Spinal cord stimulation with sympathetically independent pain and sympathetically maintained pain

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Background: Complex regional pain syndrome (CRPS) is categorized into sympathetically maintained pain (SMP) and sympathetically independent pain (SIP). Spinal cord stimulation (SCS) is a promising approach in the treatment of severely disabling CRPS. Patients with good responses to sympathetic block before SCS are more likely to have positive responses to SCS than those with negative responses. This study compared the effects of SCS in patients with CRPS, of SMP and SIP categories.

Methods: This was a retrospective study of 16 patients (SMP 8, SIP 8) with CRPS who had undergone trials of SCS. Eleven of the patients had permanent SCS device implants, and the pain relief levels at 1 and 6 months were recorded.

Results: Sixteen patients with severe, incapacitating, and therapy-resistant CRPS underwent SCS trials. Five patients (SMP 3, SIP 2) had poor pain relief during the trial despite adequate coverage. The remaining 11 patients (SMP 5, SIP 6) had permanent electrode implantation performed under local anesthesia and experienced good pain relief. The difference in VAS reduction was not significant between the two groups at the 1-month follow-up (P = 0.325) and the 6-month follow-up (P = 0.779).

Conclusions: There were no statistically significant differences in VAS pain scores between the two groups. The favorable outcome in all 11 patients with only minor remaining symptoms or without remaining symptoms or severe recurrences suggests that SCS is an efficient treatment in SMP and SIP. **(Anesth Pain Med 2013; 8: 86-90)**

Key Words: Spinal cord stimulation, Sympathetically independent pain, Sympathetically maintained pain.

INTRODUCTION

Complex regional pain syndrome (CRPS) is characterized by neuropathic pain and hyperactivity of the sympathetic nervous system, and a general consensus holds that sympathetic nervous system dysfunction is critically involved in the pathogenesis of CRPS [1]. Based on the presence or absence of the sympathetic component of pain, CRPS can be subdivided into sympathetically maintained pain (SMP) and sympathetic independent pain (SIP) [2]. The usefulness of sympathetic blocks in the treatment of CRPS according to disease stage is controversial [3]. Nevertheless, sympathetic nerve block has been suggested as an important procedure in both the diagnosis and treatment of CRPS and can predict the outcome of treatment in patients with CRPS [2,3].

Clinical experience in the treatment of CRPS is based on a few controlled trials using tricyclic antidepressants and corticosteroids with limited success [4-6]. A promising approach in the treatment of severely disabling CRPS is the use of spinal cord stimulation (SCS) to inhibit sympathetic activity [2,7]. SCS is an effective therapy for early CRPS with features of SMP that promotes sympatholysis, while preserving nociceptive pathways [8-10]. Hord et al. [11] suggested a possible correlation between the temporary pain relief with a sympathetic nerve block and the later efficacy of SCS in SMP, but not in SIP. However, the studies are also reporting that SIP patients may benefit from SCS [12,13]. We therefore designed a retrospective study to compare SCS effects between patients with SMP and SIP.

MATERIALS AND METHODS

This retrospective study enrolled patients with CRPS referred to the pain clinic. The patients had to meet the following criteria: age between 19 and 65 years; CRPS type I or II according to the diagnostic criteria of the International Association for the Study of Pain (IASP) [14]; CRPS clinically restricted to one extremity, but affecting at least the entire hand or entire foot; duration of CRPS of at least 6 months;

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and a mean pain intensity of at least 5 as measured on a visual analog scale (VAS) ranging from 0 (no pain) to 100 (very severe pain), according to Jensen and McFarland. In total, 48 patients reported pain in the upper extremity or lower limb. All of the patients had signs of sympathetic dysfunction, including edema, sudomotor or vasomotor disturbances, atrophic changes, motor weakness, and sensitivity to cold.

All of the patients underwent lumbar sympathetic ganglion block or thoracic sympathetic block using 0.25% levobupivacaine. Temperature was measured simultaneously in the affected zone and the contralateral part using an infrared thermometer. A response to sympathetic ganglion block was confirmed by the local injection of 5 ml of levobupivacaine 0.25% near the lumbar chain ganglion. Success of the sympathetic block was considered by an elevation in temperature of at least 1°C in the affected limb. When no improvement was seen following sympathetic block as assessed by reduced mechanical allodynia, improved function clinically, and pain relief of more than 50% persisting longer than the expected duration of the local anesthetic, the patients were considered to have SIP. All of the patients who had undergone a sympathetic block with local anesthetic that had not resulted in pain relief were classified as having SIP. After a diagnostic sympathetic block, 27 patients were classified as having SMP and 21 patients were classified as having SIP. At this point, we performed physical therapy, somatic block, intravenous regional block, and psychological intervention, or increase the medication dose and add opioids. The 13 patients with SIP experienced pain relief or tolerated their pain with the above treatments. Among above 48 patients, we picked up 16 patients (SMP 8, SIP 8) who showed no improvement despite medical therapy or other interventional management and performed a trial of SCS devices. Based on a favorable response to a trial stimulation, we implanted the SCS system to encourage decreased opioid intake and facilitate rehabilitation.

