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Effect of verapamil as an adjuvant to Levobupivacaine in supraclavicular brachial plexus block

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Abstract

Background: The quest for searching newer and safer anaesthetic agents has always been one of the primary needs in anaesthesiology practice. Levobupivacaine, the pure *s* (-) enantiomer of bupivacaine, has strongly emerged as a safer alternative for regional anaesthesia than its racemic sibling. Also, many adjuvants have been used with local anaesthetics to reduce the time of onset and prolong the duration of analgesia in brachial plexus blocks. However, few studies are there using verapamil as an adjuvant with Levobupivacaine.

Aims: The primary aim of the study is to know the effect of verapamil (5mg) as an adjuvant to Levobupivacaine in supraclavicular brachial plexus block.

Methods: A Descriptive, Observational study was carried out in 80 ASA Grade I and II patients, undergoing upper limb surgeries under supraclavicular brachial plexus block using ultrasound machine. Local anaesthetic solution was prepared as following.

30ml 0.5% Levobupivacaine + 2ml Verapamil (5mg). The effect of Verapamil as an adjuvant to Levobupivacaine in Supraclavicular Brachial Plexus Block with regards to onset and duration of motor and sensory block, duration of analgesia, need for rescue analgesia and number of rescue analgesia in first 24 hours after surgery was evaluated. Data analysis was done with the help of SPSS Software ver 13.

Results: Mean onset time for motor block in our study group was 9.19 ± 1.86 min

The mean duration of motor block in our study group was 470.25 ± 42.00 min

The mean onset time for sensory block in our study group was 6.48 ± 2.55 min

The mean duration of sensory block in our study group was 494.88 ± 37.67 min

The mean duration of analgesia in our study group was 517.88 ± 48.24

The mean no of reuse analgesia required in the first 24 hours after surgery was 3

Conclusion: Verapamil (5 mg) 2 ml can be effectively and safely used as an adjuvant to Levobupivacaine (0.5%) 30ml in Supraclavicular Brachial Plexus Block. However, due to paucity of studies in literature, there is still scope for further study using different calcium channel blocking drugs or in different dosage strengths.

Keywords: Supraclavicular block, Verapamil, USG, Levobupivacaine

Introduction

There has always been a search for adjuvants to the local anaesthetics that prolong the duration of block but with minimum adverse effects. Calcium plays an important role in analgesia produced by local anaesthetics. The activation of N-methyl-D-aspartate receptors may lead to Calcium entry into cells and potentiation of spinal cord and plays a role in pain formation. Hence Calcium Channel Blockers may prevent central sensitization and provide better sensory motor block characteristics [1]. Verapamil, a synthetic palavering derivative, is an L- type Calcium Channel Blocker. Verapamil, a Calcium Channel Blocker, can potentiate analgesic action of local anaesthetics and reduce postoperative pain and analgesic consumption. Verapamil has been shown to have potent local anaesthetic activity reflecting inhibition of fast Sodium Channels. It induces fast Channel blocking effects similar to local anaesthetics [1].

In this Descriptive, observational study, we have studied the effect of Verapamil as an adjuvant to Levobupivacaine in supraclavicular brachial plexus block with respect to the onset and duration of sensory and motor block as well as duration of analgesia.

Aim & Objectives

The primary aim of the study is to know the effect of verapamil (5 mg) as an adjuvant to Levobupivacaine in supraclavicular brachial plexus block.

The objective of the study is to evaluate the Onset of sensory and motor blockade

- i. Duration of sensory and motor blockade
- ii. Haemodynamic variables (HR, BP, O₂ saturation)
- iii. Need of rescue analgesia
- iv. Number of rescue analgesia required in first 24 hours of
- v. Operation.
- vi. Adverse effects of Verapamil when used in combination with Levobupivacaine.

Methods

In this Descriptive Observational study, after obtaining approval from the Institutional Ethics Committee, the study was carried out in Orthopaedic operation theatre in 80 ASA Grade I and II patients, undergoing upper limb surgeries under supraclavicular brachial plexus block.

