RESEARCH ARTICLE

Effect of Dexamethasone as an Adjuvant to Bupivacaine for Ultrasound-guided Axillary Plexus Block: A Randomized, Double-blinded Prospective Study

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Abstract

Objectives: The study evaluated sensory and motor block onset time, duration, and intensity, as well as pain intensity, sedation levels, and vital signs, showing that adding dexamethasone to bupivacaine improved sensory and motor block onset time, duration, and intensity, enhanced sedation effects. Axillary plexus block is a common type of anesthesia for surgical management of upper extremity injuries.

Methods: This prospective clinical trial included 72 patients over 18 years of age who were candidates for surgical management of upper extremity injuries with the axillary plexus block approach. The patients were randomly divided into two groups: group BD [30 ml bupivacaine 0.25% with 2ml dexamethasone (n=36)] and group B [30 ml bupivacaine 0.25% with 2ml distilled water (n=36)]. The Pinprick test and Modified Bromage Scale (MBS) were used to evaluate the sensory and motor block levels. Additionally, the Visual Analogue Scale (VAS) and Ramsay Sedation Scale (RSS) were used to assess pain intensity and degree of sedation. All collected data were analyzed using IBM SPSS Statistics version 20 software.

Results: The mean age of patients in the B and BD groups was 34.41±11.11 and 36.8±13.3, respectively. According to the results, there was a significant difference in the average time of sensory and motor block onset between two groups, with group BD showing shorter onset time compared to group B (P<0.001). Moreover, the mean duration and intensity of the sensory and motor block were significantly higher in group BD (P<0.05). Additionally, the degree of sedation changes after the block started were more pronounced in group BD. There was no statistically significant difference between the two groups regarding changes in pain intensity, heart rates (HR), mean arterial blood pressure (MABP), and complications (P>0.05).

Conclusion: Adding dexamethasone to bupivacaine as a safe adjuvant drug effectively prolongs the axillary plexus block time duration and reduces post-surgery pain. Furthermore, it accelerates the onset time of sensory and motor block.

Level of evidence: II

Keywords: Adjuvant, Axillary plexus block, Bupivacaine, Dexamethasone, Ultrasonography guide

Introduction

The topic of adding dexamethasone as an adjuvant to bupivacaine for ultrasound-guided axillary plexus block is important due to its potential to enhance the quality and efficacy of regional anesthesia for upper extremity surgeries.[1]

Axillary plexus block is commonly used to provide adequate anesthesia or control pain after surgery. Compared to general anesthesia, this method has more advantages, such as low cost, fewer side effects, less pain after surgery, and a shorter duration of hospitalization.[2] The axillary plexus block is one of the most widely used for arm

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and forearm surgeries.[3] Since ultrasound has the advantage of visualization and can significantly improve the safety and effectiveness of nerve block, it has become the optimal method of choice in peripheral nerve block.[4,5]

Many clinical studies have shown the effectiveness and higher quality of the method under ultrasound guidance compared to previous methods of regional anesthesia.[6,7] Local anesthetics such as lidocaine, ropivacaine, and bupivacaine have been used for administration in nerve blocks.[8,9] Bupivacaine has a structure similar to mepivacaine, with the difference that a butyl group on the piperidine ring has made its block longer. This feature and its higher sensory block quality have made bupivacaine the most widely used local anesthetic.[10] In order to prolong the effect of local anesthetics and improve the intensity, quality, time of onset, and length of anesthesia, various drugs such as epinephrine, bicarbonate, clonidine, dexmedetomidine, and narcotics have been used along with anesthetic drugs that resulted in different results.[8,11,12]

Studies have also shown that adding corticosteroids, including dexamethasone, to local anesthetics can prolong the duration of peripheral nerve block and analgesia and reduce postoperative pain.[2,13] Dexamethasone is a synthetic corticosteroid with anti-inflammatory, analgesic, immunosuppressive, and antiemetic properties.[14] However, the mechanism of dexamethasone in prolonging the duration of nerve blocks is not fully understood, and it is thought to be caused by various factors.[12] However, it seems that the analgesic effect of dexamethasone is through the blocking of nerve fibers of group C, which is caused by glucocorticoid receptors and anti-inflammatory effects.[11,13] In addition, dexamethasone causes blood vessel contraction and reduces local anesthetic absorption.[13]

