Complex Regional Pain Syndrome (CRPS): A Systematic Approach to Treatment

Gorecki JP, Rubin, LL, Villavicencio AT

Abstract—We see a large number of patients with extremity injuries. The number of patients experiencing industrial injuries has increased commensurate with the strong economy. Many of these patients develop Complex Regional Pain Syndrome (CRPS). We have developed a systematic approach to treatment and have undertaken a retrospective analysis of these patients. Evaluations of the results, including shortcomings, have led to recent modifications in our approach. When surgical intervention becomes appropriate we enroll patients into a randomized prospective trial comparing dorsal column stimulation and endoscopic video sympathectomy. To date, both procedures demonstrate promising results. We anticipate that with acquisition of more cases, indications for one procedure over the other will become more apparent. Initial diagnosis is confirmed during evaluation by a multidisciplinary team utilizing routine radiological studies, electrical studies, thermography and diagnostic blocks. Initial therapy consists of pharmacological agents and early intensive physical therapy and desensitization. Biofeedback is employed early. When rapid modification of the pain pattern is not identified a series of closely spaced sympathetic manipulating blocks is initiated while aggressive physical therapy continues. Patients who demonstrate response to sympathetic manipulation but fail to achieve lasting relief, were offered sympathectomy. Patients simply failing sympathetic blockade were offered stimulation. This year we began our randomized trial. Intraspinal narcotics are used to salvage failures.

Index Terms—Complex regional pain syndrome, reflex sympathetic dystrophy, CRPS, sympathectomy, Spinal Cord Stimulation, SCS, causalgia

I. INTRODUCTION

Complex regional pain syndrome (CRPS) I and II are new terms that are gaining acceptance in the pain literature [1,2]. CRPS refers to a pain that follows injury, and that is located outside of the distribution of a specific neural receptive field. In addition the pain is out of proportion to the inciting injury and lasts a disproportionate period of time. The severity of the pain is not adequately defined by the observed pathology. Two treatments for CRPS have gained popularity in the recent past, endoscopic sympathectomy and Spinal Cord Stimulation (SCS). Our multidisciplinary group has initiated a randomized trial comparing these two treatments. The purpose of this paper is to review a logical approach to the management of this type of pain based upon outcome derived literature and to present pilot data from this prospective trial comparing SCS to sympathectomy.

II. MANAGEMENT APPROACH

A. Diagnosis

An organic diagnosis must be established. The history of the injury must be carefully reviewed as well as the character of the pain. The history should include careful consideration of the responses, both negative and positive, to prior therapy. The history must also evaluate potential sources of emotional and physical stress. The severity of the pain must be documented using validated tools such as the visual analogue scale [23, 24, 25]. Physical examination confirms any ongoing source of nociceptive pain and documents the presence of sensory dysfunction. Corroborative tests then include a select combination of X-ray, CT, MRI, bone scans, thermographs, electromyography (EMG)/nerve conduction studies, or responses to selective blocks. Incomplete or inaccurate tests should be repeated. Whenever a diagnosis cannot be established, symptomatic palliation is employed. An organic explanation for the pain must be established prior to proceeding with therapy and the diagnosis should be established based upon current taxonomy recommendations.

B. Pain Reduction

The elimination of pain is a principal goal of therapy. The concept is that early pain elimination reduces the potential for “pathological learning”. The elimination of pain should also allow aggressive mobilization, physical therapy, and prevent a chronic disuse state. There is no satisfactory long-term outcome data in the literature to objectively support this hypothesis. The goal of pain elimination is therefore supported only by expert opinion [4]. Desensitization is another widely used technique in the treatment of CRPS. The concept of desensitization must be intertwined with this theory of pain elimination, although this can become somewhat convoluted. The explicit goal of pain elimination supports the notion of employing strong analgesic medication in increasing doses until pain control is achieved.

C. Physical Therapy and Physical Medicine

In many respects physical therapy is the cornerstone for the management of CRPS. Many authors recommend early
and aggressive physical therapy in the successful management of CRPS, however, in terms of outcome based data this intervention remains primarily one of expert opinion. Physical medicine employs the following techniques that each achieve specific goals: edema control, contrast baths, desensitization, fluidotherapy, static splinting, TENS, range of movement, ultrasound, paraffin baths, dynamic splinting, and continuous passive motion [5]. Muscular work of the affected extremity often increases signs and symptoms of CRPS [6]. Muscular work is accompanied by increased oxygen consumption and in theory may result in the production of free radicals. An exaggerated inflammatory response has been hypothesized to be involved in the pathogenesis of CRPS [7]. For this reason, it is advisable to administer physical therapy and active exercise within the limits of pain. It becomes a difficult task indeed to balance the benefit of mobilization and the side effect of increased pain. Objective outcome based criteria to direct the aggressiveness of physical therapy is badly needed.

