Arthroplasty Today 1 (2015) 21–24

Contents lists available at ScienceDirect

Arthroplasty Today

journal homepage: http://www.arthroplastytoday.org/

Case report

Unanticipated transient sciatic nerve deficits from intra-wound liposomal bupivacaine injection during total hip arthroplasty

Wesley H. Bronson, MD, MSB, James P. Doran, BS, James Slover, MD, Donato Perretta, MD, Richard Iorio, MD *

Department of Orthopaedic Surgery, New York University Langone Medical Center's Hospital for Joint Diseases, New York, NY, USA

ARTICLE INFO

Article history:
Received 6 January 2015
Received in revised form
11 April 2015
Accepted 4 May 2015
Available online 27 May 2015

Keywords:
Arthroplasty
Liposomal bupivacaine
Exparel
Postsurgical analgesia
Postoperative neurologic deficits

ABSTRACT

Liposomal bupivacaine (Exparel®) is a novel formulation of local anesthetic used to provide extended postoperative analgesia as part of a multimodal pain control regimen in patients undergoing total joint arthroplasty. In the three total hip arthroplasty cases described, all patients exhibited a transient loss of neurologic function in the sciatic nerve distribution of the operated extremity lasting between 24 and 72 h during the immediate postoperative period. Due to the nature and duration of the deficits, it was concluded that they likely occurred as a result of unintended injection of the medication in close proximity to the sciatic nerve. To the best of our knowledge, these events have yet to be reported in the current literature. We recommend orthopaedic surgeons pay special attention during infiltration of the medication at the surgical site to avoid postoperative neurological deficits.

Introduction

Pain control after total hip and total knee arthroplasty is a major concern for both orthopaedic surgeons and their patients. Patient perceptions of success or failure are related to pain relief and speed of recovery [1]. Additionally, adequate pain control is associated with early ambulation and return of normal gait kinematics [2,3].

In recent years, there has been a shift towards multimodal pain control in total joint arthroplasty (TJA), which can include a preoperative, preemptive pharmacologic cocktail, intraoperative periarticular injections, as well as a postoperative pharmacologic pain protocol [4–6]. These protocols, which deemphasize high-dose opiate use, have been shown to be effective in reducing opiate use, improving pain scores, and permitting early ambulation. Unfortunately, the duration of action of commonly used periarticular injections is short, with bupivacaine or ropivacaine lasting only 8–12 h [7].

As an adjunct to these multimodal pain protocols, the use of liposomal bupivacaine has recently gained popularity, offering the pain relief of local bupivacaine with a longer analgesic effect. Liposome-encapsulated bupivacaine (Exparel®, Pacira Pharmaceuticals, Inc., San Diego, CA) gained FDA approval in October 2011. This Depo-Foam bupivacaine consists of spherical, lipid-based particles with encapsulated bupivacaine, allowing diffusion over an extended period of time [8,9]. It has been shown to have bimodal plasma concentration time, with an initial peak at approximately 1 h and a second peak between 12 and 24 h [8]. This formulation is designed for a single-dose injection into the surgical site with analgesia lasting up to 72 h [10]. Liposomal bupivacaine efficacy is highly technique dependent.

A systematic review analyzed the side effect profile and safety of Exparel in the published literature [11]. The most common side effects were GI disturbances, fevers, and local site irritations. Overall, however, the medication was well tolerated, with side effects occurring within lower or equal rates as bupivacaine HCl.

Here we report on 3 cases of unintended postoperative sciatic nerve deficits following local injection of liposomal bupivacaine during total hip arthroplasty. To our knowledge, these are the first cases reported in the literature.

One or more of the authors of this paper have disclosed potential or pertinent conflicts of interest, which may include receipt of payment, either direct or indirect, institutional support, or association with an entity in the biomedical field which may be perceived to have potential conflict of interest with this work. For full disclosure statements refer to http://dx.doi.org/10.1016/j.artd.2015.05.001.