The latest studies showed that dexamethasone combined with local anesthetics can significantly increase the time of peripheral nerve block. While, the results regarding the duration of analgesia, and sensory and motor block are very heterogeneous, which may be due to the type of concentration and volume of local anesthetics, the use of adrenaline, and differences in race and athnicity.[2] This heterogeneity in the findings and the uncertainty about the optimal dose of dexamethasone perineural make it necessary to conduct further controlled trials to obtain more reliable clinical evidence.[15,16] Considering that different studies have provided different doses of dexamethasone, what distinguishes the current study from other studies, the recommended dose of dexamethasone is (8 mg).[2] Although there are several studies on the addition of dexamethasone to nerve block, its effectiveness is still uncertain compared to other additives such as fentanyl, dexmedetomidine, and magnesium sulfate. For example SS Kore et al in 2022 comprised the effects of adding dexamethasone and fentanyl to bupivacaine and lignocaine in supraclavicular brachial plexus block. They showed that both of them are suitable analgesic adjuvants with local anesthetics but the duration and postoperative analgesia were superior when dexamethasone was used as an additive to local anesthetics, compared to fentanyl.[17]

We therefore asked:

1. What is the effect of adding dexamethasone to bupivacaine on the quality of axillary plexus block under ultrasound guidance for upper extremity injury surgery?
2. How does the addition of dexamethasone impact the sensory and motor block levels during the axillary plexus block procedure?
3. What is the influence of dexamethasone on pain intensity and degree of sedation following the axillary plexus block?
4. How does dexamethasone affect the onset time, duration, and quality of the axillary plexus block compared to using bupivacaine alone?

Materials and Methods

The primary outcome in this study is the evaluation of sensory and motor block onset time, duration, and intensity, as well as pain intensity, sedation levels, and vital signs. The secondary outcomes include the assessment of changes in pain intensity, heart rates, mean arterial blood pressure, and complications between the two groups.

Study design

This investigation was a double-blind, randomized clinical trial study approved by the ethical committee of Guilan University of Medical Sciences, Rasht, Iran [ID: IR.GUMS.REC.1399.650] with a registration code of the clinical trial [ID: IRCT20121216011766N7] from the Clinical Trial Registration Center of Iran. The surgery was performed on 72 patients with upper extremity trauma at Poursina Hospital, Rasht, Iran, from June 2021 to June 2022. The sample size was calculated according to Lee *et al.*'s[12] study to include 36 patients in two groups, BD (receiving bupivacaine with dexamethasone) and B (receiving bupivacaine), using block randomization with four and six block sizes. The sample size was calculated according to Lee *et al.*'s study and following formula to include 36 patients in two groups, BD (receiving bupivacaine with dexamethasone) and B (receiving bupivacaine), using block randomization with four and six block sizes.

$$N=\frac{\left(Z_{1-\alpha/2}+Z_{1-\beta}\right)^2\left(SD1^2+SD2^2\right)}{(\mu 1-\mu 2)^2}\approx 36 \quad \alpha=0/05 \;\; \beta=\%10$$

The randomization list of patients was generated using Sealed Envelope Ltd. online randomization (https://www.sealedenvelope.com/randomisation/). All patients provided consent to participate in the study. The randomization block sizes refer to number of subjects allocated to each treatment group within a randomized controlled trial. The study was blinded to both the patients and the anesthesiologist performing the nerve block. The drug administration was conducted by a colleague of the anesthesia technician, following the randomization format. The project manager was responsible for completing the questionnaire forms.

Inclusion criteria: Patients with upper extremity trauma candidates scheduled for elective surgery, aged over 18 years, and classified as American Society of Anesthesiologists (ASA) class I and II.

Exclusion criteria: Patients with diabetes, drug addiction, sepsis, infection at the injection site, sensitivity to local anesthetics, coagulopathy, kidney failure, liver failure, history of previous paresis in the operation area, or history

of surgery in the axilla.[12]

Patients were excluded if the surgery exceeded two hours, leading to anesthetic wear-off, or if the patient did not achieve adequate anesthesia during the operation, necessitating a switch to general anesthesia due to pain and restlessness.

