Systematic Review

Parameters of Spinal Cord Stimulation in Complex Regional Pain Syndrome: Systematic Review and Meta-analysis of Randomized Controlled Trials

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Background: Complex Regional Pain Syndrome (CRPS) is a chronic debilitating neuropathic pain condition characterized by autonomic and inflammatory features that typically occurs after a traumatic event. Spinal cord stimulation (SCS) has been shown to be effective in the treatment of chronic CRPS refractory to conventional treatment modalities. The collective evidence of novel parameters of SCS for treating CRPS has not been characterized extensively.

Objective: To provide evidence for the use of SCS to treat CRPS and characterize the additional benefits of various SCS waveforms.

Study Design: Systematic Review and Meta-analysis.

Methods: PubMed, Embase and CINHLA were screened for all randomized controlled trials (RCT) comparing SCS parameters for the treatment of CRPS.

Results: Four RCTs were identified that included SCS as a treatment arm for CRPS. Of these, one study compared low frequency tonic SCS (LF-SCS) versus conventional physical therapy, 2 studies compared placebo/sham SCS with LF-SCS and a multitude of waveforms, and one study compared LF-SCS with high-frequency SCS (HF-SCS). Two of the studies were rated as having a low risk of bias, one study was rated as having some concerns for bias, while the final study was rated as having a high risk of bias. A meta-analysis of 4 studies comparing conventional therapy/placebo SCS stimulation against LF-SCS revealed increased benefit of LF-SCS in pain reduction up to a month (mean difference [MD] = -1.17 points; 95% CI = -1.61 to -0.73; $P < 0.001$, $I^2 = 42\%$). Another meta-analysis of 2 studies showed that LF-SCS results in higher global perceived effect scores relative to conventional therapy/placebo SCS stimulation (MD = 1.58; 95% CI = 1.00 to 2.15; $P < 0.001$, $I^2 = 0\%$).

Limitations: A pooled analysis using different designs for RCTs was conducted. Some studies folded in multiple neuropathic pain pathologies in addition to CRPS. One study was at a high risk for bias in at least one domain.

Conclusion: LF-SCS is superior to conventional therapy/placebo SCS stimulation. However, more evidence is required to demonstrate that novel SCS parameters are superior to LF-SCS in improving pain scores and functional outcomes.

Key words: Complex Regional Pain Syndrome, spinal cord stimulation, meta-analysis, systematic review, tonic, burst, high frequency, waveform

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Complex Regional Pain Syndrome (CRPS) is a chronic neuropathic pain condition characterized by autonomic and inflammatory features that typically occurs after a traumatic event (1). The pathophysiology of CRPS is thought to result from the combination of autonomic dysfunction, inflammatory changes, and nervous system sensitization that occurs at the onset of trauma (1,2). Though the incidence of CRPS is thought to range between 6.28-26.2 per 100,000 person-years, the clinical impact of this condition is severe as patients can develop chronic debilitating pain (3,4).

The term Complex Regional Pain Syndrome was introduced in 1994 by the International Association for the Study of Pain and divided into CRPS type 1, formerly known as reflex sympathetic dystrophy, and CRPS type 2, formerly known as causalgia. Distinguishing them is the presence of a definite nerve injury in type 2. Thus, in type 2 the nature of the chronic pain is neuropathic, whereas in type 1 it is considered nociceptive, although both types may be distinct parts of a spectrum (5). As the pathophysiology of CRPS has been further elucidated, many therapies have been developed to treat and improve clinical outcomes. These include pharmacological agents, cognitive behavioral therapy, physical/occupational therapy, nerve blocks, and spinal cord stimulation (SCS) (2,6).

SCS is a minimally invasive therapy that has been utilized to treat patients with chronic neuropathic pain (7,8). Its first reported use in a patient suffering from chronic pain was in 1967 (9). The development of SCS technology has seen massive expansion and implementation since then (10,11). The mechanism of action of SCS involves the generation of electric fields within the epidural space. These fields alter the electrical potential across membranes which trigger the generation of action potentials within the dorsal columns of the spinal cord leading to segmental and supraspinal effects (12,13).

In SCS, multiple parameters are involved in the relief of neuropathic pain. The basic unit of electrical stimulation of neuromodulation is the "pulse" which is composed of a specific amount of current amplitude (measured in milliamperes) for a specific amount of time (measured in microseconds [μs]). Another component of SCS is the "frequency" which is defined as the number of pulses per second. It is the combination of these parameters that determine the extent to which external stimuli can activate neurons and axons and subsequently, the therapeutic effect on preventing the sensation of pain they may have (12).

