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High frequency spinal cord stimulation for chronic back and leg pain

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ABSTRACT

Background: High frequency stimulation (HFS) may provide pain relief without the paresthesias typical of traditional low-frequency Spinal cord stimulation (SCS).
Methods: A consecutive single-center series of patients was retrospectively reviewed to evaluate safety and efficacy of HF10 therapy. In this 24-month study, 62 patients with variables pathologies (44 patients with back failure surgery syndrome (FBSS), 18 patients with chronic peripheral neuropathic pain in the lower limbs (NeppL) were included to be treated with HF10. Pain outcomes were compared from preoperative baseline and at the conclusion of each study period. Clinical features, outcomes and complications were reviewed.
Results: 62 patients completed this study. All patients had a successful trial before the definitive implantation of a spinal cord stimulator at the low dorsal level. The mean follow-up period was 11 months, ranging from 6 to 24 months. 6 patients showed no change from baseline visual analogue scale (VAS) after permanent implant and 2 had improved during the trial but was aggravated after the permanent implant placement. At 1 month, 63% of implanted HF10 therapy subjects were responders and 77% at 6 months. The average baseline, trial and post-operative Visual Analogue Scale (VAS) was 8.1, 3.6 and 4.2 respectively. When compared to the baseline, the average reduction achieved during the VAS trial was 4.5 points, accounting for a 56% pain reduction. The long-term failure rate was 22%.
Conclusions: This study generated preliminary evidence showing improved VAS current pain scores in absence of paresthesias and increase patient satisfaction with HF10 spinal cord stimulation.

1. Introduction

Chronic pain is a widespread neurological condition that impacts more than 110 million Americans [1] and costs $560–$630 billion in healthcare expenses and lost productivity annually [2]. When conservative therapeutic options are not able to effectively alleviate chronic pain, spinal cord stimulation (SCS) is considered.

SCS is an established, effective method of treating chronic pain, and has been shown to be effective in the treatment of chronic pain in 50–70% of cases [3]. Electrical energy delivered by SCS is characterized by stimulation parameters consisting of amplitude, frequency, and pulse width [4,5]. SCS was approved to treat chronic intractable pain of the trunk and limbs [5]. SCS delivers electrical pulses via spinal epidural electrode arrays (leads) at vertebral levels associated with perceived pain [5]. SCS parameters can be altered to optimize pain relief according to individual patient preferences [4]. Traditional SCS devices are capable of delivering pulse frequencies in the range of 2 to 1,200 Hz, with typical application of approximately 40 to 60 Hz [5]. The objective of these relatively low-frequency SCS devices is to produce paresthesias (a tingling sensation) that overlap the pain distribution, with the intent of masking pain perception. Intraoperative paresthesia mapping is thus required, wherein patient feedback is solicited while adjusting

Abbreviations: HFS, High frequency stimulation; SCS, Spinal cord stimulation; HF10, High frequency stimulation delivered at 10 kHz; NeppL, neuropathic pain in the lower limbs; FBSS, back failure surgery síndrome; VAS, visual analogue scale; N, number.

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stimulation location, pulse frequency, pulse width, and amplitude. Thus, traditional SCS success depends on adequacy and durability of paresthesia coverage as well as patient tolerance of the induced sensations [5]. Achieving adequate and stable paresthesia coverage in the axial back region specifically is known to be challenging, making back pain more difficult to treat and limiting the application mostly to patients with predominant leg pain [6,7].

Assessing an approach that does not rely on paresthesias is novel to SCS and has the potential to improve the treatment of chronic back and leg pain. HF10 (rate higher than 10.000 Hz) has led to improved pain outcomes compared to conventional SCS in patients with chronic axial back pain [8]. There is evidence that employing frequencies at rates higher than 10,000 Hz decreases the paresthesias the patients experience and can shift recharge from weekly to daily recharge burden [9].

The therapeutic mechanism of SCS relies on the delivery of electrical energy to the spinal cord dorsal columns to stimulate large A and Ab afferent fibers in an anterograde fashion and downregulate activity of wide dynamic range in a retrograde fashion thus reducing pain perception [10]. One consequence of SCS-mediated anterograde Ab afferent fiber stimulation is the development of paresthesia. Unlike SCS at lower frequencies of stimulation, HFS at 4.500 and 10.000 Hz has been suggested to reduce paresthesia through a possible mechanism involving transmission block on large A and Ab afferent fibers [11]. Therefore, without anterograde transmission there is no perception of paresthesia [12]. However, it is still unknown if pain relief from frequencies near 200 Hz is due to the same mechanism [12].

