

Diltiazem Added to Local Anesthetic in Sonar Guided Coracoid Infraclavicular Brachial Plexus Block. Dose Sparing Effect

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Abstract

Background: This study was performed to evaluate the addition of diltiazem to local anesthetic during sonar guided infraclavicular brachial plexus block as regards to its intra and postoperative analgesic quality.

Methods: In a randomized, prospective double blind study, 90 patients aged between 18-70 years with ASA Grade I and II, were randomly classified into 3 groups. Group I received 30 ml containing 14 ml 0.5% bupivacaine and 14 ml lidocaine 2% plus 2 ml saline and group II received same volume of local anesthetic and diltiazem 20mg in 2 ml saline. while group III received 30 ml containing 10 ml 0.5% bupivacaine , 10 ml lidocaine 2% and diltiazem 20mg in 10 ml saline. Onset of sensory and motor block , quality of the block , postoperative analgesia, and any complications of the procedure were recorded.

Results: Onset of sensory and motor block was significantly shorter in group II compared to other groups. Quality of the block in the three groups was comparable. Significantly prolonged duration of sensory and motor block and prolonged duration of analgesia were present in group II compared to other groups. Time of first analgesic request was significantly longer in group II. Analgesic consumption was lower in group II. Hemodynamic changes and side effects were comparable.

Conclusion: The addition of 20mg diltiazem to local anesthetic solution in sonar guided infraclavicular brachial plexus block hastened the onset of anesthesia and prolonged duration of postoperative analgesia without complications and can have a dose sparing effect on local anesthetics sufficient to produce adequate block.

Keywords: Diltiazem, Infraclavicular , Sonar, Brachial Plexus Block

Introduction

The ultrasound guided infraclavicular block via the coracoid approach is an attractive technique providing an excellent block [1]. When compared to the midclavicular approach (Raj approach), the coracoid approach is associated with a lower risk of pneumothorax [2].

Peripheral nerve block, done with ultrasound guidance enables well visualization of the nerve bundle and its adjacent structures and secures an accurate needle placement with visual confirmation of the distribution of the injected local anesthetic. This results in improved quality of nerve block, shorter performance time, with reduction of the required local anesthetic volume and lower risk of intraneural, intravascular injection, and pleural puncture [3]. Unfortunately, their duration may not be adequate without adequate postoperative analgesia [4]. This limitation is addressed by adding adjunctive drugs to prolong duration and enhance quality of regional blocks. These additives include opioids, midazolam, alpha2 agonists, ketamine, neostigmine, nonsteroidal anti-inflammatory drugs, hyaluronidase, bicarbonate, calcium channel blockers and corticosteroids but none has conclusive results [5,6].

Calcium has an important role in pain transmission. Activation of N-methyl-D-aspartic acid (NMDA) receptors leads to increased intracellular calcium which initiates central sensitization in the spinal cord. So that calcium channel blockers may be effective in preventing this central sensitization [7]. Calcium ions also have an important role in the analgesia mediated by local anesthetics. Local anesthetics reduce calcium permeability and clinical investigations have shown that calcium channel blockers can increase the analgesic effect of local anesthetics. (11) Several studies suggest that the

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concomitant administration of calcium channel blockers with opioids might increase their analgesic effects [8], and that these drugs by themselves may possess analgesic properties [9].

To the best of our knowledge diltiazem had not been tried for peripheral nerve blocks and verapamil had conflicting results. The aim of this study was to investigate the effect of diltiazem as an adjuvant to local anesthetics during sonar guided infraclavicular brachial plexus block through the coracoids approach and whether it could reduce the total dose of local anesthetic sufficient to produce an adequate block.

Patients and Methods

Study center and population

This prospective, randomized double blind study was performed in Tanta university hospital, Faculty of medicine, Tanta university, Tanta, Egypt from October 2017 until December 2017, after obtaining ethical committee approval (code : 30912/ 05/ 16) and patient informed consent.

The clinical trial was registered at the Pan African Clinical Trial Registry (www.pactr.org) database. The identification number for the registry is PACTR201711002712946.

90 patients, aged 18-70 years with American Society of Anesthesiologists' status I- II scheduled for forearm and hand surgery were included. Exclusion criteria included patients with significant coagulopathy, allergy to local anesthetic or study drug, a local skin infection, known neuropathies and history of conductive heart disease.

Randomization: Computer generated random numbers concealed in sealed envelopes technique was used for randomization.