D. Pharmacology

Pharmacological management is used throughout the treatment course in conjunction with other modalities. Outcome based literature is available both for the treatment of CRPS and for the treatment of neuropathic pains. The authors believe that it is reasonable to extrapolate some data from studies of neuropathic pain and to apply these results to CRPS. Certain therapies can therefore be recommended for the management of CRPS based upon this extrapolation, however, prospective randomized outcome studies are still indicated to confirm that such therapies are specifically successful for CRPS.

Looking first at studies with data specifically dealing with CRPS, only oral steroids have been conclusively shown to be effective. Given the side effects associated with oral prednisone we reserve this agent for failures of more benign drug regimens [8]. There is limited support in the literature for successful management of CRPS with topical dimethylsulfoxide (DMSO) [9], epidural clonidine [10], and intravenous regional blockade with bretyllium or Ketanserin [11]. The limited data available reveals contradictory results for the use of nasal calcitonin and IV phentolamine. Based on the literature and the fact that nasal calcitonin is not effective in the treatment of neuropathic pain it is recommended that the use of calcitonin and phentolamine in the therapy of CRPS be limited to clinical trials [12].

Randomized controlled trials that specifically deal with the management of peripheral neuropathic pain support the use of tricyclic antidepressants, intravenous and topical lidocaine, intravenous ketamine, carbamazepine, and topical aspirin. There is limited data supporting the use of oral, topical, and epidural clonidine as well as subcutaneous ketamine in the management of peripheral neuropathic pain. The data available from studies of peripheral neuropathic pain is contradictory with regard to outcome for the following therapies: mexiletine, phenytoin, topical capsaicin, non-steroidal-anti-inflammatory drugs (NSAIDS), and intravenous morphine [12].

The current regime that is used in our clinic consists of the sequential application of the following agents: tricyclic antidepressants, carbamazepine, phenytoin, IV and topical lidocaine, topical aspirin, clonidine [any route], topical DMSO, capsaicin, NSAIDS, mexiletine, steroids, and narcotics. Randomized prospective controlled, preferably blinded, studies to evaluate the therapeutic effectiveness for CRPS are indicated for the following agents: tricyclic antidepressants, gabapentin, carbamazepine, phenytoin, clonidine, topical DMSO, mexiletine, topical lidocaine, topical capsaicin, topical aspirin, narcotics, and intravenous or subcutaneous ketamine.

E. Psychology

There is no evidence to support the hypothesis that CRPS is the result of an underlying psychological disorder or personality trait. Pain is a subjective experiential phenomenon. A number of psychological factors are known to influence the experience of pain. Pain is influenced by attitudes, beliefs, cultural norms, mood, focus of attention, motivation, and personality traits. Pain is both influenced by psychological factors, and influences the patient’s psychological response to the environment. For example, pain can induce a reactive depression. It is incorrect to separate organic pain and psychogenic pain.

The DSM IV supports this statement. The end experience of pain is rather the result of both the organic impact to the organism that results from nociceptive activation with or without central neuropathic activation, and the impact to the organism of its psychological state which is dependent upon the preexisting state of the being and that induced by sickness.

The goals of the psychological intervention in CRPS include the treatment of depression, motivation of the patient to activate, reorientation of the patient away from the view of a passive victim towards a proactive problem solver, and addressing external stresses from legal, work, health care, insurance, secondary gain and family issues. The psychological evaluation of the chronic pain patient includes a valid and reliable assessment of pain intensity, functional capacity, mood, personality, coping beliefs, and medication usage. Assessment tools include the semi-structured interview, neuropsychological testing and behavioral analysis. Psychological interventions include education, relaxation training, support therapy, cognitive and behavioral therapy, group therapy, family therapy, physical activity and exercise, vocational counseling and relapse prevention.
F. Sympathetic Blockade

Sympathetic blockade has gained widespread use through the powerful recommendation offered by expert opinion as exemplified by John Bonica. The results associated with sympathetic blockade are not proven by outcome based data. Sympathetic blockade is associated with relatively little risk and both sympathetic blockade and somatic blockade result in at least temporary pain relief. Therefore, we believe it is reasonable to employ sympathetic blockade in the management of CRPS. Sympathetic neural blockade should be done frequently enough to keep the pain at bay during therapy and sympathetic blockade is usually continued until the patient, physician or third party payer refuses further repetition. Successful sympathetic blockade must be documented by objective criteria. Lofstrom and Cousins [20] report at least 22 potential tests to document effective sympathetic blockade. Horner’s syndrome is not sufficient to document sympathetic denervation of the arm which requires blockade of at least T1 and not only C7. One simple regimen consists of demonstrating the following four elements to prove sympathetic denervation of the arm [21]: Horner’s syndrome, skin temperature 34 degree C or higher, 50% increase in skin blood flow, and complete abolition of skin resistance response.

