Journal of Clinical Anesthesia (2007) **19**, 226–229

ELSEVIER

Journal of Clinical Anesthesia

Case report

The efficacy of postoperative perineural infusion of bupivacaine and clonidine after lower extremity amputation in preventing phantom limb and stump pain

Lakshmi Madabhushi MD (Assistant Professor), Scott S. Reuben MD (Professor)*, Robert B. Steinberg MD, PhD (Assistant Professor, Director of Pain Management), John Adesioye MD (Pain Management Fellow)

Department of Anesthesiology, Baystate Medical Center, Springfield, MA 01199, USA
Tufts University School of Medicine, Boston, MA 02111-1533, USA

Received 10 May 2006; revised 20 July 2006; accepted 31 July 2006

Keywords:
Amputation;
Above-the-knee;
Analgesia;
Perineural;
Clonidine;
Pain;
Neuropathic;
Phantom limb

Abstract We report the efficacy of perioperative infusion of clonidine and bupivacaine for above-knee amputation in a patient with a history of phantom limb pain in the same extremity after a previous below-knee amputation. The patient underwent general anesthesia. Before transection, the sciatic nerve was infiltrated with 0.25% bupivacaine 5 mL and clonidine 50 μg. After the nerve was severed, a 20-gauge epidural catheter was inserted into the nerve sheath and externalized laterally through a separate skin incision. Before closure, 0.25% bupivacaine 10 mL and clonidine 50 μg was injected, and 0.1% bupivacaine and clonidine two μg/mL was infused at 10 mL/h for the first 96 hours postoperatively. There were no incidents of hypotension, bradycardia, or sedation during the infusion period. The mean postoperative pain score (from 0 to 10) for 96 hours was 1.2 $\pm$ 0.7. The patient required a total of 10 mg of oxycodone postoperatively. The patient did not report either stump or phantom pain for 12 months after surgery.

1. Introduction

Pain after amputation is a significant problem among amputees. Phantom limb pain may appear in up to 85% of patients and is usually resistant to a wide variety of treatments [1-4]. The mechanisms underlying this pain syndrome are still unknown. Complex multifactorial interactions involving peripheral nerves, central nervous system (CNS), sympathetic system, psychologic overlay [1-4], and genetic predisposition [5] have all been implicated. Peripheral nerve transection results in an afferent nociceptive barrage that initiates spinal cord hyperexcitability with expansion of the receptive fields of dorsal horn neurons that respond to the nearest intact afferents [6]. These neuroplastic changes are believed to be responsible for the development of postsurgical chronic pain syndromes, including phantom limb and stump pain [7,8]. It is believed that regional anesthesia, by preventing the establishment of central sensitization, may play a role in reducing the incidence of acute and chronic pain. In

* Corresponding author. Tel.: +1 413 794 4325; fax: +1 413 794 5349.
E-mail address: scott.reuben@bhs.org (S.S. Reuben).

0952-8180/$ – see front matter © 2007 Elsevier Inc. All rights reserved.
doi:10.1016/j.jclinane.2006.07.008

addition, because the surgical neurogenic inflammatory response may provide a source of nociceptive input into the CNS for a prolonged period, a continuous infusion of local anesthetic postoperatively may prevent the establishment of central sensitization [7]. Although perioperative epidural block may prevent the development of phantom limb pain [9-11], its use in the setting of anticoagulation is contraindicated. The perineural administration of clonidine, an α_2-adrenergic receptor agonist, reduces neuropathic symptoms after nerve injury in a rat model [12]. Peripheral nerve block for intraoperative and postoperative analgesia with local anesthetics and clonidine not only prolongs and intensifies the block but may also help in preventing sensitization induced by nerve injury during surgery [13].

We report the efficacy of perioperative infusion of clonidine and bupivacaine for above-knee amputation (AKA) in providing effective postoperative analgesia and eliminating both stump and phantom limb pain in a patient with a previous history of this chronic pain syndrome in the same extremity.

