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ORIGINAL RESEARCH REGIONAL ANESTHESIA

A comparative study between dexmedetomidine and dexamethasone as adjuvants to bupivacaine in ultrasound guided interscalene block for arthroscopic shoulder surgery

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ABSTRACT

Background & Objectives: Arthroscopic surgery is a preferred approach for shoulder surgeries due to its documented advantages of early postoperative recovery. However, postoperative pain remains a concern for which different techniques are used. Interscalene block (ISB), using dexmedetomidine (DXM) or dexamethasone (DXA) as adjuvants to local anesthetics (LA), is a common analgesic method. We conducted this comparative study to establish if any one of the adjuvants is better in terms of postoperative analgesia.

Methodology: Patients undergoing shoulder arthroscopy were assigned randomly to three groups: Group A (LA alone), Group B (ISB with DXM), and Group C (ISB with DXA). Assessment of intraoperative and postoperative hemodynamics, visual analog scale (VAS) pain scores, time to first rescue analgesic, and rescue analgesic (ketorolac) consumption were recorded.

Results: Intraoperative and postoperative heart rate and mean arterial pressure showed no significant differences among the three groups, suggesting comparable hemodynamic control. VAS pain scores were equivalent at 1, 2 and 6 h postoperatively, but at 12, 18 and 24 h, Groups B and C demonstrated significantly lower scores compared to Group A ($P < 0.001$). Time to first rescue analgesic was prolonged in Groups B and C, indicating improved and longer-lasting analgesia. Groups B and C consumed considerably less ketorolac overall than Group A ($P < 0.001$).

Conclusion: While all three groups exhibited equivalent intraoperative and postoperative hemodynamic control, the addition of dexmedetomidine or dexamethasone to local anesthetics for interscalene block prolonged postoperative analgesia, reduced pain scores at 12, 18 and 24 h, delayed time to first rescue, and decreased total analgesic consumption. Both adjuvants showed advantages over local anesthetics alone, emphasizing their potential in multimodal analgesia for shoulder arthroscopy.

Abbreviations: ISB - Interscalene block; DXM - Dexmedetomidine; DXA - Dexamethasone; HR – Heart Rate; MAP – Mean Arterial Pressure; VAS Visual Analog Scale.

Trial registry: PACTR202210507488378

Keywords: Analgesia; Analgesia, postoperative; Dexmedetomidine; Dexamethasone; Interscalene block; Pain, postoperative; Shoulder arthroscopy

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1. INTRODUCTION

Arthroscopic shoulder surgery is now performed for many surgical indications such as rotator cuff muscle tear, stiffness, instability and shoulder impingement. An appropriate pain control is an important factor for recovery after shoulder arthroscopy as controlling pain can help in increasing patient satisfaction, early rehabilitation and improving the outcome postoperatively.[1]

Interscalene block (ISB) is usually preferred for shoulder surgery as a perioperative analgesia, as it decreases the opioid need, reduces the hospital stay and decreases postoperative complications caused by pain such as frozen shoulder.[2]

The usual peripheral nerve blocks with local anesthetics provide short term analgesia unless there is a catheter inserted for infusion. So, many additives have been used to prolong the action of the single dose blockade, e. g., magnesium sulphate, anti-inflammatory drugs, dexamethasone etc.[3]

Dexamethasone (DXA) works by reducing nociceptive C-fiber activity. Possible mechanisms of action include direct effects on inhibitory potassium channels, local vasoconstrictive effects, direct effects on glucocorticoid receptors, or systemic anti-inflammatory effects.[4]

Numerous clinical trials have demonstrated the efficacious, opioid sparing activity of dexmedetomidine (DXM), a selective alpha-2 adrenergic receptor agonist when administered intravenously. These days, there is increased interest in using DXM as a local additive to local anesthetics (LA) for peripheral nerve blocks to prolong its duration of action and lessen the need for the opioids. The proposed mechanisms of DXM action in peripheral nerve block include inhibition of the release of substance P in the nociceptive pathway at the dorsal root neuron by the blockade of cyclic nucleotide-gated channels induced by hyperpolarization, as well as the inhibition of sodium channels and neuronal potassium current.[5]

The purpose of this study was to determine the time to first need of ketorolac as a rescue analgesia during the first 24 hour postoperatively, and also the total amount of rescue analgesic required according to VAS scores and patient demand in order to detect the efficacy of DXA versus DXM as adjuvants to LA.