Before deciding to try SCS treatment, all of the patients underwent a thorough psychiatric/psychological examination, but no psychic aberrations with a possible relationship to the pain were detected. For lumbar or cervical segments, dorsal column stimulation was achieved with a medial electrode position. The final positioning for optimal paresthesia coverage was based on the individual patient's response, rather than topographical landmarks. The lead was secured surgically by anchoring it to the supraspinal ligament and exteriorizing the system to a temporary transmitter for a 7-day trial stimulation period. Following successful trial stimulation, the extension lead was connected to a pulse generator that was pocketed subcutaneously in the abdominal wall. All patients were supplied with a Medtronic Itrel® or Synergy® device for ongoing stimulation. According to the patients' response, the following stimulation ranges were used: pulse width 50－450 ms, frequency 50－130 Hz, and current 1－6 V.

To assess the efficacy of treatment, SCS inactivation tests were performed every 3 months. The patient switched off the device after 30 min of acclimation in a room with a controlled temperature between 21 and 23°C to exclude temperature-induced sympathetic vasoconstriction causing pain. We considered the SCS trial results as positive when pain was relieved more than 50% in VAS score compared the baseline and negative if the pain was relieved less than 50%. Only those patients who showed positive response underwent permanent placement of the SCS device. The pain relief was labeled as excellent if the patient had 75% or greater pain relief, good if the patient had 50% or greater, fair if the patient had 25% or greater and poor if the patient had less than 25% pain relief. The Wilcoxon signed rank test was used to compare pain VAS scores and length of time between the onset of pain and initiation of SCS treatment and to compare pain VAS scores of the response to SCS trial and follow up pain relief between SMP and SIP.

RESULTS

Sixteen patients ranging in age from 21 to 59 years presenting with severe, treatment-resistant CRPS were subjected to SCS. The patients had experienced ongoing pain for a median 35 of months after an operation, fracture, or trauma. Fifteen patients had typical symptoms of CRPS type I, and these patients reported a median pain intensity level of 9 on the VAS. The pain was described as intolerable, burning, like swelling, or in response to innocuous stimuli (*i.e.*, allodynia). All of the patients had functional impairment of the limbs that prevented them from working. Preceding therapy included medication with strong opioids, antidepressants, anticonvulsants, and analgesics.

Three patients with SMP did not respond to the trial and the other 5 had permanent SCS devices implanted. Two patients with SIP did not respond to the trial and the other 6 had permanent SCS devices implanted. As shown in Table 1 and Table 2, 6 of the patients with SIP and 5 of SMP patients enjoyed more than 50% pain relief after the trial. There were no statistically significant difference in VAS pain scores

Table 1. Clinical Features of Patients and Efficacy of Spinal Cord Stimulation with SIP

Personal data / Patient no.	Age/Sex	Method	Duration of CRPS (month)	Type of CRPS	Response to SCS trial	Outcome after 1 month	Outcome after 6 month
1	45/M	L	13	1	+	Good	Good
2	59/M	L	288	1	−		
3	29/M	T	24	1	+	Good	Fair
4	41/F	L	24	1	+	Good	Poor/remove
5	46/M	L	24	2	−		
6	21/F	L	36	1	+	Good	Good
7	21/M	L	12	1	+	Good	Good
8	30/M	L	36	1	+	Good	Good

The pain relief was labeled as excellent if the patient had 75% or greater pain relief, good if the patient had 50% or greater, fair if the patient had 25% or greater and poor if the patient had less than 25% pain relief. CRPS: Complex regional pain syndrome, SCS: Spinal cord stimulation, L: lumbar sympathetic ganglion block, T: thoracic sympathetic ganglion block.

Table 2. Clinical Features of Patients and Efficacy of Spinal Cord Stimulation with SMP

Personal data / Patient no.	Age/Sex	Method	Duration of CRPS (month)	Type of CRPS	Response to SCS trial	Outcome after 1 month	Outcome after 6 months
1	49/M	L	15	1	+	Good	Good
2	44/M	T	15	1	+	Good	Poor
3	23/M	L	6	1	−		
4	21/M	L	11	1	−		
5	30/F	T	38	1	+	Good	Good
6	46/F	L	6	1	+	Excellent	Excellent
7	22/M	L	9	1	+	Good	Fair
8	57/F	L	8	1	−		

The pain relief was labeled as excellent if the patient had 75% or greater pain relief, good if the patient had 50% or greater, fair if the patient had 25% or greater and poor if the patient had less than 25% pain relief. CRPS: Complex regional pain syndrome, SCS: Spinal cord stimulation, L: lumbar sympathetic ganglion block, T: thoracic sympathetic ganglion block.

between SMP and SIP patients at 1-month follow up (P = 0.325) and 6-month follow up (P = 0.779) (Fig. 1). In one SIP patients, the effect of SCS decreased good to poor at the 6-month follow-up and removed SCS device. The age, gender, duration of CRPS symptoms and initial VAS did not influence the outcome of spinal cord stimulation. No relationship was detected between VAS score and length of time between the onset of pain and initiation of SCS treatment.

