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CASE SERIES

Spinal Cord Stimulation for Central Neuropathic Pain After Spinal Cord Injury: A Single-Center Case Series

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Purpose: Central neuropathic pain (CNP) following spinal cord injury (SCI) presents a formidable therapeutic challenge, affecting over 50% of the patients post-SCI. For those who experience CNP, conventional treatments often prove insufficient. Spinal cord stimulation (SCS) emerges as a potential intervention for chronic pain after SCI that is unresponsive to pharmacotherapy and supportive measures. However, the efficacy of SCS in alleviating CNP is notably limited. The objective of our study was to evaluate novel stimulation paradigms in SCS for patients with severe CNP after SCI, based on our extensive experience.

Patients and Methods: From a pool of 112 patients treated with SCS for chronic neuropathic pain in the Department of Neurosurgery and Neurology, we selected eight individuals (4 males and 4 females) with CNP for our case series. Burst and high frequency SCS was applied. The assessment involved utilizing the Numeric Rating Scale (NRS), the Neuropathic Pain Symptom Inventory (NPSI), and the EQ-5D quality of life scale before surgery and during a 12-month follow-up period.

Results: Over the course of the one-year follow-up, only two patients experienced satisfactory relief from pain, demonstrating the effectiveness of the stimulation. Moreover, high-frequency and burst SCS failed to show improvement in the remaining six patients.

Conclusion: Our findings suggest that, despite the incorporation of new stimulation paradigms such as burst stimulation and high-frequency stimulation, SCS does not exhibit significant effectiveness in treating neuropathic pain in patients after SCI. These findings highlight the ongoing challenge of treating CNP and emphasize the importance of investigating alternative therapeutic strategies for this group.

Keywords: spinal cord stimulation, central neuropathic pain, spinal cord injury, burst stimulation, high-frequency stimulation

Introduction

Central neuropathic pain (CNP) following spinal cord injury (SCI) is one of the most challenging types of pain to manage. Approximately more than half of patients after SCI endure chronic neuropathic pain.[1–3] Severe chronic pain significantly impacts patients' quality of life. Furthermore, chronic pain after SCI is often unresponsive to conventional treatments and proves challenging to manage.[3,4] Spinal cord stimulation (SCS) can be applied in cases of chronic pain after SCI that is refractory to pharmacotherapy and supportive treatments. However, the effectiveness of SCS in alleviating pain after SCI is limited. There is a scarcity of studies and a lack of clinical trials assessing the effectiveness of SCS in SCI pain.[5] Since the initial use of SCS for post-SCI pain treatment, there have been no randomized controlled trials examining the efficacy of this intervention.[6] A recent systematic review by Dombovy-Johnson et al included 69 patients treated with SCS for chronic neuropathic pain after SCI, categorizing the evidence as low quality based on GRADE criteria[7]. No case series of patients with CNP after SCI was treated with high frequency or burst SCS were reported. The objective of our study was to describe the effectiveness of novel stimulation paradigms in SCS for patients with severe CNP after SCI, based on our extensive experience.

Material and Methods

From a pool of 112 patients treated with SCS for chronic neuropathic pain, mostly related to persistent spinal pain syndrome (PSPS) and complex regional pain syndrome (CRPS), we selected eight individuals (4 males and 4 females) with CNP caused by SCI for our case series. Burst and high frequency SCS was applied (Figure 1). In six patients, the

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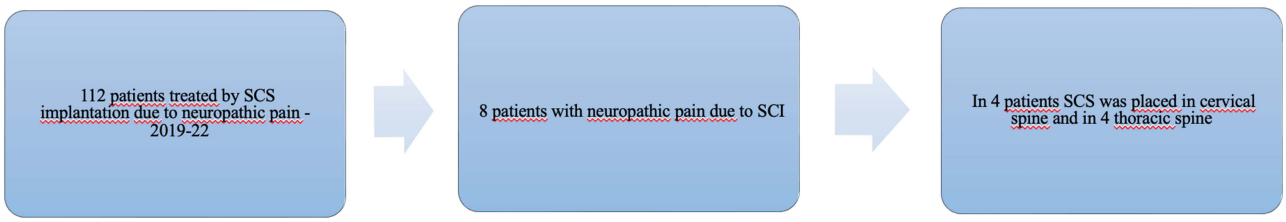