* Corresponding author. Administrative Office, 14th Floor, 301 East 17th Street, New York, NY 10003, USA. Tel.: +1 212 598 2775.
E-mail address: richard.iorio@nyumc.org

http://dx.doi.org/10.1016/j.artd.2015.05.001

Case histories

Exparel® injection protocol

At our institution, the protocol for Exparel use in unilateral total hip arthroplasty (THA) cases is as follows: 20 cc of Exparel (13.3 mg/ml) is combined with 40 cc of injectable 0.9% normal saline solution (for a total solution amount of 60 cc) and is divided equally into three 20 cc syringes. Before implanting the hip prosthesis, while the entire joint is exposed, 20 cc is injected into the pericapsular tissue (syringe #1), then 20 cc is injected in the fascia/muscle overlying the joint (syringe #2), and the last 20 cc dose is injected into subcuticular tissue beneath the incision (syringe #3).

Additionally, a periarticular injection consisting of 15 mg of ketorolac, 5 mg of Duramorph, and 40 cc of 0.25% Marcaine is infiltrated during closure of the incision (Marcaine is substituted for ropivacaine to prevent Exparel breakdown). Patient controlled analgesia (PCA), as well as preoperative and postoperative preemptive oral analgesics (celecoxib, acetaminophen, and pregabalin), are also given to THA patients.

Case 1

The patient is a 77 year-old female with a history of hypertension, hyperlipidemia, osteoarthritis, and past surgical history of laminectomy L2-L5 and posterior spinal fusion T3-S1 for degenerative scoliosis and spinal stenosis 1 year prior. She complained of pain in her right groin, buttock, and lateral thigh. She reported that the right groin pain was not relieved by the recent spine procedure, and had been getting progressively worse. Her right hip osteoarthritis was unresponsive to conservative measures. She had no preexisting sensory or motor deficits in her operative extremity due to her spine issue and was neurovascularly intact preoperatively.

She underwent right total hip replacement via a posterior approach under general anesthesia. For surgical infection prophylaxis, she received 2 g of aztreonam IVPB every 8 h over the course of 24 h (6 g total), as well as 2 g of cefazolin IVPB every 8 h over the course of 24 h (6 g total) starting at the time of surgery. The procedure was performed without any apparent deviations from routine hip arthroplasty protocol. Exparel was infiltrated following the described protocol. The operative leg was appropriately lengthened 5 mm.

Postoperative neurologic motor exam in the recovery room after regional anesthesia had resolved revealed 0/5 ankle dorsiflexion, 1/5 extensor hallucis longus, and 1/5 ankle plantar flexion. Sensory exam revealed absent sensation in common peroneal and tibial nerve distributions. The patient did not complain of any pain or discomfort. At this time a pillow was placed underneath the knee to take tension off of the sciatic nerve by flexing the knee. The patient received a morphine PCA (100 mg/100 mL) in the recovery room for overnight pain control, which was discontinued in the morning of postoperative day (POD) 1. For the remainder of her hospital stay, she was continued on an oral pain control regimen of acetaminophen 500 mg every 6 h, celecoxib 100 mg daily, pregabalin 50 mg twice daily, and oxycodone IR 5 mg every 4 h as needed for breakthrough pain. Her postoperative weight bearing status was weight bearing as tolerated (WBAT) with a walker. By POD 2, ankle dorsiflexion improved to 2/5, with extensor hallucis longus 4/5, and ankle plantar flexion 4/5. An ankle-foot orthosis was ordered for a suspected peroneal palsy after THA; however she declined to wear it.

The patient progressed with physical therapy. On POD 3, neurologic exam returned to normal with 5/5 strength and normal sensation throughout all distributions. After the patient was able to ambulate 150 feet with a wheeled walker and clear 8 stairs during her POD 3 physical therapy session, she was discharged home (our institutional mean length of stay for THA in 2014 was approximately 2.8 days). She received visiting nurse services for wound care and physical therapy. She was instructed to continue WBAT, administer enoxaparin (40 mg/0.4 ml) 0.4 ml subcutaneous injections for venous thromboembolism prophylaxis for 4 weeks, and take tramadol 50 mg every 4 h as needed for pain control. She had an otherwise unremarkable postoperative course and had no complaints or lower extremity neurological deficits at her 1 and 3 month postoperative evaluations.