Axillary plexus blocking

The patient was psitioned supine, received Normal-Saline via an intravenous catheter, and underwent standard monitoring including a 3-lead electrocardiogram (ECG), non-invasive blood pressure, and pulse oximetry. Oxygen was administered with a mask of 6 L/min, 0.02 mg/kg midazolam for sedation, and 0.5 µg/kg fentanyl to prevent tourniquet pain. Under ultrasound guidance using a Mindray M7 with a 10 MHz linear transducer probe, the axillary plexus block was performed with a 22-gauge Arrow nerve block needle. Group BD received bupivacaine 0.25% (7.5 mg) with dexamethasone (8 mg), while Group B received bupivacaine 0.25% (7.5 mg) with distilled water (placebo). Bupivacaine HCL 20mg/4ml, Myungmoon Pharm, Korea.

Block measuring

After confirming pain-free status, the orthopedic surgeon proceeded the surgery. Sensory and motor blocks were assessed every five minutes for 30 minutes. Sensory block level was evaluated using the Pinprick test criteria, and motor block was assessed with the Modified Bromage Scale.[18] (0: no ability to move fingers, 1: the only ability to move fingers, 2: the ability to move and bend the wrist, 3: full flexion of the elbow). Evaluations of sensorimotor block quality were performed at T0 and at 30, 60, 90, and 120 minutes after complete motor and sensory blockade. Vital signs of the patients were monitored throughout the procedure. Changes in pain intensity were assessed using the Visual Analogue Scale (VAS) score ranging from zero to 10 (0: no pain and 10: the most pain). The level of sedation was evaluated using the Ramsay Sedation Scale (RSS),[19] which ranges from 1 (anxious and restless) to 6 (cannot be awakened). Figure 2 Pain intensity and degree of relaxation of patients were evaluated in five-time zones (the beginning of the block, 30 minutes after the block, 60 minutes after the block, 90 minutes after the block, and 120 minutes after the block). Vital Signs (Blood Pressure, Heart Rate, Respiratory Rate, and Pulse Oximetry) as well as ECG monitoring of the patients were performed every 3 minutes using ECG Monitoring of SAADAT/Alborz, Iran. The monitoring was based on calculating the average data at the beginning of the nerve blockade as minute zero, and then by checking the average data at 60 minutes intraoperatively and 120 minutes postoperatively, respectively. In case of HR < 50 bpm, atropine 0.5 mg IV was administered, and for hypotension (a decrease in blood pressure more than 20% of baseline, or MABP < 60 mmHg), crystalloid serum was given. If there is no response, it is recommended to use Ephedrine at a dose of 10mg.

Statistical analysis

All data were analyzed using IBM SPSS Statistics version 20. Initially, the frequency of variables was reported as number (percentage) and mean ± standard deviation (SD). Subsequently, Chi-square and Fisher's exact tests were employed to compare the qualitative variables. Following the normality test, One Sample K-S, the quantitative variables in the two groups were compared using the Independent t-test and Mann-Whitney test. A significance level of less than 0.05 was utilized.

Results

According to our findings, the mean age of the patients in the B and BD group was 34.41±11.11 and 36.8±13.3 years, respectively (P=0.411), with the majority of males in both groups. The frequency of age and gender of the patients were somewhat similar in both groups, and no statistically significant difference between the two groups in terms of demographic data was reported (P>0.05). The mean onset time of sensory and motor blocks in group BD was 6.91±1.72 and 9.97± .17 minutes, respectively, while in group B it was 8.88±2.03 and 12.77±1.94 minutes, showing a significantly higher time in group B (P<0.001). The mean duration of sensory and motor blocks in group BD was 116.8±11.53 and 109.58±18.87 minutes, respectively, compared to group B with 99.16±11.68 and 87.22±9.66 minutes, indicating a significantly longer duration in group BD (P<0.001). Additionally, the intensity of sensory and motor blocks was higher in group BD than in group B. Because of we have used Bupivacaine 0.25% in this study; the duration of sensory block is much less in compare to other studies. All attempts to achieve sensory and motor blocks were successful in both groups. Nevertheless, significant differences were observed in the meantime of starting the sensory and motor block, the duration of sensory and motor blocks, and the intensity of sensory and motor blocks between groups B and BD (P<0.05) [Table 1]. The only complication noted in this study was nausea and vomiting. Among the nine patients who experienced nausea and vomiting after surgery and received ondansetron, three cases were in the BD group and six cases were in the B group (P<0.05). Most patients in group BD experienced no pain during surgery, and the requirement for additional painkillers was significantly higher in group B (P<0.05).The pain intensity score in group BD was lower than that in group B; however, no statistically significant difference was reported in the comparison between the two groups (P>0.05) [Figure 1]. Significant variations were observed in the level of sedation between the two groups (P<0.001) [Figure 2]. It was determined that the changes in the number of HR per minute and MABP were significantly different in B and BD groups after the start of the blocking.

