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Does the use of periarticular anesthetic cocktail provide adequate pain control following shoulder arthroplasty?

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Does the use of periarticular anesthetic cocktail provide adequate pain control following shoulder arthroplasty?

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Abstract

Background: Interscalene nerve block and liposomal bupivacaine have been found to provide adequate pain control following shoulder arthroplasty. We hypothesized that local infiltration of a periarticular cocktail would provide equivalent pain control compared to interscalene nerve block and liposomal bupivacaine.

Methods: Eighty-seven patients undergoing primary shoulder arthroplasty were treated with local infiltration of a periarticular cocktail (200 mg of 0.5% ropivacaine, 1 mg epinephrine, and 30 mg ketorolac), local infiltration of liposomal bupivacaine, or preoperative interscalene nerve block. The outcomes of the study were postoperative visual analog scale scores, opioid consumption, length of stay, and complications.

Results: A total of 30 patients receiving local infiltration of a periarticular cocktail, 26 receiving liposomal bupivacaine, and 31 receiving interscalene nerve block were included in the study. Patients who received local infiltration of a periarticular cocktail had a significantly lower mean visual analog scale when compared to interscalene nerve block and liposomal bupivacaine on postoperative day 0 (2.5 versus 4.0 versus 4.8, $P = 0.001$ and $P < 0.001$). Pain scores between postoperative day 0–3 were lower in patients who received local infiltration of a periarticular cocktail, but not significantly. Patients who received local infiltration of a periarticular cocktail required significantly less opioids than the interscalene nerve block group on postoperative day 0 ($P < 0.001$).

Discussion: A decrease in early postoperative pain and opioid consumption was found with local infiltration of a periarticular cocktail when compared with interscalene nerve block and liposomal bupivacaine after shoulder arthroplasty.

Level of evidence: Level II

Keywords

shoulder arthroplasty, local infiltration analgesia, local anesthetic cocktail, perioperative analgesia, postoperative pain control, opiate consumption

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Introduction

Pain control following shoulder arthroplasty has been shown to influence patient outcomes, patient satisfaction, and healthcare costs.[1,2] More recently there have been increased efforts to find multimodal regimens that control pain and decrease the use of opioids. Both regional and local anesthesia have been used in shoulder arthroplasty and have demonstrated adequate pain control.[3,4]

Interscalene nerve blocks (INBs) are a reliable method of regional anesthesia for shoulder arthroplasty and have been shown to improve postoperative pain scores, patient satisfaction, and decrease length of stay.[5,6] However, INB has been associated with postoperative complications including respiratory

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compromise and neurological palsies, as well as rebound pain leading to patient discomfort.[5,7] The benefits of regional anesthesia must be weighed against the potential risk of complications. Another option for pain control that has been shown to be highly effective in total knee and hip arthroplasty is local infiltration analgesia. This form of anesthesia involves infiltration of the periarticular tissues intraoperatively with a "moving needle" technique.[8] This can be performed using a single anesthetic agent or a cocktail of medications including ropivacaine, ketorolac, morphine, and epinephrine. This technique avoids the risks of pneumothorax and brachial plexus injury that are seen with INB.

Previous studies have found that use of local infiltration analgesia with liposomal extended-release bupivacaine (Exparel, Pacria Pharmaceuticals, Inc., Parsippany, NJ) in shoulder arthroplasty is comparable to INB in terms of pain scores, morphine consumption, and length of hospital stay.[3,9] However, other studies have shown that local infiltration analgesia with a simple cocktail of ropivacaine, epinephrine, and ketorolac in total knee arthroplasty is also associated with lower pain scores and total opiate use.[10] No previous studies have compared local infiltration analgesia with liposomal bupivacaine (LB), local infiltration cocktail (LIC), and INB for pain control following shoulder arthroplasty. The purpose of this study was to perform a prospective cohort study comparing three common methods for pain control in patients undergoing shoulder arthroplasty. Our hypothesis was that LIC would provide equivalent pain control compared to INB and LB at decreased cost.

Materials and methods

We performed a non-industry sponsored, prospective cohort study. Approval was obtained from the Henry Ford Health System Institutional Review Board prior to initiation of the study. From October 2014 through March 2018, 87 adult patients undergoing either primary anatomic or reverse total shoulder arthroplasty were consented for participation. Surgery was performed by one of three fellowship-trained orthopaedic surgeons using a deltopectoral approach. All surgeries were performed under general anesthesia in the beach chair position. Patients were excluded if their medical history revealed known allergies or intolerance to dexamethasone, bupivacaine, ropivacaine, ketorolac, epinephrine, or opioid medications; history of substantial alcohol or drug abuse; and history of current pregnancy. According to institutional protocol at the time of the surgery, patients were consecutively enrolled into the three groups. Of eligible patients, 31 patients received INB, 26 patients received LB, and 30 patients received LIC.

