Spinal Cord Stimulation for Postherpetic Neuralgia and Parkinson’s Disease: literature review

Estimulação da Medula Espinal para Neuralgia Pós-Herpética e Doença de Parkinson: revisão da literatura

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ABSTRACT

Background: Spinal Cord Stimulation (SCS) has long been studied for the treatment of chronic neuropathic pain. Nevertheless, studies have associated SCS with improvement of axial manifestations of Parkinson’s Disease (PD), which are often refractory to conservative treatment and Deep Brain Stimulation (DBS). We report a case of clinical improvement of PD’s freezing of gait (FoG) after spinal cord stimulation. Case presentation: Male patient, 82-year-old with a 10-year history of PD under a pharmacological treatment that provided resolution of tremor, but was unable to improve gait disturbance. The patient presented with severe refractory postherpetic neuralgia. A cervical epidural lead for SCS was implanted, resulting not only in improvement of neuropathic pain but also in parkinson’s posture and FoG, with an increase in gait speed. Discussion: SCS is a promising therapeutic alternative in the management of axial manifestations of PD refractory to pharmacological therapy. SCS has been thoroughly studied in the management of chronic pain, but this report and other published studies suggest that the spinal cord could also be an interesting target in the treatment of PD. Conclusion: In this report, SCS was responsible for improvement of gait and posture in a patient with refractory PD with postherpetic neuralgia.

Keywords: Parkinson’s disease; Spinal cord stimulation; Postherpetic neuralgia; Neuromodulation

RESUMO


Palavras-Chave: Doença de Parkinson; Estimulação da medula espinhal; Neuralgia pós-herpética; Neuromodulação
INTRODUCTION

Postherpetic neuralgia (PHN) is classified in the ICD-11 as a chronic peripheral neuropathic pain that persists for three months or more after acute Herpes-Zoster (HZ) cure and develops in 9% to 14% of cases. It is estimated that there are around 1 million cases in the United States. The disease is more common in white, immunocompromised and elderly people. The involvement generally follows one or two dermatomes and predominates at the thoracic, cervical and ophthalmic trigeminal levels\(^1\). Due to the refractoriness of conservative therapy, injections, percutaneous and peripheral nerve stimulation, radiofrequency, dorsal ganglion neuroablation and Spinal Cord Stimulation (SCS) are possibilities for interventional treatment\(^4\).

Parkinson’s Disease (PD) is among the most common degenerative diseases of the central nervous system. The prevalence of PD increases with age, reaching its peak incidence between 70-79 years\(^5\). Its pathophysiology involves the degeneration of nigrostriatal dopaminergic neurons in the compact portion of the midbrain and impairs the movement regulation exerted by the basal ganglia\(^6\). The main symptoms are bradykinesia, plastic hypertonia and resting tremor. Secondary motor symptoms also occur, such as freezing of gait (FoG) and, finally, non-motor symptoms, such as cognitive deficits\(^7\). The best evaluated and established surgical treatment is Deep Brain Stimulation (DBS) of the internal globus pallidus or the subthalamic nucleus of Luys. SCS has been studied as a therapeutic alternative for motor and gait dysfunction in patients with PD, especially gait freezing, with promising results. There are still several questions to be clarified about this type of treatment\(^8\).

This is the case of a patient with PD who presented with improvement of gait and posture after SCS. We also review the literature for case reports, case series and clinical trials reporting the effect of SCS on PD symptoms.

CASE PRESENTATION

We present the case of an 82-year-old man with a 10-year history of PD. The patient had a history of coronary artery disease, had undergone drug-eluting stent for 2 years, was taking Acetylsalicylic Acid (ASA) and presented a narrowing of the L4/L5 lumbar canal, and no dementia.

The patient was under pharmacological treatment for PD with high-dose dopamine agonist (Levodopa) and an anticholinergic agent (Amantadine). While the tremor was well controlled, he still presented with persistent stiffness, bradykinesia, flexed posture and gait disturbance.

The patient developed burning pain in the right flank, intensity 8/10 on the Numeric Pain Rating Scale (NPRS), in the path between the fourth and twelfth ribs, characteristic of the previous vesicular phase of Herpes-Zoster. He started treatment with Acyclovir, but did not observe any pain relief. After pain management therapy with the use of analgesics, pregabalin, multiple infiltrations, dorsal ganglion rhizotomy and physiotherapy for PD for a period of 6 months, pain intensity decreased to 6/10 on the NPRS scale.

