

Assessment of Efficacy of Liposomal Bupivacaine Versus Traditional Periarticular Injection in Pain Management After Knee Arthroplasty Surgery: A Comparative Study

Sudarshan A. Kamble

Assistant Professor, Department of Orthopaedics,
Shri Vasantnao Naik Government Medical College, Yavatmal, Maharashtra, India.

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*Correspondence to:

Dr. Sudarshan A.
Kamble,
Assistant Professor,
Department of
Orthopaedics,
Shri Vasantnao Naik
Government Medical
College, Yavatmal,
Maharashtra, India.

ABSTRACT

Introduction: Severe pain after total knee arthroplasty (TKA) is experienced by a large group of patients. Management of postsurgical pain efficiently stimulates fast healing and recovery, faster patient mobilization, less hospital stays and thus decreased cost of healthcare. The aim of present study is to compare efficacy of liposomal bupivacaine and traditional periarticular injection in postoperative pain levels following primary total knee arthroplasty.

Materials and Methods: This study was conducted in the Department of Orthopaedics, Shri Vasantnao Naik Government Medical College, Yavatmal, Maharashtra (India). A total of 30 patients who underwent total knee arthroplasty were included. 15 patients belonged to traditional periarticular injection group and 15 patients belonged to liposomal bupivacaine group.

Results: With regard to postoperative patient-reported pain scores, during the first 24 h after surgery there was no statistical difference between the 1.89 (± 2.27) in the traditional group compared to the 1.86 (± 2.23) in the liposomal bupivacaine group ($P > 0.05$), likely due to the spinal anesthetic. At the time of discharge, the mean pain scores in the traditional injection group were 3.44 (± 2.0) compared to 3.92 (± 1.74) in the liposomal bupivacaine injection group and were statistically not significant ($p > 0.05$). Most notably, the mean patient reported pain scores during the remaining hospitalization after the first 24 h until discharge were lower in the traditional injection group as compared to 4.72 (± 1.62) in the liposomal bupivacaine, which was statistically significant ($p < 0.05$).

Conclusion: Based on the results of this study, we conclude that pain control after TKA with a multimodal pain management protocol is not improved with the addition of liposomal bupivacaine compared to a traditional injection of ropivacaine.

KEYWORDS: Bupivacaine, Knee Arthroplasty, Pain, Periarticular Injection.

INTRODUCTION

Severe pain after total knee arthroplasty (TKA) is experienced by a large group of patients. Management of postsurgical pain efficiently stimulates fast healing and recovery, faster patient mobilization, less hospital stays and thus decreased cost of healthcare. Postsurgical pain control has other benefits also like improved cardiac, respiratory, and gastrointestinal function; minimizing thromboembolic complications; reduction in chronic postsurgical pain; reduced mortality in high risk individuals.¹ In the past, parenteral narcotics were most commonly used for pain management despite being its side effects and erratic pain relief.² Recently investigators have popularized multimodal pain control programs in which multiple drugs working via different

mechanisms are used in lower dosages. This method maximizes the pain control while minimizes side effects.³⁻⁷ Periarticular injection of local anesthetic is one of the methods commonly used in multi-modal pain protocols. Liposomal bupivacaine having prolonged pain controlling action had recently emerged for periarticular injection in TKA surgeries.⁸ The prolonged pain control action of Bupivacaine is based on the liposomes that function as drug carriers and offer a controlled delivery of drugs.⁹ The aim of present study is to determine efficacy of liposomal bupivacaine in comparison to traditional periarticular injection in management of postoperative pain levels following primary total knee arthroplasty.

MATERIALS AND METHODS

This study was conducted in the Department of Orthopaedics, Shri Vasantnao Naik Government Medical College, Yavatmal, Maharashtra (India). Permission was obtained from the ethical committee of the institute. A total of 30 patients underwent total knee arthroplasty were included in the study. 15 patients belonged to traditional periarticular injection of ropivacaine group and 15 patients belonged to liposomal bupivacaine group. Demographic data of all the patients was noted. All the patients were administered with multimodal pain protocol consisting of pre-emptive oral pain medications preoperatively and throughout the hospital stay until discharge.

