

Rehabilitation protocols in neuropathic pain: bibliometric review

Protocolos de reabilitação na dor neuropática: revisão bibliométrica

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ABSTRACT

BACKGROUND AND OBJECTIVES: Neuropathic pain (NP) affects the afferent somatosensory pathways, generating various symptoms, however, there is difficulty in terms of diagnosis and in the formation of treatment protocols. There is a need to search the current literature for effective resources for the treatment of peripheral neuropathy in rehabilitation. The objective of this study was to describe reproducible assessment and treatment approaches capable of reducing NP.

CONTENTS: Full articles produced between 2018 and 2022, found in the Pubmed, Scielo, Medline, Embase and Cochrane databases were included. Fifteen Boolean descriptors were used, and data were cross-referenced with the words “AND” or “OR”. The selected articles went through the *Methodi Ordinatio* of classification and organization of studies. Eleven articles were selected and used in this review, two from 2018, five from 2020, and three from 2021. Regarding the type of study, five review articles, one case study, and six intervention studies were obtained. Of these 11 studies, only three used quality of life (QoL) indicators. Most studies used combined interventions,

and in more than half of the publications transcranial direct current stimulation (tDCS) was present. The somatosensory rehabilitation method was able to redeem neuropathy through specific techniques.

CONCLUSION: The implications of the neuropathic pain treatment in terms of QoL were left in the background by the bibliometric survey carried out. It is suggested that new studies could associate analgesia techniques with rehabilitation methods, including and measuring the effects on the QoL of these patients.

Keywords: Complex regional pain syndrome, Hyperalgia, Physical therapy, Rehabilitation. Transcutaneous electrical nerve stimulation.

RESUMO

JUSTIFICATIVA E OBJETIVOS: A dor neuropática (DN) acomete as vias somatossensoriais aferentes, gerando diversos sintomas, entretanto há dificuldades em termos de diagnóstico e na formação de protocolos de tratamento. Há a necessidade de buscar, na literatura atual, recursos eficazes para o tratamento da neuropatia periférica na área da reabilitação. O objetivo deste estudo foi descrever abordagens reprodutíveis de avaliação e tratamento capazes de diminuir a DN.

CONTEÚDO: Foram incluídos artigos completos produzidos entre os anos de 2018 e 2022, encontrados nos bancos de dados Pubmed, Scielo, Medline, Embase e Cochrane. Foram usados 15 descritores booleanos, e os dados foram cruzados com as palavras “AND” ou “OR”. Os artigos passaram pelo *Methodi Ordinatio* de classificação e organização de estudos. Foram selecionados e utilizados 11 artigos, sendo dois de 2018, cinco de 2020 e três de 2021. Acerca do tipo de estudo, foram obtidos cinco artigos de revisão, um estudo de caso e seis estudos de intervenção. Desses 11 estudos, apenas três utilizaram indicadores de qualidade de vida (QV). A maioria dos estudos utilizou intervenções combinadas, e em mais da metade das publicações a estimulação transcraniana por corrente contínua (ETCC) estava presente. O método de reabilitação somatossensorial foi capaz de redimir a neuropatia por meio de técnicas específicas.

CONCLUSÃO: As implicações do tratamento da dor neuropática no quesito QV ficaram em segundo plano pelo levantamento bibliométrico realizado. Sugere-se que novos estudos possam associar técnicas de analgesia a métodos de reabilitação, incluindo e mensurando os efeitos sobre a QV desses pacientes.

Descritores: Estimulação elétrica nervosa transcutânea, Fisioterapia, Hiperalgia, Síndrome da dor regional, Reabilitação.

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HIGHLIGHTS

- This study sought to find a rehabilitation protocol for neuropathic pain by means of a bibliometric and systematized literature review.
- Few studies have assessed quality of life indicators in patients with neuropathic pain.
- Combined therapies, such as transcranial current stimulation with physiotherapy, seem to have a greater effect on the treatment and reduction of painful symptoms, but there is no specific protocol.
- The Somatosensory Reeducation method was the only resource that reported remission of neuropathic pain, regardless of the degree of involvement.
- Most of the studies found are reproducible, but few address general aspects of the patient, such as the side effects of chronic neuropathic pain and quality of life.