Due to the presence of refractory neuropathic pain, he underwent Spinal Cord Stimulation (SCS), with implantation of an epidural cervical lead over C4 to C8 levels. The Precision Artisan\(^\text{TM}\) Spinal Stimulation Electrode Kit, 16 contacts (Boston Scientific, Valencia, CA, USA) and a Precision Montage MRI rechargeable pulse generator were used. During hospitalization, the following initial settings were reached: amplitude (i) of 1.6 mA, frequency (f) of 180 Hz and pulse width (pw) of 250 ms. After one month, the settings were readjusted to i = 0.9 mA, pw = 200 ms and f = 180 Hz.

Significant improvement in pain was achieved and a considerable increase in gait speed was observed. He also presented a progressive reversal of flexed posture. Even with lower dosages of PD drugs, the improvement of gait and posture was maintained.

DISCUSSION

PHN is a painful manifestation of Varicella Zoster virus reactivation. After the initial infection, the virus may remain quiescent in the sensory ganglia of the spinal nerves, where it can initiate a process of demyelination, wallerian degeneration and
deafferentation. Such aggression manifests as neuropathic pain, characterized by burning, stabbing pain, electric or dysesthetic shock. The pain can be continuous or intermittent and is located, in most cases, in one or two dermatomes, especially in the thoracic or lumbar levels. In a study, these patients, SCS was able to improve the quality of life and improve refractory motor and non-motor symptoms. In our literature review, we identified 14 studies, comprising a total of 76 patients with PD treated with SCS. Only one study reported a postoperative complication caused by SCS, which was lead migration, a common occurrence in epidural lead neurostimulation.

In this report, a patient with PD underwent SCS for the treatment of postherpetic neuralgia pain and observed improvement of posture and gait. SCS has been demonstrated to act on suprasegmental circuits through stimulation of ascending fibers that project to the brainstem, cerebellum, basal ganglia, thalamus, and cortical areas, which could explain the improvement of SCS in PD patients. SCS can also interrupt the inhibition of the internal globus pallidus over the thalamus and the supplementary motor area (SMA), influencing the neuronal firing in this region, which is a key center for the control of the onset of gait.

Furthermore, SCS affects two postural control mechanisms differently – the reactive and the anticipatory. The cortical circuits that depend on cortical participation are more sensitive to SCS, given the increase in cortical input to the striatum, reaching the structures involved in the planning of movement, necessary during the anticipatory postural control, but not the reactive. Anticipatory Postural Adjustment (APA) mechanisms depend on thalamus-cortico-striatal loops, highly influenced by changes in attention and the environment. As part of the circuit that controls the APA, the SMA has cortical projections to the pedunculopontine nuclei (PPN), a region particularly involved in gait initiation. Since the activity of the SMA, globus pallidus and PPN are impaired in patients with FoG, SCS could be able to modulate this circuit and improve APA and gait initiation. On the other hand, the reactive mechanism of postural control to unpredictable external triggers depends on neuronal circuits involving the brainstem and spinal cord with less participation of the cerebral cortex.

Although DBS can be an effective treatment of PD, it presents limitations regarding the improvement of axial manifestations (posture and gait). Therefore, SCS could be another promising approach in patients with refractory axial symptoms of PD.

Some authors have used SCS as an alternative therapeutic option to manage motor and non-motor symptoms of PD (Table 1). Although there are few and heterogeneous studies, they present promising data that indicate SCS as an effective and safe treatment. SCS is an effective therapeutic option in the treatment of pain refractory to conservative therapies. It has been available for more than 50 years and has robust evidence supporting its efficacy and safety in the management of pain. An important component of PD, that directly affects the quality of life, is pain. Pain is one of the most common non-motor symptoms of PD and is divided by the King’s Parkinson’s Disease Pain Scale in the following domains: musculoskeletal pain, radicular pain, chronic pain, fluctuation-related pain, nocturnal pain, orofacial pain, and pain with discolouration/oedema/swelling. SCS in PD has been associated with a consistent improvement of pain, including significant reduction on the visual analogue scale of pain in patients with advanced PD and pain refractory to conservative treatment and deep brain stimulation.

In this case report, the patient underwent SCS for the treatment of postherpetic neuralgia. Besides the improvement in pain intensity, the patient also experienced an important improvement in motor symptoms of PD, including posture and gait. These results are consistent with other published studies, which have also associated SCS in PD with improvement in abnormal posture and improvement of gait. In a study with five patients with PD experiencing gait disturbance and FoG, SCS was able to improve step length, stride velocity, sit-to-stand test and FoG.