All patients underwent pre anaesthetic checkup (Pac) which included detailed history, examination and necessary investigations. Procedure was explained in patients own language and written, informed consent was obtained from each patient. Patient refusal, uncontrolled diabetes mellitus, renal or liver disease, circulatory instability, pregnant women, allergy to local anesthetic, coagulation disorder, and neurological deficit were excluded from study. Before starting the procedure, monitors were attached to the patient and all the baseline parameters such as heart rate (HR), non-invasive blood pressure (NIBP), oxygen saturation (SPO₂), electrocardiography were noted. An I.V. line of 20 gauge cannula was secured in opposite arm and I.V. ringer lactate solution started. Patients were instructed to lie in supine position, with arms by the side of body. A bolster was placed below the shoulder and head turned to opposite side. Son anatomy of patient's supraclavicular area was studied using ultrasound machine. Local anaesthetic solution was prepared as following.

30 ml 0.5% Levobupivacaine + 2ml Verapamil (5mg). After aseptic Patient preparation of the area, at a point 1.5 to 2.0 cm posterior and cephalic to midpoint of clavicle, sublamina artery pulsations were felt. A skin wheel was raised with local anaesthetic (lignocaine 2% 1.5 ml) cephalous posterior to pulsations.

The using probe was cleaned with antiseptic solution and covered with sterile transparent tandem. With the patient in the proper position, the transducer was positioned in the transverse plane immediately superior to the clavicle at approximately its midpoint. The transducer was tilted caudally to obtain a cross-sectional view of the subclavian artery. The brachial plexus was noted as a collection of hypo echoic oval structures lateral and superficial to the artery.

A 24 gauge, 1.5 inches short bevelled needle was then inserted in-plane toward the brachial plexus, in a lateral-to-medial direction. After proper placement of the needle under using guidance and negative aspiration of blood, the study

drug was injected slowly in quantities of 5 ml intermittently by confirming negative aspiration of blood. Then parameters like pulse, bp, spo₂ were noted. Surgery was started after complete nerve blockade at the surgical site. I.V fluids were given according to the nil by mouth (NBM) status of the patient. In case of supraclavicular block failure general anaesthesia was administered and patient was excluded from the study.

Sensory block was assessed by pin prick method at 0, 2, 5, 10, 25 and 30 minutes. Sensory characteristics of the block was assessed using response to pinprick to 23-gauge hypodermic needle using the Hollmen scale.

Motor block was measured at 0, 2, 5, 10, 25 and 30 minutes. Motor block was graded according to the 3-point modified Bromage score.

The duration of sensory block was defined as the time interval between complete sensory block and the return of normal sensation. Sensory block was assessed hourly for 24 hours in the postoperative room.

The duration of motor block was defined as time interval from onset of motor blockade to the time when the patients were able to lift their hand and move their fingers with normal muscle power. Motor block was assessed hourly for 24 hours in the postoperative room.

The duration of analgesia was assessed by using an 11-point (0-10) verbal numeric rating scale (VNRS) in which a score of "0" indicated "no pain" and a score of "10" indicated the "worst pain imaginable". The VNRS measurements was obtained at baseline (before placement of the block), at the time of skin incision, at the completion of the surgical procedure, and at 8 hourly interval up to 24 hours following placement of the block. Duration of post-operative analgesia was taken till the time patient asked for rescue analgesia (VNRS>3). The patients were monitored for any drug related side effects and immediate block related complications.

After surgery, patients were shifted to recovery room and were monitored for half an hour. If all the parameters like pulse, bp, spo₂ were within normal limits then patient was shifted to ward. A trained staff nurse was instructed to note the time of first onset of pain

Statistical analysis

Data was recorded in printed proforma. After data collection, data entry was done in Microsoft Excel. Data analysis was done with the help of SPSS Software ver 13. Qualitative data was presented with the help of Frequency and Percentage table. Quantitative data was presented with the help of mean and standard deviation, median and interquartile range.