Case 2

The patient is a 38 year-old female with a history of asthma, obesity (BMI 34.3), and developmental dysplasia of the hip who developed early arthritis in her right hip. She complained of severe pain in the right groin and buttock regions, no longer manageable with non-operative measures. She is former smoker of 5 pack years with a quit date 1 month prior to surgery. Preoperatively on physical exam, she was neurovascularly intact. The patient had a limb length discrepancy of 5 mm in the operative leg. She underwent a right total hip arthroplasty via a posterior approach with spinal anesthesia using 3 cc of 0.5% bupivacaine. For surgical infection prophylaxis, she received a one-time intravenous dose of gentamicin 360 mg, as well as 2 g of cefazolin IVPB every 8 h over the course of 24 h (6 g total) starting at the time of surgery. The procedure was performed without any apparent deviations from routine hip arthroplasty protocol. Exparel was infiltrated into the 3 tissue locations according to the protocol. Postoperatively, leg length measurements were restored to equal after lengthening the operative extremity by 5 mm.

In the recovery room, she exhibited full strength in her tibialis anterior, extensor hallucis longus, and gastrocnemius/soleus muscle groups in her right leg. She reported a pain level of 8/10, which was managed with a morphine PCA (100 mg/100 mL) in the recovery room and overnight after transfer to the floor. The PCA was discontinued on the morning of POD 1. For the remainder of her hospital stay, she was continued on an oral pain control regimen of celecoxib 100 mg daily, pregabalin 50 mg twice daily, oxycodone CR 10 mg twice daily, and oxycodone IR 10 mg every 4 h as needed for breakthrough pain.

By the end of POD 0, the patient was unable to fire either tibialis anterior or extensor hallucis and had decreased sensation in the superficial and deep peroneal nerve distributions on the right side. The neurologic exam remained unchanged the morning of POD 1. She was monitored closely with serial exams throughout POD 1 which demonstrated a progressive, restoration in function. By POD 2, the patient was neurologically intact with 5/5 strength and normal sensation in all distributions. The patient was made weight bearing as tolerated with crutches and was able to meet established physical therapy goals by walking 350 feet and clearing 4 stairs. At the end of POD 2, she was discharged home. She received visiting nurse services for wound care and physical therapy, was instructed to continue WBAT, administer enoxaparin (40 mg/0.4 ml) 0.4 ml subcutaneous injections for venous thromboembolism prophylaxis for 4 weeks, and take oxycodone-acetaminophen 5–325 mg as needed for pain control. She had an otherwise unremarkable postoperative course, and had no complaints or lower extremity neurological deficits at her 1 and 3 month postoperative evaluations.

Case 3

The patient is a 54 year-old male with a past medical history significant for frequent respiratory infections, presenting status-post complicated left THA. His index THA was in 2008 for osteoarthritis and was a metal on metal bearing. In 2012, he underwent

revision of the bearing surface which became infected. In 2013, he was successfully treated for the left hip periprosthetic joint infection (PJI) (group B streptococcus) with a two-stage resection and re-implantation. In late 2014, he developed another PJI with a different organism (group G streptococcus). The plan was to again treat with a two-stage resection and re-implantation. He is presenting for the second stage of his revision procedure with planned removal of the antibiotic spacer and re-implantation of a left THA. Preoperatively, he complained of severe pain in the left groin and had been using crutches to ambulate on the unipolar antibiotic spacer. On physical exam, he was neurovascularly intact.

He underwent left revision THA via a posterior approach with general anesthesia. For surgical infection prophylaxis, he received 2 g of cefazolin IV, as well as 2 g of aztreonam IVPB every 8 h over the course of 24 h (6 g total) starting at the time of surgery. A dilute betadyne wash was performed and 2 g of vancomycin powder were added to the surgical wound prior to closure. He was also continued on ceftriaxone 1 g IVPB during his hospital course. The procedure was performed without any apparent deviations from routine hip arthroplasty protocol. Exparel was infiltrated into the 3 soft tissue locations according to the protocol. Postoperatively, leg length measurements were equal.