In our literature review, only one study did not identify an improvement in motor symptoms of PD. It was, nevertheless, a case series of two patients with a follow-up of 10 days and, hence, no definite conclusion can be drawn from these findings.

Some authors have successfully used SCS as salvage therapy in patients who failed DBS. In these patients, SCS is a particularly interesting therapy that could enhance the quality of life and improve refractory motor and non-motor symptoms.
### Table 1. Literature review of spinal cord stimulation in Parkinson’s Disease.

<table>
<thead>
<tr>
<th>Author</th>
<th>Study design</th>
<th>Number of Patients</th>
<th>Symptoms treated and assessed</th>
<th>Outcome</th>
<th>Complications</th>
<th>Follow-up</th>
<th>Previous DBS/Location</th>
<th>Spinal level of stimulation</th>
<th>Frequency</th>
<th>Pulse width (µs)</th>
<th>Pulse amplitude</th>
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</thead>
<tbody>
<tr>
<td>Lima-Pardini et al.(^{10})</td>
<td>Clinical trial</td>
<td>4</td>
<td>FoG</td>
<td>Significant improvement of FoG and anticipatory postural adjustment. SCS failed to improve reactive postural responses.</td>
<td>None</td>
<td>N/A</td>
<td>Yes/STN</td>
<td>T2-T4</td>
<td>300 Hz</td>
<td>90</td>
<td>N/A</td>
</tr>
<tr>
<td>Lai et al.(^{11})</td>
<td>Case Report</td>
<td>1</td>
<td>Gait disturbance and pain</td>
<td>Improvement to gait and pain. Quality of life improvement (40% improvement in PDQ-8). VAS decreased from 7 to 3. KPPS decreased from 12 to 4.</td>
<td>Dislocation of percutaneous lead. After reoperation, symptoms improved.</td>
<td>2 months</td>
<td>Yes/STN</td>
<td>T8-T10</td>
<td>60 Hz</td>
<td>270-390</td>
<td>3.6-4.0 V</td>
</tr>
<tr>
<td>Samotus et al.(^{12})</td>
<td>Clinical trial</td>
<td>5</td>
<td>Gait disturbance and FoG</td>
<td>Improvement of mean UPDRS (33.5%), step length (38.6%), stride velocity (42.3%), sit-to-stand (50.3%) and of FoG.</td>
<td>None</td>
<td>6 months</td>
<td>N/A</td>
<td>T8-T10</td>
<td>30-130 Hz</td>
<td>200-500</td>
<td>N/A</td>
</tr>
<tr>
<td>Furusawa et al.(^{13})</td>
<td>Case series</td>
<td>5</td>
<td>Intractable lower back pain and gait disturbance</td>
<td>Improvement of affective pain and severity of motor symptoms.</td>
<td>None</td>
<td>6 months</td>
<td>No</td>
<td>T8-T9</td>
<td>Burst stimulation inter-burst rate = 40 Hz/intra-burst rate = 500 Hz</td>
<td>1000</td>
<td>N/A</td>
</tr>
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</table>