Regional sympathetic blockade with guanethidine is not indicated. Regional techniques with alternate agents may be effective but better quality data must be obtained before recommending the use of such techniques in our protocol.

G. Spinal cord and Peripheral Nerve Stimulation

Spinal cord stimulation (SCS) is a recognized therapy for the palliation of neuropathic pain. The beneficial effect of SCS may be at least partially due to its impact on the sympathetic nervous system and may even be the result of reversible sympathectomy. For this reason a number of retrospective reports are available suggesting benefit from SCS in the management of CRPS.

Kumar reported the results he obtained with SCS in 12 patients with CRPS in 1997 [13]. The follow up for the 12 patients had a mean of 41 months and 8 of these patients had prior sympathectomies. The results are quite dramatic, with all patients obtaining benefit. The outcome was excellent in 8 and good in 4. Revisions were required in 5 patients, due to lead migration and lead fracture in one case.

A report by Calvillo [14] supports the utility of SCS. Thirty-six patients were followed for 36 months. Pain scores were decreased by an average of 53% and analgesic consumption was decreased by 50%. Another report by Cooney describes 60% excellent outcome and 20% good outcome in 60 patients treated with SCS for 2 years.

Peripheral nerve stimulation (PNS) is conceptually similar to SCS. The potential advantage for PNS is the ability to concentrate the modality on a single nerve. Although this may be particularly advantageous for neuropathic pain involving one nerve these authors see a potential disadvantage for the management of CRPS since by definition the pain extends beyond the sensory representation of one nerve. Hassenbusch, in a thoughtful paper, reports the results of PNS in 32 patients [15]. Successful trial stimulation was reported for 30 patients and 19 patients (63%) maintained pain relief for 2 - 4 years. The pain score fell from 8.3 +/-0.3 to 3.5 +/- 0.4. Electrode revision was required in 8 of the 30 patients (27%).

H. Sympathectomy

Video enhanced endoscopic sympathectomy can be performed with consistent success and low morbidity. The hospital stay has been consistently reduced to less than 24 hours. When the pain of CRPS appears to be sympathetically maintained it is reasonable to consider surgical sympathectomy. Although Kux is credited with first describing endoscopic sympathectomy in 1951[18], there is a report by Goetz and Murr from South Africa dating to 1944 [16]. Singh in 1996 reports 246 endoscopic sympathectomies performed on 124 patients [17]. Successful sympathectomy was confirmed by day 2 in 244 procedures. The remaining two patients had sympathectomy confirmed by day 7 without further intervention. The hospital stay in this group of patients was more than one day in only 9 patients. Complications consisted of two pneumothoraxes and 1 Horner’s syndrome. Only 6 of the patients had a preoperative diagnosis of causalgia.

Percutaneous radiofrequency is an alternative non-invasive method of achieving sympathectomy. Wilkinson reported his results with 148 procedures on 247 limbs in 110 patients [19]. He documented successful sympathectomy in 96% at 2 years and 91% at 3 years.

The long-term outcome to be anticipated from surgical sympathectomy in patients with CRPS is difficult to ascertain. Mailis suggests that 33% of patients obtain long-term benefit from sympathectomy following positive sympathetic blockade [22]. The prognostic value of sympathetic blockade for sympathectomy may not be any better the prognostic value of somatic blockade for neurolytic procedures. Wilder et al [3] report that one third of patients who undergo permanent sympathectomy after positive local block obtain lasting relief.
III. METHODS

To date the literature does not confirm whether the results of SCS or sympathectomy sustain better results. For this reason we have initiated a randomized controlled trial comparing the two modalities. All of the patients are initially treated with the same non-surgical regimen. If they continue to demonstrate pain and if the pain is demonstrated to be sympathetically maintained pain (SMP) they are offered randomization into one of two groups—endoscopic sympathectomy or SCS. Patients who do not have SMP are not eligible for sympathectomy and are not randomized. Some literature suggests that SCS is effective through manipulation of the sympathetic nervous system. Therefore, offer such patients SCS outside of the study. Follow up is for one year. Patients who fail the modality they are randomized to are eligible for the alternative modality after a period of six months.