INB was performed 1 h prior to surgery under ultrasound guidance by a certified anesthesiologist experienced in the technique. A single dose of 40 ml of 0.5% ropivacaine was injected into the nerve sheath of the brachial plexus utilizing a 22-gauge needle of 80 mm length. The LIC contained a mixture of 200 mg of 0.5% ropivacaine, 1 mg epinephrine, and 30 mg ketorolac. The LB injection contained 20 ml of LB (266 mg) diluted in 20 ml of sterile saline. Both injections were infiltrated locally using a standardized protocol at the completion of component implantation and before incision closure. A 60 ml syringe with a 1 in., 18-gauge needle was used to administer the injection. Five milliliters were injected into the periosteum, 10 ml into the deltoid administered in 2 ml increments spread over the deltoid muscle anteriorly, 10 ml into the pectoralis major muscle (administered in 2 ml increments), and the final 15 ml were injected evenly into the subcutaneous tissue along the incision. Patients were then placed on a standardized postoperative pain regimen consisting of acetaminophen 650 mg every 8 h, oxycodone 5 mg every 4 h as needed for pain levels less than 5, oxycodone 10 mg every 4 h as needed for pain levels greater than 5, and morphine 2 mg every 4 h as needed for severe breakthrough pain during the hospital stay. Patient outcomes were self-recorded using a visual analog scale (VAS) every 4 h for 96 h in a pain diary. Opioid requirements were obtained from the medical record and pain diary after discharge. Opioid doses were converted to intravenous morphine equivalents prior to data analysis. This was performed using standardized morphine equivalent conversion factors according to the Centers for Disease Control.[11] Length of hospital stay was also obtained from the medical record and calculated from the time of surgery.

Statistical analysis

The primary outcome of interest in this study was average VAS score difference of 13 mm between the INB, LB, and LIC groups. This was based on previous literature demonstrating that a difference of 13 mm on VAS between two groups represents a clinically significant change.[12] A power analysis was performed to assess the hypothesis that a significant difference in average pain of 13 mm on the VAS would not be found between the three groups. With power of 80% (β level = 0.80, α level = 0.05), a sample size of 25 patients per group was obtained. Secondary outcomes collected included average opioid use and postoperative length of stay. Demographics and the outcomes of interest were compared between each treatment type at 4 h intervals within the first 24 h, and at each postoperative day (POD).

All results were first analyzed using analysis of variance. Then, if significant differences between groups were detected, a post hoc of least significant difference

was performed. In each table, results of ANOVA are shown in one column and, if significance was found, post-hoc tests were performed, and the results shown in the table or legend. If significant differences were not found, averages were still reported absent p-values. A general linear model univariate with post hoc of least significant difference, and Pearson's chi-square test were also used. For all analyses, $P < .05$ was considered statistically significant. Analyses were performed using SPSS software (Version 25, IBM, Armonk, NY).

Results

A total of 97 patients were evaluated for inclusion in the study. Ten patients declined participation. A total of 87 total patients were included and analyzed. Thirty patients received local infiltration analgesia with LIC, 31 patients received INB, and 26 patients received local infiltration analgesia with LB. Differences in demographic variables between the groups are presented in Table 1. In the LIC group, nine patients (31%) were using opioid pain medication, most commonly hydrocodone, for at least three months prior to their surgery compared to zero patients in the INB or LB groups.

Comparisons of postoperative VAS are shown in Tables 2 and 3. Patients in the LIC group had significantly reduced pain when compared to INB at 9–12 h and again at 17 h postoperative (3.04 versus 4.90, $P = .003$) through the remainder of POD 1. The LIC group had lower pain scores overall for the first POD (2.46 versus 3.95, $P < .001$). When compared to LB, LIC demonstrated significantly reduced pain starting immediately postoperatively (2.24 versus 5.28, $P < .001$) and lasting through the entire first POD. After POD 1, LIC had similar pain scores when compared to INB and LB.

The postoperative opioid usage per group is reported in Tables 4 and 5. Patients in the LIC group had significantly reduced average opioid consumption when compared to INB beginning at 5 h postoperative (1.12 versus 3.71, $P < .001$) and overall for the first 24 h postoperative (10.84 versus 21.42, $P < .001$). Morphine usage was also lower in the LIC group compared to LB at 5–8 h postoperative (1.12 versus 2.58, $P = .046$). Morphine usage was significantly higher on POD 3 in the LIC group compared to both LB and INB (7.54 versus 2.90 versus 2.18, $P = .033$ and .011, respectively).

