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A Retrospective, Single-Center Study Investigating the Effects of a Novel Miniature Wireless Spinal Cord Stimulation System for the Treatment of Chronic Back and Leg Pain

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Background: Spinal cord stimulation (SCS) is an evidence-based therapy for intractable chronic back and leg pain (CBLP). Most conventional SCS systems depend on an implantable pulse generator to power the system. The objective of this study was to investigate the efficacy of an externally powered wireless SCS device in patients with CBLP.

Case Report: A total of 29 patients at a single center underwent implantation of a single 8-electrode array epidurally. Responders were defined as having 50% or greater reduction in back and leg pain after a 4-week screening period. At this time, a second electrode array was placed in those patients who responded, percutaneously parallel to the first array.

Conclusion: After the 30-day screening period with the single electrode array, 28 of the 29 patients (96.6%) responded with pain relief reduction in Visual Analog Score (VAS) levels between 50% and 90%. Responsive patients were then implanted with the second electrode array. Twenty-six of the 28 (92.8 %) patients who were implanted with 2 leads reported a greater amount of overall pain relief (an additional 15% decrease) once the second device was placed. There were no procedure- or device-related complications in any of the patients. At 12 months follow-up, average VAS scores for back and leg pain did not change significantly from the early results, indicating long-term, sustainable pain relief utilizing the wireless system.
Although a single-electrode array proved to be efficacious, using 2 electrode arrays improves the anatomic coverage of the painful areas and allows for greater optionality in electrode selections to avoid plasticity.

Key words: Wireless SCS, wireless spinal cord stimulation, wireless pain relief, chronic back pain, chronic leg pain, neuromodulation, high-frequency stimulation

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BACKGROUND

Intractable chronic back and leg pain (CBLP), with or without prior spine surgery, is a debilitating condition that negatively impacts the quality of life of affected patients (1) and generates high lifetime treatment costs. Treatment options include physiotherapy, nonsteroidal anti-inflammatory drugs, opioids, (repeated) back surgery, and minimally invasive techniques, such as radiofrequency ablation, nerve blocks, and spinal cord stimulation (SCS) (2). Despite all these treatment options, low back pain still presents a treatment challenge and an unmet medical need. High-frequency SCS was reported to treat back pain in addition to leg pain and was shown in randomized controlled trial (RCT) studies to produce very stable pain relief over time, resulting in long-term remission in a majority of the patients (3) (Note: While pulse rates over 1,500 Hz were utilized in the study, Stimwave is only permitted to provide SCS therapy at frequencies <1,500 Hz. Thus, the pulse rates used in the study are not commercially available on Stimwave's products.).

Studies have shown that patients with conventional SCS systems utilizing implanted pulse generators (IPG) have a large number of complications related to the bulk of conventional system batteries, lead-related complications such as migrations and fractures, and severe pocket-pain-related issues, accounting for long-term inferior results, thus posing a significant unmet medical need (4-6). In a population of 29 patients, we hypothesized that clinically significantly superior outcomes are possible with a safer and more efficient procedure causing less trauma to the tissue of the patients.

The objective of this study was to investigate the efficacy and safety of a novel miniaturized multicontact wireless SCS stimulator utilizing an external transmitter for pain relief in selected patients with CBLP.

METHODS

Device Description

Conventional SCS systems utilize a fully implanted, rechargeable or nonrechargeable IPG, which is hardwired to the electrode arrays. In comparison, the Freedom SCS System (Stimwave, Inc. Pompano Beach, FL) is a small, cylindrical (45-cm length and 1.35-mm diameter) sealed device without a connector consisting of an 8-contact stimulator with embedded electronics and a mated receiver component (Fig. 1) (commercially available only at frequencies <1,500 Hz). A small, externally wearable rechargeable transmitter (wearable antenna assembly [WAA]) provides the energy to power the device wirelessly through the skin, using a proprietary pulse-amplitude modulation and pulse width modulation scheme, thereby avoiding the potential complications related to the implant of an IPG, for which complications have been reported in up to 40% of recipients (4-6).