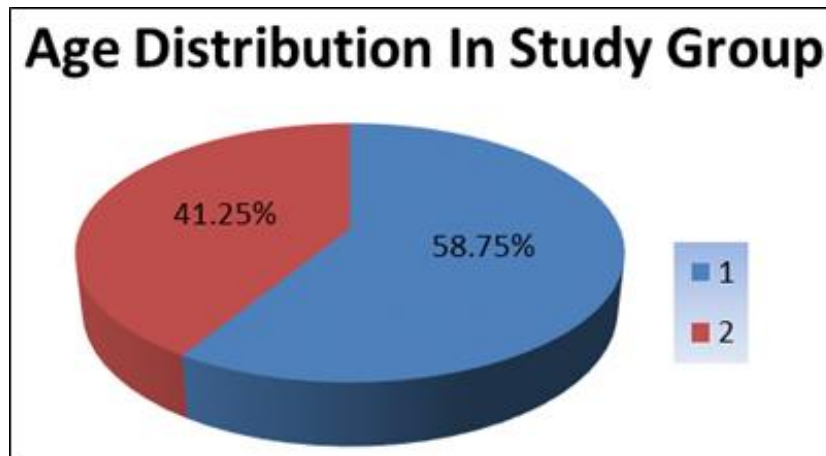
Results

80 patients aged 18yrs – 60yrs of physical status ASA grade 1 and ASA grade 2 undergoing elective upper limb surgeries were selected. Block was successful in all the patients, and all the enrolled patients completed the study.

Demographic variables and vital parameters

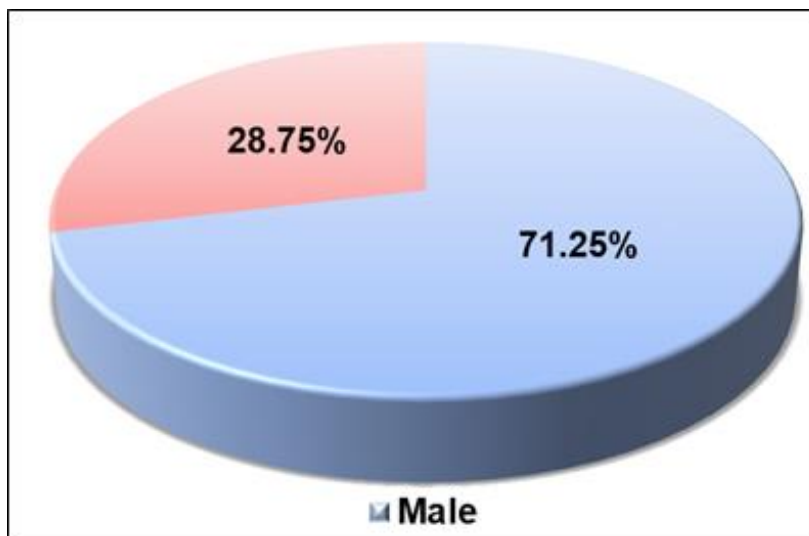
1. No of patients

- * Age 18-40 years 47 (58.75%)
- * Age 41-60 years 33 (41.25%)



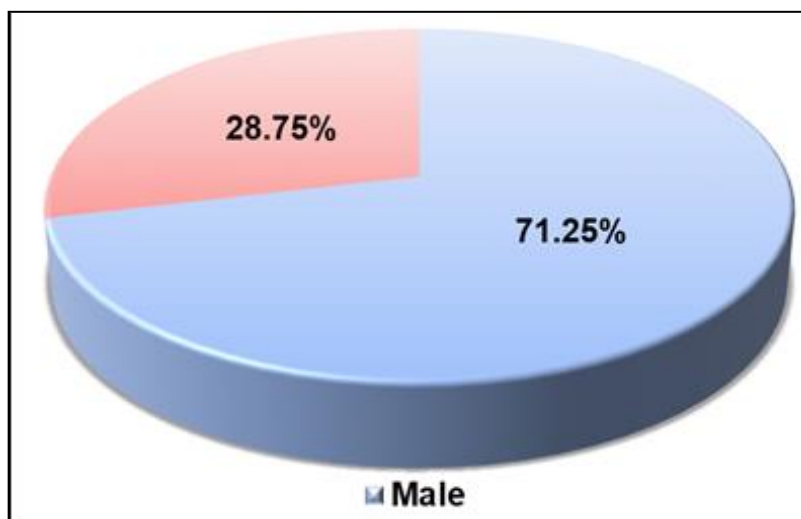
2. Gender

- * Males 57 (71.25%)
- * Females 23 (28.75%)