SCS has been typically used as a treatment modality for patients who have localized chronic pain but have been unresponsive to conventional therapies. The most frequent of these pathologies are failed back surgery syndrome, peripheral neuropathy, and CRPS (14) with some prospective studies showing that pain reduction can be sustained for prolonged periods of time (15,16).

Over the past couple of years, different waveforms and parameters of SCS have been trialed for treatments of various pain pathologies (17-19). These include stimulation frequencies as high as 10 kHz (20) along with different waveforms such as burst SCS (21, 22).

To our knowledge, a review of the SCS parameters utilized to treat CRPS has not been conducted for randomized controlled trials (RCTs). Thus, our study aimed to 1) characterize the different types of waveforms and parameters of SCS used to treat CRPS in addition to their clinical outcomes, 2) determine the waveform that patients had preferred most and had the best effectiveness, and 3) provide a narrative review of the utilization of SCS in RCTs for the treatment of CRPS.

Methods

We performed a systematic review based on conventional methodology described by Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) (23) (Fig. 1).

Eligibility Criteria

Study Types

Randomized controlled trials.

Patients

Persons with a diagnosis of CRPS.

Literature Search

Pubmed, Embase, and CINHLA were queried for full-text RCTs studying the treatment of CRPS with SCS. Keywords "Complex Regional Pain Syndrome" AND "Spinal Cord Stimulation" with an emphasis on RCTs were used to conduct the search. The software Endnote 20 (Clarivate) was utilized to conduct a search for full text articles. Articles that could not be recovered by Endnote 20 were then subsequently queried for in the Peer-Reviewed Instructional Materials Online Database or the Interlibrary Loan Internet Accessible Database via our institution.

Type of Outcome Measures

The primary outcome measurement collected was pain relief. This usually came in the form of visual analog scales (VAS) and global perceived effect (GPE), but other pain measurement data were also considered if they utilized similar reporting measures or scales indicating pain severity.

For each study, we recorded the number of patients with CRPS in each trial and the treatment modalities that were utilized for control and intervention groups. For SCS interventions, we noted the parameters that were used in the control and experimental groups whenever it was applicable. In addition to the clinical scales/scores used to characterize patients' clinical outcomes, we conducted a meta-analysis on the clinical effectiveness of low frequency (LF)-SCS on pain scores.

Inclusion Criteria

We included RCTs with patients suffering from CRPS that were treated with LF-SCS tonic, other frequencies, burst, high frequency waveforms, or had SCS implemented as part of the intervention protocol.

Exclusion Criteria

Case studies, protocol descriptions, and nonrandomized prospective studies were excluded from analysis.

Risk of Bias Analysis

All included studies were reviewed with the Cochrane risk-of-bias 2 tool for randomized controlled trials (RoB 2) (24,25). Two independent reviewers assessed each study for the 5 distinct domains outlined in the RoB 2 tool. Classifications of "low risk," "some concerns," or "high risk" were given for each study. When a disagreement was encountered, it was resolved with discussion or inclusion of a third author if necessary (Fig. 2).

Statistical Analyses

Due to heterogeneity from treatment arms and chronic neuropathic pain diagnoses, DerSimonian and Laird random effects meta-analysis was used. The weighted mean difference (MD) in pain scores and GPE