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INTRODUCTION

Neuropathic pain (NP) affects approximately 7% to 10% of the world's population¹ and affects the somatosensory afferent pathways, which can affect the central or peripheral nervous system. The clinical manifestation is complex because in addition to pain there are various associated symptoms and signs¹, including hypoesthesia, allodynia and hyperesthesia. The pain can be described as intense and chronic, and compromises the psychosocial and economic aspects of the people who suffer this type of pain². In addition to the difficulty of diagnosis, NP is difficult to treat, with low effect and low patient satisfaction when compared to pharmacological and non-pharmacological treatments³. There are several studies using drugs to relieve pain, reduce the inflammatory process and asymptomatic, with the aim of alleviating the discomfort of these patients. However, even with the numerous attempts to solve the problem, there is no drug or set of drugs that causes total analgesic effect or provides remission of the disease^{4,5}. Among the non-pharmacological options are physical rehabilitation protocols, conducted by physiotherapists and occupational therapists, with the aim of reducing the intensity of NP, improving sensitivity and providing a return to functional activities⁶. Many reports have been published on the physical approach to NP, but without delving into the psychosocial aspects, since this disease is extremely disabling and chronic, directly interfering in the QoL of this population⁷. There is a need to search the current literature for effective resources for the treatment of NP, to understand the work of the rehabilitation areas, and to access the impact on the QoL of these patients.

The present study's objective was to describe reproducible assessment and treatment approaches capable of treating NP in non-pharmacological ways, by means of a bibliometric review, and to analyze the biopsychosocial factors involved in the rehabilitation process.

CONTENTS

This is a bibliometric literature review, carried out in accordance with the descriptive and evaluative laws for this type of review⁸. There was no need for approval from the Ethics Committee for Research on Human Beings and the Free and Informed Consent Term (FICT), as this study was carried out using data from already published scientific studies.

Full articles produced between 2018 and 2022, published in any language, were included; studies with pharmacological treatment, book publications, experience reports, papers published at conferences, opinion letters, pilot studies or those not yet completed were excluded.

The databases chosen for the search were Pubmed, Scielo, Medline, Embase and Cochrane, with a filter on publication years between 2018 and 2022. The search used 15 descriptors derived from *Neuropathy*; *Allodynia*; *Hypersensitivity/Hyperaesthesia*; *Hypo-sensitivity/Hypoesthesia*; *Somatosensory rehabilitation*; *Neuropathic pain*; *Transcranial direct current stimulation*; *Pain education*; *Biopsychosocial*; *Burning sensation*; *Skin sensitivity*; *Somatosensory*; *Hypersensitivity/Hyperaesthesia*; *Funcionalidade*; *Extraterrito-*

rial neuropathic pain; *Somatosensory*; *Extraterritorial neuropathic pain*; *Transcranial direct current stimulation*; *Peripheral nerves*, combined by the Boolean operators "AND" or "OR". The descriptors used were categorized by: (a) symptoms; (b) evaluation; (c) forms of treatment, totaling 82 descriptors.

(a) The symptom descriptors were: ten on neuropathy, four on hypersensitivity, five on hyposensitivity, seven on peripheral nerves, nine on NP, five on burning sensation, three on extraterritorial NP and five on skin sensitivity;

(b) Descriptors of pain characteristics and functionality: four on biopsychosocial aspects, seven on functionality and five on restriction;

(c) Descriptors for forms of treatment: six on somatosensory rehabilitation, six on transcranial direct current stimulation and six on pain education.

After selecting the articles, those not published between 2018 and 2022 and duplicates were excluded. The selected articles went through the *Methodi Ordinatio* for classifying and organizing studies, according to the references consulted⁹.

RESULTS

Of the 82 Boolean descriptors searched in the five scientific databases, 1870 articles were found, 155 of which were included by title. Articles that were not in line with the research topic were not selected at first. After reviewing the titles of the 155 articles selected, the abstracts were read and a further 51 articles were excluded, leaving 104 (Figure 1).