2. METHODOLOGY

The research ethics committee of the Faculty of Medicine, Ain Shams University approved this prospective, randomized controlled clinical trial (No. FMASU MD 165/2022) and it was registered with the Pan African Clinical Trial Registry under the identification No. PACTR202210507488378. It was carried out in the hospital operating rooms from August 2022 to July 2023.

Ninety patients, undergoing elective shoulder arthroscopic procedure under general anesthesia, with a normal coagulation profile were involved in the trial after informed written consent. The patients of both genders, aged 21-50 y, ASA physical status I-II, were included.

Exclusion criteria included patient refusal to undergo the procedure or take part in the study, any history or presence of coagulopathy, signs of infection at injection site, past history of allergy to local anesthetics, patients with advanced medical diseases such as renal failure, cardiac, respiratory, liver or neurological diseases, failed interscalene block and the need of post-operative narcotics.

Patients were randomly divided into 3 groups using computer generated list.

2.1. Study procedure

Preoperative assessment was done including detailed personal, medical, past surgical and drug history, clinical examination, including vital data, chest examination, neurological examination and neck examination to exclude the presence of infection at the site of injection or any local causes in the neck that may be risky with performing interscalene blocks, laboratory investigations including CBC, PT, PTT, INR, liver profile, and renal profile. Intravenous line was maintained and the patients received general anesthesia in the form of 1 µg/kg fentanyl, 1–2 mg/kg propofol IV, and 0.5 mg/kg atracurium. An endotracheal intubation was inserted. 1-2% isoflurane in a 50% oxygen/air mixture and 0.1 mg/kg atracurium were used to maintain anesthesia based upon train of four monitoring. We kept

$PaCO_2$ level between 35 and 40 mmHg (normocapnia). Then interscalene block was given. Patient was placed in beach chair sitting position. Time allowed from introduction of interscalene block and beginning of surgical intervention was about 20-30 min.

2.2. Technique for interscalene block

An ultrasound device (SonoSite) with linear probe (6 mhz) and echogenic Tuohy needles were used for interscalene blocks. The syringes filled with local anesthetic drugs were prepared by a pharmacist who was blind to the study. Among additional external landmarks were the clavicle, the interscalene groove, and the lateral border of the clavicular head of the sternocleidomastoid (SCM) muscle. With the use of the ultrasound technique's "in-plane" posterior approach, the major vessels, SCM, and scalene muscles were visualized. After that, scanning continued caudally until the hypoechoic structures between the anterior and middle scalene muscles were recognized as the brachial plexus nerve roots and trunks. The block was performed by a consultant anesthesiologist with experience in regional anesthesia and was also blind to the study and medications. The patients were randomly divided into 3 groups:

Group A (control group) received 15 ml of local anesthesia solution prepared as 6 ml of 0.5% bupivacaine and 9 ml of normal saline (bupivacaine 0.2%) after negative aspiration, and divided over the 3 trunks (superior, middle and inferior).

Group B (DXM group) received 15 ml of local anesthesia solution prepared as 6 ml of 0.5% bupivacaine, 9 ml of normal saline and 0.1 µg/kg of dexmedetomidine, injected after negative aspiration divided over the 3 trunks (superior, middle and inferior).

Group C (DXA group) received 15 ml of local anesthesia solution prepared as 6 ml of 0.5% bupivacaine, 9 ml of normal saline and 8 mg of dexamethasone, injected after negative aspiration divided over the 3 trunks (superior, middle and inferior).

