

Case Report

Early Adjunct Treatment with Topical Lidocaine Results in Improved Pain and Function in a Patient with Complex Regional Pain Syndrome

Amy K.L. Hanlan, MD, Dianna Mah-Jones, MSc, and Patricia B. Mills, MHS, MD

From: GF Strong Rehabilitation Center, Vancouver, BC

Address Correspondence:
Dr. Amy Hanlan
315-3278 Heather St.
Vancouver, B.C., Canada
V5Z 4R9
E-mail:
amy.hanlan@vch.ca

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Complex regional pain syndrome (CRPS) is a pain disorder characterized by sensory, motor, trophic and autonomic dysfunction. The hallmark of the disorder is pain out of proportion of the inciting event. CRPS is difficult for clinicians to manage as there is no gold standard for diagnosis or treatment. Patients with CRPS are at risk of developing contractures, tissue atrophy, joint dislocation and severe chronic pain. While CRPS is thought to be due to peripheral and central nervous system dysfunction, there is limited understanding of the pathophysiology of CRPS. The proposed mechanisms are multifactorial and consequently, so are the proposed treatments. These treatments can be invasive, such as intrathecal drug delivery or sympathectomy, which have poor evidence for efficacy. Thus, highlighting the need for a safe, effective, and early intervention. We present a case of topical 5% lidocaine ointment as a non-invasive, inexpensive and effective adjunct treatment in the management of pain in a spinal cord injured patient presenting with early CRPS. The clinically important effect of topical lidocaine for reducing severe allodynia allowed the patient to participate in rehabilitation strategies to further manage the debilitating consequences of her CRPS, including decreased range of motion (ROM) and function. The immediate pain relief from topical lidocaine allowed the patient to tolerate physical therapy sessions directed at her CRPS. A successful outcome was measured subjectively and objectively by our patient's reduction in symptoms and improvement in ROM and function, respectively. This case study provides preliminary support for improved pain and functional outcome with early adjunct treatment of CRPS with topical lidocaine.

Key words: Complex Regional Pain Syndrome, topical lidocaine, central cord syndrome, spinal cord injury

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Complex regional pain syndrome (CRPS) is a pain disorder believed to result from dysfunction in the peripheral and central nervous systems. It is characterized by sensory, motor, autonomic, and trophic changes (1). CRPS can be categorized by perceived inciting event (type I or type II), stage of development (early or late), or features of autonomic dysregulation (warm or cold). CRPS Type I (CRPS I) develops after injury such as fracture, trauma, or prolonged immobilization, that is not associated with identifiable nerve injury. CRPS Type II (CRPS II) occurs after a defined injury to the nervous system. Currently, the diagnosis of CRPS is

based on clinical signs and symptoms. The International Association for the Study of Pain (IASP) criteria for diagnosis includes: (a) pain, allodynia, or hyperalgesia disproportionate to the initial injury; (b) evidence at some time of edema, changes in skin blood flow, or abnormal sudomotor activity in the region of pain; and (c) no other conditions that would otherwise account for the degree of pain and dysfunction (2). While there is no gold standard investigation for the diagnosis of CRPS (3), triple phase bone scan has proven useful (4).

The pathophysiology of CRPS is poorly understood, but is believed to be multifactorial (5). Mechanisms cur-

rently proposed to explain the development of CRPS include aberrant inflammation, autonomic dysregulation, nociceptive sensitization, and maladaptive neuroplasticity (1,5). Treatment strategies are targeted at these mechanisms, thus they are varied themselves. Many of these strategies are invasive, such as regional blocks or sympathectomies, and have poor success rates (6).

If CRPS persists to the chronic phase, the afflicted individual may experience spreading pain, diminished voluntary motor control, hyperpathia, and negative sensory symptoms, such as hypoesthesia (1). Symptoms can spread proximally to involve the whole limb and occasionally the contralateral limb in as many as 5% – 15% of cases (7,8). Severe chronic CRPS has led to joint dislocation, limb contractures, and chronic pain, sometimes resulting in elective amputation of the affected limb (1,9-11).

We present a case of a patient with CRPS II affecting the upper limb, diagnosed in the early phase and initially treated with topical 5% lidocaine ointment as a non-invasive management strategy.