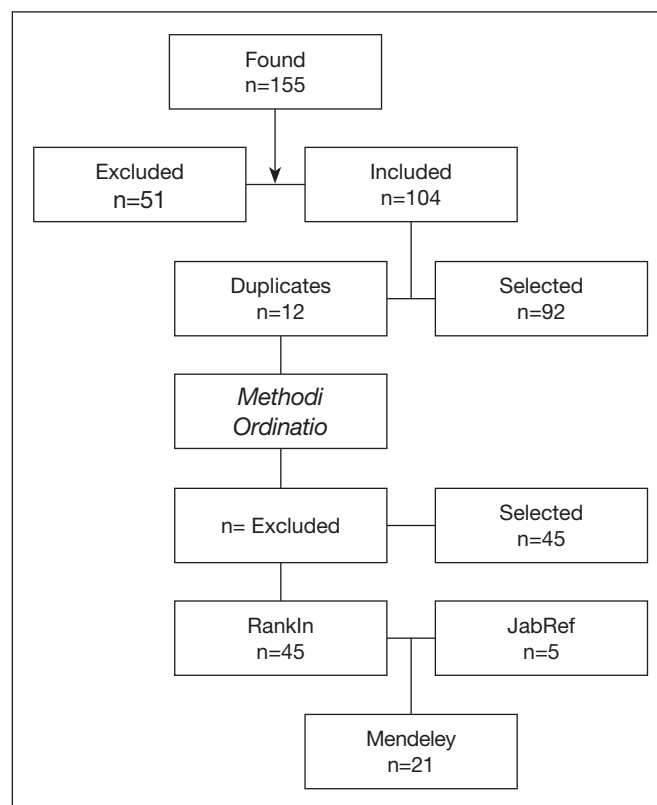


Figure 1. Flowchart of the process of including the articles to be used in this research.

Of the 104 articles selected, duplicates were removed (12 articles), leaving 92 scientific articles. The studies were carefully selected and went through the *Methodi Ordinatio* classification process, sorting the articles by impact factor, number of citations and year of publication. In the first selection phase, of the 92 articles obtained using the Mendeley® software, 21 were excluded, five of which were duplicates, six without author, one without date, six dated before 2018, two without a title and one without a journal. Five articles were excluded from the JabRef software, as two were books, two had no author and one was a duplicate. The Excel RankIn® software excluded 21 articles without ISSN. This resulted in 45 articles suitable for full reading, as shown in figure 2.

After reading all 45 articles, 34 were excluded because they were not in line with the study topic (Attachment 1). The remaining 11 articles were selected and used in this bibliometric literature review. Two articles from 2018, five articles from 2020 and three articles from 2021 were found. Regarding the type of study: four review articles, one case study and six human intervention studies. Of

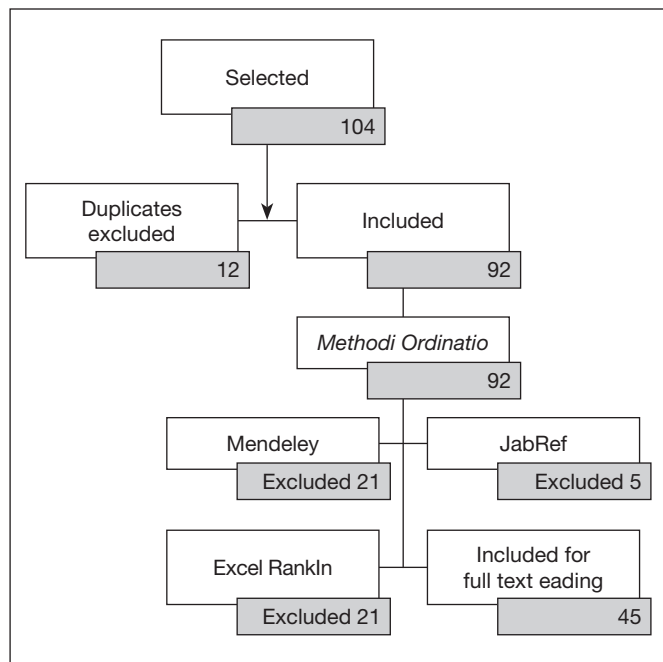


Figure 2. Process of selecting articles according to the *Methodi Ordinatio*.

the 11 studies, three used QoL indicators. Most of the studies used combined interventions (6), and in more than half of the publications transcranial direct current stimulation (tDCS) was present (Table 1).

The resources that proved most effective in relieving pain were tDCS and TENS, combined with each other or with other techniques, such as rTMS and physiotherapy with light, individualized exercises for the treatment of hypoesthesia or hyperesthesia, especially in the area of rehabilitation.