The vast array of programming options, combined with the importance of enhancing patient outcomes, highlights the need for exploratory studies to assess the efficacy of these newly designed stimulation settings. However, these studies can often be difficult to execute given the relative novelty of these stimulation parameters [4].

The aim of the trial was to ascertain degree of pain relief obtained.

2. Methods

2.1. Subjects

A consecutive single-centre series of patients was retrospectively reviewed. This study included 62 patients with variable pathologies such as FBSS and NeppLL treated with HF10 since 2016 (Table 1). The inclusion criteria were: 1) 18-year-old or older, 2) permanent HF10 implanted and follow-up at least for 6 months and 3) positive SCS trial before definitive implantation, responders (the primary outcome) were defined as having 50% or greater pain reduction with no stimulation-related neurological deficit (Table 2).

All patients who were considered for potential HF10 underwent trial stimulation before consideration of permanent implantation. A total of 73 patients underwent trial implantation, however, 5 patients are waiting for the permanent implantation, 3 had less than 1-month follow-up and 3 had a clinical fail response during the trial.

Demographic and clinical features were reviewed including etiology, pain distribution, system implanted, lead position, complications and degree of pain relief. Furthermore, Visual Analogue Scale (VAS) was used to assess baseline, trial and postoperative pain scores.

2.2. Surgical procedure

The trial was performed by placing a lead in the epidural space at the dorsal region. The wires were externalized and connected to an external pulse generator. Finally, different stimulation parameters were applied during 7–10 days until a successful stimulation was achieved.

After a positive trial, a permanent SCS with HF10 was implanted in all patients using a similar technique and connected to a battery.

The procedures were performed by the three senior authors (NS, PRE and JOF). Patients under general anesthesia for the permanent implants were placed in prone position. Exposure to the lower dorsal spine was achieved through a midline lineal incision. The yellow ligament was removed, and a midline partial laminectomy was performed to access the epidural space. The epidural paddle was placed upward in the midline. For the HF10 therapy, the upper tip was placed at D8 and D9 in 26% and 47% respectively. The wires were anchored to the muscles/fascia, tunneled to a pocket in the right-side lumbar region and connected with the implantable pulse generator (IPG). Impedances were checked, and post-operative x-rays were used to assess the position of the system.

Different hardware systems were used including the following leads: Surpass (Nevro Corp., Menlo Park, CA, USA), and Octrode (St. Jude Medical, Inc., St. Paul, Minn, USA). The IPGs used was: Senza (Nevro Corp., Menlo Park, CA, USA). HF10 stimulation was used in all the patients.

3. Results

From January 2016 to August 2018, seventy-three patients were enrolled with a trial to assess the response to the HS10 previous to undergo a permanent implant (Fig. 1). However, in three patients the trial has failed, and 8 patients did not meet the inclusion criteria. Therefore, sixty-two patients were included in the analyses. In this study the conversion rate to a permanent implant was 96%.

The demographic of the patients and the clinical features are listed in Table 1. They include gender, age, diagnosis, pain side and distribution, hardware implanted and NRS (baseline, trail and postoperative), among others.

Three patients failed their trials: with two patients, stimulation was only projected to one lower limb and despite multiple attempts at programming the system, improved coverage could not be obtained. With the other patient, coverage was uncompleted, and the sensation was unpleasant for this patient. A second attempt at open trial was performed and again this did not improve the degree of coverage and the

Table 1
Patients Demographics and clinical features. All numbers within parentheses represent percentages. FBSS: fail back surgery syndrome. NeppLL: neuropathic pain lower limbs. VAS: visual analogue scale.

Demographics	Value
Gender	
Males	40 (65)
Females	22 (35)
Age (years)	
Mean	54
Range	20–78
Diagnosis	
FBSS	44 (71)
NeppLL	18 (29)
Electrode	
Nevro	57 (92)
Octrode	5 (8)
Pain severity (VAS)	
Preoperative	8.1
Trial	3.6
Postoperative	4.2

Table 2
Patients VAS outcomes. All numbers within parentheses represent percentages. FBSS: fail back surgery syndrome. NeppLL: neuropathic pain lower limbs. VAS: visual analogue scale.

