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Original Article

Liposomal bupivacaine in total hip arthroplasty: Do the results justify the cost?

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ABSTRACT

Introduction: Liposomal bupivacaine has a paucity of data regarding narcotic requirements and hospital length of stay in comparison to other peri-articular injections, specifically in the total hip arthroplasty (THA) population.
Methods: 69 patients who underwent THA by a single surgeon were divided into two cohorts over a 3 year period in this retrospective study comparing narcotic requirements, hospital length of stay and cost. The study group (n = 29) received liposomal bupivacaine whereas a matched control group (n = 40) received a pharmacy-mixed cocktail in peri-articular structures. Statistical and clinical differences were reported in this unfunded study.
Results: No difference was found in hospital length of stay [2.9 days in the study group (range 1–14) versus 3.1 days (range 1–11) in the control group, p = 0.101], however, the study group required less narcotics per day [22.6 mg (range 5–53.3) versus 29 mg (range 6.7–80.8) in the control group, p = 0.045]. The clinical difference between cohorts averaged less than one pill per day of hospitalization. The cost per patient of the local injection was more than 11 times greater in the liposomal bupivacaine group.
Conclusion: Liposomal bupivacaine demonstrated a statistical improvement in narcotic requirements but not in hospital length of stay in comparison to a control group. The effects of liposomal bupivacaine on narcotic requirements and hospital length of stay may not justify its use in total hip arthroplasty patients given the substantial cost of these injections and the minimal clinical difference in outcomes compared to a more cost-effective injection.
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1. Introduction

Multimodal pain management in total joint arthroplasty is considered the standard of care in peri-operative pain control, with numerous studies showing improved outcomes and decreased complications.[1–5] It is well accepted that patients require adequate pain management following total joint arthroplasty to enable active participation in physical therapy and to mobilize sufficiently for safe discharge from the hospital. Opiates may be a potential hindrance to physical therapy, despite their utility as a pain modulator. Indeed the optimal pain modifier would provide peri-operative analgesia and avoid neuromuscular blockade as well as opiate-like side effects such as fatigue, constipation, nausea and dependence. Intraoperative injections of various formulations have been used for decades in an effort to decrease post-operative opiate use.

Parvataneni et al. conducted a prospective study in which they demonstrated the benefits of local peri-articular injection and its role in a multi-modal pain management strategy in total joint replacements.[6] In an effort to improve the delivery of injections administered by the surgeon at the time of the operation, a novel medication was developed using liposomal technology to allow time-released degradation of a given anesthetic. The use of this injectable time-released suspension in total hip arthroplasty (THA) is largely extrapolated from the literature on its use in total knee arthroplasty (TKA).[7,8] To our knowledge, there is only one controlled cohort study comparing standard peri-articular injections to liposomal bupivacaine in the THA population.

To add to the current body of evidence regarding peri-articular injections, we ask the following questions: (1) How does the average hospital length of stay compare between two cohorts of patients with the first receiving a pharmacy mixed peri-articular cocktail of multiple medications and the second receiving an

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injection of liposomal bupivacaine in the peri-articular tissues?; (2) What are the differences in narcotic requirements during the inpatient hospitalization between the same two groups?; (3) Is there any synergy with pre-operative epidural as part of a multimodal pain pathway within the two groups?; and (4) What is the cost difference between liposomal bupivacaine and the peri-articular injection cocktail?

2. Materials and methods

Following Institutional Review Board approval, the inpatient electronic medical records for all patients who underwent THA by a senior arthroplasty surgeon from July 2011 through August 2014 were queried. Out of 158 total hip replacements performed, the largest subgroup of patients having received a common prosthesis totaled 74. Five patients were excluded for having incomplete medical records required to answer our study questions, leaving 69 patients for inclusion in the data (Table 1). Exclusion criteria were subjects younger than 18 or older than 90 years of age, subjects who had surgery outside our study period, subjects who were undergoing revision THA, and subjects with incomplete medical records.