Attachment 1. Excluded articles

Descriptors	Reason	Quantity
Neuropathy	Out of research time	4
	Research not yet completed	2
	Abstract only	4
	Full article unavailable	5
	Disagreement with the theme	3
Hypersensitivity OR Hyperaesthesia	Full article unavailable	1
Hyposensitivity OR Hypoaesthesia	Out of research time	3
	No one was selected	
Somatosensory rehabilitation	Out of research time	5
	Full article unavailable	3
Peripheral nerves	Out of research time	2
	Article release	1
Neuropathic pain	Full article unavailable	1
	Out of research time	1
Transcranial direct current stimulation	Out of research time	1
	Full article unavailable	6
Pain education	Abstract only	3
	Full article unavailable	2
Biopsychosocial Functionality	There were no exclusions	
	There were no exclusions	
Restriction	There were no exclusions	
	Out of research time	1
Burning sensation	Full article unavailable	2
	Abstract only	
Extraterritorial neuropathic pain	No one was selected	
	Full article unavailable	1
Skin sensitivity	System/books (3)/untitled (1)	48
Ordinatio		
Total articles excluded		98
Total articles selected (1)		57

Table 1. Data from the articles found and used in this bibliometric review.

Authors	Type of study	Intervention	Conclusion
O’Neill et.al. ¹¹	Randomized controlled trial	tDCS	Reduction in pain after intervention
Li et.al. ³	Cross-over, blinded, sham-controlled clinical study	tDCS and BreESTim	Reduction in pain after the use of BreESTim
Karpov et al. ²¹	Narrative review	Several approaches	Conventional physiotherapy does not always contribute to complete recovery
Houde and Harvey et al. ¹⁸	Case study	tDCS and TENS	The combination of tDCS and TENS was more effective than the treatment of one technique alone
Ferreira et al. ¹⁵	Controlled, randomized, double-blind pilot study	tDCS + Mirror Therapy	tDCS with Mirror Therapy was more effective than the treatment with one technique alone

Continue...

Table 1. Data from the articles found and used in this bibliometric review – continued

Authors	Type of study	Intervention	Conclusion
Ferreira et al. ²⁶	Controlled, randomized, double-blind pilot study	tDCS	tDCS was effective in improving pain and functionality
Arrate and Branchet ²³	Narrative Review	Somatosensory Reeducation	The Somatosensory Reeducation method brought promising results in the treatment of peripheral neuropathy
Cho and Kim ¹⁹	Narrative Review	Acupuncture	Acupuncture can be considered promising in the treatment of peripheral neuropathy
Xue et al. ²⁰	Narrative Review	Exercises + TENS	Individualized exercises are safe for the treatment of neuropathic pain
Mansor et al. ¹⁰	Randomized controlled trial	tDCS	Application of tDCS reduced body cortisol levels
Bonifácio de Assis et al. ¹³	Randomized controlled clinical trial	rTMS + tDCS	tDCS and rTMS were effective in reducing the pain condition when combined

tDCS = transcranial direct current stimulation; BreEstim = breathing-controlled electrical stimulation; TENS = transcutaneous electrical nerve stimulation; rTMS = repetitive transcranial magnetic stimulation.

DISCUSSION

Although they are a public health problem worldwide and a major challenge for the scientific health community, this review found a few clinical studies on rehabilitation for neuropathic diseases, regardless of their etiology. As far as current knowledge is concerned, there are no more robust reviews of this approach published in the literature, as it is a subject with few established protocols.

This study shows that there is a scientific gap in rehabilitation protocols for NP treatment, despite the suffering and limitations caused to patients. Of the 11 studies found, only two used one technique in isolation, tDCS, and ended their reports by suggesting the association of techniques and a larger sample. However, the other studies presented analgesia techniques associated with other treatment protocols, proving to be more effective than isolated treatments.

It is known that tDCS has been widely used to relieve NP symptoms, with well-defined parameters. The two studies that included tDCS used an intensity of 1.5 and 2mA in a 20-minute session, but in protocols with different time periods. One study² carried out a protocol of 5 consecutive days with periodic evaluations, one week before the start of the protocol, one week after the end and 15 days after the end, showing improvements in physical aspects, pain and functionality. Another study⁶ suggests that the reduction in pain caused by the use of tDCS is due to the reduction in cortisol levels in the body, making it possible to gradually reduce the use of drugs and their adverse effects. In a single application of tDCS there was a significant reduction in cortisol levels ($p < 0.013$), while in the placebo application there was no significant result¹⁰. A relevant aspect to note is the importance of individualizing treatment protocols and their associations, since the responses are different according to each degree of pain and dysfunction.

