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Effective Sufentanil Intrathecal Pump Treatment in a Patient With Refractory Complex Regional Pain Syndrome: A Case Report

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Background: Many treatments for severe complex regional pain syndrome (CRPS) are ineffective as patients may still experience pain even after various therapeutic approaches. Therefore, it is important to consider novel and creative treatment options for patients suffering from unremitting refractory pain.

Case Report: We report the case of a patient with severe CRPS, which proved to be refractory to numerous conventional treatments. CRPS is a disease that causes chronic pain, typically in distal extremities.

Conclusions: Treatment for CRPS includes pharmacotherapy, sympathetic nerve block, and/or various surgical procedures. However, some patients may receive little benefit from these treatments with persistent severe pain despite undergoing treatment. Thus, novel treatments have been attempted to lessen CRPS-mediated pain. We present a case where one of these unconventional therapeutic approaches was utilized involving the administration of sufentanil through an intrathecal pump providing effective pain reduction in a patient with CRPS.

Key words: Complex regional pain syndrome, sufentanil, intrathecal pump, pharmacotherapy, pain

BACKGROUND

Complex regional pain syndrome (CRPS) is a disorder characterized by chronic, intense pain that occurs in response to minor sensory stimuli (1). CRPS typically occurs due to tissue damage caused by injuries, such as fractures, contusions, surgery, and crush injuries (2). CRPS tends to primarily affect the distal extremities with symptoms occurring along a regional distribution rather than following a dermatomal pattern as in other neuropathic pain conditions. Symptoms of CRPS include hyperalgesia, allodynia, abnormal skin temperature, muscle spasms, and a decreased range of motion of the affected limb (3).

There are numerous pathological processes believed to be associated with CRPS (4). These include an elevated level of inflammatory cytokines, generation of autoantibodies to adrenergic receptors, sensitization of peripheral nerves, and upregulation of adrenergic receptors on nociceptive neurons (3). Management involves multiple different treatment approaches, such as cognitive-behavioral therapy, physical therapy, surgery, and pharmacological management (2). Common medications used in the treatment of CRPS include oral corticosteroids, nonsteroidal anti-inflammatory drugs (NSAIDs), gabapentin, carbamazepine, and tricyclic antidepressants (5).

CASE PRESENTATION

A 49-year-old man with a history of CRPS reported to our pain clinic with complaints of severe pain in the

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lower extremities bilaterally. This patient had a history of recurrent blood clots related to a protein deficiency and a factor V Leiden mutation, along with a history of severe uncontrolled seizures that resulted in a prolonged hospitalization in the intensive care unit poststatus epilepticus. His hospital course was complicated, with multiple cardiopulmonary arrests and prolonged intubation and mechanical ventilation. Posthospital discharge, the patient began to suffer from severe bilateral foot pain described as sharp and burning on the plantar surface of the feet, with this pain being exacerbated upon palpation and with activity. He also complained of hyperalgesia in both his feet with swelling. The patient had a prolonged rehabilitation course and physical therapy. However, his pain continued to worsen, and eventually, he developed contractions in his feet bilaterally.

The patient was initially seen by another physician who diagnosed him with CRPS in both lower extremities. The initial treatment given was gabapentin, pregabalin, lidocaine, and capsaicin cream, though, unfortunately, these all proved ineffective. Following this, the patient received a bilateral injection of platelet-rich plasma into the metatarsal and calcaneal bursa, which provided minimal relief of pain for approximately one month. However, this pain returned with the intensity even worse in the ankles and again caused an inability for the patient to perform his daily functions.

An alternative treatment was then attempted with a lumbar sympathetic block and a lumbar sympathetic plexus thermal coagulation, though these again proved to be ineffective in controlling his pain. After this, a spinal cord stimulator trial was attempted. However, this again provided poor relief of the patient's pain. An epidural steroid injection was then completed, although this did not improve pain either. Fentanyl patches were then prescribed. Unfortunately, this caused severe itching in the patient with only a mild reduction in pain levels.

Following all of these failed prior treatments, a trial of intrathecal injection of morphine was tried. However, the patient developed severe itching and bad urinary retention. The same side effects also developed following a second trial with intrathecal hydromorphone the following month.

When the patient subsequently visited our clinic, his pain was severe and drastically affecting functionality, both psychologically and physically. We opted not to try any previously failed treatment options and discussed an intrathecal sufentanil trial. After acceptance and agreement, an intrathecal injection of 10 mcg of sufentanil provided an excellent and significant reduction of pain and he did not report any major unpleasant side effects. Following the successful trial, we implanted a 40 mL intrathecal pump with sufentanil 50 mcg/mL with an initial daily dose of only 3 mcg/24 h. The dose initially was increased by 20% every time the patient was seen in the clinic after the permanent implant. The intrathecal pump was implanted 22 months ago and at the time of this writing, the current dose is 4.20 mcg/24 h. The patient has also received several refills of the sufentanil pump medication. The patient still reports excellent relief from his daily pain and currently is planning to go back to his full-time job as a professional carpenter. As this treatment has proven to be very effective, the management is planned to remain the same with the use of the sufentanil pump (Table 1).

