

Comparison between facilitatory effects of perineural dexmedetomidine , dexamethasone or lornoxicam added to bupivacaine and bupivacaine alone in supraclavicular brachial plexus block

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Background: Supraclavicular brachial plexus block is frequently used for upper limb surgery but short duration of local anesthetics alone limits its use, various adjuncts to local anesthetics have been used to prolong the block.

Methods: 112 patients were randomly divided into four groups of 28 each. **Group I** received [20 ml bupivacaine 0.5 % + 8 ml NS 0.9% + 2 ml dexamethasone] .**Group II** received [20 ml bupivacaine 0.5 % + 9 ml NS 0.9% + 1 ml dexmedetomidine 100 mcg] .**Group III** received [20 ml bupivacaine 0.5 % + 8 ml NS 0.9% +2 ml lornoxicam 8 mg] **Group IV** received [20 ml bupivacaine 0.5 % + 10 ml NS 0.9%] as a control group .each patient received 30 ml total volume ultrasound-guided supraclavicular block. Hemodynamic variable, onset and duration of sensory and motor block and duration of analgesia were measured.

Results: Onset of sensory and motor block was significantly shorter in dexamethasone group (9.8 ± 1.6 and 11.2 ± 1.7) min , duration of sensory and motor block was significantly prolonged in dexamethasone group (1056.4 ± 53.2 and 1056.4 ± 53.2) min ,also duration of analgesia was significantly longer in dexamethasone group (1091.8 ± 51.4) min compared to other groups.

Conclusion: addition of dexamethasone, dexmedetomidine or lornoxicam to bupivacaine in supraclavicular brachial plexus block shortens onset of sensory and motor block and prolongs duration of sensory, motor block and duration of analgesia. Dexamethasone is the best in this concern as compared to other groups.

Key words: Adjuncts, Analgesia, Dexmedetomidine, Dexamethasone Lornoxicam, Supraclavicular block,

Introduction

Regional anesthesia techniques provide multiple advantages compared with general anesthesia, excellent pain control, less side-effects and shortened hospital stay. However, these advantages can be limited by relatively brief duration of action of local anesthetics (LAs) resulting in block resolution before the period of worst postoperative pain (1).

Increasing the volume (dose) of LAs may prolong the duration of analgesia, but may also increase the risk of LA systemic toxicity. Although continuous catheter-based nerve blocks can extend postoperative analgesia, their placement requires additional time, cost, and skill (2).

Various adjuncts have been used to prolong brachial block and corticosteroids have been studied recently as adjuncts to local anesthetics in regional block (3). Dexamethasone improves the quality and duration of peripheral nerve block over LA alone(4). Dexmedetomidine was first proposed as an adjuvant capable of prolonging duration of sensory and motor block produced by nerve blocks by Memiş and colleagues(5).

Aim of this study is to evaluate the effect of adding dexmedetomidine , dexamethasone or lornoxicam as an adjuvant to bupivacaine in supra clavicular brachial plexus block on the onset time and the duration of sensory and motor blocks and duration of analgesia and side effects such as hypotension ,bradycardia, nausea, vomiting, and hypoxemia.

Patients and methods:

This study is a comparative randomized double blinded controlled study and was carried out in Beni-Suef University Hospital between 6/2016 to 9/ 2017 after the approval of institutional review board and ethical committee and a written informed consent was obtained from each patient before operation.

Trial registration number was PACTR201711002773620

This study enrolled 112 ASA I & II patients, both sex aged 18-60 years undergoing elective surgery of arm, elbow or forearm. patients with a history of significant neurological, psychiatric, neuromuscular, cardiovascular, hepatic disease; pregnancy or lactating women, receiving adrenoceptor antagonist therapy, chronic analgesic therapy or peripheral vascular disease or known allergies to any of the drugs used were excluded from the study. Patients were randomly assigned into four equal groups by sequentially numbered opaque sealed envelope as follows:

Group I (n=28): received total volume 30 ml [20 ml bupivacaine 0.5 % + 8 ml normal saline + 2 ml dexamethasone phosphate] .**Group II** (n=28): received total volume 30 ml [20 ml bupivacaine 0.5 % + 9 ml normal saline + 1 ml dexmedetomidine (100 mcg)] .**Group III**(n=28): received total volume 30 ml [20 ml bupivacaine 0.5 % + 8 ml normal saline +2 ml lornoxicam (8 mg)] **Group IV** (n=28): received total volume 30 ml [20 ml bupivacaine Hcl 0.5 % + 10 ml normal saline] as a control group.