Figure 1 Number of patients with chronic neuropathic pain treated in the Department of Neurosurgery and Neurology in University Hospital Nr 2 in Bydgoszcz.

pain's pathophysiology was associated with traumatic SCI, while in the remaining two, it resulted from stroke. Level of SCI in four patients was located in the cervical spinal cord, in the other three in the thoracic spinal cord, and in the other two in the spinal conus medullaris. Table 1 presents characteristics of patients.

Clinical Findings

All patients were suffering from severe, permanent pain with neuropathic features comprising trunk and extremities. In one patient, complete tetraplegia, in the other five, lower extremities paraparesis was diagnosed. Two patients had no motor deficits.

Patient perspective and informed consent

Each patient was informed about the study details and provided written informed consent. The study adhered to the rules of the Helsinki Declaration and met the requirements of the local ethics committee (Permission Nr. 629/2018, Bioethics Committee of the Nicolaus Copernicus University in Bydgoszcz).

Timeline

We retrospectively assessed the efficacy of SCS with new stimulation paradigms in eight patients (six males and two females) hospitalized between 2019 and 2022 in the Department of Neurosurgery and Neurology at Jan Biziel University Hospital No. 2 in Bydgoszcz, Poland. The median age was 41.25 years, ranging from 20 to 62 years. The median pain duration was 8 years, ranging from 2 to 23 years.

Diagnostic Assessment

We evaluated pain using the Numeric Rating Scale (NRS) and Neuropathic Pain Symptom Inventory (NPSI), quality of life using the EQ-5D questionnaire, and the quantity of medications taken before SCS surgery.

Table 1 Patients' Characteristics

ID	Sex	Age	Injury Level	Time Since Injury in Years	Pain Area	Motor Deficit
ZD	F	20	Injury C6/C7	3	Upper limbs	None ASIA E
MB	M	42	Injury C4/C5	8	Trunk, limbs	Tetraparesis ASIA A
KS	M	42	Injury C5/C6	23	Trunk, lower limbs	Paraparesis ASIA B
SI	M	62	Injury Th4/5	6	Trunk, upper limbs	Paraparesis ASIA B
ML	F	35	Injury L1/L2	4	Right leg, lumbo-sacral area	Paraparesis ASIA D
AA	F	43	Stroke Th10/11	5	Lower limbs, lumbo-sacral area	Paraparesis ASIA C
AS	F	41	Stroke C2/C3	2	Right side of the body	None ASIA E
DG	M	45	Injury Th6/Th7	8	Upper trunk	Paraparesis ASIA A

Therapeutic Intervention

Electrode leads were implanted in the cervical area in four cases (Figure 2) and in the thoracic area in four other cases (Figure 3). In six cases, surgery was performed under general anesthesia, and surgical plate electrodes were epidurally

