The Effect of Adding Dexmedetomidine to Levobupivacaine for Interscalene Block for Postoperative Pain Management After Arthroscopic Shoulder Surgery

Züleyha K. Bengısun, MD, Perihan Ekmekçi, MD,* Burak Akan, MD,† Ayşegül Köroğlu, MD,* and Filiz Tüzüner, MD**

Objective: Arthroscopic subacromial decompression may cause substantial postoperative pain. We undertook a randomized controlled trial to examine whether adding dexmedetomidine to the local anesthetic in an interscalene brachial plexus block and subsequent patient-controlled interscalene analgesia (PCIA) regime improved postoperative pain scores, patient satisfaction, rescue analgesic requirement, and local anesthetic consumption.

Methods: A total of 48 patients aged between 18 and 65 years undergoing arthroscopic subacromial decompression were enrolled and randomized into 1 of the 2 groups. Group L (n = 25) received levobupivacaine and epinephrine, whereas Group LD (n = 23) received levobupivacaine, epinephrine, and dexmedetomidine through an interscalene catheter. Four hours after surgery, a PCIA regime was commenced. In Group L patients were administered levobupivacaine and in Group LD levobupivacaine and dexmedetomidine. Demographic and hemodynamic data, duration of motor and sensory blocks, pain VAS, side effects, PCIA demand and delivery values, consumption of lornoxicam as a rescue analgesic, and patient satisfaction were recorded for 24 hours after surgery.

Results: PCIA demand and delivery, and pain VAS values were significantly lower, and patient satisfaction was significantly higher in the dexmedetomidine group ($P = 0.004$, 0.001, 0.004, and 0.002, respectively). The side effect profile was similar between the groups. Levobupivacaine consumption was significantly lower in Group LD ($P = 0.009$). In the first 24 postoperative hours, Group LD consumed significantly less lornoxicam ($P = 0.01$).

Discussion: Addition of dexmedetomidine to levobupivacaine for interscalene brachial plexus block decreases pain scores and increases patient satisfaction after arthroscopic subacromial decompression.

Key Words: arthroscopic shoulder surgery, interscalene block, dexmedetomidine, patient-controlled interscalene analgesia

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Shoulder surgery can cause significant postoperative pain, and patients may require doses of opioid analgesia comparable with those who have undergone thoracotomy or gastrectomy.[1] Opioid-based analgesic regimes can be associated with substantial side effects. A multimodal approach to analgesia may reduce opioid requirements and decrease the incidence of side effects such as postoperative nausea and vomiting (PONV), pruritus, sleep disturbance, and constipation.[2] Nevertheless, despite multimodal analgesia, one-third of patients report severe pain in the first 24 hours after minimally invasive shoulder surgery. Continuous interscalene nerve block is accepted to be an effective and safe technique for pain control, which decreases opioid consumption and increases patient satisfaction.[3,4]

Dexmedetomidine is a potent α_2 adrenoceptor agonist that is 8 times more selective for the α_2 adrenoceptor than clonidine.[5] It has been shown to be an effective adjunct to local anesthetics in intrathecal,[6] caudal,[7] and intravenous regional anesthesia.[5] Animal[8–11] and human studies[12–15] have demonstrated that it has an effect on peripheral nerves that is thought to underpin its mechanism of action.

The efficacy of dexmedetomidine as an adjunct to interscalene block has not been examined. We undertook a randomized controlled trial to establish whether adding dexmedetomidine to levobupivacaine in an interscalene brachial plexus block and subsequent patient-controlled interscalene analgesia (PCIA) regime influenced the amount of pain reported after shoulder surgery. Secondary endpoints were patient satisfaction, rescue analgesia requirements, and local anesthetic consumption.

MATERIALS AND METHODS

We conducted a prospective, double-blind, and randomized study approved by the ethics committee in our institution (Ethics No. 08071, Date 24.06.2009). Written informed consent was obtained from 50 American Society of Anesthesiologists physical status I and II patients aged between 18 and 65 years scheduled to undergo elective arthroscopic shoulder surgery. Patients with a history of allergy to local anesthetics, severe systemic disease, difficulty in cooperating or quantifying pain using a visual analog scale (VAS), who were pregnant, or those taking adrenoceptor agonists or antagonists were excluded from the study.