IV. RESULTS: PILOT DATA

We have collected the following pilot data in the process of obtaining Institutional Review Board approval for a randomized prospective controlled trial comparing SCS to video enhance endoscopic sympathectomy for the management of patients with CRPS who failed to maintain pain relief following the conservative management protocol (outlined in the introduction). Patients are considered for this study only if they have sympathetically maintained pain syndromes (SMPS) as defined by a greater than 50% reduction in pain scores lasting at least one hour following confirmed sympathetic blockade. Patients with sympathetic independent pain syndromes (SIPS) are offered a trial of SCS independent of the study. Data is available from 11 patients. Nine patients were female and two were male. The average age is 45 years and the diagnostic break down of inciting injuries is presented in table 1. Sympathectomy was performed in four patients. Two of these patients obtained good lasting pain relief. One patient who failed to maintain pain relief after sympathectomy is successfully managing her pain with a regimen of oral methadone although narcotics did not sufficiently control the situation prior to sympathectomy. The other patient is being worked up for SCS.

SCS was employed as invasive management of CRPS in 7 patients. Fair pain control with a reduction in the pain score by less than 50% was observed in one patient who underwent a prior sympathectomy elsewhere with no benefit. Three patients experienced poor long-term pain control with SCS; two of these patients failed to obtain relief from sympathectomies performed at other institutions. The subsequent therapy for the three patients who failed SCS consisted of intrathecal narcotic analgesia (INA) in two patients and percutaneous cordotomy in one patient who suffered following a crush injury to the foot. INA has resulted in good pain control with resolution of concomitant edema in one patient but failed to result in any improvement in the second patient. There were no complications experienced by this small group of patients.

IV. DISCUSSION

The therapy of CRPS consists of concurrent interdependent administration of three major subcategories of intervention: physical therapy, psychological intervention, and pain reduction or analgesia. Each subcategory is managed with sequential, increasingly intensive interventions analogous to the WHO ladder approach to cancer pain. Within this scheme the sympathetic nervous system is no longer given the mechanistic importance once implied in the diagnostic terminology of reflex sympathetic dystrophy.

Sympathetic blockade is indicated in patients who do not achieve adequate enough pain control from pharmacological agents to exercise and remain activated. A positive response to sympathetic blockade can be used to classify the pain as a SMPS although some would argue that this classification is better made based on a response to adrenergic blockade prior to the initiation of sympathetic blockade. For patients failing pharmacological management who have SIPS, somatic blockade is appropriate. Consideration of more aggressive invasive intervention is limited to those patients who fail to maintain sufficient pain control with either sympathetic blockade or somatic blockade. For SMPS either SCS or endoscopic sympathectomy have proven to be effective. The results of our study are two premature to recommend one therapy over the other. SCS is reversible. Successful outcome following sympathectomy is more convenient since maintenance of an implanted device is not required. Our data supports the trial of SCS in patients with SIPS, although this remains to be substantiated and proven. The incidence of invasive intervention with SCS or sympathectomy is less than 20% in the group of patients referred for management in our interdisciplinary approach and should be expected to approach 5% for all patients with CRPS.

V. CONCLUSIONS

The new terminology of CRPS I and CRPS II has been accepted in the literature and appears more often both in the title and text of articles dealing with causalgia and RSD. The usefulness of the new terminology awaits confirmation. The mechanistic implication of the sympathetic in the generation or maintenance of these pain syndromes has correctly been removed from the nomenclature. The concept of sympathetic involvement in
these pain syndromes, however, persists but is now confined to the subdivision of CRPS into pain that is a Sympathetically Mediated Pain Syndrome (SMPS) or a Sympathetic Independent Pain Syndrome (SIPS). A systematic approach to the management of CRPS is justified and incorporates PT, TCA, antiepileptic agents, topical lidocaine, topical capsaicin, topical DMSO, topical ASA, clonidine, NSAID, steroids, and narcotics. There is a complete lack of outcome based data to support the value of sympathetic blockade. There is retrospective data suggesting the usefulness of SCS and sympathectomy. Both modalities deserve prospective trials demonstrating efficacy, safety and outcome. We have initiated a randomized prospective clinical trial comparing SCS to sympathectomy. The role of Intrathecal Narcotic Analgesia (INA) in the management of CRPS remains to be defined. We have organized a randomized prospective clinical trial investigating INA in benign pain and offer this therapy to patients with CRPS who fail the other modalities.

VI. TABLES

Table 1. Etiology of CRPS

<table>
<thead>
<tr>
<th>ETIOLOGY</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minor Trauma</td>
<td>4</td>
</tr>
<tr>
<td>Crush</td>
<td>2</td>
</tr>
<tr>
<td>Ulnar Nerve Transposition</td>
<td>2</td>
</tr>
<tr>
<td>Carpal Tunnel Release</td>
<td>1</td>
</tr>
<tr>
<td>Snake Bite</td>
<td>1</td>
</tr>
<tr>
<td>Laceration</td>
<td>1</td>
</tr>
</tbody>
</table>

VII. REFERENCES