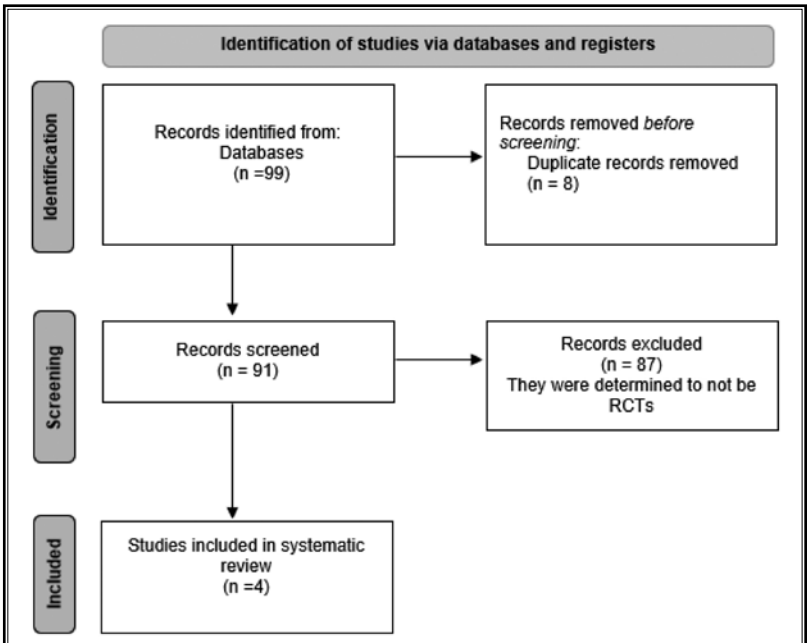

Fig. 1. *PRISMA flowchart in methodology used to identify included studies exploring the effects of various SCS waveforms in the treatment of CRPS.*

Unique ID	Study ID	Experimental	Comparator	Outcome	Weight	D1	D2	D3	D4	D5	DS	Overall
1	Kemler 2000	LF-SCS	Conventional Physical Therapy	Pain	1	+	+	+	+	+	n/a	+
2	Kriek 2017	LF-SCS	Sham	Pain	1	+	+	+	+	+	+	+
3	Sokal 2020	LF-SCS	Sham	Pain	1	+	+	+	+	+	!	!
4	Canós-Verdecho 2021	LF-SCS	Sham	Pain	1	-	-	!	+	+	n/a	-

+ Low risk ! Some concerns - High risk

Fig. 2. *Risk of bias assessment for all included studies.*

was calculated in addition to its 95% CI at time points up to one month after SCS therapy.

A *P* value < 0.05 was considered significant for pain scores. We conducted a sensitivity analysis by excluding studies in a stepwise manner to determine if the new estimate of effect size differed. Analyses were performed using RevMan 5.4 (The Nordic Cochrane Centre for The Cochrane Collaboration).

Results

Literature Search, Patient Numbers, and RCT Experimental Designs

Ninety-nine articles were gathered in our initial search. Eight duplicates were subsequently removed. Ninety-one were screened for our inclusion criteria. Four met our inclusion criteria of being an RCT studying CRPS SCS interventions and were subsequently analyzed.

Across the 4 RCTs, a total of 138 patients with CRPS were randomized into control and experimental arms. Four studies were RCTs that yielded a total of 58 patients in control interventions or standard frequencies and 80 patients in experimental frequencies. Of these, one study compared conventional physical therapy with LF-SCS, 2 studies compared placebo/sham SCS with LF-SCS and a multitude of waveforms, and one study compared LF-SCS with high frequency (HF)-SCS. The rest of the patients were enrolled in trials that had a crossover design. Only a meta-analysis comparing LF-SCS with conventional therapy/sham stimulation could be conducted. Other stimulation settings could not be pooled since there was only one RCT each that had reported data. A summary of the patients number for each RCT we reviewed can be found in Table 1.

Parameters and Waveforms Used for SCS

Two RCTs used a sham/placebo stimulation parameter for SCS while another 2 RCTs compared using SCS with physical therapy or other conventional therapies. Three of 4 RCTs used 40 Hz-60 Hz as a standard frequency of SCS along with varying parameters on pulse width (PW). Three RCTs tested different frequency parameters, such as a high 10 kHz stimulation, or in a burst pattern of 40 Hz. A summary of the control and experimental arms along with any SCS parameters that were utilized for all RCTs analyzed can be found in Table 1.

Table 1. *Intervention descriptions and SCS parameters utilized to treat CRPS.*

Study	Trial Type	Control Group Therapy	LF-SCS Parameter	Other SCS Parameters Investigated
Kemler 2000	Parallel RCT	Physical Therapy	Frequency: 85 Hz PW: 210 μsec Amp: 0-10 V using programmer	-
Kriek 2017	Crossover RCT	Placebo (100 Hz then shutoff)	Frequency: 40-60 Hz, PW: n/a Amp: n/a	500 Hz Frequency: 500 Hz PW: n/a Amp: n/a 1200 Hz Frequency: 1200 Hz PW: n/a Amp: n/a
Sokal 2020	Crossover RCT	Sham	Frequency: 40-60 Hz PW: 250-500 μsec, Amp: To paresthesia	Burst Frequency: 40 Hz PW: 250-500 μsec Amp: To comfort and 50% below perception in continuous mode 1 kHz Frequency: 1 kHz, PW:120 us Amp: 3 Amp below perceptual threshold
Canós-Verdecho 2021	Parallel RCT	Pharmacological,physical, blockages	Frequency: 40–60 Hz; PW: 250–400 MCS, Amp: n/a	10-kHz Freq: 10 kHz PW: n/a Amp: n/a

Risk of Bias Assessment

The 2 crossover studies had low levels of bias across all 5 domains plus the S domain for randomized crossover trials of the RoB 2. One parallel RCT study had a low level of bias across all 5 domains. One study had a high risk of bias in 2 domains.