Patients received 0.03 mg/kg midazolam intravenously 45 minutes before the operation as premedication. The electrocardiogram, pulse oximetry, and noninvasive blood pressure were monitored in all patients. Patients were randomized into 1 of the 2 groups using the sealed envelope technique: Group L, who later would receive an interscalene block with levobupivacaine and epinephrine; and Group LD, who would receive levobupivacaine, epinephrine, and dexmedetomidine. Anatomic landmarks were identified using the method described by Winnie.[16] After skin disinfection using chlorhexidine, the skin near the block

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From the Departments of *Anesthesiology and Reanimation; and †Orthopedics and Traumatology, Ufuk University Dr Rıdvan Ege Hospital, Ankara, Turkey.
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Reprints: Perihan Ekmekçi, MD, Department of Anesthesiology and Reanimation, Ufuk University Dr Rıdvan Ege Hospital, Konya Yolu Mevlana Blv, Balgat 86-88 06520, Ankara, Turkey (e-mail: erdogduperi@gmail.com).

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site was infiltrated with 20 mg 2% lidocaine. Peripheral nerve block was performed using a nerve stimulator (stimulation duration: 1 ms, frequency: 2 Hz, Stimuplex HNS 12; Braun Melsungen AG, Melsungen, Germany). When deltoid and/or biceps contractions were seen, the current was decreased to 0.5 mA to ensure that the amplitude of twitching was diminished. A nonstimulating catheter was advanced blindly and then withdrawn so that 2 to 3 cm of the catheter remained beyond the original position of the needle tip. After a negative aspiration test, the study drug preparation was slowly injected. Block success was defined as a negative pinprick test in the distribution of the C4-C7 dermatomes and inability to adduct the shoulder and flex the forearm. Propofol (3 mg/kg) and rocuronium (0.6 mg/kg) were then administered to induce anesthesia, which was maintained with 2% to 3% sevoflurane in 50% oxygen and air. All patients underwent minimally invasive subacromial decompression in the beach-chair position.

Patients in Group L (n = 25) were blocked with 20 mL of a mixture of 100 mg levobupivacaine (0.5%) and 50 μg epinephrine, whereas those in Group LD (n = 23) received 20 mL of a mixture of 100 mg levobupivacaine (0.5%), 50 μg epinephrine, and 10 μg dexmedetomidine through the interscalene catheter. Four hours after surgery a PCIA device was connected to the catheter and programmed to infuse at 5 mL/h, and provide a 2 mL bolus with a 15-minute lockout period. In Group L, the device delivered 0.25% levobupivacaine; in Group LD it delivered 0.25% levobupivacaine with 0.5 μg/mL dexmedetomidine. The same anesthesiologist performed all the interscalene blocks and the same surgeon performed all the arthroscopic procedures. Solutions used in the study were prepared by an anesthesiologist blinded to the participants' randomization status, as were the surgeons and anesthesiologists who conducted the postoperative evaluations.

VAS for pain (on a scale from 0 to 10) was evaluated 2, 4, 6, 12, and 24 hours after surgery. Demographic data, heart rate, mean arterial pressure, pulse oximetry, block onset time, demand and delivery values for PCIA, episodes of bradycardia (heart rate $<20\%$ of baseline), hypotension (mean arterial pressure $<20\%$ of baseline), PONV, lornoxicam consumption, and patient satisfaction were recorded. The ability to flex the elbow was considered to represent the end of motor block; the time to first flexion of the arm was recorded.

Lornoxicam, a nonsteroidal anti-inflammatory drug used to treat postoperative pain,[17] was used 8 mg intravenously as rescue analgesic when VAS scores were ≥ 4. The maximum dose administered in the first 24 postoperative hours was 16 mg. Metoclopramide (10 mg) was administered intravenously for PONV if necessary. Patient satisfaction was evaluated 24 hours after surgery using a 5-point Likert scale (completely satisfied, quite satisfied, slightly dissatisfied, dissatisfied, and very dissatisfied).

SPSS for Windows 15.0 (SPSS Inc., Chicago, IL) was used for statistical analysis. Numerical variables are reported as means, SD, and medians, whereas qualitative variables are reported as percentages. Differences in numerical variables between groups were evaluated using the Student *t* test or the Mann-Whitney test depending on distribution of variables; the χ^2 test was used to evaluate the difference in qualitative variables. Changes in pain scores, heart rate, and mean arterial pressure were evaluated using repeated measures variance analysis. Multiple comparisons were undertaken using the Bonferroni test. Statistical significance was set at $P = 0.05$. Group sample sizes of 25 and 23 achieved an 81.6% power to detect a pain VAS area under the curve (AUC) difference of 229.6 between the groups with a significance level (α) of 0.05 using a 2-sided Mann-Whitney test and making the assumption that the data are normally distributed. Pain VAS AUC scores were analyzed to achieve a more reliable result.