Patients were randomly classified into three groups 30 patients each. Group I, control group received 30 ml containing 14 ml 0.5 % bupivacaine and 14 ml lignocaine 2% plus 2 ml saline and group II received 30ml containing 14 ml 5% bupivacaine, 14 ml lignocaine 2% and diltiazem 20mg in 2ml saline . while group III received 30 ml containing 10 ml 0.5% bupivacaine , 10 ml lignocaine 2% and diltiazem 20mg in 10ml saline.

The solution to be injected was prepared by an independent anesthesiologist in identical syringes. The block was administered and observations made by anesthesiologists blinded to the solution or group allocation.

Intervention: Preoperatively, the infraclavicular block and the visual analogue scale were explained to the patients, medical history, physical examination, and indicated investigations were performed

On arrival to the operating room, basic monitors including ECG, noninvasive blood pressure, and pulse oximetry were attached. An intravenous line was inserted in the contralateral hand and an infusion of 0.9% saline at a maintenance rate was started. Prior to the block, the patient received intravenous midazolam 1mg and intravenous fentanyl 50µg and O₂ via a face mask at a rate of 3-5 liters/ minute was attached .

The patient was placed supine with the head tilted to the other side and the arm abducted to move the clavicle down and out of the way of the needle and the elbow was flexed. SonoSite

ultrasound machine (SonoSite, Washington, USA) with a 7.5-MHz fixed frequency and linear ultrasonic probe was used to perform the block.

After complete aseptic technique, the infraclavicular area was draped and 2ml lidocaine 2% were used for skin infiltration at the insertion point. The probe was put just medial to the coracoid process below the clavicle and in-plane technique was used to visualize the neurovascular bundle in the parasagittal plane. The probe was adjusted to obtain an adequate cross-sectional view of the axillary artery, with viewing all the cords in relation to the artery, including the medial, lateral and posterior sides. The 18-gauge Tuohy needle was advanced in a caudal direction, and posteriorly towards the neurovascular structures with its bevel facing superiorly till it was fully viewed. After confirming the target site with the needle positioned posterior to the axillary artery, the local anesthetic was slowly administered in a single injection with 5 ml aliquots and frequent aspiration to avoid intraneural and intravascular injection. If paraesthesia was elicited, the needle was withdrawn back 2-3 mm till no more paraesthesia was elicited before injection. If blood aspiration occurred, the needle was repositioned before injection of local anesthetic.

Sensory block was initially tested by an independent observer at five minutes intervals for 30 minutes. Sensory block was assessed using pin prick by a 22-gauge hypodermic needle at the following areas, the thenar eminence innervated by median nerve, the hypothenar region innervated by the ulnar nerve, the dorsum of the hand innervated by the radial nerve, the lateral aspect of the forearm innervated by the musculocutaneous nerve and the area over the insertion of the deltoid muscle for the axillary nerve. Motor block was evaluated using forearm flexion for the musculocutaneous, wrist extension for the radial nerve, thumb and index finger opposition, for the median nerve and thumb and little finger opposition for the ulnar nerve .The muscle power was compared in relation to the contralateral side.

Onset of the block was defined as the time from the last injection to complete loss of response to pain and complete loss of motor power. Anesthesia was considered to be at surgical level when the patient could not feel pain from the needle in tested areas and was unable to move the shoulder, elbow and/or wrist

In the operating room, sedation was administered by midazolam 0.5-1mg for anxiety and fentanyl 50µg for pain outside the operating field. Surgical block success was defined by a nerve block that allowed surgery without a rescue block, infiltration of local anesthetics, administration of analgesics for pain in the surgical field, or general anesthesia. Patients with unsuccessful block were excluded from the study

Intraoperatively, quality of the block was assessed including analgesia, muscle relaxation, and hemodynamic changes including heart rate, mean arterial pressure and arterial O₂ saturation. Hemodynamic changes were recorded every 5 minutes for the first 15 minutes and the every 10 minutes till the end of surgery.

Postoperatively the patients received patient controlled analgesia with morphine 1 mg on demand dose with lockout time 15 minutes and no basal dose The patients were evaluated for sensory and motor block by an independent observer every 30 minutes till complete recovery. The visual analogue scale was evaluated at 1,2,4,6 and 12 hours. The time to first rescue analgesic,

the duration of sensory block (time between onset and return of pin prick response), the duration of analgesia (time between onset of action and onset of pain), the total dose of analgesia consumed in the first 24 hours, the duration of motor block (time from the onset till return of complete muscle power). Hemodynamic changes and the incidence of side effects related to the drugs used (hypotension, bradycardia, respiratory depression, nausea, vomiting or to the technique (hematoma, swelling, numbness, paresthesia and pneumothorax) were recorded.

