Intrathecal Bupivacaine Monotherapy with a Retrograde Catheter for the Management of Complex Regional Pain Syndrome of the Lower Extremity

W. Porter McRoberts, MD, Catalina Apostol, MD, and Abdul Haleem, MBBS

According to the Polyanalgesic Consensus Conference guidelines, targeted intrathecal (IT) therapy is recommended for the treatment of chronic non-cancer pain when less invasive therapies fail (1). Direct analgesic delivery to the neural axis offers immediate access to receptors, bypasses the blood-brain barrier, and minimizes systemic drug interactions (2). A commonly used mixture for the treatment of intractable pain consists of morphine and bupivacaine (3). According to a retrospective study of non-cancer patients displaying opioid resistance after long-term IT infusions, addition of bupivacaine significantly lowered visual analog scale (VAS) scores and improved the quality of life. The addition of IT bupivacaine, however, provided better analgesia in patients with neuropathic pain than in patients with nociceptive pain (4,5). Some studies suggest that opioids lack a significant analgesic effect on neuropathic and idiopathic forms of pain (6) and recommend performing an initial opioid test...
to determine whether opioids should be part of the treatment plan. Opioid complications may outweigh the benefits especially in younger, non-cancer patients who need to be functional (7). Risks associated with IT opioids (respiratory depression, peripheral edema, granuloma formation) (1) are eliminated by judiciously identifying the mechanisms of pain and guiding treatment accordingly. In patients with predominantly neurogenic pain, bupivacaine monotherapy can provide a safer and more effective IT therapy than an admixture of bupivacaine and opioids.

Although IT bupivacaine is not FDA approved, multiple studies support its long-term safety in the treatment of chronic pain. A 2002 MEDLINE overview of studies employing IT bupivacaine, found this treatment acceptable for chronic pain in cancer and non-cancer patients (8). According to a 1998 prospective, cohort study, IT bupivacaine provided better pain relief than epidural dosing and toxicity was not seen at clinically relevant doses (9). IT bupivacaine was compatible with pump materials and its concentration remained stable when stored in a SynchroMed pump (Medtronic, Inc., Minneapolis, MN, USA) over 12 weeks (10). A targeted bupivacaine therapy is indicated for the treatment of complex regional pain syndrome (CRPS) patients with predominant sensory abnormalities and localized extremity pain. We present a case of intractable foot pain in a patient with CRPS II, where IT bupivacaine monotherapy provided the best analgesia with the fewest complications. We administered bupivacaine through a retrograde IT catheter, targeting the nerve roots that innervated the affected extremity.

**Case Study**

A 57-year-old woman presented to our clinic with a 2 year history of right foot pain, resulting from nerve and fascial injury following a failed plantar fasciitis procedure. The pain covered the medial and plantar aspect of the foot, and was exacerbated by walking. There was no improvement with physical therapy or pharmacotherapy (oxycodeone, lidocaine patches, tramadol, escitalopram, bupropion, and oral steroids). In the first month after surgery, the patient also underwent a calcaneal neurectomy and tarsal tunnel decompression without improvement.

In the following year, the patient consulted multiple specialists. Thorough investigation showed no evidence of nerve entrapment, infection, or malignancy. Electromyogram results suggested a possible right medial plantar nerve injury. Magnetic resonance imaging further indicated a right plantar fascia defect, likely a result of surgery. The right foot was immobilized with a cast to allow healing while the patient, now wheelchair-bound, continued treatment with minimally invasive procedures. A series of blocks provided insignificant relief: a lumbar sympathetic block, ankle nerve blocks, steroid injections, and a lumbar epidural at the L4-L5 and L5-S1 levels. Resection of the medial calcaneal branch of the posterior tibial nerve resulted in numbness without improvement in pain. A series of 8 alcohol injections provided adequate analgesia and permitted ambulation. However, pedal edema developed and the pain returned after 2 months.

The patient presented to our clinic with a 24 month history of right lower extremity pain. On exam, she had edema, reduced range of motion, allodynia, and skin color changes in the right foot (Fig. 1). After a positive lumbar sympathetic block (VAS decreased from 7/10 to 2/10 over a period of 5 days), we diagnosed the patient with CRPS type II. In addition to sympathetically mediated pain, we identified a predominant neuropathic component and advanced treatment to central stimulation. A trial at the T9 level had favorable results: VAS decreased to 2/10, activity increased, and oral opioids were discontinued.

While awaiting stimulator implant authorization, the patient also underwent dorsal root ganglion (DRG) mapping, with the expectation that if the pain improved significantly, she could receive a DRG stimulator, once approved by the FDA. DRG mapping was performed via a transforaminal epidural approach, using a shielded radiofrequency 22 gauge needle. There was a positive response at the L5 and S1 levels and a negative response (no pain relief) at L4 and S2. Unfortunately, the DRG stimulation device required a waiting period that was unacceptable to the patient given her current level of pain. We proceeded with permanent implant of a spinal cord stimulator and supplemented it with a peripheral lead to the posterior tibial nerve (Fig. 2). After one month of central and peripheral stimulation, the patient reported good pain relief (VAS 4/10) and a reduction in exacerbations from once a day to just once a month. Five months post implant, the pain returned with such severity (VAS 8/10) that the patient requested foot amputation. She was seen in the emergency room on several occasions and treated with hydromorphone drip. Ketamine infusion was attempted in another pain clinic and aborted due to dissociative symptoms. In our office, we performed a posterior tibial nerve block that gave 60 – 70% pain relief. We sus-
Six months after implant, stimulation was no longer offering significant pain relief. We decided to add an IT pump and performed IT trials with morphine and, separately, with lidocaine. Morphine offered minimal relief (VAS 7). Lidocaine decreased the pain to a VAS level of zero while producing a motor block of the lower extremities. In order to avoid this limitation, we proceeded with a clonidine trial. Based on a favorable trial (VAS 0), a Medtronic 20 mL SynchroMed II programmable pump (Medtronic, Inc., Minneapolis, MN, USA) was implanted for delivery of a continuous clonidine infusion. The IT catheter was placed in a retrograde fashion, with the tip at the L5-S1 interspace, right of the midline, in the lateral recess (Fig. 3). A myelogram with contrast solution showed excellent local spread. The patient had good pain relief (VAS 2/10) with clonidine for several days until she started experiencing headaches, night sweats, weakness, and a low blood pressure requiring treatment in the emergency room. Clonidine was discontinued.