A peri-articular injection cocktail was used up until a discrete point in time in November 2013. After this transition point, the senior surgeon began using liposomal bupivacaine, Exparel® (Pacira Pharmaceuticals Parsippany, NJ) as a peri-articular injection prior to THA closure. Thus, 2 distinct cohorts of patients were generated for comparison. Cohort 1 is our control group consisting of those patients who received a peri-articular injection comprised of: 30 mg ketorolac, 10 mg morphine and 50cc of 0.5% marcaine without epinephrine. The injection was administered in 20cc aliquots targeting the anterior capsule, iliopsoas tendon and insertion site before reduction of the prosthesis. This was followed by injecting the abductors, fascia lata, gluteus maximus and its insertion, the posterior joint capsule, short external rotators and joint synovium after final reduction of the components. Cohort 2 is the study group consisting of those patients who received peri-articular injections of liposomal bupivacaine targeting the same anatomic structures as outlines above.

Approved by the Food and Drug Administration (FDA) in October 2011, liposomal bupivacaine has grown in popularity in the total joint community.[9] Exparel® is an injectable product in which bupivacaine is encapsulated in multivesicular lipid molecules.[10] These lipid molecules degrade and reorganize slowly allowing time-released bupivacaine in contrast to the rapid metabolism of raw bupivacaine delivered in bolus form. This injection was administered using the consensus technique guidance provided by the manufacturer and recently published in 2015 by Joshi et al.[11]

Data on length of stay (in days) and narcotic usage (in morphine equivalence) was obtained from the electronic medical record. All narcotic medications from the inpatient hospital stay were included in data collection and were comprised of: oxycodone immediate release 5 mg per tablet (recorded in milligrams), oxycodone continuous release 10 mg per tablet (recorded in milligrams), hydrocodone/acetaminophen 5/325 mg per tablet (recorded in tablets given), oxycodone/acetaminophen 5/325 mg per tablet (recorded in tablets given), fentanyl (recorded in micrograms per intravenous dose), morphine (recorded in milligrams per intravenous dose), and hydromorphone (recorded in milligrams per intravenous dose).

With all medication in dosage units, they were translated into morphine equivalence using equianalgesic dose ratios in accordance with our facility inpatient pharmacy as follows:

Fentanyl (IM/IV) – 0.1 mg
Hydromorphone (PO) – 7.5 mg
Hydromorphone (IM/IV) – 1.5 mg
Morphine (PO) – 30 mg
Morphine (IM/IV) – 10 mg
Oxycodone (PO) – 20 mg

In order to obtain the parenteral morphine equivalent, the total dose of each opioid given was divided by the equianalgesic dose for that opioid, which was then multiplied by the equianalgesic dose for the new opioid and route. Opioid per day of hospitalization was obtained by dividing the total narcotic used by the hospital length of stay (in days) resulting in an average use per day (parenteral morphine mg/day).

The cost of the peri-articular injection cocktail was obtained referencing the cost to the facility. This was compared to the contracted price of liposomal bupivacaine by our facility. Contracted prices for all medications were obtained from the pharmacy acquisitions department. All prices are in U.S. dollars and represent a single patient's dose.

Table 1
Demographic Variables.

	Cohort 1 (Control) n = 40	Cohort 2 (Exparel®) n = 29	P VALUE
Age (Avg in yrs)	57.2 Range 26–76 95% CI 53.6–60.8	57 Range 34–78 95% CI 52.8–61.2	0.932
Sex			
Male	29 (72.5%)	25 (86%)	0.727
Female	11 (27.5%)	4 (14%)	
Laterality			
Right	18 (45%)	16 (55%)	0.058
Left	22 (55%)	13 (45%)	
ASA Score			
I	1 (2.5%)	1 (3.4%)	N/A
II	25 (62.5%)	21 (72.4%)	
III	14 (35%)	7 (24.1%)	
GETA			
With Epidural	36 (90%)	20 (69%)	0.342
Without Epidural	4 (10%)	9 (31%)	

ASA: American Society of Anesthesiologists physical classification score as determined by anesthesia.
GETA: General Endotracheal Anesthesia.