

Ten Consecutive Cases of Complex Regional Pain Syndrome of Less than 12 Months Duration in Active Duty United States Military Personnel Treated with Spinal Cord Stimulation

Michael H. Verdolin, MD, LCDR,
USN, MC

Eric T. Stedje-Larsen, MD, LCDR,
USN, MC

Anita H. Hickey, MD, CAPT,
USN

Complex regional pain syndrome describes a constellation of symptoms that may involve the sympathetic nervous system. Emerging consensus recommends early intervention with spinal cord stimulation to facilitate physical therapy. Isolated case reports suggest this may be an effective treatment. Ten consecutive active duty United States military personnel with newly diagnosed complex regional pain syndrome underwent early intervention with spinal cord stimulation with favorable results, including decreased pain scores and decreased opioid intake. Six received injuries directly as a result of service in Iraq or Afghanistan. These patients also had posttraumatic stress disorder, but it did not interfere with successful pain control. Additionally, 6 of 10 patients continued on active duty.

(Anesth Analg 2007;104:1557-60)

Complex regional pain syndrome (CRPS) is a clinical diagnosis based on criteria that include hyperalgesia, sudomotor, and trophic changes (1,2). It is differentiated by the presence or absence of major nerve damage as an inciting cause (1). The International Association for the Study of Pain changed the name of "reflex sympathetic dystrophy" to CRPS I, and "causalgia" to CRPS II, because not all pain in this spectrum is sympathetically maintained (1). Repeated sympathetic blockade has been used to facilitate physical therapy (2-4). However, response to sympathetic blockade is partial or absent 73% of the time (2,3,5). Likewise, surgical and radiofrequency sympathectomy provided effective pain relief in only 25% and 38% of patients at 1 yr (6,7). This may indicate a change from sympathetically mediated pain to sympathetically independent pain.

Spinal cord stimulation (SCS) is an effective therapy (3,8,9), which promotes sympatholysis while preserving nociceptive pathways. This may explain its efficacy in treating early CRPS with features of sympathetically mediated pain (3,8,9). SCS was originally considered an

application of gate theory, which postulates that proprioceptive ($A\beta$) overload at the interneuron diminishes afferent nociceptive (polymodal C fiber) input (9,10,10a). Recent investigations (11-14) suggest more complicated, multimodal mechanisms of action, including neurotransmitter release and hyper-excited wide dynamic range neuron attenuation. The exact mechanism of action of the often dramatic response to SCS is unknown (3,9,11,15). The efficacy of SCS for CRPS diminishes modestly over time, but does not disappear (16). As a result, early SCS treatment for CRPS is advocated (3,11,15).

There is only one published randomized controlled trial for SCS in CRPS (9). However, retrospective reviews and meta-analyses covering up to 5 yr of continuous treatment have validated SCS as an effective and economical treatment for CRPS (9,16-19,19a). Given the efficacy of SCS for CRPS and suggestions for early application we undertook early stimulation of 10 consecutive patients injured in military service.

METHODS

Ten consecutive patients underwent treatment in our Interventional Pain Center for CRPS Type I and II diagnosed by history and physical examination. Seven of our patients had lower extremity pain, whereas the remainder had either upper extremity or thoracic pain. Eight of our patients were male. The mean age was 27 ± 7.4 yr. The mean duration of pain before trial of spinal cord stimulation was 9.9 ± 2.5 mo. All patients had failed medical intervention, including gabapentinoids, tricyclic antidepressants, physical therapy, and other conservative treatments.

From the Department of Anesthesiology, Naval Medical Center San Diego, San Diego, California.

Accepted for publication March 7, 2007.

The views expressed in this article are those of the authors and do not reflect the official policy or position of the Department of the Navy, Department of Defense, or the United States Government.

Address correspondence and reprint requests to Michael H. Verdolin, MD, LCDR, USN, MC, Clinical Investigation Department (KCA), Naval Medical Center San Diego, 34800 Bob Wilson Drive, Ste. 5, San Diego, CA 92134-1005. Address e-mail to mhverdolin@nmcsd.med.navy.mil.