While the average day of discharge was POD 2, length of hospital stay was significantly shorter for the LIC group compared to both the INB and LB groups, 1.07 versus 1.5 versus 1.5 days ($P < .001$), respectively. One patient in the INB group sustained a phrenic nerve palsy requiring readmission for

Table 1. Patient demographics.

	LIC	INB	LB	ANOVA *P*-value
Number of patients	30 (34.5%)	31 (35.6%)	26 (29.9%)	
Males	15 (17.2%)	16 (18.4%)	12 (13.8%)	0.916
Females	15 (17.2%)	15 (17.2%)	14 (16.1%)	0.916
Mean age (SD), years	73.5 (7.8)	67.3 (12.9)	69.4 (8.1)	.054
Mean BMI, kg/m^2 (SD)	28.6 (7.0)	29.8 (5.3)	32.3 (6.5)	.090
Estimated blood loss, ml (SD)	67.7 (34.7)	128.1 (149.3)	86.54 (36.2)	**0.041***
Operative time, min (SD)	106.5 (40.0)	134.3 (27.7)	134.31 (35.9)	**0.003***
Surgery				
TSA	2 (2.3%)	15 (17.2%)	18 (20.7%)	<**0.001**
RTSA	28 (33.2%)	16 (18.4%)	8 (9.2%)	<**0.001**

ANOVA: analysis of variance; BMI: body mass index; INB: interscalene nerve block; LB: liposomal bupivacaine; LIC: local infiltration cocktail; RTSA: reverse total shoulder arthroplasty; TSA: total shoulder arthroplasty.
Note that percentages are calculated with respect to the group rather than the entire cohort.
*Post-hoc test results: Average blood loss is higher in INB versus LIC ($p = 0.014$). Average surgical time is lower in the LIC group compared to both the INB ($p = 0.002$) and LB ($p = 0.004$) groups. There were significantly more RTSAs in the LIC group compared to both the INB and LB groups ($p < 0.001$ for both). There were significantly less TSAs in the LIC group compared to both the INB and LB groups ($p < 0.001$ for both). Bold values are statistically significant.

Table 2. Pain scores by hours (mean ± SD).

Hours after surgery	LIC	INB	*P*-value LIC versus INB	LB	*P*-value LIC versus LB	ANOVA P-value
0–4	2.24 ± 1.55	2.59 ± 3.05	0.572	5.28 ± 2.23	0.001	<0.001
5–8	2.80 ± 2.43	2.93 ± 3.12	0.856	4.93 ± 2.32	0.006	0.006
9–12	2.60 ± 2.21	3.78 ± 3.05	0.045	5.09 ± 2.54	<0.001	0.003
13–16	2.60 ± 2.13	3.97 ± 3.39	0.076	4.38 ± 2.45	0.030	0.042
17–20	3.04 ± 2.11	4.90 ± 2.23	0.003	4.67 ± 2.43	0.014	0.004
21–24	2.46 ± 1.48	5.38 ± 2.13	<0.001	4.54 ± 2.48	<0.001	<0.001

ANOVA: analysis of variance; INB: interscalene nerve block; LB: liposomal bupivacaine; LIC: local infiltration cocktail.

Table 3. Pain scores by days (mean ± SD).

Postoperative day	LIC	INB	*P*-value LIC versus INB	LB	*P*-value LIC versus LB	ANOVA P-value
Day 0	2.46 ± 1.47	3.95 ± 1.75	0.001	4.80 ± 1.83	<0.001	<0.001
Day 1	3.25 ± 1.82	4.30 ± 2.16		4.14 ± 2.16		0.11
Day 2	3.29 ± 1.98	3.63 ± 1.65		4.34 ± 2.47		0.15
Day 3	2.83 ± 1.63	4.30 ± 2.16	0.053	4.14 ± 2.01	0.067	0.008

ANOVA: analysis of variance; INB: interscalene nerve block; LB: liposomal bupivacaine; LIC: local infiltration cocktail.

Table 4. Morphine equivalent use by hours (mean ± SD).