Outcomes: Duration of analgesia was the primary end point. Secondary outcomes included onset of sensory and motor block, visual analogue scale, analgesic consumption, block-related complications and the ability of diltiazem to reduce the dose of local anesthetic sufficient to produce adequate block.

Statistical analysis

For this study, it was presumed that adding diltiazem would increase the duration of analgesia by about 25% compared with local anesthetic alone. It was estimated that 25 patients will be required to permit a type 1 error of 0.05 with a power of 80%.

Thirty patients were chosen to compensate for any dropouts during the study. Continuous data were presented as mean \pm standard deviation; Categorical variables were presented as number and percentage. Continuous variables were analyzed using Student's t-test. Categorical variables were compared using the chi-square test. AP-value of less than 0.05 was considered to be significant.

Results

This study included 90 patients of the ASA physical status I and II scheduled for forearm and hand surgery. All of them had adequate block and completed the study. Consort flow diagram was used to show the patient enrollment, allocation, follow-up, and analysis (Figure 1).

The patient's characteristics including age, weight and sex and the duration of surgery were comparable in the three studied groups ($p > 0.05$) (Table 1).

As regards to block characteristics described in Table 2, the onset of both sensory and motor block was significantly shorter in

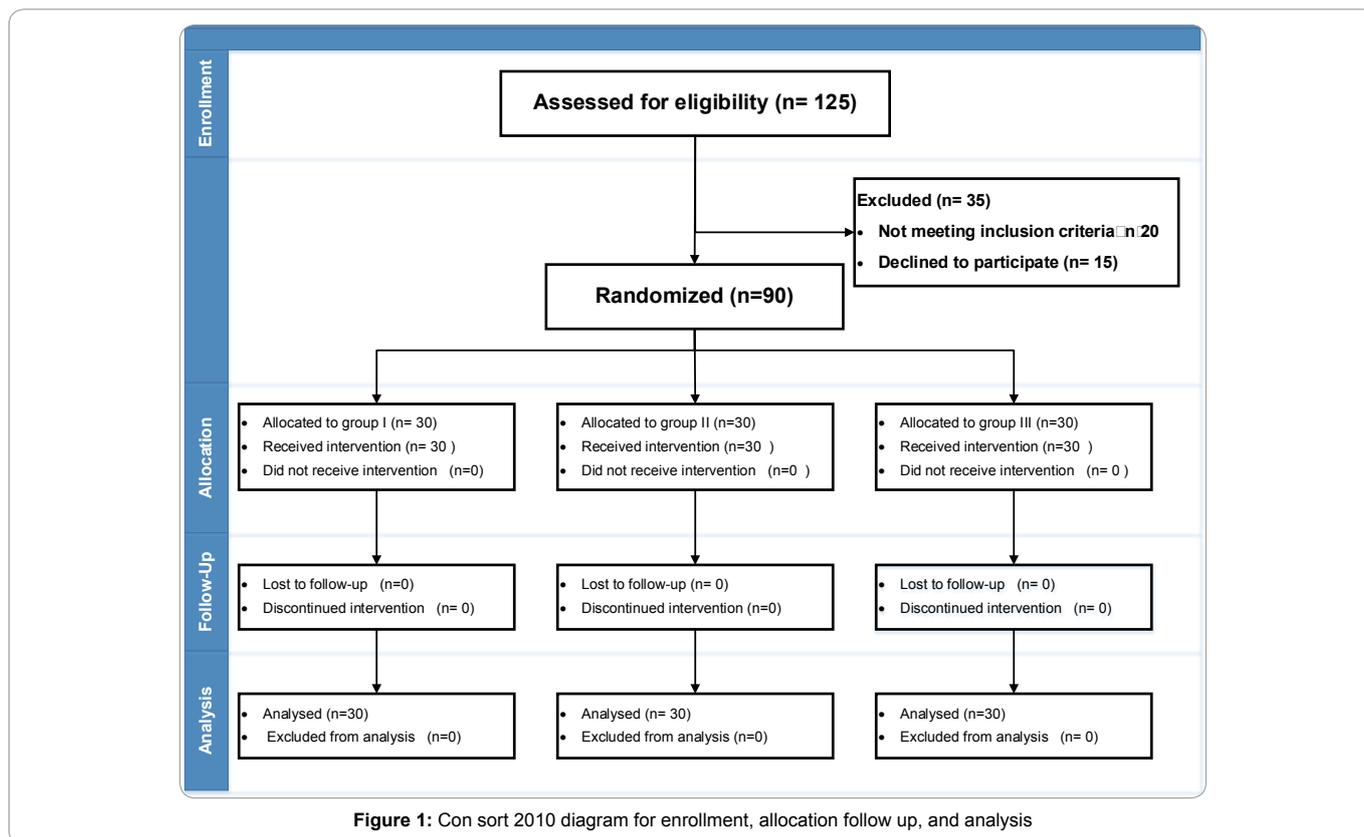


Figure 1: Consort 2010 diagram for enrollment, allocation follow up, and analysis