Patients fasted for 6 h before surgery and premedicated with midazolam 0.025 mg kg⁻¹ intravenously on the morning of surgery. In OR basal heart rate (HR); noninvasive systolic blood pressure (SBP) and diastolic blood pressure (DBP); and peripheral oxygen saturation (SpO₂) were recorded and preoperative reading was obtained. 18 G I.V. cannula was inserted in non-operated arm and lactated Ringer's solution started at 5 ml kg⁻¹h⁻¹. Oxygen was administered via a face mask at a rate of 5 L min⁻¹. The drug solutions were prepared by another anesthesiologist was not involved in the study. The anesthesiologist performing the block and observing the patient was blinded to the treatment group. Data collection were done by the same anesthesiologist who was unaware of the group allocation. Supraclavicular block was

done via the subclavian perivascular approach in supine position (back up 30 degree) with arm adducted. Under all aseptic precautions, the injection site was infiltrated with 1 ml of 1% lidocaine subcutaneously. Ultrasound guidance used to locate the brachial plexus. Block was considered successful when at least two out of the four nerve (ulnar, radial, median, and musculocutaneous) were effectively blocked for both sensory and motor.

Sensory block (four nerve territories) was assessed by pin prick test using a 3-point scale. Motor block was determined by thumb abduction (radial nerve), thumb adduction (ulnar nerve), thumb opposition (median nerve), and flexion of elbow (musculocutaneous nerve) according to the modified Bromage scale. Both sensory and motor blocks were assessed every 2 min till their onset and then every 30 min (after surgery), until they were resolved. Patients were asked to note the subjective recovery of sensation and movements which were then certified by an anesthesiologist or nurse.

Onset time for sensory block was defined as the time interval between the end of local anesthetic injection and complete sensory block (score 2) for all nerves. Duration of sensory block was defined as the time interval between the complete sensory block and complete resolution of anesthesia on all the nerves (score 0). Onset time for motor block was defined as the time interval between total local anesthetic injection and complete motor block (grade 2). Duration of motor block was defined as the time interval from complete motor block to complete recovery of motor function of hand and forearm (grade 0). HR, SBP, and DBP were also recorded at 0, 5, 10, 15, 30, 45, 60, 90, and 120 min.

Adverse effects as hypotension (20% decrease relative to baseline), bradycardia (HR <50 beats/min), nausea, vomiting, and hypoxemia (SpO₂<90%). Any need for additional medication (Fentanyl 0.5 mcg Kg⁻¹) were noted intraoperatively. Blood loss was calculated and replaced if more than the allowable blood loss.

Pain was assessed using visual analogue scale (VAS) 0-10. Nursing staff was directed to administer 1 mg kg⁻¹ meperidine intravenous when VAS ≥ 4 (rescue analgesia). The time between the complete sensory block and the first analgesic request was recorded as duration of analgesia (DOA).

Statistical methods :

Descriptive analysis of the results in the form of percentage distribution for qualitative data (minimum, maximum, mean and standard deviation) calculation for quantitative data. Cross tabulation test: For comparison between percentage values. F- Test (One way ANOVA): a test statistics calculated for comparison between means of three groups. Kruskal-Wallis test for several independent samples. Chi-square test: is used to test the statistical significance of differences in a classification system (one-way classification) or the relationship between two classification systems (two-way classification). P value < 0.05 considered significant. (SPSS) 17 was used.

Results

All patients completed the study, there were no statistical significant differences between the studied groups according to patient characteristics , Table (1).