Intraoperatively, all the patients received a periarticular injection consisting of either ropivacaine or liposomal

bupivacaine. Perioperative patient education especially to report pain control, physical therapy and expectations for discharge was completed by all the patients. Self-rated pain scores of the patients were taken during regular rounds by the nurses posted based on the established protocol. Recording of pain scores was done every 2-4 hr in the EMR. Average of the pain scores was taken during two time periods, the first 24 hr and during rest of the stay at hospital. Recording of self-rated pain score at discharge was also taken. Visual analogue scale of 0 to 10 was used for evaluation of pain scores, 0 indicating no pain and 10 indicating worst possible pain. The assessment of statistical significance of the data was done using Student's t-test. Mean pain scored at different time periods was also compared. Statistical significance was considered at $P < 0.05$.

Table 1: Patient variables

	Liposomal Bupivacaine (n=15)	Ropivacaine Injection (n=15)	P value
Age (years)	65.45±9.64	62.65 ±7.34	>0.05
BMI	33.74 ± 8.12	36.12 ± 7.23	>0.05
Length of stay	2.64 ± 0.23	2.61 ± 0.62	>0.05
Gender	Male	9	7
	Female	6	8

Table 2: Categorical pain scales

	Liposomal Bupivacaine (n=15)	Ropivacaine Injection (n=15)
▪ First 24 h	None	3
	Mild	9
	Moderate	2
	Severe	1
▪ Remaining stay	None	0
	Mild	3
	Moderate	11
	Severe	1
▪ Final	None	1
	Mild	4
	Moderate	8
	Severe	2

RESULTS

A total of 30 patients underwent total knee arthroplasty. 15 patients belonged to traditional periarticular injection group and 15 patients belonged to liposomal bupivacaine group. Demographic data of all the patients is given in Table 1. The mean age of liposomal bupivacaine group was 65.45 (±9.64) years and mean age of traditional group was 62.65 (±7.34) years. The mean body mass index in the traditional injection group was 36.12 (±7.23) and in the liposomal bupivacaine group was 33.74 (± 8.12); ($P=0.58$).

With regard to postoperative patient-reported pain scores, during the first 24 h after surgery there was no statistical difference between the 1.89 (±2.27) in the traditional group compared to the 1.86 (±2.23) in the liposomal bupivacaine group ($P > 0.05$), likely due to the spinal anesthetic. At the time of discharge, the mean pain scores in the traditional injection group were 3.44(±2.0) compared 3.92 (±1.74) in the liposomal bupivacaine injection group and this difference did not reach statistical significance ($P = 0.21$). Most notably, the

mean patient reported pain scores during the remaining hospitalization after the first 24 h until discharge were lower in the traditional injection group at 4.32 (± 1.72) compared to 4.72 (± 1.62) in the liposomal bupivacaine, which reached statistical significance ($P < 0.05$). Categorical pain scores demonstrate similar findings as the mean numerical pain scores (Table 2). There was no substantial difference in the percentage of patients who rated their pain as either mild or moderate between the traditional and liposomal bupivacaine groups during the first 24 h after surgery or at the time of discharge.