DBS: Deep Brain Stimulation; FoG: Freezing of Gait; KPPS: King’s Parkinson’s Disease Pain Scale; MDS: Movement Disorders Society; N/A: Not Available; NPRS: Numeric Pain Rating Scale; PDQ-8: Parkinson’s Disease Questionnaire; SCS: Spinal Cord Stimulation; STN: Subthalamic Nucleus; TUG: Timed Up and Go; UPDRS: Unified Parkinson’s Disease Rating Scale; VAS: Visual Analogue Scale.
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<th>Pulse amplitude</th>
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<tr>
<td>Mazzone et al.</td>
<td>Prospective case series</td>
<td>18</td>
<td>Pain and motor symptoms</td>
<td>Improvement in pain and motor symptoms. Patients who underwent burst stimulation presented with a more acute response to treatment</td>
<td>None</td>
<td>12 months</td>
<td>High cervical</td>
<td>Tonic stimulation group: 130-185 Hz; Burst stimulation group: inter-burst rate = 40 Hz/intra-burst rate = 500 Hz</td>
<td>Tonic stimulation group: 60-210; Burst stimulation group: 0.2-0.9 mA</td>
<td></td>
<td></td>
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<td>Pinto de Souza et al.</td>
<td>Clinical trial</td>
<td>4</td>
<td>Postural instability and gait disturbance</td>
<td>50 to 65% improvement in gait measurements and 35 to 45% in UPDRS III</td>
<td>None</td>
<td>6 months</td>
<td>Yes/STN T2-T4</td>
<td>300 Hz</td>
<td>90</td>
<td>N/A</td>
<td></td>
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<tr>
<td>Agari et al.</td>
<td>Prospective case series</td>
<td>16</td>
<td>Abnormal posture, gait disturbance and pain</td>
<td>Mean VAS decreased from 8.9 to 2.3. There was no significant improvement of total UPDRS motor score, but among motor subscres, there was significant improvement of gait, Improvement of posture</td>
<td>None</td>
<td>12 months</td>
<td>Yes (7 patients)/ N/A</td>
<td>T7-T12</td>
<td>5-20 Hz</td>
<td>210-330</td>
<td>0-4 V</td>
</tr>
<tr>
<td>Akiyama et al.</td>
<td>Case report</td>
<td>1</td>
<td>Painful camptocormia with Pisa syndrome</td>
<td>Improvement of pain and posture. UPDRS improved from 48 to 34 points and TUG test improved from 15 s to 7 s</td>
<td>None</td>
<td>6 months</td>
<td>Yes/STN T8-L3</td>
<td>7 Hz</td>
<td>250-450</td>
<td>2.5-3.5 V</td>
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<td>Chakravarthy et al.</td>
<td>Prospective case series</td>
<td>15</td>
<td>Pain and motor symptoms</td>
<td>59% reduction in VAS. 73% of patients presented with improvement in the 10-meter walk test and 64% experienced improvement in the TUG test</td>
<td>None</td>
<td>4-33 months (mean: 22)</td>
<td>Yes (8 patients) / STN</td>
<td>C2-T12</td>
<td>Burst stimulation: inter-burst rate = 40 Hz / intra-burst rate = 500 Hz / Tonic stimulation: 10-40 Hz</td>
<td>1000</td>
<td>0.15-4.5 mA</td>
</tr>
<tr>
<td>Nishioka and Nakajima</td>
<td>Case series</td>
<td>3</td>
<td>Intractable chronic pain, motor symptoms</td>
<td>There was significant improvement in VAS score and UPDRS II</td>
<td>None</td>
<td>12 months</td>
<td>No</td>
<td>T8-L1</td>
<td>5-65 Hz</td>
<td>60-450</td>
<td>0.45-5.8 V</td>
</tr>
<tr>
<td>Thevathasan et al.</td>
<td>Case series</td>
<td>2</td>
<td>Motor impairment</td>
<td>There was no improvement in UPDRS motor score</td>
<td>None</td>
<td>10 days</td>
<td>No</td>
<td>High cervical</td>
<td>130-300 Hz</td>
<td>200-240</td>
<td>2.4 V</td>
</tr>
<tr>
<td>Hassan et al.</td>
<td>Case Report</td>
<td>1</td>
<td>Resting tremors, bradykinesia and shuffling gait. Abdominal tremors and neuropathic pain.</td>
<td>VAS decreased from 8 or 9 to 0 or 1. Relief from motor symptoms and gait in UPDRS and 10-meter walk test. The tremors largely disappeared. Rigidity decreased. Shuffling gait and posture at baseline improved. Masked facies improved</td>
<td>None</td>
<td>24 months</td>
<td>No</td>
<td>C2</td>
<td>40 Hz</td>
<td>500</td>
<td>0.3-1.1 mA</td>
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<td>Landi et al.22</td>
<td>Case Report</td>
<td>1</td>
<td>Pain, dysesthesia, and paresthesia. Motor impairment</td>
<td>VAS decreased 70%, Improvement in gait, postural stability, bladder control, incontinence and dysesthesias. Subjective evaluation of quality of life (EQ-VAS) improved 60%. UPDRS unchanged.</td>
<td>None</td>
<td>16 months</td>
<td>Yes/STN</td>
<td>T9-T10</td>
<td>30Hz</td>
<td>250</td>
<td>1.8-2.5 V</td>
</tr>
<tr>
<td>Fénelon et al.23</td>
<td>Case Report</td>
<td>1</td>
<td>Lower limb neuropathic pain, motor symptoms</td>
<td>Motor score and UPDRS were reduced by 50%. Amplitude reduction of tremor. Pain relief. Rigidity and bradykinesia improved.</td>
<td>None</td>
<td>24 months</td>
<td>No</td>
<td>T9-T10</td>
<td>70-130 Hz</td>
<td>410</td>
<td>3.5 V</td>
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CONCLUSION

In this case report, spinal cord stimulation was able to provide improvement of gait and posture in a patient with PD. Other studies have also published results that support the spinal cord as a potential neurostimulation target for the management of refractory PD.

REFERENCES


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