	Group I	Group II	Group III	P value		
				P1	P2	P3
Age (years)	46.5 \pm 12.4	43.4 \pm 13.3	44.9 \pm 11.8	0.451	0.678	0.708
Weight (kg)	78.3 \pm 21.6	75.6 \pm 20.9	77.8 \pm 24.5	0.690	0.842	0.762
Sex (male/female)	8/12	13/7	11/9	0.113	0.342	0.519
Duration of surgery(min)	71.3 \pm 12.3	73.8 \pm 13.5	72.7 \pm 11.6	0.544	0.713	0.784

Data are presented as mean \pm SD

P1 group I compared to group II, P2 group I compared to group III, P3 group II compared to group III

Table 1: Patients demographic data and duration of surgery in different studied groups.

group II (15.4 ± 1.3 and 18.6 ± 2.9 minutes respectively) compared to either group I (18.5 ± 2.4 and 22 ± 2.6 minutes respectively) or group III (17.9 ± 3.1 and 21 ± 3.2 minutes respectively) ($P < 0.05$) while group I and III did not differ significantly ($P > 0.05$)

The duration of both sensory and motor block was significantly longer in group II (428 ± 26.2 and 353 ± 31.5 minutes respectively) compared to either group I (368 ± 22.5 and 310.5 ± 30.3 minutes respectively) or group III (361 ± 26.4 and 307.7 ± 31.6 minutes respectively) ($P < 0.05$). Comparison of group I and III revealed non-significant difference ($P > 0.05$).

Intra and postoperative hemodynamic parameters did not show any significant changes in the three studied groups at any time of

measurements and none of the patients developed hypotension, bradycardia or desaturation ($P > 0.05$) (Table 3 and 4).

The visual analogue scale measured at the first, second and twelve hours showed non-significant difference between the three groups while at the fourth and sixth hours, it was significantly lower in group II compared to either group I or III while at these times group I and III showed comparable values (Table 5).

The time of first rescue analgesic which describes the duration of analgesia was significantly longer in group II (445.4 ± 33.3 minutes compared to both group I (346.5 ± 35.4) and III (351.9 ± 31.8) ($P < 0.05$) while group I and III were comparable ($P > 0.05$) (Table 6).

	Group I	Group II	Group III	P value		
				P1	P2	P3
Onset of sensory block (min)	18.5 ± 2.4	15.4 ± 1.3	17.9 ± 3.1	0.001*	0.497	0.002*
Onset of motor block (min)	22 ± 2.6	18.6 ± 2.9	21 ± 3.2	0.001*	0.285	0.017*
Duration of sensory block (min)	368 ± 22.5	428 ± 26.2	361 ± 26.4	0.001*	0.372	0.001*
Duration of motor block (min)	310.5 ± 30.3	353 ± 31.5	307.7 ± 31.6	0.001*	0.776	0.001*

Data are presented as mean ± SD

P1 group I compared to group II, P2 group I compared to group III, P3 group II compared to group III

*Denotes significance ($p < 0.05\%$)

Table 2: Characteristics of the block in different studied groups.