In the recovery room, he exhibited full strength in his gastrocnemius/soleus muscle groups of his left lower extremity, but 0/5 strength in his extensor hallucis longus and tibialis anterior muscles. Sensory exam also revealed numbness in the superficial peroneal and deep peroneal nerve distributions. At this time he was positioned with his left hip in extension and knee in flexion and underwent serial physical exams. He reported a pain level of 3/10, which was managed with hydromorphone 25 mg/250 mL PCA in the recovery room and overnight after transfer to the floor. The PCA was discontinued on the morning of POD 1. For the remainder of her hospital stay, he was continued on an oral pain control regimen of celecoxib 200 mg daily, pregabalin 50 mg twice daily, oxycodone CR 10 mg twice daily, and oxycodone IR 10 mg every 4 h as needed for breakthrough pain.

On POD 1, his motor and sensory exam remained unchanged. Serial exams showed a slow, but progressive, restoration in function. The patient was made weight bearing as tolerated with a rolling walker. By POD 2, the patient was neurologically intact throughout the left lower extremity except for 4+/5 strength in tibialis anterior and 4/5 in extensor hallucis longus muscles. Sensation to light touch was intact in all distributions. By the morning of POD 3, he was neurologically intact with 5/5 strength and intact sensation throughout his left lower extremity. He was able to meet established physical therapy goals by walking 150 feet and clearing 4 stairs. At the end of POD 3, he was discharged home. He received visiting nurse services for wound care and physical therapy, was instructed to continue WBAT with wheeled walker, take aspirin 325 mg twice daily and to wear foot pumps for 18–20 h daily for venous thromboembolism prophylaxis for 4 weeks, take amoxicillin 875 mg twice daily for 4 weeks for infection prophylaxis, and take oxycodone-acetaminophen 5–325 mg as needed for pain control. He had no neurological deficits at his 2 week evaluation.

Discussion

Liposomal bupivacaine (Exparel®) is a novel medication that can provide long lasting pain relief as part of a multimodal pain regimen [10,12–16]. In the three THA cases described, the patients exhibited a transient loss of neurologic function in the affected extremity lasting between 24 and 72 h. We believe this occurred as a result of unintended injection of the medication in close proximity to the sciatic nerve. The three patient cases were performed by two different surgeons at the same institution. Each of the surgeons followed the injection protocol. While all patients had risk factors for experiencing a neurologic deficit—one had prior spine surgery, one patient had DDH, and the third had multiple previous hip surgeries—none of the patients had excessive lengthening of the limb or a preoperative neurologic deficit.

Aggressive injection of the medication around the short external rotators and pericapsular fat during total hip arthroplasty may result in unanticipated sciatic nerve anesthesia. These occurrences do not appear to be reported in the current literature. Surgeons who use liposomal bupivacaine as part of a multimodal pain treatment regimen need to be aware of the possibility of inadvertent sciatic nerve injection. We recommend that orthopaedic surgeons pay special attention during infiltration of the medication as unintended transient postoperative anesthetic-induced deficits have the potential to be confused with more serious causes of neurologic deficits. Delaying neurologic work-up or imaging, ankle-foot orthosis fitting, and operative intervention in the setting of painless sciatic nerve injury without suspicion of surgical insult, hematoma, or preoperative susceptibility until liposomal bupivacaine effects dissipate at 48–72 h postoperatively seems prudent. Unlike cases of traumatic injury to the sciatic nerve by retractor or stretch, the transient anesthetic episodes exhibited in these three cases were not associated with pain or dysesthesia in the sciatic nerve sensory distribution. Ultimately, it is our hope that surgeons be able to identify similar cases of neurologic deficits due to liposomal bupivacaine injections in order to avoid unnecessary, expensive, and potentially harmful evaluations, treatments, and re-operations.

Summary

In the three total hip arthroplasty cases described, all patients exhibited a transient loss of neurologic function in the sciatic nerve distribution of the operated extremity lasting between 24 and 72 h during the immediate postoperative period. Due to the nature and duration of the deficits, it was concluded that they likely occurred as a result of unintended injection of liposomal bupivicaine (Exparel®) in close proximity to the sciatic nerve. To the best of our knowledge, these events have yet to be reported in the current literature. We recommend orthopaedic surgeons pay special attention during infiltration of the medication at the surgical site to avoid postoperative neurological deficits.