Meta-analysis

LF-SCS Versus Conventional/Placebo

Four studies reported pain scores and standard deviations or standard errors for patients who received LF-SCS. These studies were compiled for meta-analysis which revealed a significant reduction in pain scores favoring LF-SCS over conventional therapy or placebo stimulation (MD = -1.17 points; 95% CI = -1.61to -0.73; $P < 0.001$, $I^2 = 42\%$) (Fig 3). Two studies were pooled for a meta-analysis on GPE which revealed that LF-SCS significantly raised GPE scores relative to conventional therapy/placebo (MD = 1.58; 95% CI = 1.00 to 2.15; $P < 0.001$, $I^2 = 0\%$).

Sensitivity Analysis

A sensitivity analysis was conducted on the 4 studies that were used for the meta-analysis on pain score reduction. The analysis was performed by excluding individual trials and evaluating its effect on the pooled estimate of pain score reduction. No significant findings were uncovered with this process (Fig. 4, Table 2).

Discussion

To our knowledge, this is the first systematic review conducted regarding the parameters used for SCS in RCTs for CRPS treatment. Some reviews have described the multiple pathologies that SCS has been used to treat, including failed back surgery syndrome, peripheral neuropathy, and refractory angina pectoris (7,8). The last review that mentioned SCS as a treatment modality for CRPS specifically was conducted by Stephen Bruehl in 2015 (1). At that time, only one RCT had been published for the treatment of CRPS (26). Since then, new RCTs have been published that have utilized different SCS parameters to assess clinical effectiveness

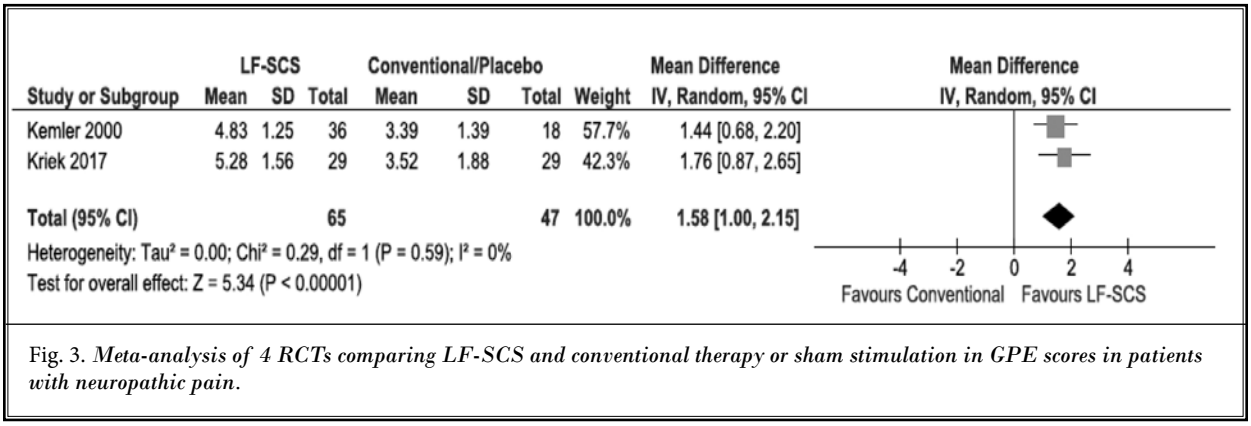

Fig. 3. *Meta-analysis of 4 RCTs comparing LF-SCS and conventional therapy or sham stimulation in GPE scores in patients with neuropathic pain.*