DISCUSSION

CRPS is a type of neuropathic pain condition that is believed to have a worldwide prevalence between 5.5 to 26.2 per 100,000 persons per year and most frequently presents in women between the ages of 50 and 70 (6). Prior to the onset of symptoms, patients usually suffer some sort of trauma, such as a fracture or surgery, which is believed to play a critical role in triggering the development of the disease (2). Additionally, it is believed psychological factors, such as depression, are associated with the development of CRPS as cognitive-behavioral therapy has been shown to alleviate symptoms in some patients (7). Patients with CRPS experience extreme pain that typically lasts for a transient period, with most cases resolving within one year. However, in 20% to 30% of cases, this condition may become chronic and remain despite attempts to control it with treatment (8).

There are many different treatment options available for patients suffering from CRPS. In the past, NSAIDs were given to these patients to control inflammation though this has been brought into question as clinical trials have not shown this to be effective (9,10). However, bisphosphonates have shown to be effective in helping reduce pain, likely through modulating levels of various inflammatory cytokines (11). Additionally, gabapentin has been shown to lower pain levels in patients with CRPS related to its effect in blocking calcium channels, and thus reducing the release of neurotransmitters by nociceptive neurons (12). Other drugs like ketamine and vitamin C may also be given as they inhibit N-methyl-d-aspartate receptors in the central nervous system and prevent oxidative damage,

respectively (13,14). If pharmacological treatments prove to be ineffective, nonpharmacological methods may be tried, such as plasma exchange therapy or sympathetic nerve block, which have both been shown in various studies to be effective in treating these patients (15,16). Surgical treatment may also be used in patients with CRPS with this often involving the implantation of a spinal cord stimulator. These devices tonically stimulate the axons of neurons in the dorsal column causing a reduction in neuronal hyperexcitability and a change in neurotransmitter levels, and thus may be effective in reducing pain in patients with CRPS (17,18).

Some patients with neuropathic pain conditions, such as CRPS, may not respond to traditional treatments, such as those previously described (19). Because this was the case for our patient, we attempted an unconventional treatment that involved the administration of sufentanil through an intrathecal pump. Sufentanil is an analog of the opiate fentanyl, and thus exerts strong analgesic effects, primarily by acting as an agonist at the mu-opioid receptor (20). Sufentanil is typically administrated intravenously and is often used in combination with other medications in the induction and maintenance of anesthesia for surgery (21,22). Sufentanil may also be administered intravenously for treatment of post-operative pain with studies showing a higher efficacy of sufentanil compared to fentanyl in alleviating pain following surgery (22). However, there are few reported cases involving the administration of sufentanil through an intrathecal pump to treat chronic pain. When sufentanil was used for this purpose, it was shown to be highly effective in alleviating CRPS-mediated chronic pain (23). Furthermore, clinical trials have been done that show sufentanil may suppress severe pain in patients, though this was not the case for all patients in the study (24). In addition, sufentanil has the added benefit of producing less downregulation of the opioid receptor compared to morphine, which often causes this effect when given chronically (25). Because of this, there is reduced tolerance to sufentanil compared to other opiates, such as morphine, which mitigates one of the downsides of chronic opioid use for treating CRPS (25,26). Another potential drawback involving the use of opioids for CRPS is the development of opioid-induced hyperalgesia, which occurs when nociceptive neurons undergo sensitization when patients are exposed to opioids (26,27). However, this has been shown to be more associated with morphine with some reports even showing that the substitution of morphine for sufentanil may reverse opioid-induced hyperalgesia (28). Additionally, while there is the risk of some adverse effects developing with chronic sufentanil use, this can be dealt with by beginning patients on a relatively small dose and then escalating it as needed while carefully monitoring for the development of toxicity. Because of the factors discussed above, we believe sufentanil should be considered as a treatment for patients suffering from CRPS that is refractory to other forms of treatment.

Table 1. Session number and corresponding treatment administered at that session.

Session No	Treatments Administered
Session 1	Oral gabapentin, pregabalin, lidocaine, and capsaicin cream
Session 2	Platelet-rich plasma injection
Session 3	Lumbar sympathetic plexus block and thermal coagulation
Session 4	Insertion of spinal cord stimulator
Session 5	Epidural steroid injection
Session 6	Fentanyl patches
Session 7	Intrathecal morphine injection
Session 8	Intrathecal hydromorphone injection
Session 9	Intrathecal sufentanil injection
Session 10	Intrathecal sufentanil pump insertion

CONCLUSIONS

CRPS is a debilitating condition that affects many people around the world. Patients suffering from this condition experience severe, chronic pain, which often interferes with their ability to accomplish everyday tasks. The pathophysiological mechanisms behind the development of this condition are still not completely understood, though numerous physiological changes are believed to occur which trigger its development. Treatment is often pharmacological though there are other potential options available. However, many of these treatments are ineffective as patients may still experience pain even after numerous therapeutic approaches are tried. Because of this, it is important to develop new and creative treatments for patients suffering from this refractory pain. In this case, therefore, we discussed how the intrathecal administration of sufentanil was able to control pain in a patient with severe CRPS when numerous other conventional treatments failed. Thus, it is important to consider more novel therapies, such as sufentanil intrathecal administration, in treating patients suffering from severe refractory pain related to CRPS.

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