Evaluation of liposomal bupivacaine versus immediate release bupivacaine in post-operative pain after knee surgery

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BACKGROUND

The management of post-operative pain holds many challenges. The use of narcotics, including PCA (patient controlled analgesia), and femoral nerve blocks can limit ambulation, increase the length of hospital stays, and cause adverse events that hinder overall recovery. Liposomal bupivacaine is a non-opioid anesthetic indicated for the management of post-operative pain. Studies have shown that the use of liposomal bupivacaine has been associated with a decrease in opiate use after total knee arthroplasty, and can offer multimodal pain management through the maximization of pain control while decreasing side effects. The purpose of this study is to determine the effectiveness of using liposomal bupivacaine for patients undergoing partial or total knee arthroplasty in comparison to femoral nerve block with or without post-operative PCA.

The development of a liposomal formulation of local anesthetics stems from the desire to alter the pharmacokinetics of conventional local anesthetics, specifically to alter the short duration of action. Local anesthetics typically have a short duration of action (≤ 7 hours), at which point opiates are typically used to control pain[3]. The liposomal formulation of bupivacaine has a duration of action that is significantly longer (~96 hours), and undergoes both short-term, first-order absorption and longer-term zero-order absorption[3,4]. This leads to a two peak phenomenon when looking at plasma concentration over time[2]. The clinical implications of this longer duration and two peak phenomenon are a more sustained and progressive disruption of sensory neural transmission.

Two articles from the Journal of Arthroplasty, as well as a review article evaluating liposomal bupivacaine for knee replacement surgery, have described the effects of using liposomal bupivacaine on length of stay, patient reported pain scores, and average opioid usage[1,2,5]. These articles evaluate the effectiveness of liposomal bupivacaine compared to conventional therapy, and while the articles by Surdam et al. and Harrison note a trend in improved pain scores and decreased narcotic use, the article by Bagsby suggests that liposomal bupivacaine is not superior to conventional therapy. This shows the continued need for research into the overall effectiveness of liposomal bupivacaine on post-procedural pain, and how it compares to conventional therapy.

OBJECTIVE

The primary outcome of this study is to determine the effect liposomal bupivacaine in addition to conventional therapy compared to conventional therapy alone on post-operative pain control after partial or total knee replacement. Secondary outcomes evaluated included length of stay, time to ambulation, and patient reported pain scores on post-op day 1 and day 2, in the two patient populations.

METHODS

- This is a single-center, retrospective, cohort study was conducted in a 353 bed academic medical center
- Medical records were used to identify patients over the age of 18 who have undergone knee replacement and received peri-operative liposomal bupivacaine in addition to conventional therapy or conventional therapy alone
- Data on 150 patients was collected, with 100 patients receiving liposomal bupivacaine and 50 control patients
- Data on age, gender, type of surgery performed, pain scores, opiate and non-opiate pain medications used in the post-anesthesia care unit (PACU) and post-PACU, time to ambulation (50 feet), and length of stay was collected and analyzed
- The primary outcome of pain control was measured through morphine equivalents required post-operatively

RESULTS

Table 1: Demographics and data analysis

	Control	Liposomal Bupivacaine	P
N	50	100	
Male	15	38	0.91
Female	24	58	
Age (mean)	68	66	0.26
Total Knee Replacement	35	82	0.096
Partial Knee Replacements	15	18	
Length of Stay (mean)	2.98	1.9	<0.0001
Time to Ambulation (mean)	1.76	0.38	<0.0001
Time to D/C from PT (mean)	3.10	1.78	<0.0001
Pain Score at 24 hours (mean)	4.69	4.11	0.18
Pain Score at 48 hours (mean)	4.46	3.71	0.078
PACU Morphine Equivalents (mean)	7.00	4.89	0.085
Non-PACU Morphine Equivalents (mean)	51.33	28.73	0.0003
Daily Morphine Equivalents (mean)	21.11	12.65	0.0016
PCA Use	43	8	<0.0001

Figure 1: Opioid requirements (in morphine equivalents)

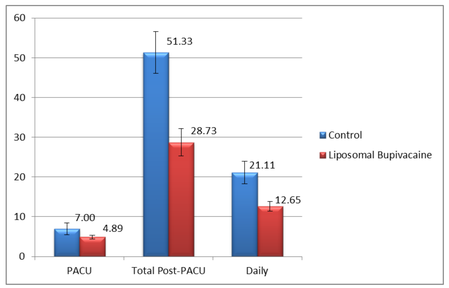


Figure 2: Mean Length of stay (in days)