STUDY DESIGN

This was a retrospective single-center study, which had institutional review board approval. The objective of the study was to assess the feasibility, performance, and safety of the implantation procedure and the treatment efficacy of a novel, fully implantable, miniaturized wireless SCS device (Freedom 8A; Stimwave, Inc.). The first phase of the study consisted of the implantation of a single permanent SCS device with a screening period of 4 weeks, and the second phase consisted of the implant of a second permanent SCS device (Fig. 2). Patients were followed for a total period of 12 months. To be enrolled in the study, patients had to be at least 18 years old, have a history of chronic medically intractable low back and leg pain with or without prior surgery, have an initial Visual Analog Score (VAS) of more than 50 mms, pass a psychological evaluation, and have the cognitive ability to use the external transmitter. Exclusion criteria were visceral pain, hyperalgesia or allodynia of the lower back, allergies to system components, active cancer treatment, drug dependence, pregnancy, and inability to comply with the study requirements.

Procedure

A total of 29 patients (14 men and 15 women, aged 19–87 years) with medically intractable CBLP were selected according to accepted and recommended clinical criteria. Under intravenous anesthesia, they underwent percutaneous implantation of one epidural SCS device in the anatomic midline. A Tuohy needle was used to enter the epidural space at a 45° paramedian approach under fluoroscopic guidance. The track for the needle was injected with a solution of 5 mL of bupivacaine 0.5% and 5 mL of lidocaine 2%. Once the contact array was placed at the top of the T8 vertebrae level, the receiver element was connected to the inner lumen of the extruded stimulator body. The neurostimulator was fixated using an anchor injected through the fascia at the primary implant site. The receiver pocket was made approximately 2-cm long, 10 cm distal from the electrode array entry point, and a Touhy needle was utilized to tunnel the receiver the full length of the track to the secondary subcutaneous receiver pocket. The distal portion of the receiver was coiled, sutured to

itself to eliminate any sharp ends, and then sutured to the fascia. The pocket was then closed with subcutaneous and then subcuticular sutures.

All patients were programmed subthreshold with a bipole covering T9-T10, with parameters as preferred by patients. After the 4-week screening period, responders received a second device placed percutaneously and parallel to the first one and staggered with the top electrode placed at the T9 vertebrae level. The second stimulator was secured in a similar manner to the original stimulator and tunneled to the previous pocket. Patients were programmed based on parameters proven to be efficacious during the trial period. The second electrode array stimulator allowed for optimization of therapy creating alternative programming options. All patients in the study used a single WAA device to power and provide stimulation parameters to both SCS stimulators.

Clinical Assessment and Follow-Up

Responders were defined as having 50% or greater reduction in back or leg pain VAS scores at the end of the 4-week screening period. Follow-up was carried out at 3, 6, and 12 months after the first implant.

Statistical Analyses

All analyses were based on the intent-to-treat principal, meaning that all 29 patients participated in all analyses. Because some patients were not responders and were explanted at the 4-week follow-up, missing follow-up data were imputed by using baseline values.

Changes in back and leg pain VAS scores and in Oswestry Disability Index (ODI) scores were compared with paired t-tests. The test comparing baseline to 1 month was a 2-sided test of Ho: $\Delta = 0$ versus Ha: $\Delta \neq 0$, where Δ is the difference in the scores; this was a test of the effect of the first implant. The test comparing 1 to 3 months tested the same hypotheses; this was a test of the effect of the second implant.

The tests comparing 6 to 3 months and 12 to 3 months were noninferiority tests of the stability of the changes. The changes (increases in VAS or ODI scores at 6 and 12 months) had to be significantly less than the minimum clinically important difference (MCID) to be considered stable. The tests comparing 6 and 12 to 3 months were one-sided noninferiority tests of Ho: $\Delta >$ MCID versus Ha: $\Delta <$ MCID. The MCID for a 10-point VAS is 1.2 points for leg pain and 1.6 points for back pain. The MCID for ODI is 12.8 points (7).

Fig. 1. The Freedom-8A SCS neurostimulator with 8 electrodes, a microchip, and a miniature receiver embedded into the inner lumen of the stimulator body.