Hours after surgery	LIC	INB	*P*-value LIC versus INB	LB	*P*-value LIC versus LB	ANOVA P-value
0–4	4.29 ± 2.93	3.23 ± 3.02		2.78 ± 2.52		0.13
5–8	1.12 ± 2.11	3.71 ± 2.95	<0.001	2.58 ± 2.90	0.046	0.001
9–12	1.15 ± 2.01	3.61 ± 2.61	<0.001	2.43 ± 2.85	0.064	0.001
13–16	1.63 ± 2.16	4.65 ± 3.47	<0.001	2.45 ± 2.38	0.302	<0.001
17–20	1.61 ± 2.44	3.39 ± 3.96	0.026	2.70 ± 2.77	0.191	0.009
21–24	1.05 ± 1.91	2.84 ± 4.46	0.036	2.10 ± 2.69	0.239	0.01

ANOVA: analysis of variance; INB: interscalene nerve block; LB: liposomal bupivacaine; LIC: local infiltration cocktail.

respiratory compromise. There were no complications in the LB or LIC groups.

Discussion

INBs and local infiltration analgesia with LB have been used with success for perioperative pain control in shoulder arthroplasty. Our study found that local infiltration with a simple cocktail is associated with significantly reduced pain scores and opiate consumption on POD 0 when compared to INB and LB. Following POD 0, these differences were not statistically significant. LIC offers another cost-effective alternative that can be used to manage pain control following the procedure.

Table 5. Morphine equivalent use by days (mean ± SD).

Postoperative day	LIC	INB	*P*-value LIC versus INB	LB	*P*-value LIC versus LB	ANOVA P-value
Day 0	10.84 ± 7.85	21.42 ± 11.28	<0.001	15.04 ± 9.09	0.109	<0.001
Day 1	11.49 ± 10.74	9.11 ± 11.43		8.98 ± 9.53		0.599
Day 2	9.19 ± 9.58	5.21 ± 10.79		12.83 ± 17.00		0.081
Day 3	7.54 ± 10.41	2.18 ± 6.11	0.011	2.90 ± 4.13	0.033	0.014

ANOVA: analysis of variance; INB: interscalene nerve block; LB: liposomal bupivacaine; LIC: local infiltration cocktail.

These analgesic methods have varying mechanisms of action to help control pain. Anesthetics such as ropivacaine and bupivacaine work by inhibiting the transmission of action potentials in sensory nerve fibers.[13] When used as a perineural infiltration, such as with INB, this results in a widespread anesthetic effect that can be used both intra- and postoperatively for pain control.[4] When used locally such as with LIC or LB, the inhibition of local nociceptors limits transmission of pain signals. A depot formulation such as LB helps to slow systemic absorption and prolong the local effects.[14] Adjuvants such as epinephrine can be used to constrict the local vasculature, delaying absorption, and prolonging the effects of the infiltration.[13] Ketorolac is included as a non-steroidal anti-inflammatory medication to control pain caused by the local inflammatory response to surgical trauma. When ketorolac is used in a LIC, it has been shown to provide superior pain control compared to cocktails that do not include ketorolac.[15] Therefore, the LIC is a multimodal therapy, which acts to control varying types of pain with multiple adjuvant medications at the site of surgery. Studies have shown that absorption of locally injected medications, including ropivacaine, bupivacaine, and ketorolac, does not lead to systemically toxic levels.[14,15]

LICs with the same medications used in this study have been well studied in hip and knee arthroplasty. Most of these authors used the same combination of medications as were used in this study.[8,16] Other authors also add morphine to their cocktail, but all have achieved similar success.[17,18] A randomized controlled trial of total knee patients showed improved patient satisfaction and decreased pain scores in the first 24 h postoperatively with use of a multimodal periarticular cocktail.[18] Bagsby et al.[17] compared LB to a traditional LIC in total knee patients and found improved pain control with the LIC throughout the hospital stay. Previous studies in shoulder arthroplasty patients have compared INB and LB and found no significant difference in pain control.[3,9] Our results are consistent with these studies, showing comparable results between the methods of analgesia. In comparison to INB, LIC was associated with decreased VAS scores on POD 0. VAS was similar between the two groups from 0 to 16 h postoperatively; however, after 16 h the LIC group demonstrated lower pain scores. This may be related to the duration of action of the INB, which is on average 18 h as reported in Goon et al.[19] After the nerve block wears off, patients have been found to have an increase in rebound pain compared to a more consistent pain profile in patients who do not receive a block. From Table 2, it appears that the block started to wear off at 9 h postoperatively for this study group and patients likely experienced rebound pain at approximately 21–24 h. The LIC group also did not demonstrate a dramatic increase in pain scores over the course of POD 0, suggesting more even pain control. When compared to LB, LIC was associated with significantly lower VAS at all time points on POD 0. These results demonstrate better pain control using a multi-ingredient cocktail for local injection rather than using a single long-acting agent. Physicians must determine if there is an additional benefit of using a more expensive long-acting agent when a mix of cheaper agents achieves improved pain control.