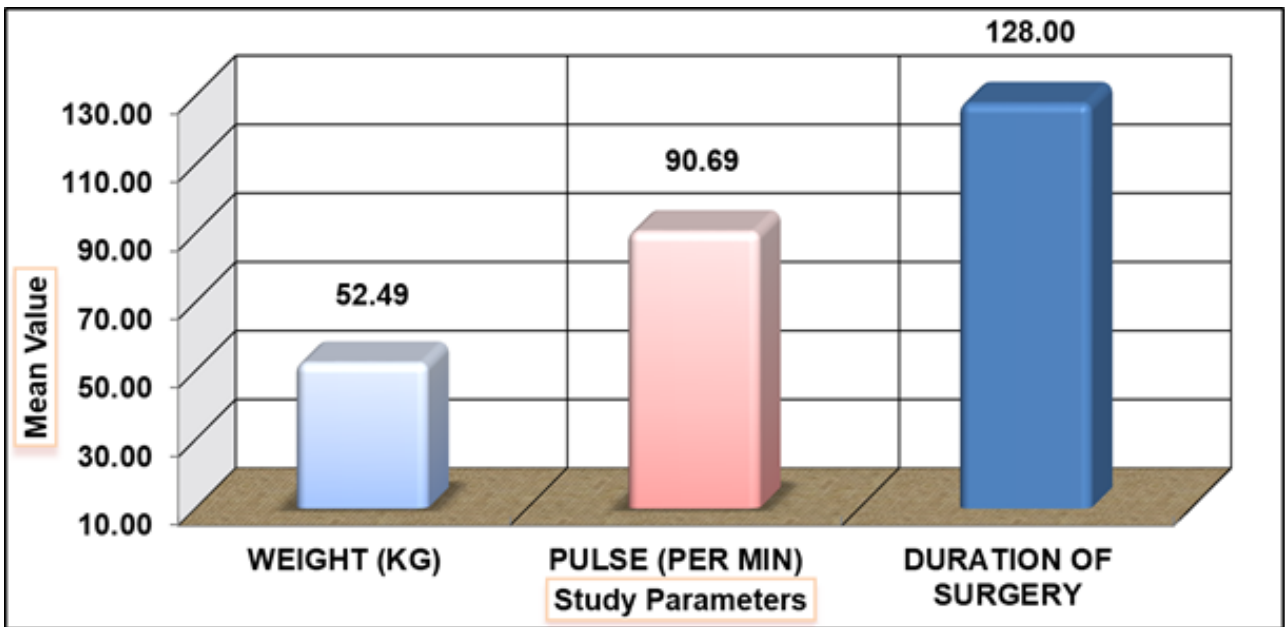


3. ASA grade

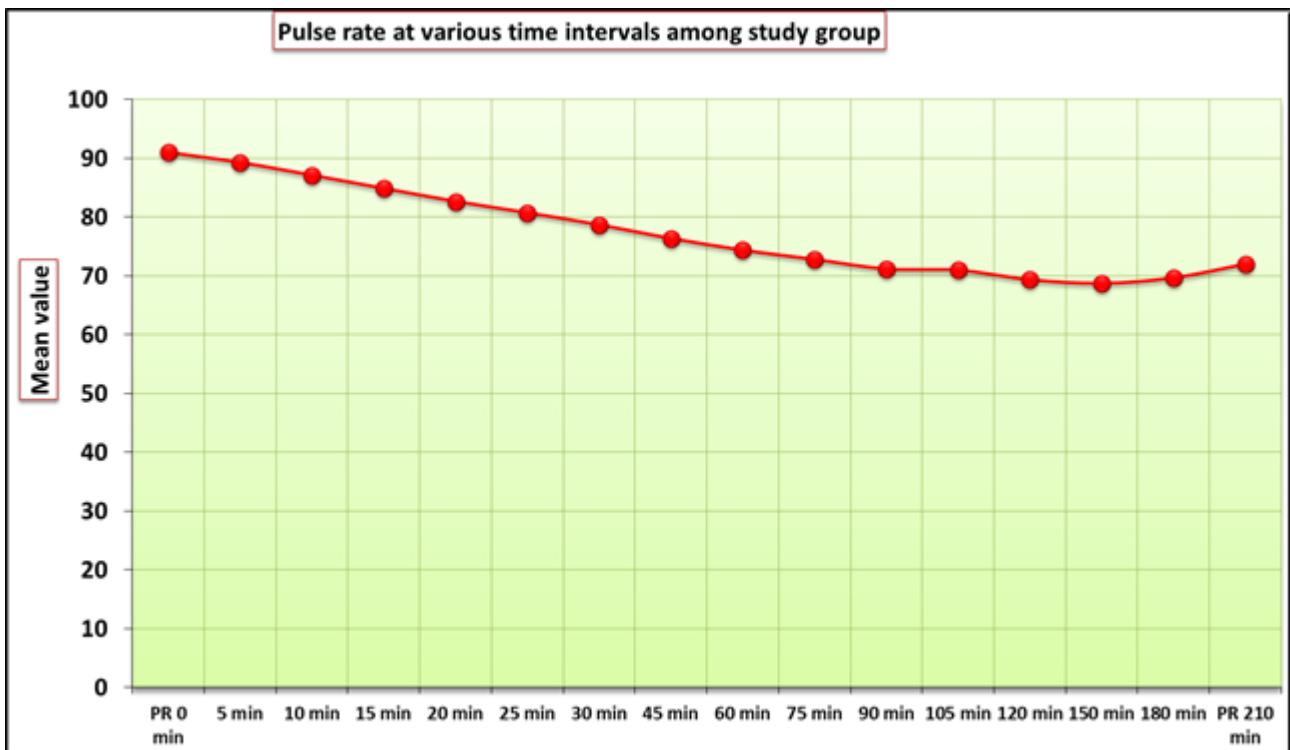
- * Grade 1 68 (71.25%)
- * Grade 2 127(15%)



