Liposomal Bupivacaine for Interscalene Block in Ambulatory Rotator Cuff Repair

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Abstract

We conducted a retrospective study of the effectiveness of liposomal bupivacaine for analgesia in interscalene block for patients undergoing ambulatory rotator cuff repair. Postoperative opioid use, the primary outcome measure, was markedly reduced, and pain scores were significantly lower, as compared to use of plain bupivacaine block in a historical control group. Furthermore, most patients found that the duration of pain control was longer than their own prior plain bupivacaine interscalene block.

Keywords: Liposomal bupivacaine; interscalene block; ambulatory; rotator cuff repair.

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Introduction

Liposomal bupivacaine (LB), a liposome-encapsulated form of the local anesthetic bupivacaine, was approved for injection into the surgical field in 2011 (1). Animal and early clinical studies were supportive of its long-lasting analgesic potential, though later studies and meta-analyses did not find significant prolongation of analgesia when LB injected into the surgical field was compared to injection of plain bupivacaine in the surgical field (2) or was compared to bupivacaine interscalene nerve block (ISB) (3). This drug has also been incorporated into transversus abdominus plane (TAP) blocks, and is reported to reduce opioid requirements, particularly in the setting of cesarean delivery (4). In 2018, the drug received approval for use in ISB for shoulder surgery, and is reportedly most effective when used as an admixture with plain bupivacaine (1). Some investigators have reported favorable effects of LB in this setting (5,6), but a number of randomized trials have not been supportive of this drug when compared to ISB with plain bupivacaine (7,8).

Because long-lasting analgesia is important in ambulatory orthopedic patients, we evaluated LB in our shoulder surgery population, ensuring specific injection within the fascial confines of the interscalene groove. We evaluated the effects of LB mixed with bupivacaine on postoperative opioid requirements and pain scores in patients undergoing rotator cuff repair. We deliberately recruited patients who had previously undergone this operation with plain bupivacaine ISB, so

that they could serve as their own controls in reporting their experience with pain control and duration of analgesia. We hypothesized that opioid requirements on postoperative days 1-3 would be 50% lower than for those for a control group who had received plain bupivacaine ISB for the same surgical procedure.

Methods

This prospective, quality improvement project was initiated for presentation to our pharmacy. We subsequently obtained IRB approval for retrospective analysis of the data. Patients presenting for ambulatory rotator cuff repair, who had a history of prior rotator cuff repair with single-shot ultrasound-guided ISB within four years of the current operation, were recruited to participate. Other inclusion requirements were: age over 18 years, ASA class 1-3, and able to provide consent for participation. Pediatric patients, pregnant patients and those with contraindications to peripheral nerve blockade, including severe pulmonary disease, were excluded. Patients with chronic shoulder pain requiring opioids for management were also excluded.

After informed consent was obtained, intravenous access was obtained and monitors placed in the preoperative holding area. The patients underwent ultrasound-guided ISB, with the injectate consisting of 10mL of bupivacaine 0.5% and 10mL of LB 1.3%. In order to ensure a surgical block for the surgery, the needle tip was guided into the interscalene groove between the C5 and C6 nerve roots, ensuring that the fascia lining the middle scalene muscle was traversed, and that the solution accumulated directly between the two nerve roots during injection. The first four mL of the injectate consisted of plain 0.5% bupivacaine, with the remainder administered in the same location as a mixture of the two agents. Pacira, the manufacturer of LB, provided the drug at no cost for this investigation.

In the operating room patients received a standardized anesthetic of propofol infusion and ketamine 15-20mg, with preserved spontaneous ventilation. If deemed necessary for aberrations

in vital signs or rapid respiratory rate, small doses of fentanyl were also permissible. Postoperatively, patients were taken to the post-anesthesia care unit, where recovery occurred and the first postoperative pain scores were assessed. Before returning home, the patients received a self-assessment journal for recording pain scores and oral analgesics during the first three days after surgery, as well as the duration of perceived motor block.