Following extubation and the end of the procedure, each patient was transferred to the post-anesthesia care unit (PACU). Intraoperative parameters; heart rate (HR) and mean arterial blood pressure (MAP) were recorded as follows: baseline measurements (BL), after intubation (AI), 10 min after interscalene block, mid-operative measurements (MO), before extubation (BE) and after extubation (AE). In the PACU data was recorded every 30 min for one hour. Visits on the first day was performed at 1, 2, 6, 12, 18 and 24 h postoperatively for 24 hours and Pain was recorded at rest. Time of first postoperative analgesic demand or when the VAS score was ≥ 3. Rescue analgesia (ketorolac 30 mg) was given slow intravenously, total amount of analgesics used was recorded. Side effects of drugs, e.g., respiratory depression, postoperative nausea and vomiting (treated by 0.1 mg/kg of ondansetron), bradycardia (treated by 0.01mg/kg of atropine) and pruritus were recorded in the first 24 h postoperatively.

2.3. Sample size

PASS 11 was utilized to calculate the sample size, with power set to 95% and alpha error at 5%. Previous research, as reported by Kataria et al.,[6] indicated that patients undergoing arthroscopic shoulder surgery who took dexmedetomidine had shorter duration of analgesia (19.30 ± 3.80 vs 22.40 ± 2.16 h, respectively), and this was after accounting for a 20% dropout rate. Based on these findings, a sample size of at least 90 patients was deemed sufficient to meet the study objectives.

2.4. Statistical analysis

The data was analyzed using SPSS (Statistical Package for Social Science) version 27.0. Quantitative data were presented as median (IQR) if not stated, or as mean ± standard deviation (SD). To express the qualitative data, percentage and frequency were utilized. In cases when the ANOVA test yielded a favorable result, post-hoc

Table 1: Comparison between groups as regard demographic data and ASA classification.

Demographic data		Group A (n = 30)	Group B (n = 30)	Group C (n = 30)	F/X2	P-value
Age (y)		32.93 ± 7.2	33.13 ± 7.6	33.80 ± 6.4	0.1 [f]	0.885
BMI (kg/m^2)		26.80 ± 2.3	27.34 ± 2.0	27.08 ± 2.1	0.5 [f]	0.62
Gender	▪ **Female**	6 (20.0)	7 (23.3)	4 (13.3)	1.02 [x2]	0.602
	▪ **Male**	24 (80.0)	23 (76.7)	26 (86.7)		
ASA	▪ **I**	25 (83.3)	24 (80.0)	24 (80.0)	0.15[x2]	0.93
	▪ **II**	5 (16.7)	6 (20.0)	6 (20.0)		
Operation time (min)		96.67 ± 19.4	99.00 ± 17.7	96.67 ± 18.3	0.2 [f]	0.852

Data expressed as mean ± SD or n (%), proportion, f = one way ANOVA test, X2 = chi square