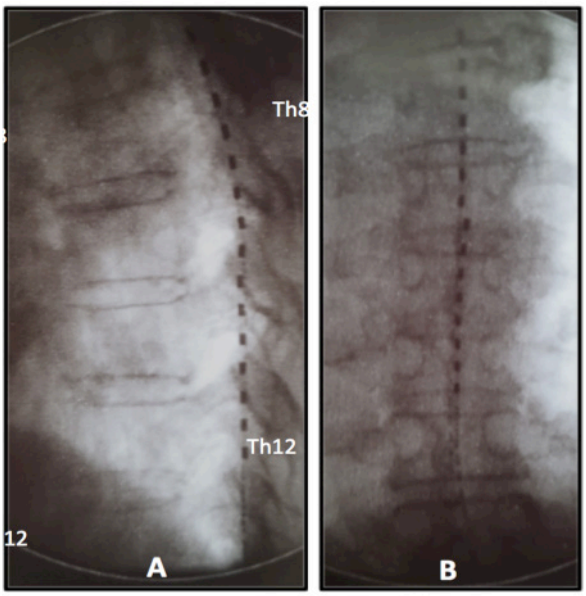

Fig. 2. Lateral (A) and anteroposterior (B) image showing distribution of 2 octopolar neurostimulator electrode arrays spanning the T8-T10 vertebral levels in the epidural space.

RESULTS

The 29 study patients averaged age 67 years at the time of the first implant (range, 18–87 years). Forty-eight percent were men.

After the 4-week screening period using a single SCS device, 28 of 29 patients (96.5%) responded to therapy,

Table 1. VAS and ODI scores over time.

Statistic (n = 29)	Mean (SD) or *P* Value at Time				
	Baseline (BL)	1 Month (1 m)	3 Months (3 m)	6 Months (6 m)	12 Months (12 m)
Score: VAS leg	7.9 (0.92)	4.6 (1.4)	3.0 (1.5)	2.7 (1.3)	2.6 (1.5)
Score: VAS back	7.9 (0.82)	5.3 (1.1)	3.4 (1.0)	2.8 (0.77)	2.4 (0.95)
Score: ODI	45 (3.7)	24 (7.1)	19 (5.1)	17 (4.1)	16 (3.7)
Change: VAS leg	NA	3.2 (1.1)*	1.5 (0.78)*	0.34 (0.77)*	0.41 (0.87)*
Change: VAS back	NA	2.6 (0.86)*	1.9 (0.59)*	0.62 (0.73)*	0.97 (0.98)*
Change: ODI	NA	21 (5.6)*	4.6 (3.6)*	1.7 (1.9)*	3.5 (2.2)*
t-test** Change: VAS leg	NA	$P < 0.001$	$P < 0.001$	$P < 0.001$	$P < 0.001$
t-test** Change: VAS back	NA	$P < 0.001$	$P < 0.001$	$P < 0.001$	$P < 0.001$
t-test** Change: ODI	NA	$P < 0.001$	$P < 0.001$	$P < 0.001$	$P < 0.001$
Percent change: VAS leg	NA	42% (14%)*	36% (18%)*	5.6% (29%)*	9.4% (33%)*
Percent change: VAS back	NA	33% (11%)*	37% (12%)*	15% (17%)*	25% (23%)*
Percent change: ODI	NA	48% (13%)*	18% (11%)*	8.0% (8.1%)*	17% (7.8%)*

with greater than 50% improvement in back or leg pain. One patient (3.4%) reported lack of efficacy and was explanted. The 28 successfully screened patients were subsequently implanted with a second SCS device. Twenty-six of the 28 implanted patients (92.8%) self-reported a greater amount of overall pain relief with the 2 SCS devices as compared with treatment with a single device.

Table 1 shows the absolute and percentage changes in VAS and ODI scores at 1 month versus baseline, at 3 months versus 1 month, and at 6- and 12 months versus 3 months, using the intent to treat (ITT) population. The *P* values from the paired t-tests for the changes are also listed. All of the hypothesis tests were highly significant ($P < 0.001$) and rejected all of the null hypotheses indicating: 1) significant pain and disability reduction with a single system; 2) significant improvement in these dimensions with 2 systems compared with one; and 3) stability in the improvement at both 6 and 12 months.

Patients reported mean pain score reductions of 5.1 for back and 5.2 for leg pain at 6 months as compared with baseline VAS scores (Fig. 3). At the 12-month follow-up, mean VAS scores for back and leg pain did not change significantly as compared with 3 months, with mean pain score reductions of 69% for back and 67% for leg pain, indicating stable long-term pain relief.

The patients' mean level of disability, as measured by the ODI, improved significantly by an average of 48% at the end of the trial (Fig. 4). At 12 months, the scores decreased 64% from baseline, from 45 (severe disability) to 16 (minimal disability), a reduction of 2 categories.

At 12 months, 16 patients (55%) were able to completely stop taking oral opioids. The remaining patients considerably reduced opioid use (Fig. 5). The average reduction at 12 months was 90%.