HR	Baseline	5min	10 in	15 min	25 min	35 min	50 min	65 min	80 min
Group I	100 ± 5.2	99 ± 3.5	93 ± 4.2	90 ± 3.6	88 ± 4.1	89 ± 3.4	91 ± 3.2	88 ± 2.2	87 ± 3.3
Group II	97 ± 8.2	96 ± 4.5	94 ± 3.2	91 ± 2.8	89 ± 3.3	86 ± 5.4	88 ± 5.2	86 ± 3.5	88 ± 2.5
Group III	99 ± 6.2	97 ± 3.6	95 ± 2.7	93 ± 2.1	87 ± 4.1	88 ± 3.9	90 ± 4.7	87 ± 2.8	90 ± 0.7
P1	0.342	0.113	0.557	0.497	0.554	0.274	0.128	0.324	0.682
P2	0.701	0.224	0.221	0.063	0.217	0.634	0.471	0.578	0.136
P3	0.546	0.589	0.459	0.096	0.563	0.387	0.215	0.489	0.317
MAP									
Group I	98.2 ± 23.3	95.6 ± 25.6	93 ± 19.2	96.7 ± 21.5	91.4 ± 21.2	89 ± 19.4	91 ± 21.2	91 ± 20.3	93 ± 22.3
Group II	99 ± 18.2	94 ± 24.5	92 ± 22.2	95.1 ± 23.9	89 ± 21.3	88 ± 19.6	89 ± 20.4	89 ± 22.5	91 ± 24.5
Group III	99 ± 19.2	95 ± 22.6	95 ± 21.7	93 ± 22.1	90 ± 23.3	88 ± 21.9	90 ± 18.7	87 ± 24.8	90 ± 22.7
P1	0.645	0.574	0.652	0.425	0.745	0.658	0.652	0.645	0.574
P2	0.612	0.825	0.247	0.105	0.821	0.635	0.812	0.795	0.236
P3	0.754	0.561	0.189	0.327	0.712	0.875	0.721	0.685	0.741

Data are presented as mean ± SD; HR= heart rate, MAP= mean arterial pressure

P1 group I compared to group II, P2 group I compared to group III, P3 group II compared to group III

Table 3: Intraoperative hemodynamic changes in different studied groups.

H R	15Min	30min	1Hour	2 hours	4 hours	6Hours	8Hours	12 hours	24 hours
Group I	89 ± 5.2	87 ± 4.6	92 ± 2.3	93 ± 2.6	86 ± 2.1	88 ± 2.4	90 ± 3.4	89 ± 2.2	85 ± 2.7
Group II	88 ± 8.2	86 ± 4.5	91 ± 3.2	90 ± 2.8	84 ± 3.3	86 ± 4.4	89 ± 4.6	88 ± 3.4	84 ± 3.1
Group III	90 ± 6.2	89 ± 4.6	93 ± 2.1	93 ± 2.4	86 ± 2.5	88 ± 2.3	91 ± 2.3	90 ± 1.8	86 ± 1.5
P1	0.744	0.756	0.658	0.128	0.325	0.415	0.652	0.452	0.623
P2	0.695	0.563	0.632	0.741	0.854	0.865	0.632	0.523	0.603
P3	0.508	0.268	0.387	0.158	0.374	0.408	0.471	0.329	0.389
MAP									
Group I	90.2 ± 21.4	90.6 ± 22.6	90 ± 20.2	89.6 ± 20.5	90.4 ± 19.2	88 ± 21.4	90 ± 20.3	92 ± 16.3	93 ± 18.4
Group II	89 ± 19.2	88 ± 24.5	90 ± 21.3	88.1 ± 22.4	89 ± 20.4	87 ± 22.6	89 ± 20.7	90 ± 18.7	92 ± 19.5
Group III	91 ± 18.2	91 ± 20.6	92 ± 20.4	90 ± 20.2	90 ± 21.1	88 ± 20.9	91 ± 19.2	92 ± 15.8	94 ± 17.6
P1	0.742	0.456	0.952	0.741	0.723	0.702	0.665	0.358	0.93
P2	0.785	0.748	0.658	0.702	0.912	0.947	0.625	0.941	0.702
P3	0.589	0.369	0.647	0.595	0.698	0.685	0.825	0.398	0.458

Data are presented as mean ± SD; HR= heart rate, MAP= mean arterial pressure

P1 group I compared to group II, P2 group I compared to group III, P3 group II compared to group III

Table 4: Postoperative hemodynamic changes in all groups.

	Group I	Group II	Group III	P value		
				P1	P2	P3
First hour	2.3 ± 1.7	2.2 ± 1.8	2.4 ± 1.6	0.856	0.852	0.875
Second hour	2.9 ± 1.6	2.8 ± 1.7	3 ± 1.5	0.758	0.789	0.912
4th hour	3.5 ± 1.3	2.7 ± 1.1	3.6 ± 1.4	0.013*	0.775	0.007*
6th hour	5.5 ± 2.2	3.2 ± 1.5	5.7 ± 1.6	0.001*	0.689	0.001*
12th hour	4.5 ± 1.8	4.3 ± 2	4.6 ± 1.5	0.685	0.816	0.514

Data are presented as mean ± SD; *Denotes significance ($p < 0.05\%$)

P1 group I compared to group II, P2 group I compared to group III, P3 group II compared to group III

Table 5: Visual analogue scale (VAS) in different studied groups .