Copyright © 2007 International Anesthesia Research Society
DOI: 10.1213/01.ane.0000264087.93163.bf

Table 1. Demographics of 10 Consecutive Cases of Complex Regional Pain Syndrome (CRPS) in Active Duty United States Military Personnel Including Mechanism of Injury

Age	Sex	Source of injury	Pain Site	Diagnosis	SMP or SIP	PTSD	Symptom duration
21	M	Scorpion sting	Left foot	CRPS I	SMP	No	6 mo
28	M	Terrorist explosion and gun shot wound	Right shoulder	CRPS II	SIP	Yes	11 mo
34	M	Helicopter crash	Right knee	CRPS I	SMP	Yes	12 mo
23	M	Terrorist explosion	Left leg	CRPS II	SIP	Yes	10 mo
22	M	Terrorist explosion	Right leg	CRPS II	SMP	Yes	12 mo
27	M	Terrorist explosion	Bilateral legs	CRPS II	SMP	Yes	11 mo
45	F	Rib resection	R chest wall	CRPS I	SMP	No	11 mo
24	M	Terrorist explosion	Left ankle	CRPS II	SMP	Yes	12 mo
24	F	Sprain	Right ankle	CRPS I	SMP	No	9 mo
24	M	Motor vehicle crash	Right ARM	CRPS II	SMP	No	5 mo

Mean age 27 ± 7.4 yr; symptom duration before spinal cord stimulation 9.9 ± 2.5 mo.

SMP = Sympathetically maintained pain, SIP = sympathetically independent pain; PTSD = posttraumatic stress disorder.

All patients underwent sympathetic blockade. In the eight patients, who demonstrated a sympathetically maintained component, defined as greater than 50% diminution of their pain and no appreciable motor block, without permanent resolution of symptoms, a minimum of two blocks were performed. The repeat block was timed if possible with a scheduled physical therapy appointment. In all these cases, the series of blocks, combined with physical therapy failed to permanently relieve or reverse the clinical findings of CRPS. The demographics, including mechanism of injury, are presented in Table 1.

All patients who met criteria for posttraumatic stress disorder were followed by a psychiatrist. All patients underwent a trial of SCS lasting 5–7 days with devices from either Advanced Bionics (Valencia, CA) or Medtronic (Minneapolis, MN). The trial was considered successful in those who reported more than 50% of pain relief from baseline while using the stimulator. Compliance with physical therapy during the trial was interpreted as a positive predictor for implantation. Patients were referred to a behavioral psychologist to assess psychological optimization, including posttraumatic stress disorder (PTSD). Patients with somatization disorder were disqualified. All patients for implantation had favorable psychological screening. Following assessment, patients were implanted with dual-lead 16-electrode systems.

We retrospectively reviewed these patients' medical records and prepared this summary with consent of our Institutional Review Board. Routine assessment 3 mo and 6 mo after implantation included numeric rating scales (NRS) and opioid doses calculated in morphine equivalents. The changes from Pre-SCS NRS and opioid dose were then subjected to statistical evaluation using a two-tailed Student's *t*-test.

RESULTS

This retrospective, observational case series demonstrated a pooled mean NRS of 1.6 ± 1.5 at 6 mo after spinal cord stimulator implantation, representing a

decrease from a pre-SCS NRS of 7.8 ± 1.3 ($P < 0.001$) (Fig. 1). Mean daily morphine equivalents diminished from 103.5 ± 79 to 22 ± 15.8 mg ($P = 0.003$) (Fig. 2). In the war wounded cohort, pooled mean NRS decreased from 8 ± 1.4 to 1.8 ± 1.7 and morphine equivalent consumption decreased from 140 ± 81 mg to 33.3 ± 18.2 mg ($P = 0.004$, $P = 0.02$). The CRPS II subset showed a δ NRS of 6.5 ± 2.3 ($P < 0.001$) and a decrease in opioid consumption of 81.67 ± 17.2 mg ($P = 0.006$). All patients became compliant with physical therapy.

DISCUSSION

American Civil War physician, Silas Weir Mitchell, is credited as the first modern physician to describe causalgia, (CRPS II). He wrote, "Long after every other trace of the effects of a wound has gone, these neuralgic symptoms are apt to linger, and too many carry them throughout the long years this final reminder of the battlefield." (20); His description of neuropathic war wounds still resonates. In the present Middle East conflict, improved armor protects vital areas including the head, neck, and thorax, resulting in a battlefield survival rate of approximately 90%. Injuries are mostly from improvised explosive device attacks, which cause survivable extremity wounds and traumatic amputation (21). Along with physical injuries, most victims suffer PTSD, manifested by hypervigilance, sleep disturbance, and emotional lability (22).

Recent consensus among experts suggests that using SCS earlier in the course of CRPS will improve quality of life and success of rehabilitation (3,9,11). Based on the favorable responses to trial stimulation, we implanted SCS systems to encourage decreased opioid intake, facilitate rehabilitation, and importantly allow for repatriation with often distant commands and families. Six of our 10 patients were wounded as a result of service in Iraq or Afghanistan. One patient with CRPS I was stung by a scorpion, resulting in necrosis of the foot.