When a diagnosis of CRPS II was suspected, the patient was managed with topical 5% lidocaine ointment and upward titration of pregabalin until the maximum dose (600mg/day) while awaiting definitive diagnosis via bone scan. The patient noted an immediate, dramatic improvement in her allodynia and hyperesthesia following lidocaine application, allowing her to rapidly increase the function and range of motion (ROM) of her hand through participation in physical therapy modalities, such as occupational and physiotherapy, which remain first-line in the treatment of CRPS (12,13). After bone scan confirmation of the CRPS II diagnosis, she was treated with a 12-day tapering course of oral prednisone (initial dose of 50 mg) and calcitonin via nasal spray (200 units) for 2 months.

CLINICAL PRESENTATION

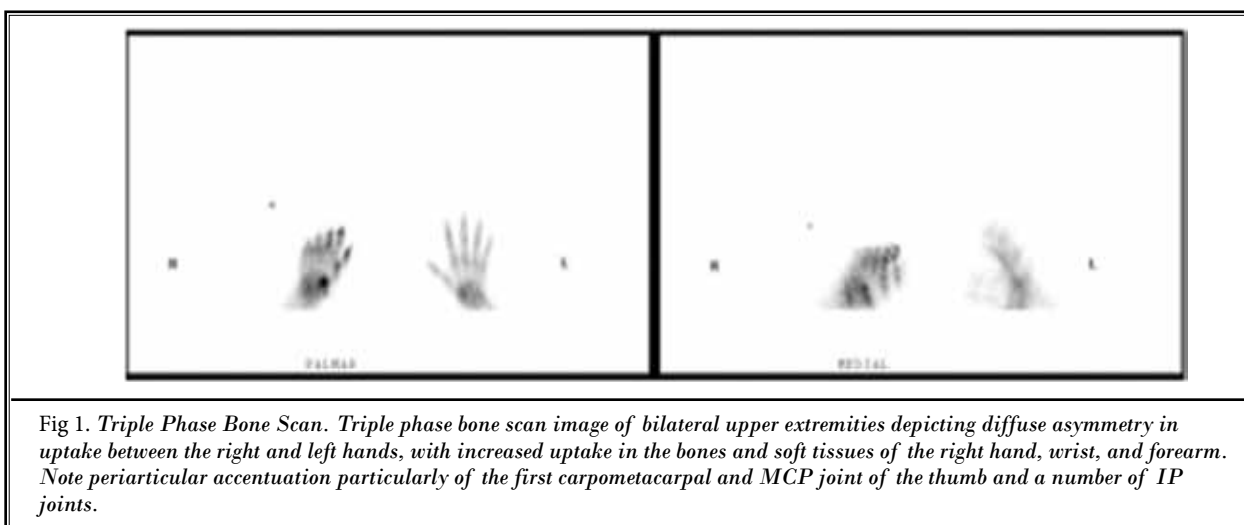
A right hand dominant 65-year-old woman was admitted to our tertiary rehabilitation hospital approximately 2 months after she sustained a traumatic cervical spinal cord injury (SCI) resulting in a central cord syndrome. When examined on admission, she was found to have a C5 AIS D (American Spinal Injury Association Impairment Scale) incomplete SCI as well as a painful, swollen right hand. Her right hand adopted a closed posture. She exhibited severe allodynia to light touch and movement. This degree of pain was out of keeping with her initial injury. The second and third digits were swollen and shiny, with no evidence of C7

radiculopathy on neurological examination (reflex was present and brisk at the ipsilateral triceps). There was pain on application of pressure to all of the metacarpophalangeal (MCP) and interphalangeal (IP) joints on the affected side, especially those of the second and third digits, with no previous history of trauma to that hand. In addition, she had limited ROM of her right shoulder secondary to pain, with evidence of spasticity affecting primarily the pectoralis major and elbow flexors (score of 1+ on the Modified Ashworth Scale). She protected the arm and was unable to utilize the hand for functional activities despite having at least partial preservation of motor power on examination, with full testing of strength limited by pain. A diagnosis of CRPS was suspected.