However, no statistically significant difference was seen in the comparison between the two groups (P>0.05). The reduction in the level of O2Sat after starting the block was reported in both groups, while it was significantly higher in group B compared to group BD (P<0.05) [Table 2]. According to the CONSORT diagram, all 72 patients were included in the study, and no factors leading to withdrawal from the study were reported. Based on the randomization pattern, the 72 patients were divided into two groups of 36 and analyzed [Figure 3].

Table 1. Demographical data and clinical characteristics of the patients in group BD and group B

Variables		Group B Number (%)	Group BD Number (%)	P-value*
Gender	*Male*	26 (72.2)	24 (66.7)	0.680
	Female	10 (27.8)	12 (33.3)	
Age (year)	*18-20*	5 (13.9)	5 (13.9)	0.880
	21-30	12 (33.3)	11 (30.6)	
	31-40	8 (22.2)	7 (19.4)	
	41-50	8 (22.2)	7 (19.4)	
	50<	3 (8.3)	6 (16.7)	
Sensory and motor blocking	*Successful*	36 (100)	36 (100)	1
	Failed	0 (0.0)	0 (0.0)	
The intensity of sensory blocking	*Full sensation*	0 (0.0)	0 (0.0)	<0.001
	Mild sensation	14 (38.9)	1 (2.8)	
	No sensation at all	22 (61.1)	35 (97.2)	
The intensity of motor blocking	*Full flexion of the elbow*	0 (0.0)	0 (0.0)	0.002
	The ability to move and bend the wrist	2 (5.6)	0 (0.0)	
	The only ability to move fingers	18 (50.0)	6 (16.7)	
	No ability to move fingers	16 (44.4)	30 (83.3)	
Pain during the surgery	*Yes*	14 (38.9)	3 (8.3)	0.002
	No	22 (61.1)	33 (91.7)	
Need additional painkillers	*Yes*	11 (30.6)	3 (8.3)	0.017
	No	25 (69.4)	33 (91.7)	
Complications	*Yes*	6 (16.7)	3 (8.3)	0.470
	No	30 (83.3)	33 (91.7)	