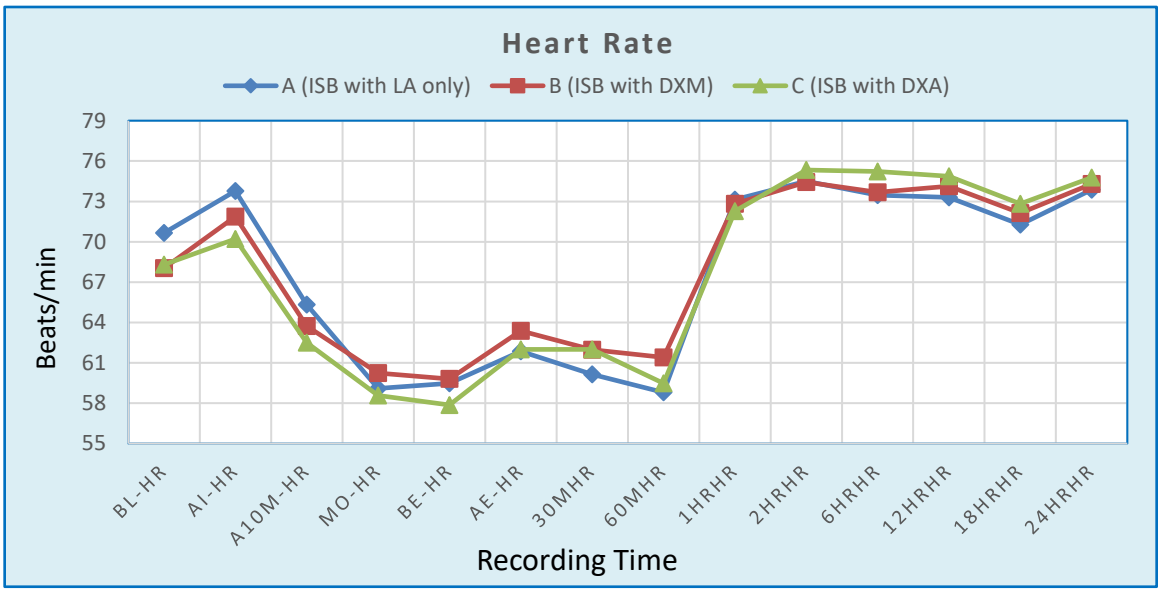

Figure 1: Comparative intraoperative and postoperative heart rate data.

testing was employed to compare subgroups pairwise. When comparing the means of various subgroups of a variable, one-way analysis of variance (ANOVA) was used to assess the difference (multiple testing). When analyzing non-parametric data, the Kruskal-Wallis test was employed to compare several subgroups. A pairwise comparison was made if the test was positive. The ratios between the qualitative measures were compared using the Chi-square (X2) test of significance. A 95% confidence interval and a 5% allowable margin of error were established. Consequently, the $P < 0.05$ was deemed significant.

3. RESULTS

We assessed 106 patients for eligibility in the study, 16 patients were excluded as 7 did not meet the inclusion criteria, 5 refused to participate while 4 patients received postoperative narcotics. So, 90 patients (30 for each group) completed the study.

There was no significant difference ($P > 0.05$) in the demographic data among the three groups, including