When evaluating morphine requirements in patients undergoing total knee arthroplasty, studies have shown decreased morphine usage for the first 48 h after surgery with use of LIC.[16] However, comparisons of LIC with LB in total hip and knee arthroplasty show a larger decrease in opiate usage with LB.[20,21] Studies comparing INB with LB in total shoulder arthroplasty show similar opiate usage.[3,9] One study showed lower opiate consumption with INB compared to LB; however, they used an indwelling catheter rather than a single injection.[22] In this study, results were consistent with the total shoulder literature. LIC was associated with decreased opiate use when compared to INB on POD 0. There was not a significant decrease in morphine equivalent usage when comparing LIC and LB. This is likely to be related to the formulation of LB, which is designed to release anesthetic slowly over the course

of a number of days.[14] Opiate use was significantly increased in the LIC group on POD 3. This may be related to the prevalence of preoperative opiate usage in this group as 31.0% (nine patients) were using opioid medications for at least three months prior to their surgery, and therefore, did not demonstrate the equivalent decrease in opiate usage on POD 3 as in the other two groups. There were no patients using preoperative opiates in the LB and INB groups. Despite this, the LIC group still had adequate pain control compared to the other groups which indicates that this may be a good option for analgesia in that population.

Complications of INB have been evaluated in numerous studies.[7,23,24] In a prospective study of 218 patients, Weber and Jain[24] found a failure rate of 13% and abnormal neurologic responses in 5% of patients at 24 h. Other studies have reported rates of acute complications as high as 16%, with persistent neurological complications in 4.4%.[23] Of note, bupivacaine is associated with higher risks of central nervous system and cardiac toxicity when compared to ropivacaine when administered intravenously.[25] These risks are lower with the liposomal formulation of bupivacaine and with local injection, but are important factors to consider.[24,26] Our study is consistent with these results with only one patient sustaining a phrenic nerve palsy after INB and no complications following LB or LIC. However, in patients with medical comorbidities who may be placed at higher risk of complications with general anesthesia, the combination of regional anesthesia with INB and sedation is the more reasonable option.

In terms of healthcare costs, length of stay was significantly shorter in the LIC group. This has potential implications for overall system-wide cost savings as this can lead to decreased costs for the patient and increased availability of beds to support higher surgical volumes. With increasing emphasis on outpatient surgery, LIC can provide reliable pain control for patients being discharged immediately following shoulder arthroplasty. Additionally, there is a large difference in cost for each of these methods of analgesia. The average wholesale cost of LB in our region is $315 and the physician fee for INB based on *Current Procedural Terminology* code 64415 is $1583. In comparison, the total wholesale cost of the LIC at our institution is $24.68, making it a highly cost-effective alternative to INB and LB.

There are several limitations to our study. The patients in the LIC group underwent a higher proportion of reverse compared to anatomic shoulder arthroplasty and included chronic opiate users, which may have been confounding factors. The LB and INB groups did not include chronic opiate users. However, it is encouraging that these chronic pain patients still demonstrated good pain control. Additionally, recent research has shown that postoperative pain is equivalent between TSA and RTSA.[27] The study participants were not blinded to their intervention due to the invasive nature of the INB. Blinding of the surgeon was not thought to be necessary as the surgeons were not involved in data collection. However, residents or mid-level providers who were also not blinded made the decision to discharge patients based on recommendations from physical and occupational therapy. Therefore, we do not believe that the decision to not blind surgeons influenced our length of stay measurements. Another limitation is the use of VAS, which is a subjective measure of pain level and can limit the patient's ability to detect subtle changes in pain and these differences may not be clinically significant.[28] Finally, patient compliance, defined as the completeness with which the patient recorded opiate intake and pain scores, was a limitation. Compliance with pain diaries was over 80% on POD 0–1 in all groups, but decreased to 40–50% on POD 2–3.

Conclusion

A decrease in early postoperative pain and opioid consumption was found with LIC when compared with INB and LB after shoulder arthroplasty. These findings suggest that LIC provides similar pain relief and opioid requirements at a decreased cost compared to INB or LB.

Authors' note

This work is not based on previous communication to a society or meeting.

Contributorship

EK wrote the first draft of the manuscript, all authors reviewed and edited the manuscript and approved the final version of the manuscript.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical Review and Patient Consent

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Trial Registration

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