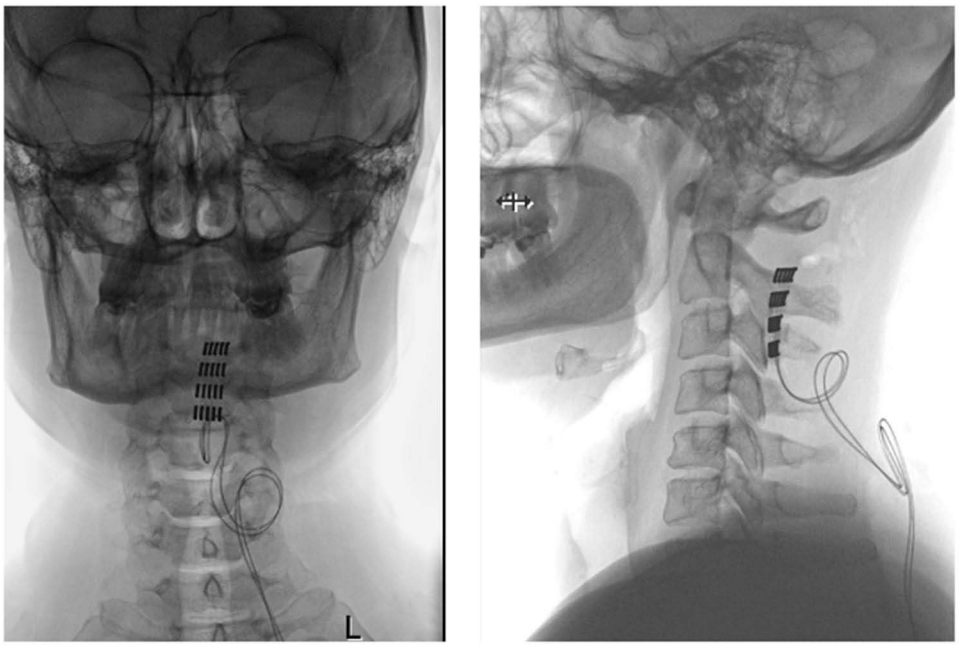

Figure 2 20-contact electrode (PENTA™) by Abbott Co. USA placed on cervical segment in a female patient after the post-stroke myelopathy with significant pain relief over 50% after Burst SCS.

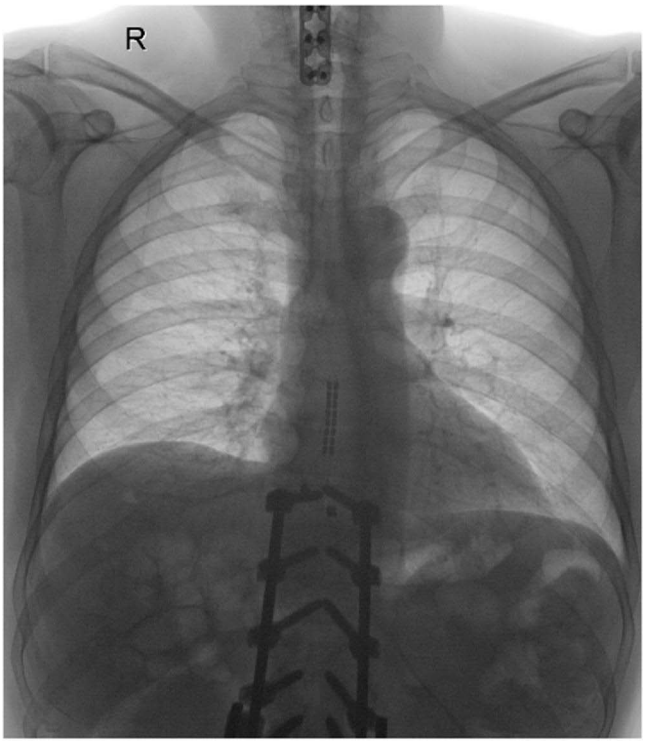

Figure 3 2×8 electrode plate (Artisan™) by Boston Scientific, Massachusetts, USA implanted in a surgical way in a male-patient after traumatic SCI on Th12 level. 1.2kHz SCS without improvement.