TABLE 1. Demographical Data

	Group L (n = 25)	Group LD (n = 23)
Age (y)	50.4 ± 12.9	55.9 ± 8.5
Weight (kg)	77.5 ± 11.0	76.5 ± 12.5
Sex (F/M)	17/8	16/7
ASA (I/II)	10/15	6/17
Duration of surgery (min)	85.9 ± 27.0	84.1 ± 33.1
Block onset time (min)	17.9 ± 10.1	15.4 ± 8.8
Nausea (n [%])	5 (21.7)	4 (18.2)
Vomiting (n [%])	2 (8.7)	0

Values are mean ± SD. Numbers for nausea and vomiting are the number of patients who complained of nausea and vomiting.

P values were not significant.

ASA indicates American Society of Anesthesiologists; F, female; M, male.

RESULTS

Demographic data were broadly comparable between the groups (Table 1). There were no statistically significant differences in perioperative hemodynamic parameters. No surgical complications were observed. No patients were excluded from the study as a result of a failed block, but in Group LD 1 patient was excluded when the catheter was accidentally dislodged, and another because the surgery was converted to an open procedure. Mean duration of surgery was 85.9 ± 27.0 minutes in Group L and 84.1 ± 33.1 minutes in group LD ($P = 0.834$). The onset time of sensory block was 17.9 ± 10.1 minutes in group L and 15.4 ± 8.8 minutes in group LD ($P = 0.375$). Duration of motor block was 15.6 ± 9.6 hours in Group L but significantly shorter at 9.6 ± 8.6 hours in group LD ($P = 0.032$). Pain VAS values were lower in Group LD at all time points ($P = 0.004$; Fig. 1), whereas patient satisfaction was higher ($P = 0.002$). The AUC for the pain VAS

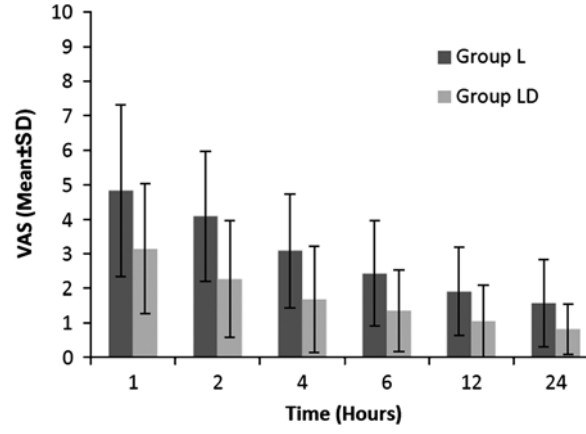

FIGURE 1. Mean arterial pressure changes in time.

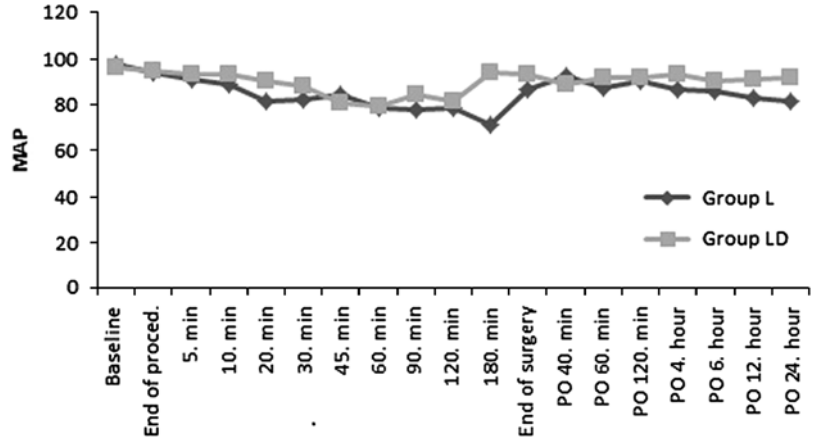

FIGURE 2. Heart rate changes in time.

