an appropriate physiotherapy program, along with psychotherapy, physical therapy, and pharmacological treatment, addressing the physical, psychological, and social aspects of the condition.

This systematic review highlights the significant role of rehabilitation in the context of the interdisciplinary management of neuropathic pain. However, it also reveals a paucity of evidence regarding various rehabilitation practices for the treatment of this complex condition. Consequently, further research is needed to ascertain the most effective rehabilitation interventions for patients suffering from neuropathic pain.

Conflict of Interest

Authors declare that they do not have any conflict of interest.

References