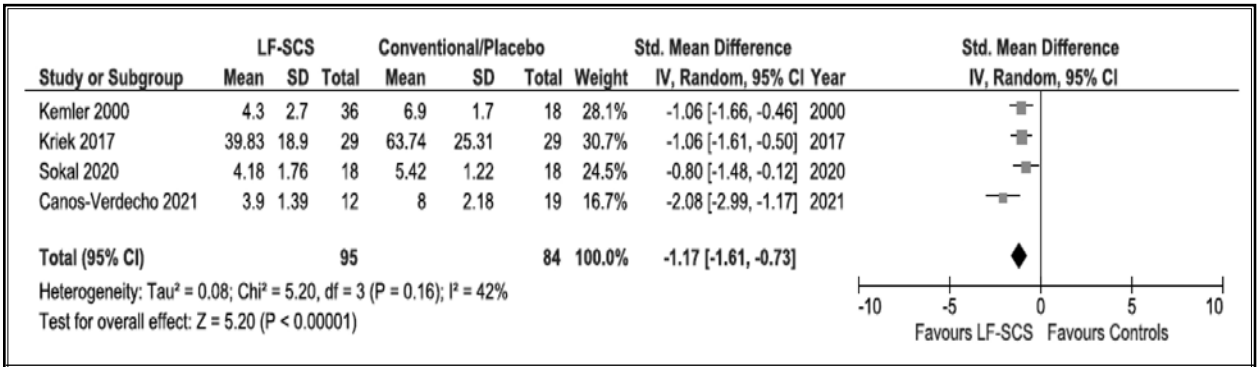

Fig. 4. *Meta-analysis of 4 RCTs comparing LF-SCS and conventional therapy or sham stimulation in reducing pain scores in patients with neuropathic pain.*

Table 2. *Sensitivity analysis of identified studies with omitted study to explore random effects estimates.*

Study Removed	Standard Mean Difference (95% CI)	Test for Overall Effect: Z	*P* value
None	-1.17 (-1.61 to -0.73)	5.2	< 0.001
Kemler 2000	-1.24 (-1.89 to -0.59)	3.75	< 0.001
Kriek 2017	-1.25 (-1.91 to -0.58)	3.67	< 0.001
Sokal 2020	-1.30 (-1.85 to -0.75)	4.04	< 0.001
Canos-Verdecho 2021	-0.99 (-1.34 to -0.64)	5.55	< 0.001

or improved outcomes for patients with CRPS patients (18,27-29). We sought to review the updated literature and provide a comprehensive summary about the treatment effectiveness of SCS historically for CRPS along with the new SCS parameters being investigated.

Our review uncovered only 4 RCTs with a total of 138 patients studying the effects of SCS for the treatment of CRPS. This may reflect the rare incidence of CRPS which has been estimated to range from 5.46-26.2 per 100,000 person-years (30,31) making larger trials difficult to pursue. In addition, SCS bears a high upfront cost (32,33) which may prevent institutions from investigating and implementing its use. Nevertheless, there is evidence to suggest that SCS is a cost-effective treatment for CRPS (34).

The RCTs that we analyzed recruited patients with CRPS either exclusively or folded in patients with CRPS along with other patients with chronic neuropathic pain, such as failed back surgery syndrome. This made conducting an analysis of the clinical effectiveness of SCS in CRPS trials difficult as data for the patients with mixed pain are not typically presented in a manner that stratifies for the specific pain pathology. Neuropathic pain is a complex condition of nervous system disease in which pathophysiology mechanisms are still being elaborated on (35). It is not possible to make an assessment currently whether the pathologies of CRPS or other chronic pain conditions are equivalent. Therefore, caution should be exercised when interpreting clinical data that fold in multiple pain pathologies under one treatment paradigm. We would recommend future studies to stratify their data by the specific pain pathology or design trials in which only one pain pathology is studied.

Our review was able to document the different SCS waveforms that were utilized in each RCT for their patients with CRPS. However, we found differences in the extent to which studies describe the entire SCS parameter that they programmed into each device. Some studies did not include certain aspects of SCS stimulation, such as the pulse width or the amplitude generated. In addition, the parameters can be adjustable by the patients themselves so that they can customize their own programming to achieve the best results (36). We believe that a complete description of the parameters used for the SCS paradigm is crucial to improve reproducibility and allows clinicians to have a better understanding of how to deliver SCS as a therapy for CRPS or other neuropathic pain pathologies.

