Dorsal root ganglion stimulation in the treatment of complex regional pain syndrome, following a spinal cord injury

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ABSTRACT

Complex regional pain syndrome is a chronic pain condition that presents symptoms from the autonomous nervous system, as well as motor and sensory disturbances. Thus, because of the complexity of its symptoms, it becomes difficult to find the appropriate treatment for this syndrome.

The aim of this thesis, is to examine the effectiveness of dorsal root ganglion stimulation as a treatment for complex regional pain syndrome, following a spinal cord injury. The research strategy, for the identification of the relevant literature, included data retrieved from articles in English, from Greek and foreign bibliography, as well as from internet sources. The results showed great effectiveness for dorsal root ganglion stimulation, in comparison with other conventional treatments. According to several studies, significant improvement was observed in the fields of patients' pain relief and mood and quality of life, while excellent pain-paresthesia overlap was reported. Furthermore, due to the unique anatomical position of the dorsal root ganglion, no lead migrations or differences in paresthesia's intensity -due to postural changes- were reported. In addition, according to long-term outcomes, therapy habituation did not occur in patients that had dorsal root ganglion stimulation treatment and as a result, there was no loss of the therapeutic effect over time. Thus, dorsal root ganglion stimulation for complex regional pain syndrome following a spinal cord injury, is estimated to be beneficial. Nevertheless, more research is needed in order to receive more accurate results.

Key words: dorsal root ganglion stimulation, complex regional pain syndrome, spinal cord injury, spinal cord stimulation

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VOLUME 74 | ISSUE 2 | APRIL - JUNE 2023

Introduction

Complex regional pain syndrome (CRPS) is a pain disorder that usually occurs after a surgery, an injury or a vascular accident. It is a chronic and progressive condition that involves the extremities and patients may experience vascular, sensorimotor and trophic changes [1,2]. According to the International Association for the Study of Pain (IASP), there are two types of CRPS: (a) CRPS type I (also known as Reflex Sympathetic Dystrophy or RSD) and (b) CRPS type II (also known as causalgia) [3]. The most common symptoms of this pain syndrome include hyperesthesia and allodynia, however patients can also experience changes in skin temperature and color, sweating, swelling of the affected area, muscle atrophy and decreased range of motion of the affected joints [4]. The clinical diagnostic criteria for CRPS (Budapest criteria), have recently been revised. These criteria describe CRPS as "an array of painful conditions that are characterized by a continuing regional pain that is seemingly disproportionate in time or degree to the usual course of any known trauma or other lesion. The pain is regional and usually has a distal predominance of abnormal sensory, motor, sudomotor, vasomotor, and/or trophic findings. The syndrome shows variable progression over time [5]. Establishing a treatment for CRPS that has both efficacy and long-term outcome, is difficult [6]. However, there is evidence that that early treatment may lead to improved results [7]. Therapies for both types of CRPS focus on pain relief, improvement of function of the affected extremity, decreased edema and increased range of motion of the affected joints [8].

Spinal cord stimulation (SCS) is considered to be a therapeutic option for the treatment of chronic pain, thus it is used for the treatment of CRPS when other treatments have failed. SCS has been successfully applied since 1967, for treating chronic pain in the trunk and limbs [9]. The neurostimulation system that is used, consists of stimulation leads implanted near the spinal cord and a pulse generator that produces electrical stimulation pulses [10,11]. Despite the benefits of this therapy, there are limitations and deficiencies, including changes in the intensity of stimulation due to posture related changes, lead migration and therapy habituation [12-14]. Furthermore, SCS seems not to cover completely some painful areas such as low back, groin, pelvis, buttocks and neck [15]. As a result, different neurostimulation techniques needed to be found.

Neuromodulation of the dorsal root ganglion (DRG) is an alternative treatment targeting the exact anatomical area that has been affected by CRPS and is difficult to be approached with any other traditional treatment [16]. The DRG is located within the spinal foramen in the lateral epidural space and houses the cell bodies of the primary sensory neurons, which are responsible for modulating sensory information and transferring it to the spinal cord. There are several types of DRG neurons, categorized by their size and function [17]. Recent studies have shown that DRG stimulation is safe and effective even for patients that in the past had a SCS treatment that failed [18]. In addition, DRG stimulation seems to cover in great extent the area of paresthesia and leads to pain relief, without the danger of lead migration or changes related to the intensity of stimulation because of patient's postural changes [19].

A review of the current literature was performed by using the online PUBMED, COCHRANE and PEDro database and the following keywords: dorsal root ganglion stimulation, complex regional pain syndrome, spinal cord injury, spinal cord stimulation. Inclusion criteria included: (a) date of publication, later than 2000 (b) subjects diagnosed with complex regional pain syndrome following a spinal cord injury, (c) mental state ensuring cooperation during the performance of tests.