Acknowledgments

The Department of Orthopaedic Surgery at the New York University Langone Medical Center's Hospital for Joint Diseases received an unrestricted grant from Pacira Pharmaceuticals, Inc.

References

[1] Bayley KB, London MR, Grunkemeier GL, Lansky DJ. Measuring the success of treatment in patient terms. Med Care 1995;33:AS226.
[2] Dickstein R, Heffes Y, Shabtai EI, Markowitz E. Total knee arthroplasty in the elderly: patients' self-appraisal 6 and 12 months postoperatively. Gerontology 1998;44:204.
[3] Singelyn FJ, Deyaert M, Joris D, Pendeville E, Gouverneur JM. Effects of intravenous patient-controlled analgesia with morphine, continuous epidural analgesia, and continuous three-in-one block on postoperative pain and knee rehabilitation after unilateral total knee arthroplasty. Anesth Analg 1998;87:88.
[4] Ranawat AS, Ranawat CS. Pain management and accelerated rehabilitation for total hip and total knee arthroplasty. J Arthroplasty 2007;22(7 Suppl. 3):12.
[5] Ranawat CS, Ranawat AS, Mehta A. Total knee arthroplasty rehabilitation protocol: what makes the difference? J Arthroplasty 2003;18(3 Suppl 1):27.

[6] Meftah M, Wong AC, Nawabi DH, Yun RJ, Ranawat AS, Ranawat CS. Pain management after total knee arthroplasty using a multimodal approach. Orthopedics 2012;35(5):e660.
[7] Borgeat A, Ekatodramis G. Anaesthesia for shoulder surgery. Best Pract Res Clin Anaesthesiol 2002;16(2):211.
[8] Bergese S, Onel E, Portillo J. Evaluation of DepoFoam bupivacaine for the treatment of postsurgical pain. Pain Manag 2011;1:539.
[9] Chahar P, Cummings III KC. Liposomal bupivacaine: a review of a new bupivacaine formulation. J Pain Res 2012;5:257.
[10] Gorfine SR, Onel E, Patou G, Krivokapic ZV. Bupivacaine extended-release liposome injection for prolonged postsurgical analgesia in patients undergoing hemorrhoidectomy: a multicenter, randomized, double-blind, placebo-controlled trial. Dis Colon Rectum 2011;54(12):1552.
[11] Portillo J, Kamar N, Melibary S, Quevedo E, Bergese S. Safety of liposome extended-release bupivacaine for postoperative pain control. Front Pharmacol 2014; Apr 30;5:90.
[12] Cohen SM. Extended pain relief trial utilizing infiltration of Exparel, a long-acting multivesicular liposome formulation of bupivacaine: a phase IV health economic trial in adult patients undergoing open colectomy. J Pain Res 2012;5:567.
[13] Smoot JD, Bergese SD, Onel E, Williams HT, Hedden W. The efficacy and safety of DepoFoam bupivacaine in patients undergoing bilateral, cosmetic, submuscular augmentation mammoplasty: a randomized, double-blind, active-control study. Aesthet Surg J 2012;32(1):69.
[14] Golf M, Daniels SE, Onel E. A phase 3, randomized, placebo-controlled trial of DepoFoam(®) bupivacaine (extended-release bupivacaine local analgesic) in bunionectomy. Adv Ther 2011;28(9):776.
[15] Bramlett K, Onel E, Viscusi ER, Jones K. A randomized, double-blind, dose-ranging study comparing wound infiltration of DepoFoam bupivacaine, an extended-release liposomal bupivacaine, to bupivacaine HCl for postsurgical analgesia in total knee arthroplasty. Knee 2012;19(5):530.
[16] Bagsby DT, Ireland PH, Meneghini RM. Liposomal bupivacaine versus traditional periarticular injection for pain control after total knee arthroplasty. J Arthroplasty 2014 Aug;29(8):1687.