There were no procedure-related complications, no hardware failures, no infections, and no undesirable side effects of the system.

DISCUSSION

The qualitative feedback of the implanted patients suggests that leg and back pain reduction is being improved with the second SCS device due to improved anatomic coverage. At the 12-month follow-up, average VAS scores for back and leg pain did not change significantly, indicating stable long-term pain relief.

ODI scores are additional measurements, demonstrating that SCS therapy can impact patients on a day-to-day basis and allowing them to return to normal activities. The ODI scores in this study decreased significantly at 12 months, demonstrating considerable improvements in functionality.

Traditional SCS trials with percutaneous electrodes externalized to an external power source are typically limited in duration of up to 15 days (9) because of the risks of infection of up to 7.5%. The novel miniaturized wireless SCS device used in the present study eliminates percutaneous extensions and allows for a trial period of any chosen duration, after which a second, staggered device may be implanted to improve SCS efficacy long term and offer a greater option for programming against plasticity.

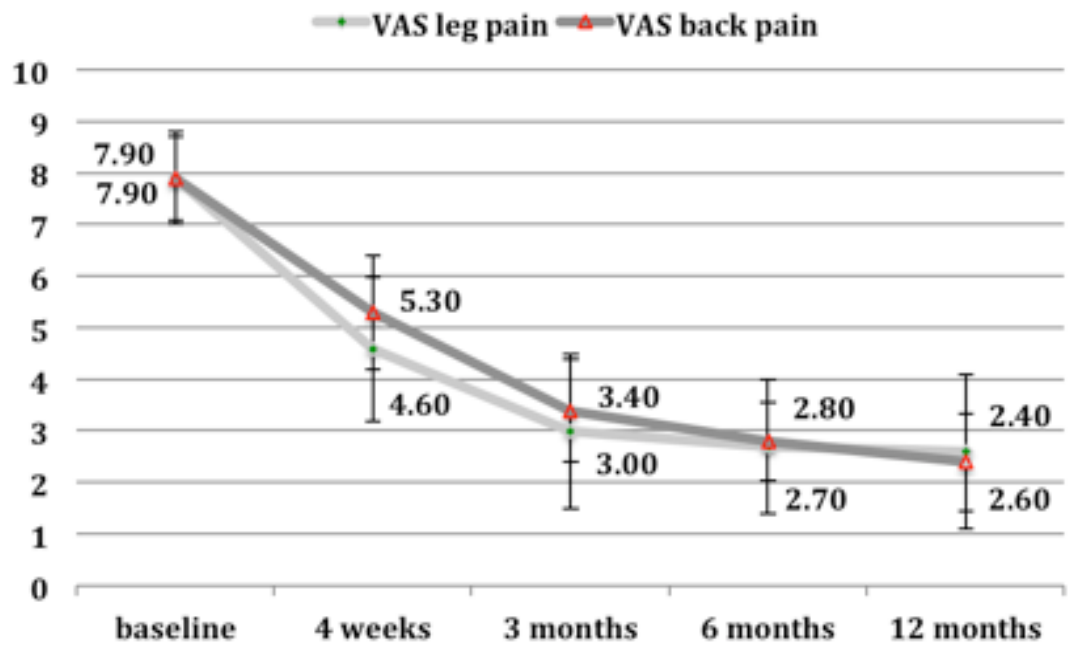

Fig. 3. VAS score/back and leg pain.