Diagnosis	N° patients	Patients improved	VAS baseline	VAS postoperative	VAS Improvement
FBSS	44	17 (77%)	8.1	4.2	3.9 (48%)
NeppLL	18	7 (78%)	8	4.3	3.7 (46%)
Total	62	24 (77%)	8.1	4.2	3.9 (48%)

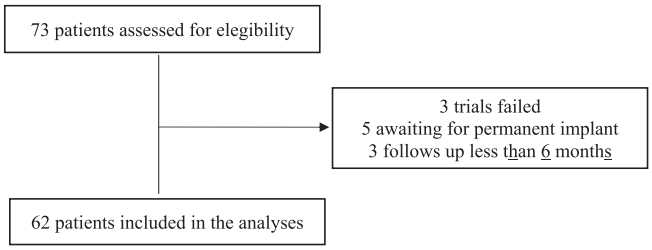

Fig. 1. Study subject flow.

sensation was also unpleasant. In the rest of a permanent SCS was implanted.

Regarding their diagnosis, the majority (67%) were classified as FBSS and only 33% as NeppLL.

For those patients with FBSS or NeppLL leads were placed at the level of D8 and D9 in 26% and 47% respectively. Data is not available for the remaining patients. Lead position for HF10 therapy was based on extensive empirical observation that most patients respond to stimulation application near T9/ T10, while allowing for patient variation by covering T8 to T11.

The average baseline, trial and postoperative VAS was 8.1, 3.6 and 4.2, respectively. When compared to the baseline, the average reduction achieved during the trial VAS was 3.6 points, accounting for a 56% pain reduction. At 6 months, in the group with FBSS, 77% of the patients (34 out of 44) improved the VAS with the HF10 therapy achieving an average reduction of pain of 3.9 points (48%) compared with the baseline VAS. In those patients with NeppLL, this therapy diminishes the pain in 78% of the patients (14 out of 18) with an average pain reduction of 3.7 points (46%) points compared with the baseline VAS. Pain relief occurred in the absence of paresthesia. At 1 month, 63% of implanted HF10 therapy subjects were responders and 77% at 6 months.

Almost all patients with FBSS and amelioration degree of pain (88%) were younger than 65 years old. However, in the group of patients with FBSS but without improvement after being treated in the pain clinic, two patients (40%) were older than 65 years old.

Although all patients had a successful trial before the definitive hardware implantation, the long-term failure rate was 22% (14 out 62 patients). With two of these patients the stimulation was never effective after the definitive implant procedure.

The mean follow-up period was 11 months ranging from 6 to 24 months. During the follow-up period, six patients (10%) underwent further procedures. A total of 6 system revisions were performed. Two revision was related to an infection, three for lead migration and one because of erosion of the skin in the site of the IPG.

There was no mortality related to the procedure and there was only one case of postoperative infection treated with oral antibiotics with favorable results.

4. Discussion

4.1. SCS in the treatment of BFSS and NeppLL

The rapid pace of development of neuromodulation technology and the introduction of novel SCS programming parameters underscores the need to investigate the efficacy of these methods in alleviating pain and improving patient outcomes [4].

We present a work assessing the safety and efficacy of HF10 therapy, which is an innovative spinal cord stimulation (SCS) system for the management of chronic back and leg pain. This system delivers electrical stimulation pulses at high frequency (10,000 Hz) as compared with traditional low-frequency SCS systems (typically around 50 Hz). Previous work suggests that the higher frequency system may treat back and leg pain to a greater degree.

HF10 therapy involves application of short-duration (30 μs), high-frequency (10 kHz), low-amplitude (1 to 5 mA) pulses to the spinal epidural space in such a manner as to not produce paresthesia, which some patients find uncomfortable, and also, obviating the requirement of paresthesia mapping [8,13]. Previous prospective studies have indicated that HF10 therapy is able to treat patients with chronic back pain and that the results are sustained for 2 years [14,15].