*Chi-square & Fisher exact test by considering significant level<0.05

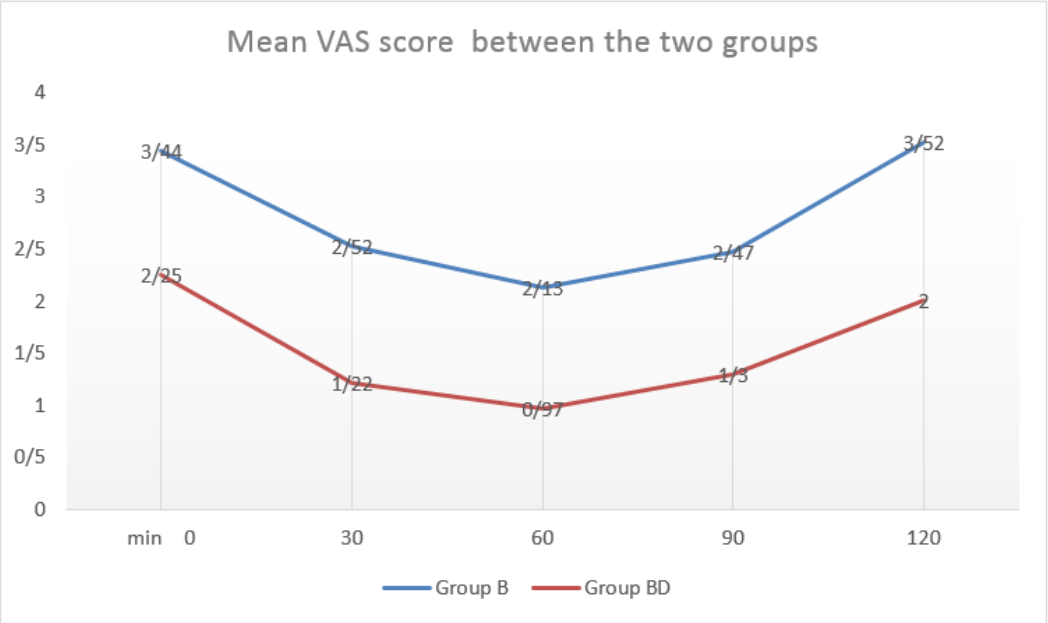

Figure 1. The mean changes in pain intensity according to the Visual Analogue Scale (VAS) after the axillary plexus block in group BD (bupivacaine 0.25% with dexamethasone) and group B (bupivacaine 0.25% with distilled water) , no statistically significant difference was reported in the comparison between the two groups (P>0.05)

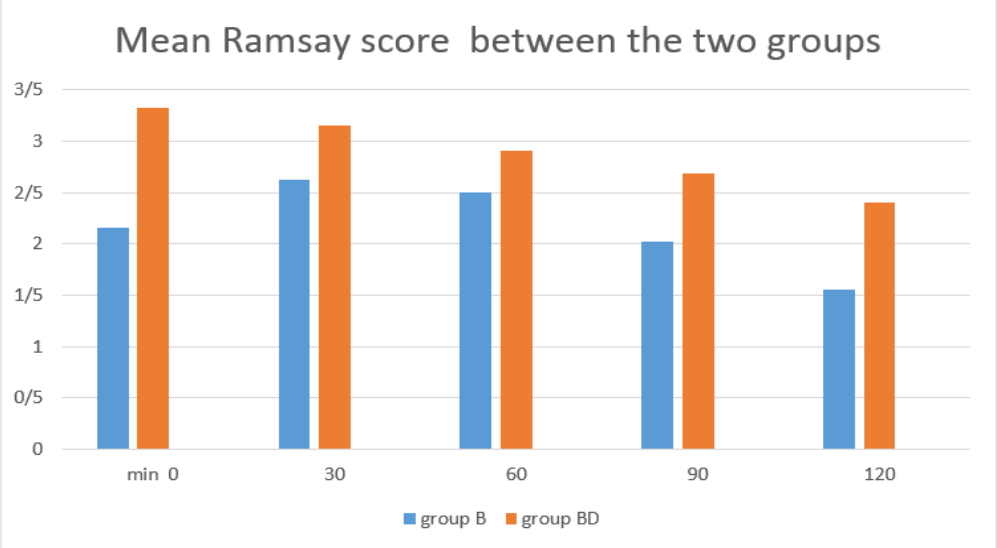

Figure 2. The mean changes in sedation degree according to the Ramsay Sedation Scale (RSS) after the axillary plexus block in group BD (bupivacaine 0.25% with dexamethasone) and group B (bupivacaine 0.25% with distilled water)

Table 2. The reduction in the level of O2Sat after starting the block was significantly higher in group B compared to group BD

Variables		Time zero (Min)	Time 60 (Min)	Time 120 (Min)	F in the group	*P-value in the group	F between groups	*P-value between groups
HR	*B*	90.47±20.99	83.00±19.19	81.75±16.42	7.78	0.001	12.93	0.349
	BD	84.94±20.31	78.22±15.46	80.47±15.43	5.86	0.01		
MABP	*B*	99.11±2.93	89.90±6.92	91.39±39.32	9.22	<0.001	0.80	0.431
	BD	96.56±13.29	90.64±11.05	91.88±11.68	4.47	0.026		
O_2Sat	*B*	99.30±0.74	98.27±0.77	98.30±0.57	32.42	<0.001	3.51	0.041
	BD	99.50±0.65	98.83±0.84	99.02±0.60	11.5	<0.001		