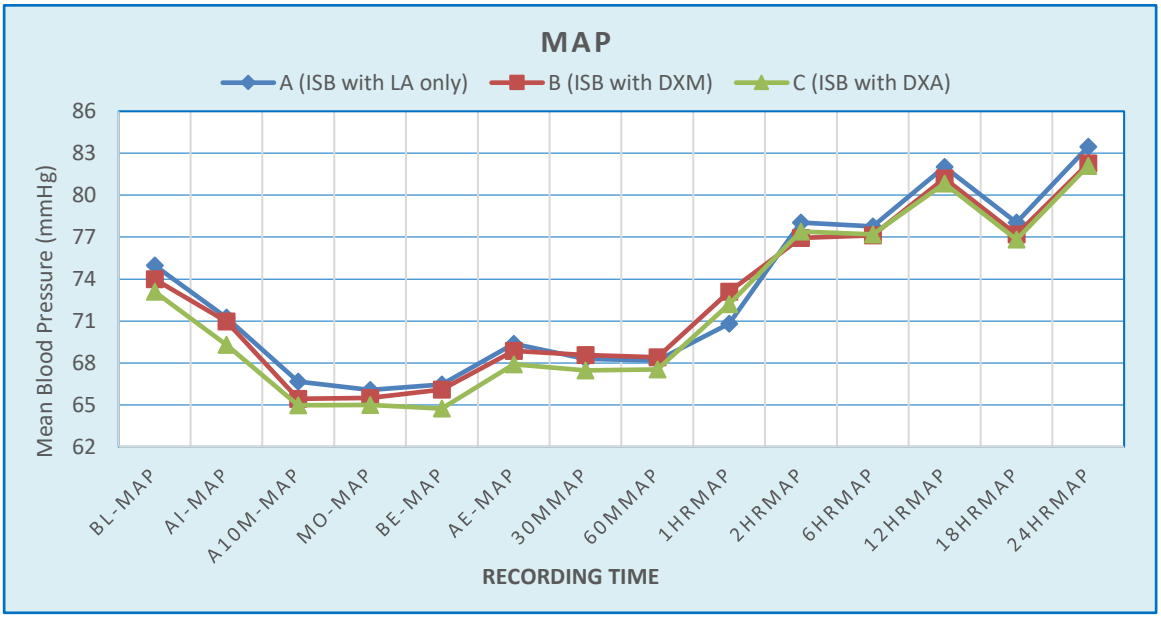

Figure 2: Comparative intraoperative and postoperative mean arterial blood pressure data

Table 2: Comparison between groups as regard postoperative VAS data.

Recording Time (h)	Group A (n = 30)			Group B (n = 30)			Group C (n = 30)			P value
	Range	Median	IQR	Range	Median	IQR	Range	Median	IQR	
1	0-2	0	0-1	0-1	0	0-1	0-1	0	0-1	0.513
2	0-2	0	0-1	0-2	0	0-1	0-1	0	0-1	0.633
6	0-2	0	0-1	0-2	0	0-1	0-1	0	0-1	0.257
12	1-7	4 [a]	2-6	0-2	0 [b]	0-1	0-1	1 [b]	0-1	**< 0.001**
18	1-7	3 [a]	2-5	0-2	1 [b]	0-1	0-2	1 [b]	0-1	< **0.001**
24	2-8	4.5[a]	3-6	0-6	2 [b]	1-4	0-6	2 [b]	1-4	**< 0.001**

Data expressed as median, range and IQR, P = value done by Kruskal Wallis test, different letter donate pairwise comparison; P < 0.05 shows significant difference

age, sex, BMI, ASA classification and length of operation. (Table 1).

When the groups were compared in terms of intra- and postoperative HR, there was no statistically significant difference found (P > 0.05) (Figure 1).

Groups were compared for intra and postoperative MAP and there was no statistically significant difference between the groups (P > 0.05) (Figure 2).

Postoperative pain data in terms of VAS scores at intervals for 24 h was compared among 3 groups where group A showed higher VAS scores at 12, 18 and 24 h postoperatively than the other groups (Table 2).

Groups were compared regarding time to first rescue analgesic (TR-keto) and ketorolac dose (A-keto) and there was significantly difference as Group A showed higher ketorolac consumption and earlier time to first rescue analgesic (Table 3).

4. DISCUSSION

Arthroscopic shoulder surgery, which is commonly favored over open procedures due to early postoperative recovery and rehabilitation, may nonetheless be accompanied by postoperative pain. [7]

ISB is the preferred method for analgesia during shoulder surgery, as it successfully lowers the need for opioids and associated negative side effects, which include nausea, vomiting and respiratory depression, thereby imparting multiple benefits such as minimizing the duration of hospitalization and mitigating the occurrence of postoperative complications that are commonly induced by pain, such as the development of frozen shoulder.[2]

DXM, a highly selective α2-adrenoceptor agonist, has been extensively studied in various surgical contexts for its sedative and analgesic properties. Its use in arthroscopic shoulder surgery is particularly notable due to its potential to enhance patient comfort and recovery outcomes. DXA, a potent corticosteroid, is often used for its anti-inflammatory and immunosuppressive effects, which can be beneficial in controlling postoperative pain and swelling in shoulder surgeries.[8] It is being used to extend the action of peripheral nerve blocks. Many theories suggest that DXA inhibits nociceptive C-fiber activity through local vasoconstriction, direct inhibition of potassium channels, direct action on glucocorticoid receptors, or systemic anti-inflammatory effects, although the precise mechanism of action is still unknown.[4]

Several previous studies focused on the use of DXM and DXA in post-operative pain management. Peršec et al. explored the effectiveness of DXM and DXA when administered epidurally in managing postoperative pain and reducing oxidative stress and inflammation in thoracic surgery. [9] In another trial, Gadallah et al. assessed the

Table 3: Comparison between 1st rescue time and ketorolac dose data.