Arle et al. has suggested that when utilizing HF10, smaller fibers are potentially used when transmission blockages occur in the large fibers, which could potentially maintain the pain-relieving effects, while at lower frequencies the overall effect of stimulation may decrease the threshold for activation. Theoretically, the cumulative effect is that there is inhibition of large diameter sensory afferent fibers and activation of medium and small diameter sensory afferent fibers [11].

4.2. Effectiveness and complications

In two previous randomized, controlled trials of patients with predominant leg pain, SCS was found to be more effective than reoperation [16] and conventional medical management [17]. In the reoperation study, SCS was more effective in treating persistent radicular pain after lumbosacral spine surgery and often obviated the need for reoperation. In the conventional medical management study, more subjects randomized to SCS had a significant reduction in leg pain. These results along with those of the SENZA-RCT study suggest that HF10 therapy may be even more effective in comparison [5].

The SENZA-RCT study provides the first scientifically rigorous, randomized, controlled trial demonstrating the superiority of HF10 therapy over traditional SCS in the long-term treatment of both back and leg pain [5]. Findings showed HF10 significantly decreased VAS pain scores compared to conventional stimulation and was associated with a pattern of vibration sensation more similar to preoperative baseline than conventional stimulation [4]. Corcondingly, our study showed a relief of the pain with 77% of the patients with FBSS and 78% of the patients with NeppLL. Remarkably, these results were superior with previous studies of 50% of patients attaining 50% pain relief achieved with traditional SCS [5]. Also, in the SENZA-RCT study the success of HF10 therapy was nearly superior for both back and leg pain, two thirds of subjects receiving HF10 therapy achieved remitter status for back and leg pain, and over one third decreased or eliminated opioid analgesic usage at 12 months [5].

Comparison of SENZA-RCT results for leg pain to published literature is challenging, due to different inclusion/exclusion criteria (limited to predominant leg pain patients) and reporting methods. Nevertheless, leg pain relief for traditional SCS in the SENZA-RCT is consistent with previous reports [6,7,16,17]. In our series, cases with NeppLL diminishes the pain for 78% of the patients with a 46% average and 3.7 points pain reduction were observed.

Finally, Grider et al. [20] provide a systematic review of the efficacy of spinal cord stimulation for chronic pain reporting significant (Level I to II) evidence of the efficacy of spinal cord stimulation in lumbar FBSS; whereas, there is moderate (Level II to III) evidence for high frequency stimulation [20].

4.3. Safety

In terms of safety, the incidence of study-related advert events over 24 months was presented only with 6 patients, with no stimulation-related neurological deficits in treatment group, and only three revisions for migration of the lead. Historically, lead migration has been the most frequently reported complication of SCS with rates ranging from 2.1 to 23% [18,19]. In the SENZA-RCT study, using a percutaneous technique, lead migration rates were comparatively low (3 to 5.2%), likely due to improved device technology, implantation techniques, and patient selection in recent years [5]. In our study, performing an open technique lead migration rate was 5%.

5. Limitations

There are evident limitations in our study that prevent us from generalizing our results and making wide recommendations based on them. The most important one is its retrospective design and the intrinsic bias associated. Nonetheless, rare conditions are not usually suitable for prospective studies. The statistical power of the study was diminished by the small size of the sample.

In addition, the absence of prospectively collected data resulted in the lack of other important outcome measures addressing quality of life, pain relief, associated depression and anxiety.

Despite the sample being fairly homogenous regarding the clinical features and diagnosis, the differences in the underlying etiology may limit generalized recommendations to all subgroups of patients. Nevertheless, our study presents new data supporting the efficacy of HF10 in BFSS, NeppLL and FP, and encourages further research with prospective designs. Finally, the wide range in follow-up may prevent us of reaching conclusions and recommendations regarding the long-term efficacy.

6. Conclusions

HF10 stimulation improved VAS pain scores compared to the pre-operative baseline. In spite of this extent of intractable pain, HF10 therapy demonstrated favorable safety and efficacy.

Further large-scale prospective studies are needed to clarify the role of shuffle technology in the SCS armamentarium.

Author contributions

S.-T.B wrote the manuscript. S.-T.B., S.M., and M.-A.M performed research, collected patient information, and helped to analyze data; Y.-M.A., and H.F-G.B performed bioinformatics and biostatistical analysis; D.M., N.S., and J-OF. designed the research, directed the work, analyzed data and provided funding.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.inat.2020.101009.

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