HR: Heart Rate, MABP: Mean Arterial Blood Pressure, O2Sat: percentage of oxygen saturation

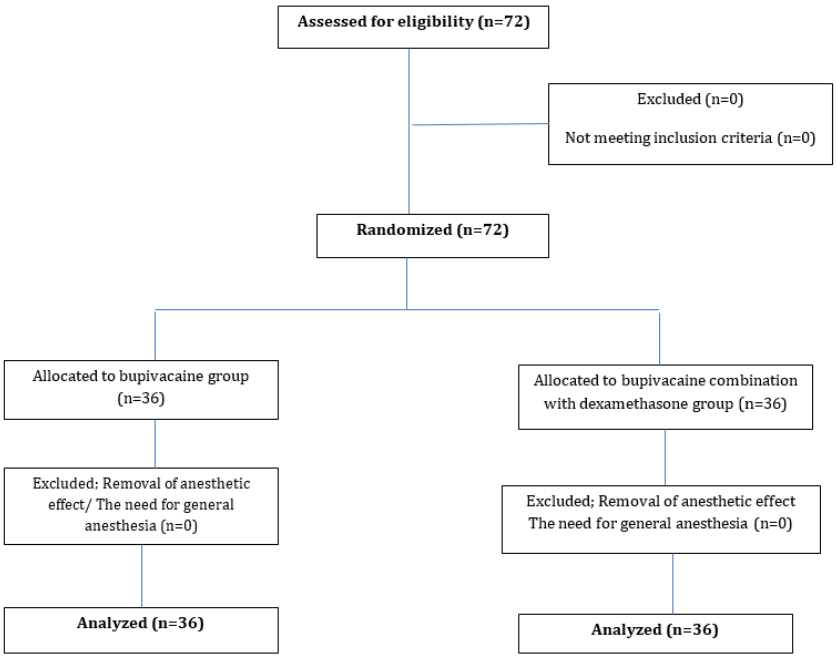

Figure 3. CONSORT flow diagram of the survey

Discussion

USG provides an effective reliable block that has increased safety because of better visualization of anatomy and needle placement. The utilization of ultrasound guidance for large nerve blocks reduces the risk of side effects related to intra-arterial injection and nerve damage. Some studies, like the Sakae study, have incorporated 4 mg of dexamethasone into 20 ml of ropivacaine 0.75%. However, relying solely on ultrasound guidance for diagnosing the brachial plexus and subsequently using a nerve locator to identify the injection site is considered outdated compared to newer ultrasound techniques.[20,21] Many adjuvants such as adrenaline, clonidine, steroids, neostigmine, midazolam, magnesium sulphate, dexmedetomidine, and opioids like tramadol, fentanyl, and morphine have been used in peripheral nerve blocks to improve the quality, duration, and avoid using toxic doses of local anesthetics.[17,22] The current investigation on the effect of dexamethasone and bupivacaine on the adequacy of axillary plexus block under ultrasound guidance demonstrated a significantly shorter onset of blocking and longer duration of sensory and motor blocks in group BD compared to group B. Furthermore, similar to our findings, studies have shown that adding dexamethasone to local anesthetics resulted in an increase in the duration of sensory and motor block.[23,24] Based on Pinprick criteria and MBS, it was reported that adding 8 mg of dexamethasone to bupivacaine significantly increases the intensity of sensory and motor block in axillary plexus block.