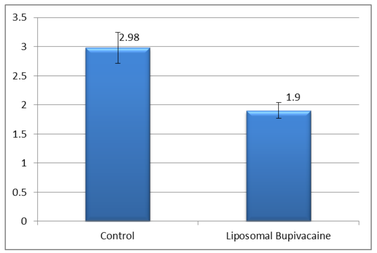


Figure 3: Patient reported pain scores

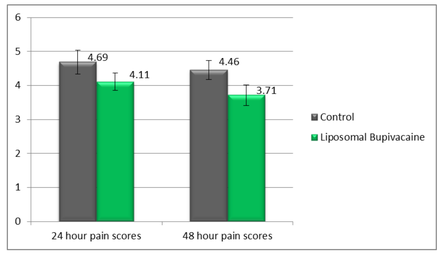


Figure 4: Mean time to ambulation (in days)

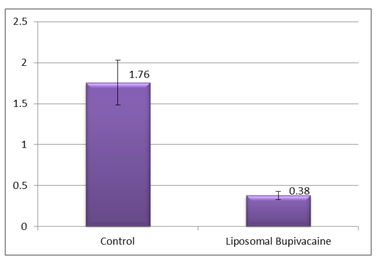
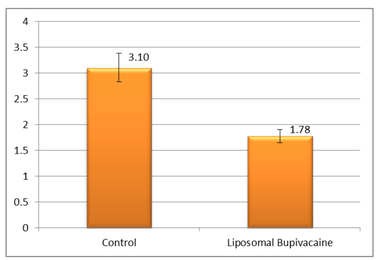


Figure 5: Mean time to discharge from physical therapy (in days)



DISCUSSION

- A total of 150 patients who had knee arthroplasty surgery were retrospectively evaluated, with 100 patients receiving liposomal bupivacaine injections
- Compared to the control sample, a reduction in opiate requirements, as determined by morphine equivalents, was seen with liposomal bupivacaine post-PACU, but not in the PACU (p = 0.0003 and p = 0.085, respectively)
- When examining secondary outcomes, a statistically significant decrease in length of stay and time to ambulation was seen in the liposomal bupivacaine group (length of stay: 1.9 days vs 2.98 days, p < 0.0001; time to ambulation: 0.38 days vs 1.76 days, p < 0.0001). However, liposomal bupivacaine showed no statistical difference in pain scores, either at 24 or 48 hours (p = 0.18 and 0.078, respectively)
- A subgroup analysis that removed patients with extended lengths of stay (two from control and one from liposomal bupivacaine) revealed similar results. Length of stay and daily opiate requirements remained statistically different (p <0.0002 and p = 0.0008, respectively). Opiate requirements in the PACU remained similar (p = 0.16)
- Several clinical trials have been conducted with liposomal bupivacaine in knee replacement surgery
  - A study in press by Surdam et al.[1] shows that liposomal bupivacaine decreases the opiate requirements POD1, while other reports vary regarding opiate use. A review article by Harrison[2] reports that extended release bupivacaine significantly decreases narcotics used, while Bagsby et al.[5] reports no difference in opiate usage.
  - The study by Bagsby et al. also shows that liposomal bupivacaine does not decrease reported pain scores when compared to conventional therapy.
  - The preliminary findings of a large clinical trial by Barrington and Emerson[6] show that liposomal bupivacaine decreases overall length of stay.

CONCLUSION

Our data support several clinical trials, suggesting that a protocol outlining the use of liposomal bupivacaine in knee replacement surgery may lead to better patient outcomes and satisfaction. These data have been used as the basis for updating current practice at Gwinnett Medical Center, leading to the addition of liposomal bupivacaine to the formulary for use in knee replacement surgery.

DISCLOSURE

Authors of this presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation:

- No authors have anything to disclose

REFERENCES

[1]Surdam JW, et al. The Use of Exparel (Liposomal Bupivacaine) to Manage Postoperative Pain in Unilateral Total Knee Arthroplasty Patients. J Arthroplasty (2014).
[2]Bupivacaine Effective for Knee Replacement Pain. Medscape. Mar 14, 2014.
[3]Candiotti K. Liposomal bupivacaine: an innovative nonopioid local analgesic for the management of postsurgical pain. Pharmacotherapy 2012 Sept.; 32 (9 Pt 2):19S-26S.
[4]Tong YC, Kaye AD, Urman RD. Liposomal bupivacaine and clinical outcomes. Best Pract Res Clin Anaesthesiol. 2014 Mar;28(1):15-27.
[5]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):1687-90.
[6]Barrington JW, Emerson RH Jr. Liposomal bupivacaine: the first 1,000 cases in a new era. Presented at the 2014 Annual Meeting of the American Academy of Orthopaedic Surgeons; New Orleans, LA; March 14, 2014. Paper 675.