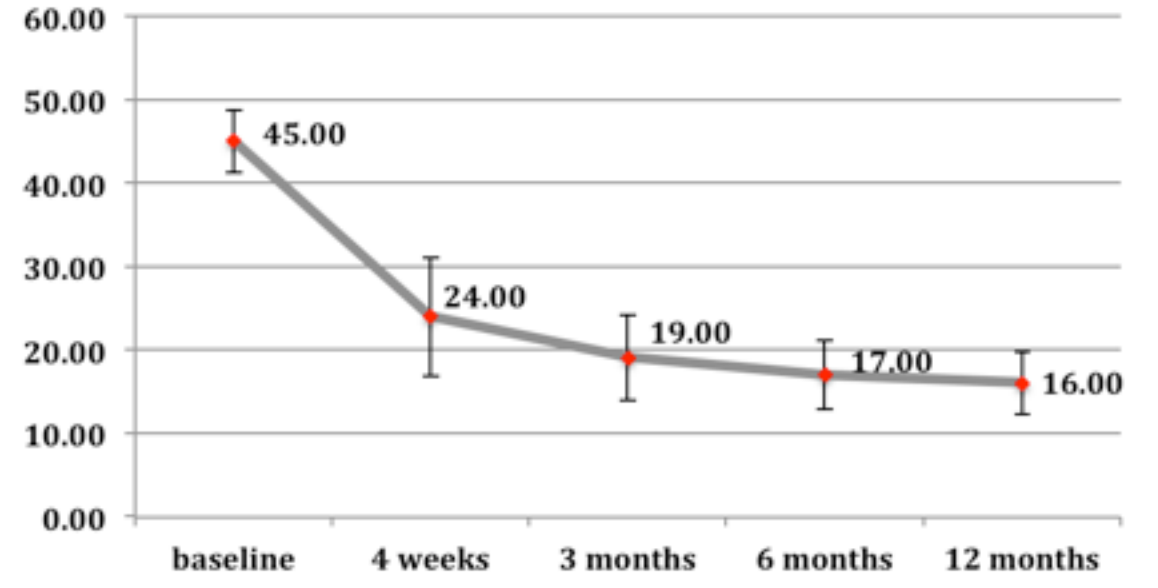

Fig. 4. Functionality (measured by the ODI).

Even if the screening trial with externalized percutaneous components is abbreviated to minimize the risk of infection, it remains present. Furthermore, if an infection does not become apparent until after a costly IPG has been implanted, the entire implanted system generally requires removal, interrupting treatment until the infection has been successfully treated and a new system can be implanted (10). No infections were seen in this study. Some clinicians utilize "on-table-trials" and "all-in-one" implants, proceeding to IPG implantation in a single stage, and have reported overall results comparable to those achieved with more prolonged trials. This study supports the concept of a "direct to perm" or "permanent trial" with this wireless system. Because there is no cut down or IPG, the device can be easily removed if the patient does not obtain relief.

Safety

Surveillance radiographs were obtained at 3 and 12 months to assess SCS device position. Asymptomatic caudal device migration of up to 5 mm was noted in the absence of clinical manifestations. With the superior anatomic coverage of 2 parallel electrode arrays, migration could easily be compensated by modifying the active contacts. A wireless SCS system is capable of reducing complication rates, such as pocket pain, because most of these are linked to the battery component of a conventional system (11). An important aspect to consider is that according to Bendel et al (12), who studied 2,737 SCS implant procedures and identified all procedures complicated by infection (2.45%), the IPG pocket was the most common site of an SCS-related infection and it leads to explantation of the device in 77.6% of the cases. With this new system, the IPG pocket is not required and less infections overall are expected.

Limitations

Although the present study showed a high trial success rate for the wireless SCS system during the 4-week screening period compared with prior SCS literature, there was no control group using alternative technology or sham therapy, so definitive conclusions cannot be made. The difference between no therapy and a single implant, or between a single or dual system, is self-reported and confounds the effect of the therapy and the placebo effect. The single-stage wireless SCS implants lack the distinction between trial and permanent placement and can be considered a "permanent trial."

We did not compare effects on leg or back pain depending on the frequency used. Such tests are possible with already implanted patients because the SCS device allows for choosing low-, intermediate-, or high-frequency SCS via the software, without any further technical limitations (Note: While pulse rates over 1,500 Hz were utilized in the study, Stimwave is only permitted to provide SCS therapy at frequencies <1,500 Hz. Thus, the pulse rates used in the study are not commercially available on Stimwave's products.).

CONCLUSIONS

Our study was a single center, retrospective nonrandomized and noncontrolled study demonstrating the safety and effectiveness of a novel wireless SCS system for the treatment of chronic back or back and leg pain refractory to standard medical management. A significant and stable reduction in pain and improvement in disability and opioid reduction was shown using the new SCS system.

This SCS device opens up a wider spectrum of therapeutic paradigms in the management of neuropathic pain syndromes. Further research in larger groups and in prospective RCTs may provide definitive proof of efficacy of the device.

Authorship Statement

Dr. Rainov treated patients and collected the data at the study site (MVZ Wirbelsaeulenzentrum and Praxisklinik München-Taufkirchen). Drs. Rainov, Haritonov and Niek Vanquathem prepared the manuscript. All authors reviewed the manuscript critically and approved the final version.

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