Current Standard for SCS

Conventional SCS has been defined as a tonic pulse, released at a constant frequency of 40 Hz-80 Hz and a fixed PW of 200-450 μs (37) In our review, the first instance of SCS usage was introduced as a treatment arm in an RCT for CRPS to compare its efficacy against conventional physical therapy (PT) (26,38). They published a prospective RCT (38) to determine if the combination of SCS with PT was more effective than treatment with PT alone. Patients in the SCS + PT combined cohort were implanted with a pulse generator (Itrel III, model 7425, Medtronic) subcutaneously in the left lower anterior abdominal wall and connected to an electrode by a tunneled extension lead. The stimulus delivered was characterized by the following parameters: frequency = 85 Hz, PW = 210 μs, with patients being allowed to adjust stimulus intensity from 0 to 10 V. Pain was assessed using the VAS and the McGill Pain Questionnaire. In addition, patients rated the global perceived effect while functional improvements were also measured (38).

They reported (38) that at 6 months, the cohort assigned to the SCS + PT had their VAS scores reduced by 2.4 cm, whereas scores increased by 0.2 cm in the PT alone group. Fourteen of 36 (39%) patients in the SCS + PT group scored a 6 for the GPE compared to only 1/18 (6%) in the PT alone group. SCS was reported to be successful in 20/36 (56%) patients, with 18/36 (50%) patients scoring 50% lower than their baseline VAS scores. However, the treatment did not result in any functional improvement. Interestingly, a 2-year follow-up study revealed that the patients' VAS scores were decreased by 2.1 cm in the SCS + PT group compared to no change in VAS scores in the PT only controls (39).

However, in a 5-year follow-up study, SCS + PT produced similar results to those assigned to the PT only group (40). Of note, 13 patients were lost to follow-up at 5 years.

Since then, several RCTs included in our review have reproduced the therapeutic effect that LF-SCS has on patients with CRPS. Our meta-analysis of 4 RCTs showed that LF-SCS significantly reduced pain scores relative to conventional therapy or placebo, at least within the first month of treatment. Given the nature of some trial designs included in our study, a pooled analysis of more long-term outcomes was not possible.

Adjusted Parameters of SCS Used to Treat CRPS

We found that subsequent RCTs investigated the effects of changing SCS parameters to determine if it achieved different levels of pain reduction (18,27-29). The first RCT to our knowledge to implement the use of multiple SCS parameters to treat CRPS was conducted by Kriek et al (18) in 2017. In a randomized double-blinded crossover approach, patients diagnosed with CRPS that was resistant to conventional therapy were exposed to the following SCS parameters: standard (40 Hz), burst (frequency: 500 Hz, PW: 1000 μs, interspike interval: 1000 μs), 500 Hz and 1200 Hz. Pain scores were measured using VAS, McGill Pain Questionnaire (MPQ), Numeric Rating Scale (NRS-11), and GPE surveys.

At the end of the crossover period, 14 (48%) of their patients preferred the standard frequency stimulation and 15 (52%) preferred one of the nonstandard stimulation modalities. Of those that preferred the nonstandard parameters, 6 (20.7%) preferred 500 Hz, 4 (13/8%) preferred 1200 Hz, 4 (13.8%) preferred burst while 1 (3.4%) preferred placebo (38). All active stimulation settings were significantly better in reducing VAS and McGill MPQ pain scores relative to placebo stimulation. Nonstandard frequencies achieved similar pain relief as standard frequencies. However, the GPE scores were improved with their preferred stimulation compared with standard stimulation. These findings support the use of standard SCS frequency parameters in the treatment of CRPS as both the Kemler trial (38) and the Kriek trial (18) found clinically significant decreases in pain scores after its use. However, the issue of long-lasting pain relief from CRPS using SCS still remains an objective to study further.

Burst Stimulation, 1 kHz, Clustered Tonic

One RCT in our analysis tested the efficacy of burst stimulation, a 1 kHz frequency, and clustered tonic SCS on their pain-relieving capabilities in CRPS (28). In their randomized semi-double-blinded crossover placebo-controlled trial, they observed a significant reduction in self-reported pain for each treatment type. At baseline, their patients' VAS scores were mean ± SD = 8.13 ± 0.9. VAS scores of the sham, standard (40 Hz, PW = 250-500 μs, amplitude until paresthesia) and 1 kHz (PW = 120 μs, 3 Amp); and clustered tonic (40 Hz, PW=250-500 μs, amplitude until comfortable) SCS parameters had scores of 5.42 ± 1.22, 4.18 ± 1.76, 5.17 ± 1.40, and 5.27 ± 1.33 respectively (28). Patients from all treatment arms including sham saw significant pain relief from SCS and nonstandard parameters exhibited comparable pain-relieving effects to standard parameters. However, it is noteworthy that this trial included patients whose neuropathic pain was due to both failed back surgery syndrome (17) and CRPS (5). Of the 5 patients with CRPS who underwent the interventions, one had no follow-up while another failed the trial. Of the 3 patients who finished the follow-up, 2 preferred the 1 kHz stimulation while one preferred the standard frequency (28). Therefore, we cannot make any strong conclusions as to whether patients with CRPS prefer any specific SCS stimulation parameter for this trial. In addition, there are no data from a long-term follow-up study to determine whether the therapeutic effects of LF-SCS and nonstandard SCS persist.