	Group I	Group II	Group III	P value		
				P1	P2	P3
Time to first rescue analgesic (min)	346.5 ± 35.4	445.4 ± 33.3	351.9 ± 31.8	0.001*	0.615	0.001*
Total analgesic consumption (mg)	15.3 ± 2.6	9.6 ± 2.9	16.8 ± 3.5	0.001*	0.132	0.001*

Data are presented as mean ± SD; *Denotes significance ($p < 0.05\%$) .

P1 group I compared to group II, P2 group I compared to group III , P3 group II compared to group III.

Table 6: Time to first rescue analgesic and total analgesic consumption in different studied groups

	Group I	Group II	Group III	P value		
				P1	P2	P3
Nausea and vomiting	2 (6.6%)	2 (6.6%)	1 (3.33%)	1.0	0.548	0.548
Parasthesia	0	0	0	-	-	-
Hematoma formation	1 (3.33%)	2 (6.6%)	1 (3.33%)	0.548	1.0	0.548
Hypotension	2 (6.6%)	3 (10%)	1 (3.33%)	0.632	0.548	0.292
Bradycardia	1 (3.33%)	2 (6.6%)	0	0.548	0.311	0.147

Data are presented as number (%)

P1, group I compared to II, P2, group III compared to group I, P3, group II compared to group III

Table 7: Incidence of complications in different studied groups.

Total analgesic morphine consumption in the first 24 hours was significantly lower in group II (9.6±2.9 mg) compared to both group I (15.3 ± 2.6 mg) and III (16.8 ± 3.5 mg). ($P < 0.05$) while group I and III were comparable ($P > 0.05$) (Table 6).

The incidence of side effects was similar and non-significant in the three studied groups (Table 7).

Discussion

In this study, it was found the addition of diltiazem 20mg to the mixture of lignocaine 2% and bupivacaine 0.5% during sonar guided infraclavicular brachial plexus block through the coracoid approach succeeded in shortening the onset of sensory and motor block and improving the quality of postoperative analgesia by increasing its duration and decreasing the total analgesic consumption without significant side effects. Also when administered with a lower dose of local anesthetic diltiazem gave comparable results with adequate block characteristics

There was significant improvement in the onset of both sensory and motor block with the addition of the calcium channel blocker diltiazem in a dose of 20 mgs. This is in agreement with previous animal and human studies which suggested that inhibition of calcium entry through calcium channels may play a role in analgesia development [10-17].

The onset of both sensory and motor block was different than previous studies of sonar guided block [1-3]. This can be explained by the higher dose and concentration used in this study which was 30 ml, lignocaine 2 % and 0.5% bupivacaine with or without diltiazem. and the definition of the onset in this study

which was the time from drug injection till complete loss and not diminished loss of sensation and motor power. Most of the previous studies used lower concentrations of local anesthetics. The higher dose and concentration in this study allowed the rapid onset of action.

The clinical efficacies of the calcium-channel blocker for pain relief has been documented in several studies Local anesthetics reduce the calcium permeability and clinical investigations have shown they potentiates the analgesic effect of local anesthetics Iwasaki et al., [11] concluded that the calcium-channel blocker potentiated lignocaine-induced sensory block at the level of peripheral nerves in rats. Ohmori *et al.*, [12] studied the effect of adding calcium-channel blocker in procaine for local conduction block and found that sensory block by procaine of peripheral nerves was hastened by the use of a calcium-channel blocker. Omote *et al.*, [13] in a study conducted on rats, have suggested that

calcium-channel blocking drugs potentiated the analgesic effects of morphine at the level of the spinal cord .Omote *et al.* [14] in another study reported that intrathecal calcium-channel blocker verapamil potentiated the local anesthetic during spinal anesthesia ... Kim et al., [15] and Choe et al., [16] also found that preemptive addition of verapamil to epidural bupivacaine decreased the analgesic consumption and possibly decreased the central sensitization. Khanna et al., [17] studied the effect of diltiazem during regional intravenous anesthesia using lidocaine 0.5% and concluded that diltiazem was effective in hastening onset, reducing tourniquet pain, and increasing tourniquet tolerance, thereby contributing to better perioperative analgesia.

In contrary to our results, the study of Reuben et al., [18] and Lalla et al., [19] found a non-significant difference in the onset of sensory block of brachial plexus block with the addition of the calcium channel blocker verapamil. Tabaalzavareh et al., [20] found that addition of verapamil to epidural local anesthetic solution failed in improving the sensory block level and postoperative analgesia.