A group of authors¹¹ carried out a study with tDCS and a placebo group, in which the patients themselves applied the stimulation for five consecutive days over four weeks, 20 minutes a day, at a setting of 1.5mA. The results showed a reduction in pain through pre- and post-intervention tests. Another study¹²

used rTMS or tDCS for 5 consecutive days, in 2 blocks of stimulation separated by an interval of 30 days, totaling 10 days of stimulation. After the evaluations, the results showed a reduction in pain intensity, especially after the fifth session of each block. However, no significant improvements were found in the structure of the nerve, only a transient analgesic effect¹³. Both studies reported on the efficiency of tDCS or rTMS in patients with neuropathies, but mentioned that the technique alone is not as beneficial as in combination, demonstrating that combined therapies, such as tDCS with physiotherapy, seem to have a greater effect on the treatment and reduction of painful symptoms, but without a specific protocol.

As in the study¹¹, another study used tDCS associated with another technique, in this case mirror therapy (MT)¹⁴, showing that despite the same tendency to respond with an analgesic effect, there was a greater benefit for the group that associated tDCS with MT than for the group that used placebo tDCS, with a permanent result at follow-up 3 months after the end of treatment¹⁵. Some authors¹⁶ used a protocol with a similar study design, but the result was different due to the number of participants. The participants themselves controlled the intensity of tDCS with a stimulator that works through breathing, aided by a face mask (Breathing-Controlled Electrical Stimulation - BreEStim). Each application lasted 20 minutes, with a three-day break in between. Airflow was measured through surface electrodes up to the median nerve in real time, and the intensity was gradually increased according to tolerance. All the participants (10 individuals) tolerated the protocol well and all showed a reduction in pain immediately after using BreEStim, but there was no difference when associated with tDCS. The authors justify this negative result with the association of tDCS because only two patients participated until the end of the protocol¹⁶.

A case study of a patient with complex regional pain syndrome^{17,18} received one tDCS session a day for 5 consecutive days in isolation, with no reduction in pain. Afterwards, the patient received the same tDCS protocol combined with low-frequency TENS (3Hz, 400us) for 25 minutes. The second protocol, with the association, was more effective than the first, with pain

reduction continuing for nine days. However, on the Visual Analog Scale (VAS), the patient reported a minimum pain of 3 (3/10), not achieving complete analgesia. The authors suggested further studies to confirm the hypothesis that the associated techniques cause analgesia for patients with NP¹⁸. It was clear from these protocols using tDCS that few studies have assessed QoL indicators in patients with NP. Their main objectives were based on pain relief and mobility.

TENS used in acupuncture settings can adjust conduction and relieve the clinical symptoms of patients with neuropathy. A narrative review evaluated the effects of acupuncture on diabetic neuropathy in animal and human models⁴, with the aim of observing whether Chinese medicine outperforms Western medicine in its treatment. The results show that acupuncture can be considered an effective and promising treatment method for diabetic neuropathy. Acupuncture and moxibustion can accelerate microcirculation and reduce neural hypoxia, but the authors suggest more extensive studies for more conclusive results¹⁹.

TENS associated with physiotherapy exercises is part of the treatment for peripheral neuropathy, but little is known about which exercises to perform and how effective they are. One study²⁰ carried out a TENS-associated exercise protocol associated with aerobic exercises and exercises without resistance, to avoid exacerbation of pain. The authors used acupuncture parameters for its application (2 Hz and 200 ms), as they are within safe limits and do not present adverse effects. Individualized exercises are safe for patients with NP.

According to one study²¹, physiotherapy for the treatment of neuropathy is often carried out with the affected limb immersed in water. The exercises were carried out at minimum amplitude and at a slow pace in order to avoid exacerbating the pain, with an initial duration of 5 to 7 minutes, which could be extended to 10 to 15 minutes. Its treatment protocol for hand injuries consisted of immersing the injured hand in water, then instructing the patient to carefully lift one finger at a time and then perform circular movements. Other resources can be associated with the exercises, such as iontophoresis, phonophoresis, magnetic therapy, acupuncture, high frequency, use of pulsed current, therapeutic mud or electrostimulation adjacent to the injury site. However, the authors pointed out that conventional physiotherapy does not always contribute to a complete recovery from neuropathy²². Most of the studies found were reproducible, but few addressed general aspects of the patient, such as the side effects of chronic NP and QoL.