As the patient was on a low dose of pregabalin on admission, this was slowly increased to the maximum dose (600 mg per day) over a period of 2 weeks. As an adjunct therapy, topical lidocaine 5% ointment was also prescribed the same day that the pregabalin dose was first increased, to be applied 3 times a day while awaiting confirmation of the diagnosis by triple phase bone scan. The patient was encouraged to apply the lidocaine 5% ointment herself using a gloved left hand. A neoprene glove appropriately sized for the patient was then applied to the right hand over the lidocaine ointment, acting as an occlusive dressing. The patient noted a dramatic improvement within 20 minutes of applying the lidocaine to the affected hand for the first time, which occurred before the first increased dose of pregabalin was administered. She reported pain reduction of her allodynia on Numeric Rating Scale (NRS) from 9/10 to 5/10. The pain relief lasted approximately 2 hours, and returned with future re-applications of lidocaine. The reduction in the allodynia of the hand allowed the patient to immediately begin to participate in physical therapy treatments for CRPS including desensitization techniques and contrast baths (Table 1). It also permitted functional use of her arm in self-care exercises with therapy, increased ROM of the fingers and compliance with other aspects of her SCI rehabilitation, such as using a walker for ambulation. The lidocaine did not improve the shoulder pain associated with ROM or the pain elicited by pressure on the MCP and IP joints. The swelling and shiny appearance of her hand slowly improved over the following week. The patient experienced no side effects from the lidocaine. Her only complaint was that the pain relief lasted only 2 hours at a time; this was improved when a glove was applied following topical application.

Table 1. Occupational therapy techniques. Listed are the occupational therapy techniques employed as part of the patient's CRPS treatment.

Intervention	Description
Desensitization	Contrast baths Graded tactile challenges Graded passive stretching
Positioning	Custom foam cone splint Rolyan finger sleeve Custom resting splint in position of function
Heat	Warm paraffin wax prior to manual handling or active exercises
Manual Handling	Active stretches of connective tissue around radius and ulna, at radio-carpal joints and at finger joints Hold-relax techniques to fatigue the antagonist muscles Proprioceptive input to finger extensors during active extension Eccentric and concentric muscle work into supination, wrist extension and finger extension
Active Use with Verbal Guidance	Remedial activities for grasp and release, opposition and manipulation Self-care activities (dressing, feeding, grooming, bathing) Home-making activities (food preparation, cleaning, shopping)



A week following initiation of the lidocaine, a triple-phase bone scan was performed demonstrating diffuse asymmetry in uptake between the right and left hands, with increased uptake in the bones and soft tissues of the right hand, wrist, and forearm (Fig. 1). There was periarticular accentuation particularly of the first carpometacarpal and MCP joint of the thumb and a number of IP joints. This bone scan was reported by the radiologist as consistent with a diagnosis of CRPS.

Following the bone scan, although she was making functional gains with the hand and had reasonable pain control with the lidocaine, she continued to experience pain on deep palpation of the MCPs and IPs of the hand and with ROM of the shoulder. Therefore a 12-day tapering course of oral prednisone (initial dose of 50 mg

and calcitonin via nasal spray (200 units) for 2 months was introduced. The patient continued using the lidocaine and showed ongoing improvement in terms of increased ROM of the fingers and decreased swelling and shiny appearance of the digits (Fig. 2). However, at the end of the prednisone and calcitonin regimen, the shoulder pain and pressure-induced pain of the finger joints persisted. Fortunately, the improvement in the allodynia was sufficient to allow her to continue to participate and make gains with therapy. Two months after the diagnosis of CRPS, she discontinued use of the lidocaine as her allodynia completely resolved (NRS 0/10). The function of the right arm improved to the point where she returned to right hand dominance with self-care activities (Table 2).