Variables	group A (n = 30)	Group B (n = 13)	Group C (n = 15)	F	P-value
1st rescue time (h)	9.37 ± 2.9 [a]	22.69 ± 0.7 [b]	21.53 ± 1 [b]	249.714	**< 0.001**
ketorolac dose (mg)	68 ± 17.5 [a]	30 ± 0.0 [b]	34 ± 10.6 [b]	49.343	**< 0.001**

Data expressed as mean ± SD, f = one way ANOVA test, different letter donate post hoc test (Tukey) comparison significant difference

efficacy of bupivacaine combined with DXA and DXM for relief of postoperative pain after abdominal surgery. [10]

A recent Egyptian study by Khalil et al. investigated the comparative effectiveness of DXA and DXM as additive to bupivacaine in pediatric nerve blocks. in addition, Sugiyama et al. discussed the use of DXM and DXA in enhancing post-operative analgesia and reducing opioid consumption in penile prosthesis implantation. [11,12] We compared the efficacy of DXM and DXA as an additive to bupivacaine in shoulder surgery. Patients included in this study were divided randomly into three groups.

The current results revealed that, at various surgical time points, there were statistically non-significant variations in HR and MAP between the three groups. It is obvious that the three interscalene block regimens provide similar intraoperative and postoperative hemodynamic management and stability due to the lack of substantial changes in HR and MAP. There was also no bradycardia nor hypotension associated in any of the three groups. These findings indicated that perioperative interscalene block, with or without the adjuvant's DXA and DXM, allowed adequate maintenance of HR and MAP within normal physiological limits for all three groups.

The effect of DXA or DXM on HR and MAP during arthroscopic shoulder surgery is a critical concern due to the need to maintain hemodynamic stability in elderly patients. A recent retrospective analysis by Zhang et al.[13] investigated the usage of remifentanil along with intravenous DXM anesthesia combined with brachial plexus block in elderly patients undergoing shoulder arthroscopy. The study found that patients receiving this combination had lower MAP and HR levels at different time points post-operative compared to those who received remifentanil continuous pump injection. Additionally, these patients experienced lower pain levels, stress-induced markers, lower incidence of adverse reactions and shorter operating times.

In contrast, Eldin Abdel Hamid compared the infusion of DXM with fentanyl in prospective randomized research involving patients undergoing arthroscopic shoulder surgery while under general anesthesia.[14] Up to two hours into the recovery period, the treated group experienced a statistically significant decrease in both MAP and HR following the administration of DXM. They also reported more sedation, improved pain control, a better surgical field, and higher surgeon's satisfaction when compared to the fentanyl group.

However, in their randomized controlled experiment, Kang et al. did not find any appreciable differences in blood glucose levels between the DXA-taking patients and the control group. This finding could imply stability in hemodynamic parameters like HR and MAP.[15]

The VAS pain scores for each of the three groups were also compared. After surgery, the group differences were not significant at one, two or six hours. At these early postoperative time intervals, the median VAS values were zero for each of the three groups. Nonetheless, there were notable variations in the VAS pain ratings across the groups at 12, 18 and 24 h following surgery ($P < 0.001$). Group A had a considerably higher median VAS score at 12 and 18 h than Group B and C. In a similar vein, Group A scored higher on the VAS at 24 h (median 4.5 h) than did Groups B and C (median 2). These findings indicated that in the initial 6-h postoperative period, interscalene block alone or with DXA or DXM provided effective analgesia, as evidenced by the low median VAS scores. However, in the 12 to 24-h period, DXA and DXM appeared to increase the analgesic duration and improve pain management. Kong et al. found that intravenous DXA and DXM administration dramatically lengthens the time patients need for their first rescue analgesic following a single-shot interscalene brachial plexus block in patients undergoing arthroscopic shoulder surgery.