inserted above the level of the SCI. Percutaneous SCS implantation was not feasible in cases of high-level spinal cord injury, particularly in the cervical and thoracic regions, or in the presence of post-traumatic or post-surgical scars in the spinal canal. In these situations, an open surgical approach was applied. In two cases, surgery was performed under local anesthesia, involving percutaneous electrode implantation under fluoroscopic control. An external pulse generator was connected, and a two-week trial stimulation was conducted. In the surgical method, following successful electrode implantation and connection to the pulse generator, the generator was placed in a subcutaneous pocket located in the subcostal area in one-stage surgery, and no trial stimulation was performed. Following electrode implantation, patients received subperceptional stimulation, either in burst or at 1.2 kHz frequencies. This was because most of them did not experience paresthesia, except for two patients who reported sensation during intraoperative testing in percutaneous procedure. We implemented new stimulation paradigms based on burst stimulation in four cases and high-frequency stimulation in the remaining four cases. Burst stimulation consisted of intermittent packets of high-frequency stimuli in a 40-Hz burst mode, with five spikes at 500 Hz per burst, a pulse width of 1 ms, and 1-ms interspike intervals delivered in constant current mode.[8] High-frequency stimulation was programmed with a frequency (f) of 1.2 kHz, pulse width (PW) of 120–800 μs, and amplitude of 1–6 Amp. The 1.2 kHz stimulation was below the perceptual threshold. Patients receiving high-frequency stimulation were provided with a non-rechargeable IPG (Precision Novi^{TM}) manufactured by Boston Scientific Co., Massachusetts, USA, and a surgical paddle electrode (Artisan^{TM}) or linear 3–4 electrode. Patients undergoing burst stimulation received a surgical paddle electrode (PENTA^{TM}) and an IPG (internal pulse generator) (Proclaim^{TM}) by Abbott Co., Austin, USA.

Follow-Up and Outcomes

We assessed the efficacy of SCS with new stimulation paradigms in eight patients (six males and two females) for a period of 12 months. We evaluated pain using the Numeric Rating Scale (NRS) and Neuropathic Pain Symptom Inventory (NPSI), quality of life using the EQ-5D questionnaire, and the quantity of medications taken during the 1 year after implantation.

Results

Stimulation demonstrated effectiveness in only two patients, leading to a reduction in pain on the NRS scale by more than 50%. These two patients, showcasing preserved motor and sensory function, exhibited satisfactory results with SCS using burst and a 1.2kHz waveform. Detailed results are presented in Table 2.

Discussion

The primary finding of our study confirms the thesis that SCS, in general, is an ineffective method for treating chronic neuropathic pain after SCI. SCS may not be effective in complete SCI when paraplegia is present.[9] Mechanism of action of conventional SCS is based on segmental spinal inhibition, activation of descending inhibitory system, and cortical

Table 2 Results of the Intervention

ID	Level	Brand	Lead	Mode	Impl	NRS	NRS 1Y	NPSI B	NPSI1Y	EQ-5DB	EQ-5D 1Y	Imp
ZD	C4-C6	Boston Scientific	Artisan	1,2KHz	Open	7	3	30	20	12	8	**60%**
MB	C3-C4	Abbott Proclaim	Penta	Burst	Open	10	10	87	90	15	15	0%
KS	C2-C3	Abbott Proclaim	Penta	Burst	Open	10	9	90	89	14	14	10%
SI	Th4	Boston Scientific	Linear 1x8	1,2kHz	Percut	8	8	45	45	13	13	0%
ML	Th8	Boston Scientific	Artisan	1,2 kHz	Open	7	7	25	23	10	9	0%
AA	Th8	Boston Scientific	Linear 1x8	1,2KHz	Percut	10	10	40	43	11	9	0%
AS	C2	Abbott Proclaim	Penta	Burst	Open	9	4	23	12	10	8	**55%**
DG	Th4	Abbott Proclaim	Penta	Burst	Open	7	6	21	19	11	11	10%

Abbreviations: SCI, spinal cord injury; SCS, spinal cord stimulation; CNP, central neuropathic pain.