Discussion

The search resulted in 25 studies. After checking titles and summaries, 11 articles were rejected as irrelevant to the subject. Of the 14 remaining publications, 5 were rejected due to specific reasons. After reviewing the reference lists of the included studies, 9 more studies were included. Finally, there were 18 studies included in the present review (Figure 1).

The role of dorsal root ganglion stimulation in the

VOLUME 74 | ISSUE 2 | APRIL - JUNE 2023

treatment of CRPS

In a prospective study, Elliot S. Krames changed the common opinion that the DRG is not involved in the development of neuropathic pain. Instead, he proved that it is not only involved in the development of neuropathic pain, but also affects the process of chronicity, from acute to chronic pain [20]. Huygen et al., in 2019, evaluated the effects of dorsal root ganglion stimulation in 49 patients with CRPS type I or in patients with failed back surgery syndrome (FBSS) followed by CRPS type II. According to the results, patients with CRPS type II had an 43.7% average reduction of pain at 12 months post-implant, with 60% of them reporting a 50% pain relief, using the visual analog pain scale (VAS). Patients with CRPS type I, had an 46.8% average reduction of pain, with 33.3% of them reporting 50% pain relief. In addition, there was improvement in subjects' quality of life, as well as in their total mood disturbance [21]. In 2014, Long Liem et al., trialed a DRG-SCS device in 51 patients and examined its effectiveness in pain relief, using the VAS and the Brief Pain Inventory (BPI) scales and in the quality of life and mood of the subjects, using the questionnaires: EQ-5D-3L, Profile of Mood States (POMS) and the McGill Pain Questionnaire. The subjects also captured their pain and paresthesia distributions on body maps. Between baseline and the 12-month follow-up, overall pain was reduced by 56%, while pain localized to the legs, feet and back was reduced by 62%, 80% and 42%, respectively. Also, sixty per cent of patients reported more than 50% improvement in their pain. Furthermore, subjects reported high levels of satisfaction related to the results of their treatment and benefits in mood and quality of life. It is noteworthy that the coverage of pain-paresthesia area was precise and remained stable during those 12 months of the study [22].

Comparison of DRG stimulation and SCS

Timothy R. Deer et al., in 2017, directly compared the safety and efficacy of DRGS and SCS for CRPS and causalgia. At the primary end point, patients using DRG stimulation had a higher score related to treatment success (81.25%), compared to the corresponding score of traditional SCS (55.7%), while the same score at the 12-month follow-up was 74.2% for the DRG team and 53% for the SCS team. In addition, the DRG team reported a minimum change, related to the intense of paresthesia due to postural changes of the subjects, rating of 0.1±1.6, while the SCS team had a mean difference of 1.8 ± 3.0 between supine and upright intensity of paresthesia. Both groups reported improvements in SF-36 scores, but DRG patients improved even more on the physical component score, general health and social functioning, compared with SCS patients. Last but not least, at 12-month follow-up, 94.5% of the patients in DRG group, reported that they felt paresthesia only in their painful area, in contrast with 61.2% of the patients in SCS group [23]. Another comparison between DRG stimulation and SCS took place in 2019, when Robert M. Levy et al., compared therapy habituation among these two techniques, in patients with CRPS I or II. For both groups, mean percentage of pain relief (PPR) was greater at the end of the trial period than all the other follow-ups (DRG=82.2% and SCS=77.7%). After the permanent DRG system implantation, there were not significant differences on this percentage during the 12 months of the study (PPR range= 69.3-73.9%). On the other hand, PPR for SCS team at 1 month was 66.9%, while at 9 and 12 month was 58.3% and 57.9%, respectively. Furthermore, the percentage of subjects reported at least 50% pain relief from baseline, was for both teams highest after the end of the trial period (DRG=89% and SCS=86.1%). This responder rate decreased to 74% at 1 month for the DRG group, but remained stable for the rest of the study. On the contrary, for the SCS group, this percentage continues to decline, reaching 61.1% at 12 months [24].

Safety of DRG stimulation

Regarding the safety of DRG stimulation, Deer et al. in 2013, mentioned 17 events during their study. Three of them were considered as adverse events and involved pain increase after the procedure of implantation, while the other complications were related to lead migration, device inactivation and reactions to antibiotics [25]. 86 safety events were

VOLUME 74 | ISSUE 2 | APRIL - JUNE 2023

reported by Liam et al. in 2014, half of them related to the device, such us lead migration and fracture or temporary motor stimulation [22]. In their study, Deer et al. compared the safety between DRG stimulation and SCS. The results showed that patients of the DRG team had a higher rate of adverse events (46.1%), than the patients of the SCS team (26.3%). This might be due to longer operative times in DRG stimulation team, than in the SCS team [23].

The results of using dorsal root ganglion stimulation as a treatment in CRPS patients are encouraging. However, evidence of long term results and effectiveness of this treatment is lacking.

Conflict of Interest

The authors declared no conflicts of interest.