The primary outcome for this study was oral opioid requirement on postoperative days 1-3. We considered a reduction of opioid use of 50% to be clinically significant, compared to comparable data from the control group (n=27) of a prior trial that we had conducted which evaluated the effects of LB injected into the surgical field (9). Secondary outcomes included NRS pain scores (from 0 to 10) on the first three postoperative days, motor block duration, and the patients' qualitative comparison to their prior nerve block duration.

Statistical analysis:

Based on opioid requirements for the control group of a prior trial (9), and with our hypothesis specified as a 50% reduction in postoperative opioid use during the first three days after surgery, we

calculated that 25 patients would be required for this study.

Descriptive statistics were calculated using medians and inner quartile ranges for continuous variables and counts and percentages for categorical variables. Opioid requirement and pain scores distributions were compared by day and across days with Mann Whitney U tests. Linear mixed models were fit to account for within person variance across days and confirm results of non-parametric testing. Missing data was removed from any comparison and testing.

Results

27 patients were approached to participate in the study, and one patient declined. 26 patients provided consent to participate in this investigation. One patient was excluded due to chronic, unremitting shoulder pain and long-term opioid use for management. Of the remaining 25 patients, all turned in their self-assessment journals, or provided the appropriate feedback over the phone. Two of these 25 patients did not provide complete data for postoperative day three. Demographics for the patients are presented in Table 1.

Table 1 Demographic Data.

	Historical Control Group (n=27)	Liposomal Bupivacaine Group (n=26)
Age	58.2 ± 7.2	54.3 ± 12.6
Male	15 (55.5)	14 (53.8)
Right Side	15 (55.5)	15 (57.7)
BMI	31.5 ± 4.8	30.0 ± 5.8
ASA Class		
1	1 (3.7)	2 (7.7)
2	21 (77.8)	17 (65.4)
3	5 (18.5)	7 (26.9)

BMI – body mass index; ASA – anesthesiology physical classification. Categorical variables shown as a numerical value (percentage), continuous variables are shown as means + or – standard deviation.

Oral opioid use was significantly lower on days 1 through 3 for the patients receiving the ISB with LB (Table 2), compared to the control group who had received plain bupivacaine ISB for rotator cuff repair. NRS pain scores were also significantly lower on all three days; these decrements were clinically relevant as well. Mixed models agreed with these results longitudinally, both for oral opioid requirements (β=-31.2, CI=(-41.2, -21.2), p <.001) and for reported NRS pain scores (β=-3.3, CI=(-4.7, -1.9), p <.001). The reported mean duration of motor block was 25.5 (14.8) hours.

In the qualitative assessment, 92% (n=23) of the patients reported that pain control lasted distinctly longer than it had with their prior bupivacaine ISB. All of these patients responded that they would desire LB for a future nerve block, while the two patients who did not have a perceived prolongation of block duration were not favorable toward use of this drug again.

Discussion

In this retrospective QI study, we found significantly reduced oral opioid requirements and NRS pain scores for ISB utilizing a mixture of LB and bupivacaine, on postoperative days 1, 2 and 3, compared to a historical control group which had received ISB consisting only of plain bupivacaine. The reduction in opioid use in the patients receiving LB was consistent with our hypothesis. Pain scores reported on the first three postoperative days were reduced by more than two units on the NRS scale, which substantiates clinical, as well as statistical, significance. In addition, 92% of the patients reported that the block incorporating LB lasted meaningfully longer than a prior block with plain bupivacaine alone for shoulder surgery.

These results stand in contradistinction to several other studies which have evaluated LB in the setting of RCR or shoulder arthroplasty. Kim et al assessed RCR patients in a randomized, controlled trial, in which ISB was provided with mixed LB and bupivacaine and compared to bupivacaine with dexamethasone (7). They noted no significant differences in pain scores, opioid requirements or duration of the block. Similarly, Flaherty, et al assessed this mixture in ISB in patients undergoing RCR, with similar postoperative opioid usage. The authors did note modest improvement in pain scores at 24 hours and 72 hours, but not 48 hours (8).