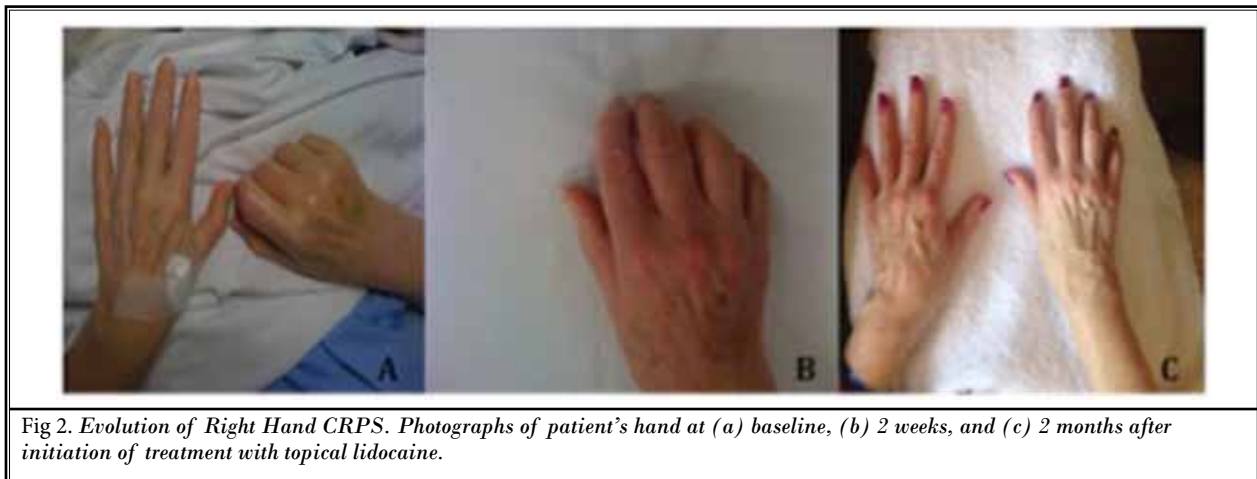


Table 2. Range of motion and functional measurements. Measurements at baseline, 1 week, 3 weeks, and 2 months after initiation of topical lidocaine therapy.

Measures	Baseline	1 week	3 weeks	2 months
Numeric Rating Scale for allodynia pain	9/10	5/10		0/10
Range of motion – (Active flexion/extension in cm)				
Digit 2	3/6	/8	/8.5	0/10
Digit 3	1/6	/8	/9	0/9.5
Digit 4	0.75/5	/7	/8	0/8
Digit 5	1/3	/6	/6	0/6.25
Strength – Maximum grip				
Affected hand			745 gm	18 lbs
Contralateral hand			18 lbs	32 lbs
Strength – Lateral pinch				
Affected hand			3 lbs	6 lbs
Contralateral hand			8 lbs	9 lbs
Strength – 3 point pinch				
Affected hand			2 lbs	5lbs
Contralateral hand			5lbs	7 lbs

Range of motion of the fingers was initially assessed using the Hines Digit-o-Meter, as recommended by the American College of Orthopedic Surgeons. Measurement of composite finger flexion and extension was performed by placing the flat end of the Digit-o-Meter on the palmar crease and flexing and extending the fingers to maximum. The distance is recorded in centimeters from the palmar crease to the tips of the fingernails.

DISCUSSION

This is a case in which adjunctive therapy with topical 5% lidocaine ointment in a patient with early CRPS II elicited a clinical reduction in allodynic pain immediately allowing manipulation of the hand in physical therapy, thereby allowing increased ROM of the fingers and improved function of the hand.

This patient was classified as early CRPS II as she had an identifiable nervous system lesion from her traumati-

ic SCI, and was diagnosed within 2 months of onset of her symptoms, which started a few weeks after the SCI. Epidemiological studies show that 6% of CRPS cases are in patients with SCI (15). Early diagnosis of CRPS is critical as the resolution rate is more favorable if diagnosed in the first year: 74% versus 36% with diagnosis within the next 6 years (1). CRPS that progresses to the late phase can show ipsilateral spread of the painful area or

inclusion of the contralateral side, suggestive of central sensitization of pain. This can lead to invasive and costly interventions including spinal cord stimulation (16), intrathecal drug delivery (17), and partial or complete amputation of the affected limb (9,18). The recurrence rate of CRPS in the residual limb following amputation is as high as 48% and can cause phantom pain in as many as 41% (9).

CRPS is thought to have a peripheral sensitization component whereby the density of sodium channels increases, their activation threshold decreases, and the current across the membrane increases thus amplifying the pain response (5). Local peripheral sensitization following tissue or nerve trauma contributes to hyperalgesia and allodynia, both key diagnostic features of CRPS (3). Lidocaine is a common local anesthetic that acts peripherally by blocking fast voltage-gated sodium channels on the neuronal cell membrane, thus preventing the depolarization and propagation of action potential in sensory nerves (19). A further consideration is that topical anesthetics including lidocaine first impede conduction of myelinated autonomic B fibers, which regulate vascular smooth muscle tone, followed by blockade of nonmyelinated C fibers and, finally, myelinated A fibers, which regulate pain and temperature (20). Therefore topical lidocaine may act to modulate both the autonomic dysregulation and nociceptive sensitization components of CRPS.