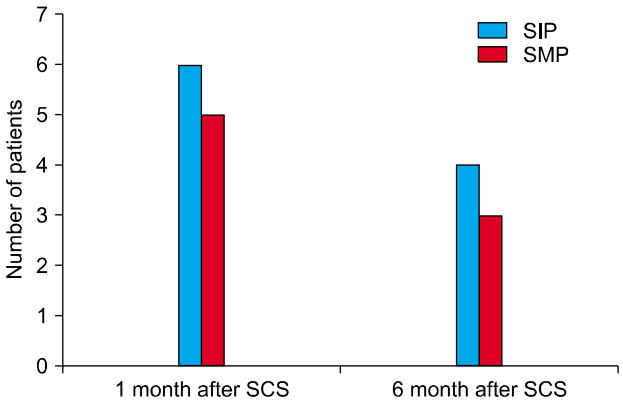

Fig. 1. Number of good responders (50% or greater pain relief to SCS) at 1 month and 6 months after SCS in SIP and SMP. There were no significant differences between two groups (P = 0.325 after 1 month, P = 0.779 after 6 months). SIP: sympathetically independent pain, SMP: sympathetically maintained pain.

DISCUSSION

CRPS can be subdivided into SMP and SIP. SMP implies that an abnormal response of the sympathetic nervous system maintains the pain [2]. Our results confirmed that there was no difference between the two, although SMP responds better to stimulation [11].

A positive response to a sympathetic block in CRPS-I is a reliable predictor of the outcome of SCS. Hord et al. [11] reported that patients with a good response to sympathetic block before SCS are more likely to have a positive response during their SCS trial than those with a negative sympathetic block. Verdolin et al. [12] reported that SIP also responded well to SCS. Eijs et al. [13] suggested that SCS provided effective pain relief in SIP patients.

Our results contradict those of Hord et al. [11] in that no significant correlation was found between SIP and SMP. The mechanism behind the beneficial effects of SCS is largely unknown. SMP implies that an abnormal response of the sympathetic nervous system maintains the pain. Vasodilation obtained by inhibiting sympathetically mediated vasoconstriction could be involved in the mechanism of pain relief by SCS [15]. The theoretical basis for this therapy is blockade of sympathetic fibers in the spinal cord dorsum. The predominant mechanism in patients having CRPS with SMP is most likely suppression of the cutaneous sympathetic vasoconstrictor activity exerted mainly via the α1-adrenoreceptors and antidromic vasodilation mediated by a calcitonin gene-related peptide release by peripheral terminals [16]. This effect on the microcirculation could not be demonstrated in patients with associated sympathetically independent pain [17].

Kemler et al. [17] suggested that the pain relief in patients with CRPS and SIP conferred with SCS does not depend on vasodilation. Eijs et al. [13] found SCS to be extremely successful in the treatment of early CRPS with SIP. To explain the relationship between SIP and the response to SCS, we considered a few possibilities. Several neurophysiologic mechanisms have been proposed. Roberts et al. [18,19] reported inhibitory effects on the central sympathetic system and the activation of descending inhibitory pathways by supraspinal orthodromic SCS stimulation of the periaqueductal gray matter. The release of γ-amino butyric acid (GABA) by SCS may actually inhibit the release of excitatory amino acids in the dorsal horn, thereby suppressing neuronal pain transmission.

In the present study, five patients of eight SIP patients were responders to SCS therapy and four out of eight SMP patients had a reduction of $>25\%$ of the VAS score after 6 months. Although the response rate was slightly better for SIP patients than for SMP, the difference was not statistically significant. Because patients in this study were refractory to other treatments and reported a median pain intensity level of 9 on the VAS, only reduction of $>25\%$ of the VAS score might be meaningful.

In this study, we had several limitations. First, the number of patients was too small for us to draw a solid conclusion. Second, we evaluated the effect with the only VAS. This measurement is not sufficient to evaluate the effect of treatment objectively. Third, the study is retrospective. So, prospective study would be necessary to assess the predictive value of SMP and SIP in patients undergoing SCS.

Based on our data, we suggest that patients having CRPS with SIP can be treated successfully with SCS. Therefore, SCS should be considered in patients with CRPS who are refractory to medical therapy or interventional treatments, regardless of whether the pain has a sympathetic component. Controlled studies are still necessary to establish the long-term benefits of SCS.

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