The somatosensory re-education method was the only treatment report that showed a reduction in neuropathy symptoms, meeting all five classifications of the disease. This method was able to rehabilitate patients from hypoesthesia to CRPS, using specific techniques for each level. In this sense, the somatosensory re-education method showed promising results³, as it provided treatment for all five types of neuropathy, from hypoesthesia to CRPS²³. A 2020 study presented a rehabilitation protocol for hypoesthesia, in which the patient performed the “connect the dots” exercise with a pencil. The patient, blindfolded, felt the movement that a third person made with a pencil in the hypoesthetic territory. The exercise was performed four

times a day for five minutes. Afterwards, the patient could move on to the “touch everything” technique, with the aim of sharpening the perception of different textures and comparing it with the healthy limb. This exercise could be performed four times a day for five minutes.

In addition to the techniques described above, vibratory stimulation can be used to stimulate the hypoesthetic area, with a frequency of between 30 and 120 Hz, without causing pain²⁴. Vibrotactile counter-stimulation is used to treat static mechanical allodynia. Unlike the techniques for rehabilitating hypoesthesia, the treatment of allodynia aims to find the area of skin to be avoided in order to reverse the pain. In these cases, a “no touch” prescription may be recommended, so that this area of skin has as little contact as possible with the external environment. A multidisciplinary team is recommended to cover all the patient’s biopsychosocial aspects affected by the primary physical injury²⁵. Articles on non-pharmacological treatment in the field of physiotherapy need to focus on the patient as a whole, covering the biopsychosocial context, QoL, levels of physical activity and treatment costs. Only three studies looked at these aspects, demonstrating how important this global, often multidisciplinary approach is for reintegrating patients into the social context^{11,15,26}.

Patients with nerve injuries have many difficulties in their daily lives, as pain often prevents them from carrying out many activities. The biopsychosocial aspects surrounding this type of injury are an extremely important issue. There is a need to check whether the treatment techniques used can improve the QoL of each patient. One study¹¹ addressed some of these aspects during its evaluations¹, using the SF-36 QoL questionnaire to observe secondary results, along with an assessment of physical fitness levels. It was observed that the use of tDCS, as well as benefiting physical issues, helped to improve the functional capacity and QoL of patients with diabetic polyneuropathy. The authors also suggested that further studies should look at the social and emotional context of the participants, in addition to QoL.

The Beck Depression Inventory is a test widely used to assess factors that affect the biopsychosocial context in various diseases. One study²⁶ used a structured questionnaire including demographic data, characteristics of the injury, affected side, severity of pain, symptoms of depression and anxiety, as well as VAS and the McGill questionnaire to qualify pain. The State-Trait Anxiety Inventory was also used to measure two different components of anxiety, state and mood traits. Their treatment protocol used a combination of tDCS and MT. In addition to the questionnaires described, the authors used the SF-36 QoL questionnaire to measure their results, thus covering the patient as a whole.

The third study that assessed QoL² used, like the other studies, the SF-36 QoL questionnaire to assess lifestyle habits and physical activity. Five sessions of tDCS induced improvements in physical health, body pain, physical functions and functional capacity in patients with diabetic polyneuropathy²⁶.

As limitations, few studies were found focusing on QoL and the biopsychosocial aspects evaluated in NP interventions, summarizing the results in combined therapies focused on the

physical and structural aspects of the body. Most of the studies found were reproducible, but few addressed aspects such as the secondary effects of chronic NP and QoL.

CONCLUSION

The literature review shows that tDCS is an effective technique for analgesic control when combined with other types of treatment. With regard to rehabilitation, the somatosensory rehabilitation method was the only one capable of reducing the symptoms of neuropathy using specific techniques. These are two resources that are easy to acquire and apply, reproducible and inexpensive.

In general, the studies were not clear enough to solve the research question, and the patients' QoL took a back seat. It is suggested that new studies associate analgesia techniques with treatment methods for the rehabilitation of neuropathy, focusing on the effects on patients' QoL.

AUTHORS' CONTRIBUTIONS

Jessika Mehret Fiusa

Statistical Analysis, Data Collection, Project Management, Research, Methodology, Writing - Preparation of the Original, Software

Sibele de Andrade Melo Knaut

Conceptualization, Project Management, Writing - Review and Editing, Supervision, Validation

Emerson Carraro

Conceptualization, Resource Management, Project Management, Methodology, Writing - Review and Editing, Supervision, Validation

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