The war-wounded were injured in separate improvised explosive device attacks or motor vehicle crashes

Daily Mean Pooled Pain Numeric Rating Scale Pre-SCS, 3, and 6 Months Post SCS Implant

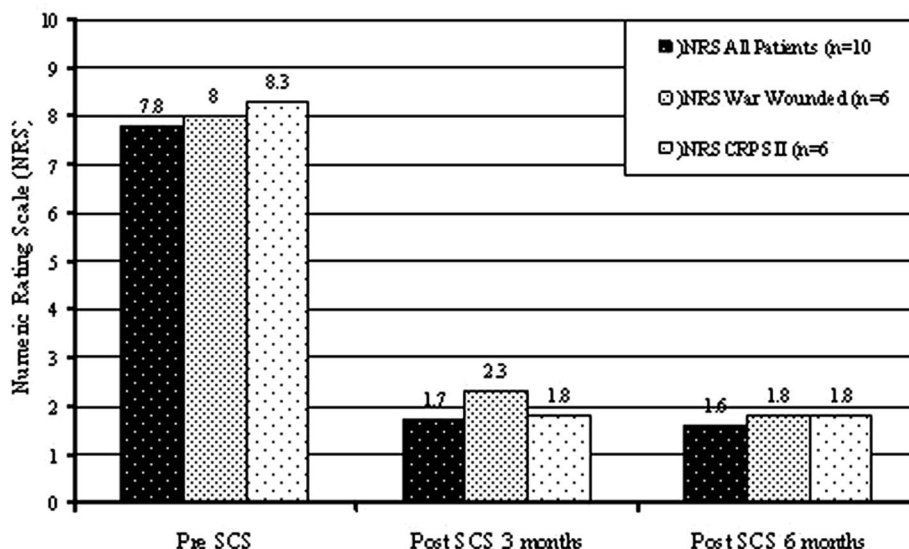


Figure 1. Daily mean pooled pain numeric rating scale pre, three months, and six months after spinal cord stimulator implantation.

Daily Mean Pooled Morphine Equivalents Pre-SCS, 3, and 6 Months Post SCS Implant

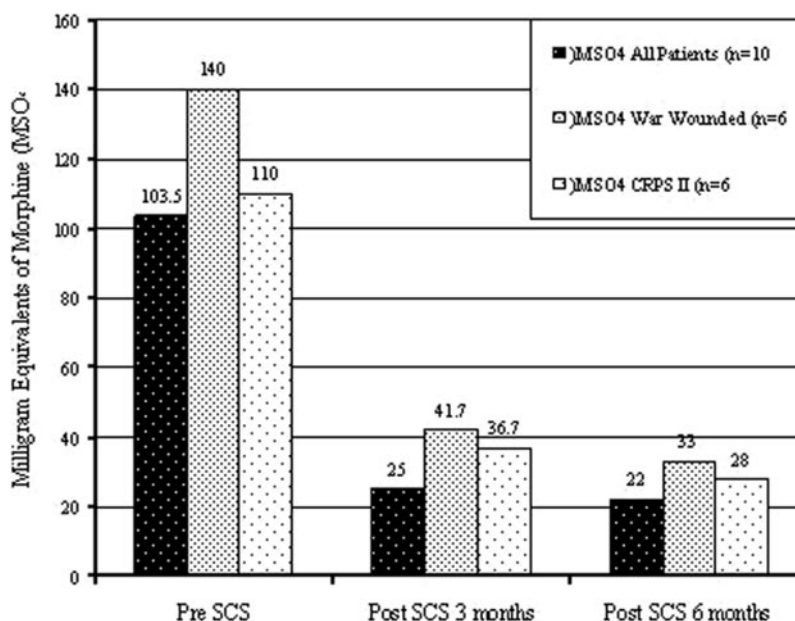


Figure 2. Daily mean pooled morphine equivalents pre, three months, and six months after spinal cord stimulator implantation.

and had PTSD. These survivors had multiple extremity fractures and required repeated orthopedic procedures. Before consultation at our tertiary care Pain Center, all patients were noncompliant with physical therapy and were receiving moderately large doses of opioids. Typically, major psychological comorbidities, such as PTSD, may be considered disqualifying for SCS (23,24). However, all responded favorably to SCS, regardless of the presence of PTSD.

Our results confirm that although sympathetically mediated pain may respond best to stimulation, sympathetically independent pain also responded well to SCS. Because only 2 of 10 patients had sympathetically

independent pain, the data were not broken out for statistical analysis.

We conclude that early consideration for SCS should be given to those with CRPS, particularly CRPS II of <12 mo duration, whether there is a sympathetic component to their pain or not. SCS efficacy does not appear to be impaired by PTSD. Additional benefits of SCS appear to be decreased opioid use, improved compliance with physical therapy, and a short-term propensity toward retention of active duty military personnel. The enthusiasm with which these results may be applied to other populations should be tempered by the short period of follow-up in a small, retrospective observational case series.