Chazapi et al. reported increased sensory and motor block intensity by adding 4 mg of dexamethasone to 0.75% ropivacaine for axillary plexus block with no effect on the onset of the sensory and motor block.[23] similarly; some other studies reported no changes in the sensory and motor block onset after adding dexamethasone to the local anesthetic.[23,25] In the current study, most patients in the group BD experienced no pain during surgery. In line with our findings, Clement et al. reported that adding 8 mg of intravenous dexamethasone to the anesthetic significantly reduced the need for fentanyl infusion through patient-controlled analgesia (PCA).[26]

In the Badran study, following the induction of general anesthesia with an adequate dose of fentanyl and midazolam for analgesia, an interscalene nerve block was administered with 8 mg of dexamethasone and 30 ml of 5% bupivacaine for shoulder surgery, potentially introducing bias into the evaluation of pain control.[14,24] Steroid suppresses the synthesis and secretion of various inflammatory mediators, which prolongs the period of analgesia up to 48 hours,[27] and dexamethasone acts on glucocorticoid receptors, which increases the activity of potassium-inhibit channels on C fibers.[13]

Kim et al. showed that adding 5 mg of dexamethasone as an adjuvant drug to levobupivacaine 0.5% in the brachial plexus block increased the period of pain control up to 48 hours after surgery without any notable complications.[28] VAS Score in group BD was lower than in group B; however, no significant difference was seen in pain intensity changes between the two groups.

Contrary to our results, Badran et al.'s study showed that patients in the dexamethasone group had lower VAS scores at 6, 12, and 24 hours after surgery compared to the control group.[14]

Additionally, the results of Aleboyeh et al.'s study indicated that the VAS score of pain intensity during the early stages after surgery (recovery time, 2 and 4 hours after surgery) in the dexamethasone group was significantly lower than the control group. However, at 6 hours after surgery, the pain intensity was similar in the two groups.[29] According to the RSS criterion, the RSS score was significantly higher in group BD than in group B.

However, Moshari et al. observed significant differences in the RSS score among three groups of bupivacaine with dexamethasone, bupivacaine with dexmedetomidine, and bupivacaine alone on the supraclavicular block. Specifically, the dexamethasone group exebited more positive effects on the supraclavicular block with a shorter onset of the sensory block. Additionally, the mean duration of the sensory and motor block in the bupivacaine with dexamethasone and the bupivacaine with dexmedetomidine groups was longer than the bupivacaine group.[30]

Based on our findings, the variations in HR and MABP changes following the initiation of the block were noteworthy within each group, with no statistically significant distinction between the two groups. Nevertheless, the decline in O2Sat was markedly more pronounced in group B. Consistent with our results, previous studies have indicated that the HR frequency per minute exhibited a similar pattern in both the case and control groups.[23,25]

In a study by Mashari et al., it was noted that the reduction in O2Sat ten minutes after the commencement of the surgery was significantly lower in the dexamethasone group compared to the dexmedetomidine group.[30] In the present study, the only complication observed in the patients was nausea and vomiting, which were more frequent in group B. Previous studies have mentioned that dexamethasone has been shown to reduce postoperative complications, including nausea and vomiting.[14,31] There is an ongoing debate regarding the use of dexamethasone as an adjuvant to local anesthetic solutions, with some suggesting that intravenous dexamethasone may serve as an alternative to peripheral dexamethasone in peripheral nerve blocks. Recent studies in this field have indicated that both peripheral and systemic dexamethasone can increase the duration of block compared to placebo. However, it is important to note that the use of single-dose intravenous dexamethasone may be associated with complications such as hyperglycemia, postoperative infection, and delayed wound healing.[32,33]

Limitations

Our study does present some limitations. First, the conclusions of the study are specific to the bupivacaine solution that was used. More trials are required for other local anesthetic solutions. Second, the dose of dexamethasone we used was 8 mg and not adjusted to the weight of the patient. Moreover, we did not include another

group with intravenous administration of the same dose of dexamethasone, so we cannot exclude the possibility that prolongation of analgesia occurred because of the systemic effects of dexamethasone.

Conclusion

This current study demonstrated that the combination of dexamethasone and bupivacaine significantly shortened the onset of sensory and motor block in the axillary plexus block. It also improved patient relaxation, prolonged the duration and intensity of sensory and motor block, and reduced pain during surgery and the need for additional painkillers.

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Authors Contribution:

Hossein Khoshrang: Conceived and designed the literature review; collected the data; wrote the paper.

Mohammad Haghighi: Conceived and designed the analysis; collected the data; wrote the paper.

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Saeed Hemmati: who collected the data and wrote the paper.

Roxana Azizi: who collected the data and wrote the paper.

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Declaration of Informed Consent: The participants provided their written consent to participate in the study.

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