Furthermore, in an ultrasound-guided interscalene block, Margulis et al. examined the effects of adding DXM and DXA to ropivacaine. They came to the conclusion that both medications worked well, but that DXM was a safer option when using DXA would have negative effects.[16] Another case series highlighted the potential of combining DXA and DXM e in an interscalene block, showing significant postoperative opioid reduction and prolonged analgesic effects.[17] A recent systematic review by Wei et al..[18] examined the efficacy of DXA and DXM as additive to brachial plexus block in shoulder arthroscopic surgery. This review provided insights into their role in managing acute pain following the surgery. The most significant outcomes were observed with the concurrent administration of intravenous DXA and DXM, including extended analgesia, decreased opioid dosages, and decreased pain scores.

On the other hand, a randomized, controlled trial by Cabaton et al. investigated whether combining DXA and DXM provides better analgesia compared to intravenous DXA alone. The study suggested that the addition of DXM is accompanied by more hypotensive episodes.[19] Rodrigues et al.[8] found that after arthroscopic shoulder surgery, the analgesic period of interscalene blocks was prolonged by both DXA and DXM.

The time to the first rescue analgesia and the total amount of postoperative rescue analgesic needed varied significantly across the three groups, according to the data. Group A had a significantly shorter time compared to Group B and C ($P < 0.001$). This result indicates that

interscalene block alone provided a shorter duration of postoperative analgesia versus when DXA or DXM were added. Similarly, the total postoperative ketorolac consumption was significantly higher in Group A versus Group B and C. The lower ketorolac requirements in the adjuvant groups imply better and prolonged analgesia with DXA and DXM as adjuncts.

These findings correlate with the postoperative VAS scores, where Groups B and C had lower pain ratings at 12 and 24 hours compared to Group A. The extended first rescue times and reduced analgesic needs further demonstrate that combining DXA or DXM with interscalene block improves and prolongs postoperative pain relief.

DXA and DXM with ropivacaine for ultrasound-guided interscalene brachial plexus block for shoulder arthroscopic procedures was compared in another study by Shekar et al.[20] They found that adding DXM to ropivacaine accelerated the onset, prolonged the duration of sensory blocking, and delayed the need for rescue analgesia more effectively than adding DXA. The additive effect following combination of DXA and DXM appears to offer a better and longer duration of analgesia throughout the postoperative phase.

5. LIMITATIONS

We didn't assess the motor function after the block whether it was blocked or not, also pain scores on movement were not assessed.

6. CONCLUSION

While all three groups exhibited similar intraoperative hemodynamic control, the addition of dexamethasone or dexmedetomidine to interscalene block prolonged postoperative analgesia, reduced pain scores at 12-24 h period, delayed demand of first rescue, and decreased total analgesic requirement. Both adjuvants showed advantages over interscalene block with local anesthetics only, emphasizing their potential in multimodal analgesia for shoulder arthroscopy.

7. Future scope

The addition of either dexmedetomidine or dexamethasone into standard interscalene block can improve the quality of care for patients undergoing shoulder surgeries.

On behalf of all the contributors I will act and correspond with the journal from this point onward at all stages of refereeing and publication, also post-publication. All authors have contributed intellectually to the manuscript and the manuscript has been read and approved by all the authors. All authors read and approved the final manuscript.

8. Ethics considerations

This study was approved by the research ethics committee at the Faculty of Medicine, Ain Shams University (No. FMASU MD 165/2022) and registered retrospectively with Pan African Clinical Trial Registry, identifier: PACTR202210507488378. Written informed consent was obtained from all patients.

9. Availability of data

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

10. Competing interests

The authors declare that there were no conflicts of interest.

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12. Authors' contribution

PN: conduction of the study work.

OM: manuscript editing.

SG, ES: literature search.

AM: statistical analysis and review.

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