However, some studies have found favorable outcomes with the use of LB. Vandepitte et al evaluated mixed LB and bupivacaine for ISB in a randomized trial for patients undergoing major shoulder surgery. The primary outcome, worst pain experienced by the patients, was significantly lower for the LB group in the first postoperative week (5). In a multi-center study in which ISB with LB-bupivacaine plus bupivacaine was compared to a control group with injection of saline placebo, the LB-bupivacaine group had significantly improved pain scores and a 65% reduction in opioid requirements (6).

We believe that LB may be of greater utility for prolonged analgesia when deliberately injected within the fascial envelope that encloses C5 and C6 in the interscalene groove. We specified that the injectate be placed within these fascial confines, as evident on ultrasound imaging, for our study, which may explain the prolonged analgesia provided by LB. The patients had well-controlled pain for the first

Table 2 Continuous Values.

Variable	Total median (IQR)	Control median (IQR)	Treatment median (IQR)	P-Value
Duration	46 (24 - 61)	60 (48.5 - 77.5)	24 (14 - 30)	<.001
Pain_1	4.1 (1.85 - 7)	6.2 (3.8 - 8.2)	3 (0 - 4.2)	<.001
Pain_2	5 (2.1 - 7)	6.6 (5 - 7.8)	3 (0 - 5)	<.001
Pain_3	5 (3 - 6.5)	6 (5 - 7.5)	3.1 (0 - 5.1)	<.001
Combined Pain Days 1-3	5 (2.2-7)	6.2 (4.67 - 8)	3 (0-5)	<.001
OME_1	15 (7.5 - 37.5)	37.5 (22.5 - 60)	7.5 (0 - 15)	<.001
OME 2	15 (0 - 37.5)	37.5 (30 - 45)	5 (0 - 15)	<.001
OME 3	15 (0 - 32.5)	32.5 (18.8 - 46.9)	0 (0 - 7.5)	<.001
Combined OME	15 (0-37.5)	37.5 (22.5 - 52.5)	7.5 (0 - 15)	<.001

three postoperative days. Other studies in which LB has been utilized for ISB, while specifying injection between the nerve roots, have been less detailed about the specific site of injection with regard to the fascia bounding the groove (5,7,8), and this may help to explain a relative lack of efficacy. While speculative, this may explain our excellent outcomes with regard to opioid use and pain scores for the first 72 hours after surgery.

Our study was also unique in specifically selecting patients who had received prior single shot bupivacaine ISB, which allowed subjects to act as their own control. While patients' perceptions are necessarily subjective and qualitative, there was a very high degree of appreciation of a prolonged duration. Over 90% of patients stated that the block lasted longer with the mixture of LB-bupivacaine than with their prior nerve block utilizing plain bupivacaine.

This study has several limitations. Foremost, it was a non-blinded comparison to prior, historical data, rather than a randomized trial. We chose this design because the study was formulated initially as a QI project for presentation to our pharmacy committee; after completion, we decided to report our results as a retrospective, observational investigation. In a study such as this which is not blinded, a placebo effect cannot be discounted. In addition, while no specific funding was provided for this study, the manufacturer of LB, Pacira, provided the drug at no cost. Finally, patient reports of improved duration with LB are necessarily qualitative, since they had not recorded exact durations of their previous bupivacaine nerve block.

Conclusion

In this retrospective evaluation of LB mixed with bupivacaine for ISB for rotator cuff repair, we found that opioid use was markedly reduced, and pain scores were significantly lower, as compared to use of plain bupivacaine in a historical control group. Furthermore, most patients found that the duration of pain control was longer than with a prior plain bupivacaine ISB.

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