In this study the intraoperative anesthetic quality of anesthesia and hemodynamic changes were comparable in the three studied groups. The three studied groups were comparable as regard to the cases which needed analgesic, sedative, or local nerve block supplements. This can be explained by the use of sonar guided technique which allowed good visualization of the nervous structures and optimum perineural deposition of the anesthetic solution with resultant high success rate and adequate anesthesia [21].

Postoperatively, the hemodynamic changes were similar in the three groups with non-significant incidence of hypotension or bradycardia. The visual analogue scales were similar at 1 and 2 and 12 hours in the three groups but it was significantly lower in the group II receiving diltiazem and normal dose local anesthetic solution at 4 and 6 hours. The duration of both sensory and motor block was significantly longer in group II compared to the other 2 groups, the duration of analgesia was longer and the total 24 hours analgesic consumption was lower in group II compared to either group I and III. This antinociceptive effect of diltiazem is in accordance with previous results concluding the analgesic properties of calcium channels blockers [11-17].

In contrary to the results of this study other researchers lalla et al., [18] and Ruben et al., [19], found that despite increasing the duration of anesthesia, there was no significant increase in the duration of analgesia and the analgesic consumption was not reduced. This can be explained by the lower concentration of bupivacaine used in their studies.

In this study, trying to decrease the dose of local anesthetic, with the addition of diltiazem resulted in comparable block results. The comparison of group I receiving normal dose of local anesthetic without additive drug and group III receiving a smaller dose of local anesthetic combined with diltiazem 20 mg revealed similar results in all parameters of comparison either intra or postoperatively. The dose sparing effect of diltiazem in this study was documented by the comparable block characteristics, including onset and duration of both sensory and motor block. Intraoperative quality of anesthesia, visual analogue scores, duration of analgesia and analgesic consumption.

This may indicate that diltiazem may have a dose sparing effect on local anesthetics. On the other hand this decrease in the total dose may be due to the use of sonar guided techniques which allows decreasing the volume or dose of local anesthetic sufficient for adequate block [22].

This dose sparing effect can be also attributed to the use of multimodal approach which consisted of the combination of two types of local anesthetics with an additive plus the use of sonar guided block which allowed adequate nerve localization with good deposition of the local anesthetic. This resulted in a higher success rate, shorter procedure time, high block quality and lesser complications. This multimodal approach was advised by the

American association of anesthesiologist during the management of acute pain [23].

The incidence of side effects in the three studied groups was similar and self-limited and this can be explained by the use of sonar guided technique with optimum visualization and optimum deposition of the local anesthetic with neither intraneural nor intravascular injection [1-4].

The addition of calcium channel blocker in this study may decrease the dose of local anesthetic sufficient to have acceptable block with adequate intra and postoperative analgesia

The primary mode of action of local anesthetics is through the sodium channel and axonal conduction blockade. Diltiazem, a calcium channel blocker of the benzothiazepines group, blocks the sodium channels in a dose-dependent manner in addition to calcium channels and has a local anesthetic action [9,24]. Local anesthetics reversibly block the conduction of nerve impulses by preventing increases in the permeability of nerve membrane to sodium ions. Calcium movement is essential for normal sensory processing and plays a role in axonal conduction and synaptic transmission [8]. Direct inhibition of voltage dependent calcium conductance and the consequent lowering of calcium ions of the peripheral nerves possibly caused the potentiation of sensory and motor block onset.

Limitation of this study is that the dose sparing effect may be due to the use of diltiazem or the use of multimodal approach including combination of two different local anesthetics and the use of sonar guided block. So it has to be tried with other techniques of block to detect its efficacy or to compare it with other additives.

Conclusion

From this study it can be concluded that the addition of the calcium channel blocker, diltiazem 20 mgs to the local anesthetic combination of lignocaine 2% and bupivacaine 0.5% during sonar guided infraclavicular brachial plexus block through the coracoid approach. Shortened the onset of both sensory and motor block and improved the postoperative analgesia by increasing its duration and lowering the postoperative total analgesic consumption with minimal side effects. Diltiazem may reduce the total dose of local anesthetic sufficient for adequate block

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References

1. Desroches J. The infraclavicular brachial plexus block by the coracoid approach is clinically effective: an observational study of 150 patients. *Can J Anaesth*. 2003;50(3):253-257.
2. Azmin FMT, Choy YC. Regional infraclavicular blocks via the coracoid approach for below-elbow surgery: a comparison between ultrasound guidance with, or without, nerve stimulation. *South Afr J Anaesth Analg*. 2013;19(5):263-269.
3. Hopkins PM. Ultrasound guidance as a gold standard in regional anaesthesia. *Br J Anaesth*. 2007;98(3):299-301.