- 4. Mean weight (kgs) 52.49±7.66
- 5. Mean duration of surgery (min) 128 ± 33.65
- 6. Mean baseline pulse rate (min) 90.69±10.29

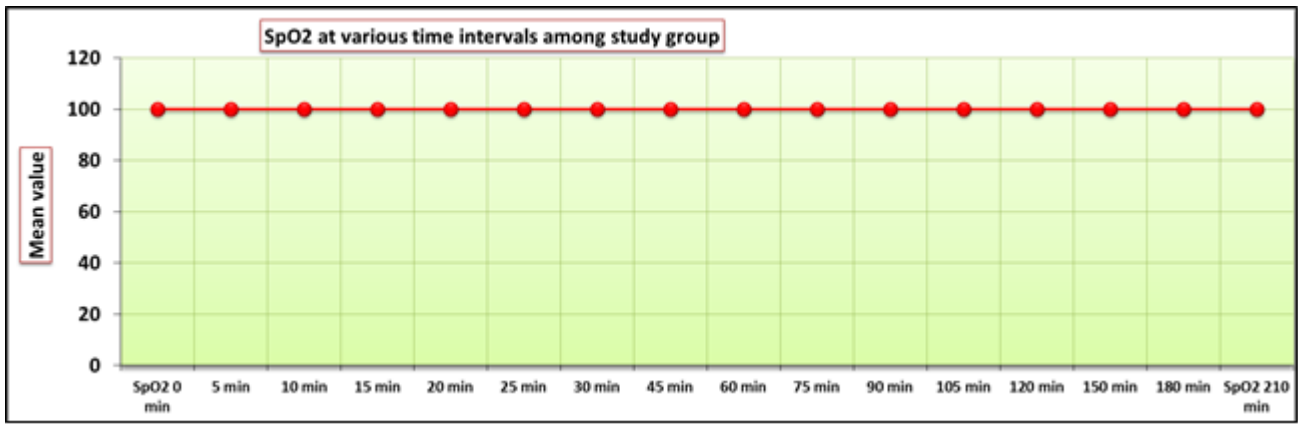


The lowest mean pulse rate was 68.71 ± 8.65/min at 150 the min after giving block