The component of central sensitization in late CRPS is postulated to occur due to activation and upregulation of glutamate receptors in nociceptive pathways that are continuously firing from persistent or intense noxious input (5). This process can be exacerbated by alteration in the central nervous system with loss of descending inhibition of spinal neurons and facilitation of nociceptive activity by excitatory neurons projecting from the rostroventral medulla (21). This loss of inhibition of incoming pain messages from the periphery may enhance excitability of thalamocortical nociceptive networks, setting up a chronic pain cycle (22,23). The favorable outcome in pain control with the early use of lidocaine in our patient leads us to hypothesize that treating peripheral sensitization seen in early CRPS may prevent central sensitization by modulating the incoming pain messages from the periphery.

However, improvement in pain does not necessarily equate to improvement in function. The lidocaine allowed our patient to engage in recognized physical therapy activities for management of CRPS, such as de-

sensitization techniques and contrast baths (24). Having our patient apply the lidocaine ointment herself was in itself a desensitization technique. Without the lidocaine effect on the allodynia, our patient would not have tolerated the physical therapy sessions. Oerlemans and colleagues (13) report that patients who participated in physical therapy compared to no therapy resulted in better functional outcomes as assessed by active ROM. Therefore topical lidocaine should not be used in isolation, but in combination with rehabilitation strategies to improve function in the affected extremity.

While no large clinical trials exist on the use of lidocaine for CRPS, lidocaine by alternate routes of administration has been reported for the treatment of CRPS. Vorobeychik and Giampetro (25) reported a case in which a patient with CRPS in the early phase following spine surgery responded well to an epidural infusion of bupivacaine and hydromorphone followed by topical lidocaine 5% patch. Topical lidocaine delivered via patch has been shown to have promising effects on pain reduction in late CRPS in an open-label trial (26). In a study by Schwartzman and colleagues (27), intravenous lidocaine infusion in patients with late CRPS has been shown to decrease mechanical and thermal allodynia with mostly mild side effects in 32.6% of the patients; however, one patient had a seizure. The effectiveness of this intervention strategy on its own was short-lived with the patients returning to their baseline level of pain within 6 months.

Finally, an important consideration is that the formulation, delivery system, and method of application of lidocaine may affect clinical response. Devers and Galer (26) reported patients with chronic neuropathic pain in an open-label trial responded to the lidocaine 5% patch despite a previous poor response to EMLA cream. Lidocaine delivered via gel may have better skin penetration than lidocaine delivered via patch according to a small comparative study (28), although no clinical trials exist to show superiority between the 2 methods. In addition, occlusion after application of lidocaine may increase absorption and shorten onset of action (29). In the case of our patient, use of the glove after application also prevented the spread of the ointment to other surfaces. Fortunately, the safety profile of topical lidocaine is favorable regardless of formulation, with minimal systemic exposure (28). However, there is some systemic exposure as measured by blood levels (28), indicating that tissue absorption of the product occurs beyond the superficial layer of the skin. While topical

lidocaine has a limited side effect profile, factors that influence transdermal absorption and tolerance, such as lidocaine allergy, advanced age, potential for medication interactions, and relevant comorbidities, should be assessed on a case by case basis.

CONCLUSION

This case demonstrates a possible role for topical lidocaine in CRPS as a relatively safe, non-invasive, inexpensive adjunct therapy that permits the utilization of physical therapy strategies for improving pain, ROM, and function of the affected limb. Given that lidocaine formulation and method of application may affect clinical response, we recommend trialing lidocaine 5% in ointment base up to 4 times a day, followed by an oc-

clusive dressing, such as clothing (e.g., gloves, socks) or bandages, to prevent transfer of the ointment to other surfaces and allow absorption. As with all single subject reports, the results with our patient should be interpreted with caution, and ideally confirmed in a randomized controlled trial. Nevertheless, the advantages of topical lidocaine treatment include its relative lack of systemic side effects and its ease of use as an add-on therapy, and therefore can easily be added as a potential management strategy in this patient population.

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