4. Enneking, F. Kayser. Local Anesthetics and Additives. *Anesth Analg*. 2001;92(3):32-36.
5. Jason A. Patacsil, Maura S. McAuliffe, Leah S. Feyh, Lorie L. Sigmon. Local Anesthetic Adjuvants Providing the Longest Duration of Analgesia for Single-Injection Peripheral Nerve Blocks in Orthopedic Surgery: A Literature Review. *AANA*. 2016;84(2):95-103.
6. Brummett CM, Williams BA. Additives to local anesthetics for peripheral nerve blockade. *Int Anesthesiol Clin*. 2011;49(4):104-116.
7. Park J, Luo ZD. Calcium channel functions in pain processing. *Channels (Austin)*. 2010;4(6):510-517.
8. Miranda HF, Bustamante D, Kramer V, et al. Antinociceptive effects of Ca²⁺ channel blockers. *Eur J Pharmacol*. 1992;217(2-3):137-141.
9. Del Pozo E, Ruiz-Garcia C, Baeyens JM. Analgesic effect of diltiazem and verapamil after central and peripheral administration in the hot plate test. *Gen Pharmacol*. 1990;21:681-685.
10. Brian Cox. Calcium Channel Blockers and Pain Therapy. *Current Review of Pain*. 2000;4:488-498.
11. Iwasaki H, Ohmori H, Omote K, et al. Potentiation of local lignocaine-induced sensory block by calcium channel blockers in rats. *Br J Anaesth*. 1996;77:243-247.
12. Ohmori H, Iwasaki H, Omote K, et al. Potentiation of procaine-induced local sensory block by verapamil in rats. *Masui*. 1996;45(9):1100-1104.
13. Omote K, Sonoda H, Kawamata M, Iwasaki H, Namiki A. Potentiation of antinociceptive effects of morphine by calcium-channel blockers at the level of the spinal cord. *Anesthesiology*. 1993;79(4):746-762.
14. Omote K, Iwasaki H, Kawamata M, Satoh O, Namiki A. Effects of verapamil on spinal anesthesia with local anesthetics. *Anesth Analg*. 1995;80(3):444-448.
15. Kim JS, Park JH, Kang SG, Choe HG, Han YJ, Choe H. Analgesic Effect with Epidural Bupivacaine and Verapamil in Lower Abdominal Surgery. *Korean J Anesthesiol*. 1996;31(2):239-245.
16. Choe H, Kim JS, Ko SH, Kim DC, Han YJ, Song HS. Epidural verapamil reduces analgesic consumption after lower abdominal surgery. *Anesth Analg*. 1998;86(4):786-790.
17. Puneet Khanna, Virender Kumar Mohan, RaniA chanpa Sunder. Efficacy of diltiazem as an adjunct to lignocaine in intravenous regional anesthesia. *Saudi J of Anaesth*. 2013;7(3):305-309.
18. Scott S. Reuben, John P. Reuben. Brachial Plexus Anesthesia with Verapamil and/or Morphine. *Anesth Analg*. 2000;91:3379-3383.
19. Lalla RK, Anant S, Nanda HS. Verapamil as an Adjunct to Local Anaesthetic for Brachial Plexus Blocks. *MJAFI*. 2010;66(1):22-24.
20. Morteza HeidariTabaeizavareh, Mahmoud OmraniFard, AbassMoalemi. The effect of verapamil as an adjuvant agent with local anesthetic on sensory block level, hemodynamic and postoperative pain. *Pak J Med Sci*. 2012;28(2):259-262.
21. A McNaught, U Shastri , N Carmichael1, et al. Ultrasound reduces the minimum effective local anaesthetic volume compared with peripheral nerve stimulation for interscalene block. *Br Journal of Anaesthesia*. 2022;106(1):124-130.
22. MojganVazin, Kenneth Jensen, Danja L. Kristensen, Mathias Hjort, et al. Low-Volume Brachial Plexus Block Providing Surgical Anesthesia for Distal Arm Surgery Comparing Supraclavicular, infraclavicular, and Axillary Approach: A Randomized Observer Blind Trial. *BioMed Res Int*. 2016;2016:7094121.
23. American Society of Anesthesiologists Task Force on Acute Pain Management. Practice guidelines for acute pain management in the perioperative setting: an updated report by the American Society of Anesthesiologists Task Force on Acute Pain Management. *Anesthesiology*. 2012;116(2):248-273.
24. Fox AP, Nowycky MC, Tsien RW. Single-channel recordings of the three types of calcium channels in chick sensory neurons. *J Physiol*. 1987;394:173-200.