in Group LD was significantly lower than in Group L ($P = 0.006$). No significant difference in the incidence of PONV was observed (Table 1). Neither hypotension nor bradycardia was observed in either group (Figs. 2, 3). Eight patients (34.8%) in Group L reported being completely satisfied compared with 17 (77.3%) in group LD ($P = 0.002$; Table 2). In the first 24 postoperative hours, the patients in Group LD consumed significantly less lornoxicam than did Group L (8.0 ± 11.8 and 20.2 ± 17.5 mg, respectively, $P = 0.01$; Table 3). Total local anesthetic consumption was significantly lower in Group LD compared with Group L (129.4 ± 11.8 and 141.3 ± 17.1 mL, respectively, $P = 0.009$; Table 3). Patients in Group LD made significantly fewer PCIA demands and fewer boluses were delivered: demand values were 18.7 ± 18.2 and 59.8 ± 71, respectively; delivery values were 13.7 ± 13.6 and 28.8 ± 18.8; $P = 0.004$ and 0.001, respectively.

DISCUSSION

We found that adding dexmedetomidine to the local anesthetic mixture used for interscalene block and subsequent PCIA regime decreased pain scores, local anesthetic consumption, and rescue analgesic requirements, and increased patient satisfaction after arthroscopic shoulder surgery.

Although arthroscopic shoulder surgery is associated with less tissue damage, patients often report severe pain afterward. Interscalene plexus block is an effective way of managing this acute pain.[18] Levobupivacaine is widely used for peripheral nerve blockade as it has a greater margin of cardiovascular safety than the racemic mixture when used in large doses.[19] Levobupivacaine and bupivacaine seem to be equipotent for brachial plexus block. Baskan et al[20] compared 40 mL 0.25% levobupivacaine with the same volume of 0.25% bupivacaine for the posterior approach to the brachial plexus block, and reported that the onset times, and duration of anesthesia and analgesia were similar.

A variety of drugs has been used as adjuncts to local anesthetics in peripheral nerve blocks, including opioids, magnesium, and α_2 adrenoreceptor agonists.[21] The latter exert their analgesic effects by inhibiting norepinephrine release mediated by α_2 receptors located at nerve endings.[22] Brummett et al[8] reported that a short period of analgesia is observed after local injection of dexmedetomidine, implying that it has a peripheral effect. The same investigators also reported that dexmedetomidine is more effective in a rat sciatic nerve model when injected perineurally rather than

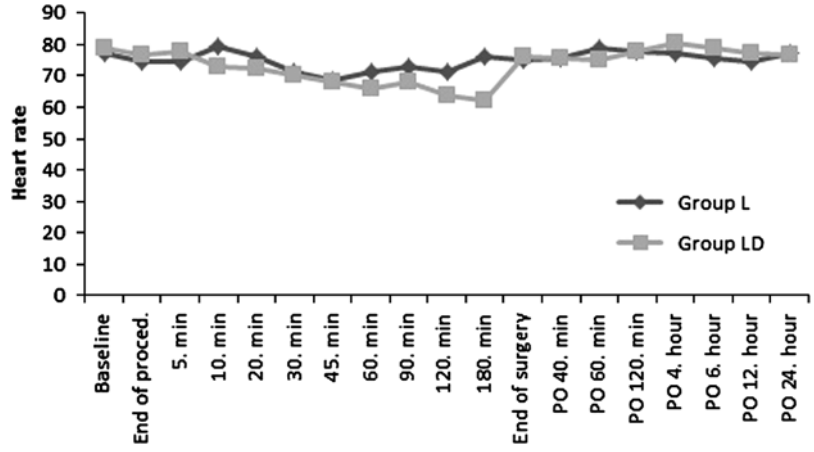

FIGURE 3. Changes in VAS scores over time (h) after arthroscopic shoulder surgery. Pain scores were significantly lower in Group LD (who received levobupivacaine and dexmedetomidine) compared with Group L (who received only levobupivacaine) at all times.

TABLE 2. Patient Satisfaction

	n (%)	
	Group L (n = 23)	Group LD (n = 22)
1	8 (34.8)	17 (77.3)
2	3 (13)	4 (18.2)
3	10 (43.5)	1 (4.5)
4	0 (0)	0 (0)
5	2 (8.7)	0 (0)

$P = 0.002$.