REFERENCES

1. Stanton–Hicks M, Janig W, Hassenbusch S, et al. Reflex sympathetic dystrophy: changing concepts and taxonomy. Pain. 1995;63:127-33.
2. van Eijs F, Stanton-Hicks M, Van Zundert J, et al. Complex regional pain syndrome. Pain Pract. 2010;11:70-87.
3. International Association for the Study of Pain (IASP). Classification of Chronic Pain: Descriptions of Chronic Pain Syndromes and Definitions of Pain Terms, 2nd ed. (Revised). Washington DC: IASP Press;1994.
4. Veldman PH, Reynen HM, Arntz IE, et al. Signs and symptoms of reflex sympathetic dystrophy: prospective study of 829 patients. Lancet 1993;342:1012-16.
5. Harden RN, Bruehl S, Stanton-Hicks M, et al. Proposed new diagnostic criteria for complex regional pain syndrome. Pain Med. 2007;8:326-31.
6. Levy RM. Evidence-based review of neuromodulation for complex regional syndrome: a conflict between faith and science? Neuromodulation 2012;15:501-506.
7. Harden RN, Oaklander AL, Burton AW, et al. Complex regional pain syndrome: Practical diagnostic and treatment guidelines, 4th edition. Pain Med. 2013;14:180-229.
8. Harden RH, Bruehl S, Perez RSGM, et al. Development of a severity score for CRPS. Pain. 2010;151:870-76.
9. Shealy CN, Mortimer JT, Reswick JB. Electrical inhibition of pain by stimulation of the dorsal columns: preliminary clinical report. Anesth Analg. 1967;46:489-91.
10. Kemler MA, Barendse GA, van Kleef M, et al. Spinal cord stimulation in patients with chronic reflex sympathetic dystrophy. N Engl J Med 2000;343:618-24.
11. van Eijs F, Stanton-Hicks M, Van Zundert J, et al. Evidence-based interventional pain medicine according to clinical diagnoses. 16. Complex regional pain syndrome. Pain Pract 2011;11:70-87.
12. Deer TR, Pope J, Hayek S, et al. Neurostimulation for the treatment of axial back pain: a review of mechanisms, techniques, outcomes, and future advances. Neuromodulation 2014;17(suppl 2):52-68.
13. Liem L, Russo M, Huygen FJPM, et al. A multicenter, prospective trial to assess the safety and performance of the spinal modulation dorsal root ganglion neurostimulator system in the treatment of chronic pain. Neuromodulation 2013;16:471-82.
14. Atkinson L, Sundaraj SR, Brooker C, et al. Recommendations for patient selection in spinal cord stimulation. J Clin Neurosci 2011;18:1295-302.
15. Stuart RM, Winfree CJ. Neurostimulation techniques for painful peripheral nerve disorders. Neurosurg Clin N Am. 2009;20:111-20.
16. Krames ES. The dorsal root ganglion in chronic pain and as a target for neuromodulation: a review. Neuromodulation 2015;18:24-32.
17. Kishi M, Tanabe J, Schmelzer JD, et al. Morphometry of dorsal root ganglion in chronic experimental diabetic neuropathy. Diabetes 2002;51:819-24.
18. Ajax Yang, Corey W, Hunter. Dorsal root ganglion stimulation as a salvage treatment for complex regional pain syndrome refractory to dorsal column spinal cord stimulation: A case series. Neuromodulation 2017;20(7):703-07.
19. Alo KM, Yland MJ, Redko V, et al. Lumbar and sacral nerve root stimulation (NRS) in the treatment of chronic

VOLUME 74 | ISSUE 2 | APRIL - JUNE 2023

pain: a novel anatomic approach and neuro stimulation technique. Neuromodulation 1999;2:23-31.

20. Elliot S Krames. The role of the dorsal root ganglion in the development of neuropathic pain. Pain Medicine 2014;15:1669-85.
21. Frank JPM Huygen, Liong Liem, Harold Nijhuis, et al. Evaluating dorsal root ganglion stimulation in a prospective Dutch cohort. Neuromodulation 2019;22(1):80-6.
22. Liong Liem, Marc Russo, Frank JPM Huygen, et al. One-year outcomes of spinal cord stimulation of the dorsal root ganglion in the treatment of chronic neuropathic pain. Neuromodulation 2015;18(1):41-9.
23. Deer TR, Vevy RM, Kramer J, et al. Dorsal root ganglion stimulation yielded higher treatment success rate for CRPS and causalgia at 3 and 12 months: a randomized comparative trial. Pain 2017;158:669-681.
24. Robert M Levy, Nagy Mekhail, Jeffrey Kramer, et al. Therapy habituation at 12 months: spinal cord stimulation versus dorsal root ganglion stimulation for complex regional pain syndrome type I and II. J Pain.2020;21(3-4):399-408.
25. Deer TR, Grigsby E, Weiner RL, et al. A prospective study of dorsal root ganglion stimulation for the relief of chronic pain. Neuromodulation 2013;16:67-72.

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