DISCUSSION

Multimodal pain management protocols use multiple agents with different mechanisms to modify nociceptors and different regions of the common pain pathways resulting in reduced use of opioid agents and their adverse effects. Peri-articular injection of local analgesia is one of the methods used commonly. To establish the efficiency of periarticular injections in reducing postoperative pain in TKA various studies has been conducted.¹⁰ Peri-articular injections consisting local anesthetics such as bupivacaine and ropivacaine as well as adjuvants like morphine and epinephrine have successful results in pain management in TKA.⁹ Bupivacaine has been used successfully as continuous infusion to control pain after TKA.¹¹ The half-life of bupivacaine is 3.5 hours and its action last upto 9 hours.¹⁰ Liposomal bupivacaine is superior to this and has been shown to provide analgesia upto 72 h after hemorrhoidectomy, decreasing the consumption of opioids.¹² Liposomes are microscopic structures consisting of a phospholipid bilayer encapsulating an aqueous core and confers characteristic drug release patterns from the aqueous core, leading to increased stability and longer duration of drug release. Currently available liposomal bupivacaine consists of vesicles of bupivacaine loaded in the aqueous chambers using DepoFoam® technology. Each particle is composed of a honeycomb like structure of numerous internal aqueous chambers containing encapsulated bupivacaine.¹³ The present study was undertaken to determine whether a PAI of liposomal bupivacaine provided a benefit as a component of an established multi-modal pain management protocol compared to a traditional PAI. The results demonstrates that after the initial 24 h, inpatient self-reported pain scores were actually higher in the liposomal bupivacaine group compared to the traditional PAI group. Liposomal bupivacaine PAI provided inferior pain control compared to the less expensive traditional PAI in a multi-modal pain control program in patients undergoing TKA. The inferior pain control in the liposomal bupivacaine group may be explained by slow release of the drug from the liposomes, which limits the amount of free bupivacaine present at the site of action.

Lombardi AV et al¹⁴ conducted study to determine if an intraoperative intraarticular and soft-tissue injection of local anaesthetic, epinephrine, and morphine has a beneficial effect for total knee arthroplasty. A control group of 138 patients (181 knees) received no intraoperative injection. The study group of 171 patients (197 knees) received intraoperative injection of 0.25% bupivacaine with epinephrine and morphine with 2/3 injected into the soft tissues and 1/3 injected into the joint. Patients having bilateral simultaneous procedures received a divided dose. The pain treatment protocol otherwise was identical. Pain, sedation, rescue narcotic usage, narcotic reversal and blood loss were examined. Pain levels during the immediate postoperative period, blood loss, and bleeding indices were reduced with injection. Considerably more control patients required rescue doses of narcotics. Preemptive analgesia with soft tissue and intra-articular injection of long-acting local anesthetic with epinephrine and morphine provides better pain control in the immediate postoperative period, decreases blood loss, and decreases the need for rescue narcotics and reversal agents. This simple, inexpensive method provides an effective adjunct to a multimodal approach in improving the postoperative course of primary total knee arthroplasty. In a prospective, blinded study conducted by Schroer WC et al¹⁵ liposomal bupivacaine was randomized against bupivacaine and incorporated into a comprehensive multimodal pain management protocol. 111 primary TKAs were randomized to receive PAI: 58 patients received 266 mg (20cc) liposomal bupivacaine mixed with 75 mg (30cc) 0.25% bupivacaine, and 53 patients received 150 mg (60cc) 0.25% bupivacaine. Visual analog pain scores and narcotic use were determined. No pain score differences occurred between study and control patients: Day 1: 4.5/4.6 ($P=0.73$); Day 2: 4.4/4.8 ($P=0.27$); or Day 3: 3.5/3.7 ($P=0.58$). Narcotic use was similar during hospitalization, 51.8/54.2 ($P=0.34$). This finding does not justify the routine use of liposomal bupivacaine.

Recently published review articles stated that bupivacaine liposomal decreased postsurgical pain over placebo.¹⁶

A white paper sponsored by the manufacturer suggests that bupivacaine liposomal reduces opioid-related adverse events that may lead to decreased patient length of stay.^{16,17} Candiotti K¹⁸ carried out a literature review and reported that when compared to bupivacaine, positive results are present whereas Chahar P et al¹³ commented that more adequately powered trials are needed to establish its superiority over plain bupivacaine.

In summary, this study demonstrates that a periarticular injection of liposomal bupivacaine in primary TKA patients is not associated with a significant improvement in post-operative pain or narcotic usage.

CONCLUSION

This study found no benefit to intra-articular injection of liposomal bupivacaine, with the possible negative effect of increased pain throughout the remaining hospital course after the initial 24 h. Based on the results of this study, the authors conclude that pain control after TKA with a multimodal pain management protocol is not improved with the addition of liposomal bupivacaine compared to a traditional injection. Based on the results of this study, the authors would specifically recommend that more trials are required to establish its superiority over plain form of drug.

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