2. Case report

A 68-year-old, 81-kg man presented for elective left AKA due to ischemic necrosis secondary to peripheral vascular disease. He had a left below-knee amputation two years earlier, after which he reported stump and phantom pain. His medical history was significant for hypertension, diabetes, chronic atrial fibrillation, and a St Jude aortic valve necessitating daily warfarin therapy. Warfarin was withheld 6 days before AKA surgery, and he received subcutaneous enoxaparin 80 mg (one mg/kg) every 12 hours until the day before surgery. The patient underwent uneventful general anesthesia. Intraoperatively, the sciatic nerve trunk was dissected and infiltrated with 0.25% bupivacaine 5 mL and clonidine 50 μg before transection. Afterward, a 20-gauge, multiorificed, epidural catheter was inserted into the nerve sheath and sutured in place. The catheter was then externalized laterally through a separate skin incision. Before closure, 0.25% bupivacaine 10 mL and clonidine 50 μg were administered through the catheter. Bupivacaine 0.1% and clonidine 2 μg/mL were infused at 10 mL/h for the first 96 hours postoperatively. Enoxaparin 80 mg was initiated every 12 hours for 24 hours after surgery. Pain scores, vital signs [blood pressure (BP), heart rate (HR), respiratory rate] and sedation scores were recorded every 4 hours. Pain scores were recorded on a numerical rating scale (NRS) from 0 to 10 (0 = no pain, 10 = worst imaginable pain), whereas sedation scores were measured on a numerical scale of 1 to 5 (1 = completely awake, 2 = awake but drowsy, 3 = asleep but responsive to verbal commands, 4 = asleep but responsive to tactile stimulus, and 5 = asleep and not responsive to any stimulus). Intravenous (IV) fentanyl 25 μg every 5 minutes as needed was prescribed while the patient was in the postanesthesia care unit (PACU), and oxycodone 5 to 10 mg every 4 hours as necessary was prescribed while he was on the surgical ward. There were no incidents of hypotension (blood pressure, <20% baseline), bradycardia (HR, <60 bpm), or excessive sedation (score, >3) during the infusion period. The 96-hour mean NRS pain score was 1.2 ± 0.7, and the mean sedation score was 1.8 ± 0.3. The patient required no fentanyl in the PACU, but he did receive a total of 10 mg oxycodone postoperatively for the first 96 hours during the infusion. The patient reported the absence of both stump and phantom pain at monthly intervals during the first 12 months postoperatively.

3. Discussion

We report the efficacy of a perioperative perineural infusion of bupivacaine and clonidine for analgesia after AKA in a patient with a previous history of phantom limb and stump pain in the same extremity. This technique provided excellent postoperative analgesia with minimal supplementary opioid use while preventing the recurrence of both stump and phantom limb pain.

Although first described in 1649 [1], the etiology of phantom limb pain still remains unknown, and numerous analgesic techniques aimed at relieving the symptoms of this chronic pain syndrome have proved disappointing [1-4]. Three factors may contribute to the development of persistent, postamputation phantom pain by inducing central sensitization at different times relative to surgery: pre-amputation pain, noxious intraoperative stimuli, and acute postoperative pain [7,8,14,15]. Continuous epidural analgesia may be an effective analgesic technique for lower limb amputation. Initial clinical trials showed a beneficial effect on the reduction of phantom and stump pain [9-11], whereas a later study failed to confirm any benefit [16]. Epidural analgesia is contraindicated in the setting of anticoagulation and may result in hypotension, sedation, respiratory depression, pruritus, urinary retention, and motor block. Continuous regional analgesia by perineural block is a potential technique for managing pain after lower extremity amputation [17-21]. This technique may be a safer alternative to epidural analgesia for geriatric patients who have multiple comorbidities. Furthermore, perineural catheters are not contraindicated in the setting of perioperative anticoagulation. However, clinical investigations evaluating the efficacy of continuous perineural analgesia in reducing long-term phantom and stump pain have been equivocal, with some studies reporting efficacy [17,18,21], whereas others showed no long-term beneficial effect [19,20]. Unfortunately, many of these studies had significant design flaws including the fact that they were not prospective, randomized, or blinded; they used either no control group or historical controls; they investigated a heterogeneous study group; and/or they lacked sufficient power to reach a firm conclusion.