modulation.[5] Since the SCS modulate ascending medial and lateral pathways as well as descending nociceptive inhibitory pathways, which are responsible for supraspinal analgesic mechanism of SCS, interruption of transmission on level of injury can alternate this mechanism.[10] Electrodes are placed epidurally and cranially in the damaged area of the spinal cord. Therefore, when the damage is incomplete, and residual afferent tracts are preserved, stimuli induced by SCS can be transmitted and can inhibit perception of pain. Conventional dorsal cord stimulation in patients with neuropathic pain after SCI usually failed to improve clinical state in complete SCI, in one-third of patients with incomplete SCI, it was helpful.[11] In a study on predictors of SCS effectiveness in different types of pain, Kumar et al observed that all cases with incomplete paraplegia and pain below the level of the lesion demonstrated satisfactory pain relief, whereas patients with complete paraplegia showed no benefit from SCS.[12] New hope was connected with the introduction of new paradigms of SCS, such as high-frequency stimulation or de Ridder's burst stimulation.[8] Several randomized controlled studies supported the efficacy of modern SCS modes in neuropathic pain in failed back surgery syndrome (FBSS)-PSPS and CRPS.[13–16] Singular case reports present successful treatment of neurogenic pain with the application of one of the new paradigms of SCS-Burst stimulation with two eight-pole electrode leads.[17] The 10kHz stimulation might induce greater neural inhibition directly, potentially resulting in pain alleviation, particularly when the leads are positioned above the level of injury. However, it is important to note that this approach was not utilized in the study under consideration.[14]

The authors obtained satisfactory results with the electrode placed below the level of injury, which is remarkable. The authors concluded that the residual function of the spinothalamic tract (STT) might be responsible for the positive effects of SCS although SCI was complete and STT was damaged. In another case report of CRPS caused by incomplete SCI (AIS B), SCS was applied with an 80% improvement.[18] In our series, relief of pain was demonstrated only in patients with incomplete SCI. In 6 out of 8 patients no trial stimulation was performed. Probably majority of them would not have received permanent implants and would have been excluded from the study. The reason was not to perform surgery under general anesthesia twice: at first implantation of lead and secondarily removal of the paddle lead or implantation of pulse generator. In cases of PSPS or ischemic pain, where the effectiveness of tonic stimulation and new, more effective modern algorithms is documented, if the patient does not experience significant pain relief during a trial of SCS, permanent implantation of stimulator is not recommended. No complications associated with infection or lead migration, lead breakage or other hardware malfunction in our case series were observed, although these adverse events are not rare in patients after SCI.[5] According to several reports, burst SCS does not increase activity in dorsal column nuclei.[6] Thus, it may attenuate pain without sensory perception in subthreshold level. Burst stimulation was expected to suppress pain to a greater extent than conventional tonic stimulation.[19] The 1.2 kHz stimulation, which is sub-perception stimulation compared to tonic stimulation, did not demonstrate its superiority in pain relief. This finding aligns with our previous observations concerning FBSS treatment.[20] In this study, none of the new paradigms of SCS proved to be effective in this disabling CNP syndrome.[21] On the other hand, in the rat's CNP model, the reversal of hyperalgesia was achieved by repetitive SCS at a low frequency with the activation of spinal neuronal progenitors facilitated by chronic, low-dose gabapentin treatment.[22] Further studies are needed to elucidate the mechanisms of action of SCS in concurrent pharmacological facilitation in CNP, and other alternative methods of neuromodulation could be explored.

Limitations

The study has a retrospective nature, and there is a limited amount of collected data. The effects of SCS were measured post-intervention and one year later. During this period, patients were receiving different analgesic medications, and subjective assessments could be influenced by medications and changes in mood, as the majority of examined individuals had varying degrees of mood alterations or depressive disorder.

Conclusion

Our findings suggest that, despite the incorporation of new stimulation paradigms such as burst stimulation and high-frequency stimulation, SCS does not exhibit significant effectiveness in treating neuropathic pain in patients after SCI, and these results are consistent with the existing literature. Nonetheless, the therapy may yield satisfactory results for a specific subset of patients with incomplete spinal cord injuries, where there is no total damage and motor functions remain intact. Hence, SCS can prove effective in such cases. These results underscore the persistent challenge in addressing CNP, emphasizing the need for further exploration of alternative therapeutic approaches in this population.

Compliance with Ethics Guideline

Bioethical committee at Nicolaus Copernicus University reviewed and approved the study protocol (No. 629/2018). The present work was implemented under the guidance of the principles of the Declaration of Helsinki.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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