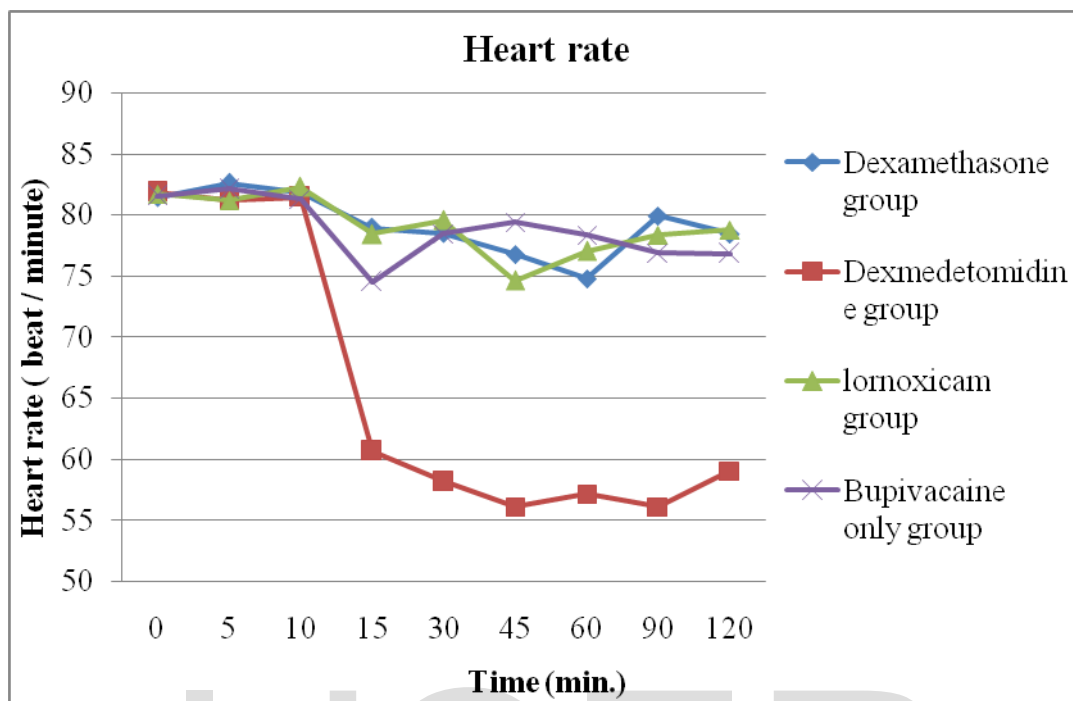
Table (1): Comparison between all groups according to age, sex and ASA

	Dexamethasone (n=28)	Dexmedetomidine (n=28)	lornoxepam (n=28)	Bupivacaine only (n=28)	P value
Age (Year)	42.9±4.9	41.3±5.0	42.5±3.1	42.4±3.9	0.553
Sex (M/F)	12/16	10/18	11/17	9/19	0.859
ASA (I/II)	21/7	20/8	22/6	23/5	0.801

SD: Standard deviation**: P-value < 0.05 (Significant) P-value > 0.05 (Non significant)

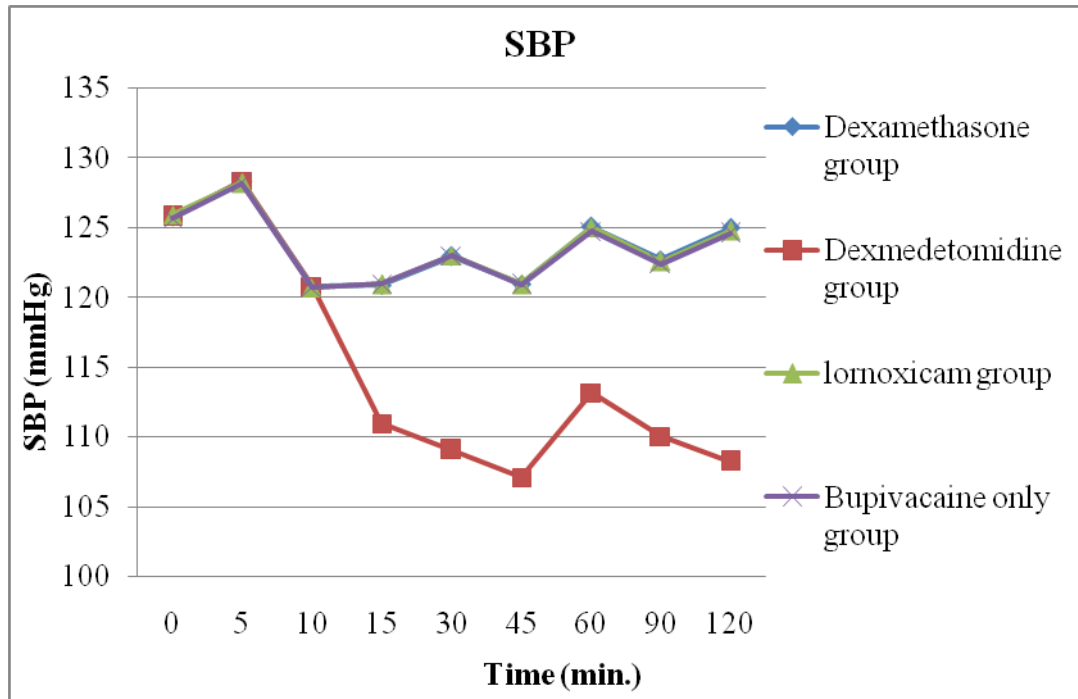
Comparison between groups according to intraoperative heart rate showed the HR in dexmedetomidine group was statistically significant lower than other groups from 15th min. figure (1).