High Frequency SCS

Currently, another available alternative to standard SCS involves the delivery of HF pulses. Previous randomized trials for neuropathic pain have shown that HF systems may be superior to standard parameters (41,42). Our review uncovered one RCT that examined pain relief provided by HF-SCS compared to standard SCS and conventional treatment (27). In their parallel 3-armed RCT, patients allocated to the conventional treatment (pharmacological, physical, nerve blocks) saw a decrease of 1.4 (15.1%) in NRS-11 scores relative to their baseline at 3 months. Patients allocated to the LF-SCS and HF-SCS lowered their NRS-11 scores by 5.7 (61.8%) and 5.9 (63.8%) respectively. These effects seem to persist after one year of follow-up. In this trial, both LF-SCS and HF-SCS were found to have significantly decreased pain scores with no significant difference between these 2 SCS parameters. However, HF-SCS appears to have the added advantage of the absence of paresthesia as well as removing the need for intraoperative mapping (43,44). Other prospective

studies have found that patients preferred these HF systems over LF-SCS (42,44).

Patient Preference in SCS Treatment

It has been described that patients undergoing SCS treatment have their own preferences for specific parameters they prefer (45,46). Zhao et al (47) explored the value of a Bayesian preference-optimization algorithm to select patients for specific SCS parameters. In their study, they developed a preference model that predicted stimulation preferences for patients requiring SCS. These data could potentially assist clinicians in choosing patients that may benefit with certain SCS parameters to limit trial and error time.

In addition to insufficient improvement after a trial of SCS, decay in SCS pain relief also occurs in a sizable percentage of patients (48). However, salvage therapy after shifting patient SCS parameters has shown to be successful in reducing pain scores after a decline in effectiveness from their initial SCS parameters (49). Thus, the literature supports the practice of determining patient preference for their SCS treatment; regular follow-ups should be conducted to determine whether those parameters need to be adjusted to maintain significant pain relief throughout the course of their therapy.

Limitations

Some limitations exist within our methodology. In our literature search, we did not prompt databases to display any results aside from RCTs. This may have affected the amount of data we were able to curate for the study. However, our search criteria were able to include RCTs that met our inclusion criteria and allowed for a meta-analysis to be conducted on the effects of LF-SCS on pain scores.

Some of the RCTs we analyzed did not include solely patients diagnosed with CRPS, but other types of neuropathic pain conditions, such as failed back surgery syndrome. Though these data were included in our meta-analysis, it was only a small portion of the total study population. However, we acknowledge that such practices make data analysis difficult and we advise against its use in further studies.

Though our analysis found a significant reduction in pain scores after patients received LF-SCS, longitudinal data of patient outcomes were limited. Our pooled analysis was only able to be performed on outcomes up to one month as that was the approximate latest timepoint all included studies shared. Nevertheless, our study has revealed these limitations and can help inform further research to extend their follow-up periods. SCS is still being studied as a therapeutic device to treat neuropathic pain. As new parameters are likely being developed, a proper outline of investigation should be employed to determine their therapeutic effectiveness.

Conclusions

SCS has been shown to be therapeutic in the treatment of patients with CRPS. Our meta-analysis of 4 RCTs of LF-SCS demonstrates significantly reduced pain scores relative to conventional/placebo therapy.

Recently, there has been increased interest in the utilization of nonstandard waveforms, such as burst or HF stimulation. However, the number of RCTs utilizing nonstandard SCS to treat CRPS is severely lacking. Moreover, long-term data showing their persistent therapeutic effects are limited. Nevertheless, studies have shown that some patients prefer nonstandard SCS; their potential to reduce pain levels appears to be equivalent to LF-SCS. More evidence is required to inform the development of SCS devices that patients can program to deliver their preferred SCS stimulation and more longitudinal evidence is required to demonstrate their effectiveness.

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