REFERENCES

1. Stanton-Hicks M, Janig W, Hassenbusch S, et al. Reflex sympathetic dystrophy: changing concepts and taxonomy. *Pain* 1995;63:127–33.
2. Baron R, Janig W. Complex regional pain syndromes—how do we escape the diagnostic trap? *Lancet* 2004;364:1739–41.
3. Wilson PR, Stanton-Hicks M, Harden RN, eds. CRPS: current diagnosis and therapy. *Progress in pain research and management*, Vol. 32. Seattle: IASP Press, 2005.
4. Cepeda MS, Lau J, Carr DB. Defining the therapeutic role of local anesthetic sympathetic blockade in complex regional pain syndrome: a narrative and systematic review. *Clin J Pain* 2002;18:216–33.
5. Maneksha FR, Mirza H, Poppers PJ. Complex regional pain syndrome (CRPS) with resistance to local anesthetic block: a case report. *J Clin Anesth* 2000;12:67–71.
6. Forouzanfar T, van Kleef M, Weber WE. Radiofrequency lesions of the stellate ganglion in chronic pain syndromes: retrospective analysis of clinical efficacy in 86 patients. *Clin J Pain* 2000;16:164–8.
7. Bandyk DF, Johnson BL, Kirkpatrick AF, et al. Surgical sympathectomy for reflex sympathetic dystrophy syndromes. *J Vasc Surg* 2002;35:269–77.
8. Baron R, Fields HL, Janig W, et al. National Institutes of Health Workshop: reflex sympathetic dystrophy/complex regional pain syndromes—state-of-the-science. *Anesth Analg* 2002;95:1812–16.
9. De Andres J, Van Buyten JP. Neural modulation by stimulation. *Pain Pract* 2006;6:39–45.
10. Melzack R, Wall PD. Pain mechanisms: a new theory. *Science* 1965;150:971–9.
- 10a. Grabow TS, Tella PK, Raja SN. Spinal cord stimulation for complex regional pain syndrome: an evidence-based medicine review of the literature. *Clin J Pain* 2003;19:371–83.
11. Stanton-Hicks M. Complex regional pain syndrome: manifestations and the role of neurostimulation in its management. *J Pain Symptom Manage* 2006;31:S20–4.
12. Shelden CH, Paul F, Jacques DB, Pudenz RH. Electrical stimulation of the nervous system. *Surg Neurol* 1975;4:127–32.
13. DeLeo JA. Basic science of pain. *J Bone Joint Surg Am* 2006;88:58–62.
14. Deuchars SA, Trippenbach T, Spyer KM. Dorsal column nuclei neurons recorded in a brain stem-spinal cord preparation: characteristics and their responses to dorsal root stimulation. *J Neurophysiol* 2000;84:1361–8.
15. Harney D, Magner JJ, O’Keeffe D. Early intervention with spinal cord stimulation in the management of a chronic regional pain syndrome. *Ir Med J* 2005;98:89–90.
16. Kemler MA, de Vet HC, Barendse GA. Spinal cord stimulation for chronic reflex sympathetic dystrophy—five year follow-up. *N Engl J Med* 2006;354:2394–6.
17. Mailis-Gagnon A, Furlan AD, Sandoval JA, Taylor R. Spinal cord stimulation for chronic pain. *Cochrane Database Syst Rev* 2004;CD003783.
18. Kemler MA, Barendse GA, van Kleef M, et al. Spinal cord stimulation in patients with chronic reflex sympathetic dystrophy. *N Engl J Med* 2000;343:618–24.
19. Taylor RS, Van Buyten JP, Buchser E. Spinal cord stimulation for complex regional pain syndrome: a systematic review of the clinical and cost-effectiveness literature and assessment of prognostic factors. *Eur J Pain* 2006;10:91–101.
- 19a. Taylor RS. Spinal cord stimulation in complex regional pain syndrome and refractory neuropathic back and leg pain/failed back surgery syndrome: results of a systematic review and meta-analysis. *J Pain Symptom Manage* 2006;31:S13–19.
20. Mitchell SW, Morehouse GR, Keen WW. Gunshot wounds and other injuries of nerves. *Clin Orthop Relat Res* 1982;163:2–7.
21. Nelson TJ, Wall DB, Stedje-Larsen ET, et al. Predictors of mortality in close proximity blast injuries during Operation Iraqi Freedom. *J Am Coll Surg* 2006;202:418–22.
22. West AN, Weeks WB. Mental distress among younger veterans before, during, and after the invasion of Iraq. *Psychiatr Serv* 2006;57:244–8.
23. North RB. Psychological criteria are outcome measures as well as prognostic factors. *Pain Forum* 1996;5:111–14.
24. North RB, Kidd DH, Wimberly RL, Edwin D. Prognostic value of psychological testing in patients undergoing spinal cord stimulation: a prospective study. *Neurosurgery* 1996;39:301–10.