Figure (1): Comparison between all groups according to heart rate per minute



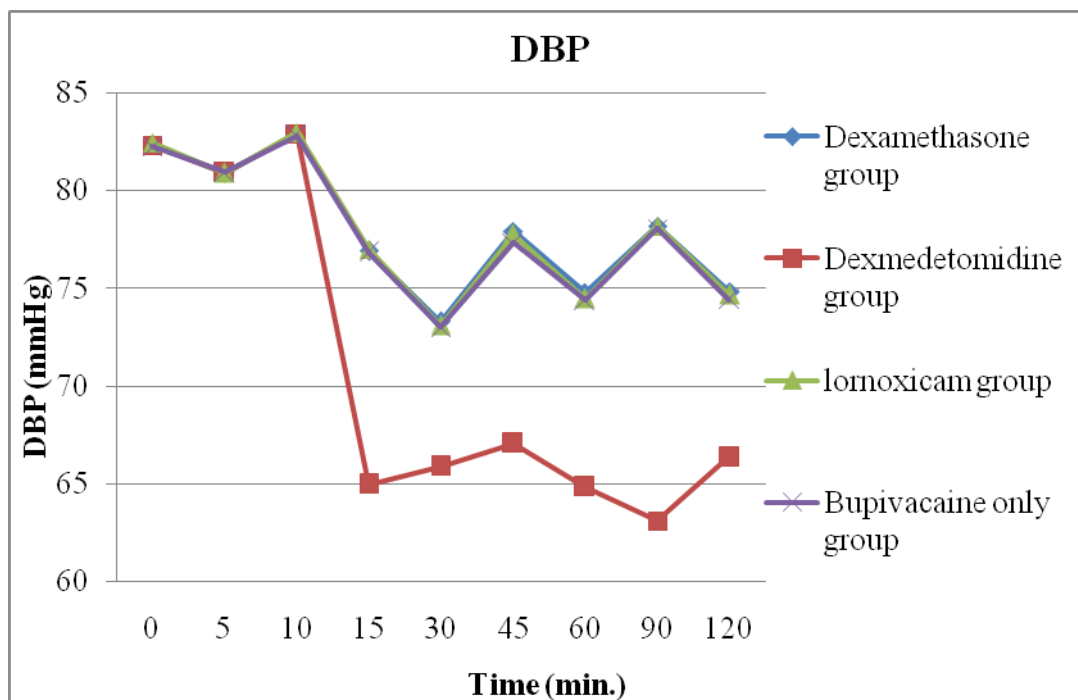
Comparison between groups according to systolic blood pressure, SBP in dexmedetomidine group II was statistically significantly lower than other groups from 15th min. figure(2).

Figure (2): Comparison between all groups according to systolic blood pressure



Comparison between all groups according to diastolic blood pressure DBP in dexmedetomidine group was statistically significant lower than other groups from the 15th min figure (3).