A bupivacaine trial was then attempted and gave 100% pain relief. Therapy was switched to a hypobaric...
bupivacaine infusion (Medisca Inc., Plattsburgh, NY, USA): 3 mg/day with 2 – 4 mg boluses up to 10 times per day. After multiple dose adjustments meant to decrease a bupivacaine-related perineal anesthesia and extremity motor block, the pump was programmed to deliver an infusion of 3 mg/day and 1.85 mg bupivacaine boluses, up to 10 times a day. The patient experienced 90 – 95% relief using a daily average of 4 boluses that lasted between 30 minutes and 4 hours. This enabled her to ambulate for 10 – 15 minutes at a time and perform chores without her electrical scooter. We helped her experiment with positioning during boluses, and found that a left lateral decubitus position, with the right foot elevated, minimized the unwanted sensory blockade in the opposite foot and perineum. Although pain still peaked between boluses (VAS 8), the patient discontinued narcotics and considered her current pain level a significant improvement over her initial condition.

**Discussion**

CRPS presents a therapeutic challenge due to its many presentations and multifaceted pathophysiology. Although we know that both peripheral and central mechanisms are involved, a better understanding of the underlying pathology is needed. There is no approved treatment algorithm and clinical interventions are often applied empirically, to counter the various symptoms as they arise (11). As part of our treatment, we tried several invasive modalities, starting with stimulation and later advancing to an IT pump. An ideal starting point in our investigations was finding the anatomic source for the pain. DRG mapping was essential in identifying the L5 and S1 levels as the best targets for therapy. Based on this information, we threaded a retrograde catheter to these levels of the spinal nerve roots. In order to maximize analgesia and avoid undesirable side effects, we decided to test various IT drugs, sequentially. We started with an initial morphine trial that was negative, thus allowing us to eliminate opioids from the treatment algorithm. Continued testing, showed that clonidine and bupivacaine provided the best pain control. Clonidine had severe side effects, leaving bupivacaine as the preferred agent. A dual targeted approach involving a retrograde catheter and bupivacaine IT monotherapy gave the best results in our patient.

CRPS presents an obvious therapeutic challenge. We believe, both central and peripheral mechanisms are involved. However symptoms vary and there is no approved treatment algorithm, to date. According to Stanton-Hicks et al (12) interventional treatment can be generally divided in 3 stages: minimally invasive therapies (blocks), more invasive therapies (stimulators, IT pumps), and surgical ablations (sympathectomy) as a last resort. Secondary to the poorly understood nature of CRPS and lack of clinical consensus, a variety of specialties may be involved in the treatment. Neurodestructive procedures (neurectomy, sympathetic ablation, and neurolytic alcohol blocks) were performed in the early stages of treatment, and likely exacerbated our patient’s situation by inducing post-sympathectomy neuralgia. According to the latest Practical Diagnostic and Treatment Guidelines for CRPS, neuro-destructive procedures are best relegated to terminally ill patients (11). We believe that non neuro-destructive second stage interventions should be the main treatment for CRPS and that the pain practitioner should be at the center of treatment planning.

IT bupivacaine monotherapy is infrequently used for CRPS treatment. A 1999 case study by Lundberg and colleagues (13) examined the effects of continuous IT bupivacaine infusion in 2 patients with CRPS-I. The authors concluded that this treatment provided some pain relief but did not stop the associated symptoms of edema from spreading to the entire extremity or the opposite limb. They did not recommended IT bupivacaine in preference to other pain treatment regimens for CRPS-I. Our findings, however, support the use of IT bupivacaine monotherapy for CRPS treatment when...
In conclusion, this case report described a CRPS patient, with neuropathic symptoms, resulting in debilitating right foot pain. She had undergone repeated minimally invasive blocks and several neuro-destructive procedures as part of her initial treatments, and experienced an exacerbation of pain. We subsequently advanced her treatment to more invasive techniques, and found that IT monotherapy with bupivacaine offered the best relief with the least severe side effects. The patient reported 100% pain relief after treatment with bupivacaine boluses, delivered through a retrograde catheter at the L5-S1 level. Unfortunately, she had some degree of motor block in her left foot and minimal bladder incontinence. Overall, she felt the treatment increased mobility and function. This case illustrates the benefit of characterizing CRPS patients among 3 main classes: sensory abnormalities with limited neuropathic pain, vasomotor abnormalities, or RSD (sp)-like symptoms. Treatment can then be targeted to the particular symptoms. Our patient benefited from individualized treatment, with IT monotherapy through a retrograde catheter. We endorse a targeted therapy and practitioner tenacity to seek alternate treatments as symptoms evolve.
References