1 indicates completely satisfied; 2, quite satisfied; 3, slightly dissatisfied; 4, dissatisfied 5, very dissatisfied.

systemically, although they state that the underlying mechanism is unclear.[23] In a study conducted by Wahlander et al,[24] intravenous 0.5 μg/kg loading and 0.4 μg/kg/h infusion dose of dexmedetomidine were used as an adjunct to thoracic epidural analgesia established using 0.125% bupivacaine and caused a significant decrease in heart rate and blood pressure when used systemically. By administering dexmedetomidine perineurally, we aimed to increase the quality and duration of regional anesthesia while avoiding the adverse effects associated with systemic use, such as hypotension, bradycardia, and sedation.

A variety of doses of dexmedetomidine has been used in peripheral nerve blocks as an adjunct to local anesthetics. Esmaoglu et al[12] added 100 μg to 40 mL 0.5% levobupivacaine for axillary brachial plexus block and reported faster onset and longer duration of block and postoperative analgesia. In another study, Swami et al[15] compared 1 μg/kg dexmedetomidine with 1 μg/kg clonidine as adjuncts to bupivacaine in supraclavicular brachial plexus block, and reported that dexmedetomidine prolonged sensory and motor blockade, increased the quality of analgesia, and delayed the need for first rescue analgesia. Ammar and Mahmoud[14] used 0.75 μg/kg dexmedetomidine as an adjunct to 30 mL 0.33% bupivacaine in single-shot ultrasound-guided upper extremity blocks and found that the onset of sensory and motor block was faster, the duration of analgesia was prolonged, and pain scores and opioid requirements were reduced.

TABLE 3. Maintenance Characteristics and Postoperative Analgesic Outcomes

	Group L (n = 25)	Group LD (n = 23)	*P*
Total local anesthetic consumption (mL)	141.3 ± 17.1	129.4 ± 11.8	0.009*
Total rescue analgesic consumption (mg)	20.2 ± 17.5 (median = 16) (0-56)	8 ± 11.8 (median = 0) (0-40)	0.010*
Demand	59.8 ± 71.0 (median = 38) (3-330)	18.7 ± 18.2 (median = 17) (0-66)	0.004*
Delivery	28.8 ± 18.8 (median = 22) (3-73)	13.7 ± 13.6 (median = 12) (0-52)	0.001*
VAS AUC	510.7 ± 298.4	281.1 ± 232.8	0.006*

Total demand is calculated as the total number of demands made by the patient. Total delivery is calculated as the number of deliveries made by the patient-controlled interscalene analgesia device. Total anesthetic consumption is calculated as the sum of basal infusion rate and number of deliveries multiplied by the concentration of local anesthetic.

VAS AUC indicates area under the curve for visual analog scale values.

In our study, 0.5 μg/mL dexmedetomidine was also added to 0.25% levobupivacaine for the postoperative PCIA with a background infusion. We found no statistically significant difference in the onset time compared with those who received only levobupivacaine, which can be explained by the relatively low dose of dexmedetomidine used. Nonetheless, the duration of analgesia was prolonged, and the total local anesthetic and rescue analgesic requirements were lower, similar to the findings of previous studies.

Continuous infusion through an interscalene catheter for pain management after arthroscopic subacromial decompression treats pain on movement more effectively than a single injection.[25] We used a continuous background infusion rate of 5 mL/h with patient-controlled boluses. This is the first time that dexmedetomidine has also been used as an adjunct to the drugs that comprise the postoperative analgesic regime.

Dexmedetomidine may cause hypotension and bradycardia in high doses, as well as sedation and anxiolysis.[26] Other investigators have found that 2.5 μg/mL dexmedetomidine as an adjunct to single-shot axillary block increased the quality of analgesia but caused bradycardia, although not hypotension.[12] In our study, 0.5 μg/mL dexmedetomidine did not seem to cause any hemodynamic changes either as a bolus or infusion, which may reflect the lower dose of dexmedetomidine that we used.

In conclusion, our randomized trial showed that when dexmedetomidine is used to augment the action of levobupivacaine in a single-shot interscalene block followed by PCIA for 24 hours after arthroscopic shoulder surgery, analgesia and patient satisfaction seem to be improved without increasing the incidence of side effects. Better pain relief was reflected in reduced pain VAS scores (our primary outcome measure), and reduced local anesthetic and rescue analgesia requirements. This study is limited by the low number of patients. Future studies should focus on establishing the optimal dosage of dexmedetomidine in this setting.

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