Figure (3): Comparison between all groups according to Diastolic blood pressure



Comparison between groups according to SPO₂ showed no statistically significant difference between all groups

Comparison between all groups according to Sensory block: onset of sensory block was statistically significant lower in dexamethasone group and duration of sensory block was statistically significant prolonged in dexamethasone group compared to other groups, according to motor block: onset of motor block was statistically significant lower in dexamethasone group and duration of motor block was statistically significant prolonged in dexamethasone group compared to other groups, also duration of analgesia was statistically significant prolonged in dexamethasone group compared to other groups. Table (2)

Table (2):-

		Dexamethasone (n=28)	Dexmedetomidine (n=28)	lornoxiam (n=28)	Bupivacaine only (n=28)	P value
Sensory block (min)	Onset time	9.8±1.6	13.0±0.9	16.0±1.1	18.9±1.3	0.001**
	Duration	1056.4±53.2	754.7±65.2	651.3±59.4	233.9±34.0	0.001**
Motor block (min)	Onset time	11.2±1.7	16.1±1.0	18.0±1.0	22.5±1.2	0.001**
	Duration	1013.0±63.0	701.7±56.9	598.4±24.0	207.8±15.8	0.001**
Duration of analgesia (min)		1091.8±51.4	774.8±67.2	671.1±76.0	241.4±33.4	0.001**

Regarding side effects, there was statistically significant increase in incidence of hypotension and bradycardia in dexmedetomidine group (8 patients - 28.6 %)

compared to other groups, other side effects: nausea and hypoxemia there were no significant difference between groups.

Comparison between all groups according to need for additional intra operative medication (Fentanyl 0.5 mcg Kg⁻¹) the need for additional intra operative medication was significant lower in dexmedetomidine group compared to other groups table (3)

Table (3): Comparison between groups according to need for additional intra operative medication

	Dexamethasone (n=28)	Dexmedetomidine (n=28)	loronoxcam (n=28)	Bupivacaine only (n=28)	P value
Fentanyl 0.5 mcg Kg⁻¹ (n %)	3(10.7)	1(3.6)	4(14.3)	5(17.8)	0.385

Discussion

Supraclavicular brachial plexus block widely used regional nerve block to provide anaesthesia and analgesia for upper limb surgery provides a rapid and dense anesthesia and analgesia of the entire upper limb ⁽⁶⁾.

In our study, 112 patients divided to 4 equal groups (n=28 each) in **Group I**, **Group II**, **Group III** dexamethasone, dexmedetomidine loronoxcam was used as adjuvant to bupivacaine respectively and in **Group IV** bupivacaine was used alone. The onset of sensory and motor blockade was significantly shorter and

duration of sensory and motor blockade and duration of analgesia were significantly longer in group I compared to group II, III and IV.

Golwala MP et al⁽⁷⁾ and Yadav RK et al⁽⁸⁾ found significant earlier onset of sensory and motor block in the local anesthetic plus dexamethasone group than in the control group.

However Vieira et al.⁽⁹⁾ performed ultrasound-guided interscalene brachial plexus block in 88 patients scheduled for shoulder arthroscopy with 20 ml of the local anesthetic mixture with dexamethasone adjuvant, no significant reduction in onset of sensory and motor blockade in between two groups. This discrepancy may be due to the difference in the LA volume and site of block.

Trabelsi et al.⁽¹⁰⁾ conducted ultrasound-guided supraclavicular brachial plexus block in 60 patients undergoing upper extremity surgery using 15 ml of 2% lidocaine + 2 ml of adjuvant (8 mg dexamethasone, 100 mg tramadol, 2 ml saline). They also found a significant prolongation of duration of analgesia with dexamethasone group compared to tramadol group.

Choi S et al, collected data from nine trials (801 patients) were included with patients receiving either Local Anaesthetic (LA) alone or LA with perineural dexamethasone (4-10mg)⁽¹¹⁾. Their conclusion was that dexamethasone prolonged analgesic duration for LA.

The mechanism of the analgesia produced by corticosteroids is not fully understood. This effect may be mediated by their anti-inflammatory or immune-suppressive effects^(12, 13). Corticosteroids also cause skin vasoconstriction on topical application.

Steroids bind to intracellular receptors and modulate nuclear transcription. However, dexamethasone produced a relatively rapid effect which cannot be explained by the above mechanism⁽¹⁴⁾. Many authors believe that the block prolonging effect of dexamethasone is due to its local action and not a systemic one⁽¹⁵⁾.

They said that steroids may induce analgesia by blocking transmission in nociceptive c-fibres and suppressing ectopic neuronal discharge. Local application of methylprednisolone blocks transmission in c-fibres but not in *a* and *B* fibres⁽¹⁶⁾. Steroids might have effect by altering the function of potassium channels in the excitable cells⁽¹⁷⁻²⁰⁾

Esmoglu et al.⁽²¹⁾ added dexmedetomidine to Levobupivacaine in axillary brachial plexus block observed that sensory and motor block onset time were significantly shorter in group LD (levobupivacaine + Dexmedetomidine) than in group L (levobupivacaine) and This study was the basis for dose selection of dexmedetomidine (100 µg) in our study. Agarwal et al.,⁽²²⁾ dexmedetomidine was used as adjuvant to bupivacaine in supraclavicular brachial plexuses block significantly shortens the onset time and prolongs the duration of sensory and motor block.

Biswas et al.⁽²³⁾ added dexmedetomidine as an adjuvant to levobupivacaine and found that it significantly shortens the sensory and motor onset time and prolongs the duration of sensory and motor block.

Gandhi et al.⁽²⁴⁾, also found administering perineural dexmedetomidine as part of a brachial plexus block resulted in a prolongation of motor block duration. Masuki et al., suggested that dexmedetomidine induces vasoconstriction via adrenoceptors⁽²⁵⁾ possibly this vasoconstriction around the site of injection, delaying the absorption of local anesthetic and prolonging its effect.

Esmoglu et al., observed bradycardia in 7 out of 30 patients in study group while we observed 8 out of 28 patients. In our study heart rate, systolic blood pressure and diastolic blood pressure was decreased from base line in the group II (bupivacaine + dexmedetomidine) after 15th min ($p < 0.05$) when compared to other groups.

Presynaptic activation of α_2 adrenoceptor in central nervous system inhibits the release of norepinephrine, terminating the propagation of pain signals

and their postsynaptic activation inhibits sympathetic activity, thereby decreasing HR and BP ⁽²⁶⁾.

Our study showed decrease in onset of sensory and motor block, increase in duration of sensory, motor block and duration of analgesia in group III (bupivacaine + lornoxicam) when compared to group IV (bupivacaine only) but less than group I,II.

Sen and his colleagues show that addition of NSAID (lornoxicam) to lidocaine for IVRA shortens the onset of sensory and motor block, decreases tourniquet pain, and improves postoperative analgesia without causing any side effects ⁽²⁷⁾.

Lornoxicam might produce a peripheral analgesic effect via NO-c GMP pathway and the opening of K⁺ channels. Buritova and Besson also suggested that lornoxicam shows antinociceptive effect in predominantly peripheral site ⁽²⁸⁾. These mechanisms may explain why the analgesic effect of lornoxicam in IVRA was better than the systemic administration for tourniquet pain.

Additional intraoperative medication (fentanyl 0.5 mcg kg⁻¹) was less in group II when compared other groups as dexmedetomidine has a sedative effect. Ozalp et al. ⁽²⁹⁾ and Esmaoglu et al. adding dexmedetomidine as adjuvant in brachial plexus block observed that patients was sedated throughout the surgery.

Though the exact mechanism of action is not known, centrally-acting alpha-2 agonists produce analgesia and sedation by inhibition of substance P release in the nociceptive pathway at the level of the dorsal root neuron and by activation of alpha-2 adrenoceptors in the locus coeruleus⁽²⁹⁾.

Limitation: Addition of adjuvant (dexamethasone , dexmedetomidine or lornoxicam) in supraclavicular brachial plexus block shortens onset of sensory and motor block, prolongs duration of sensory , motor block and duration of analgesia but to give a better insight of its efficacy, safety profile, and cost effectiveness; need to be applied in a larger study population and in different nerve blocks.

Conclusion: we can conclude that addition of adjuvant as dexamethasone , dexmedetomidine or lornoxicam to bupivacaine in supraclavicular brachial plexus block shortens onset of sensory and motor block and prolongs duration of sensory , motor block and duration of analgesia than using bupivacaine alone and dexamethasone is the best in this concern as compared to other groups .

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