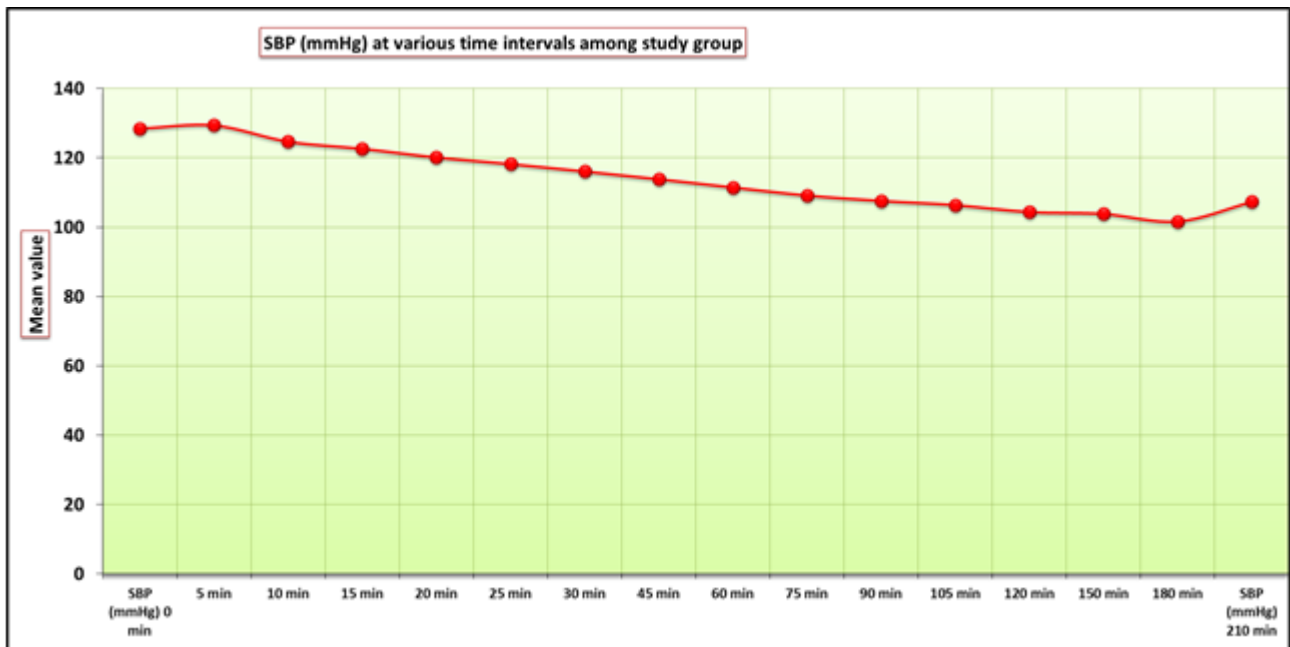
- 7. Mean Baseline Spo2 99.98 ± 0.22 %

* The Lowest recorded mean Spo2 in our study group is 99.91 ± 0.36% at 15 min after giving the block



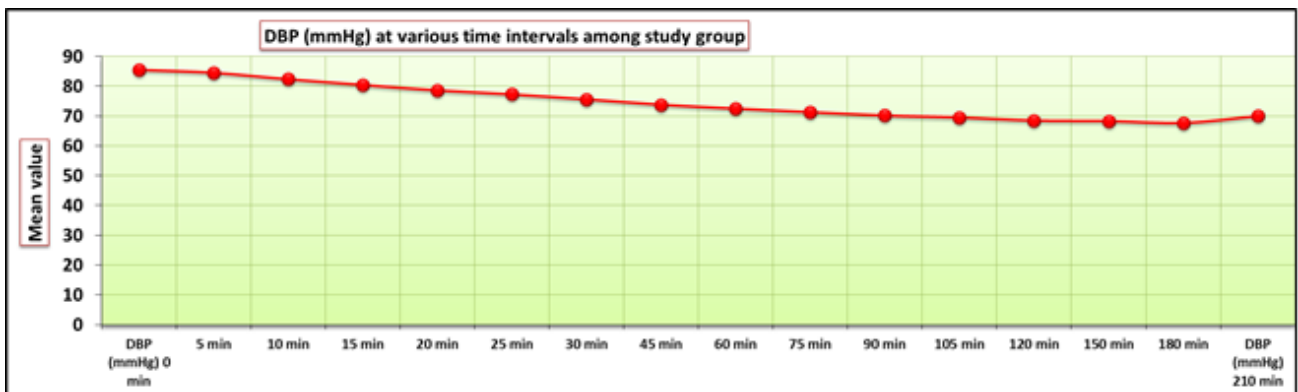
8. Mean baseline systolic blood pressure (MMHG) 128.48 ± 7.66

* The lowest mean systolic blood pressure was 101.67 ± 6.02 mm of Hg at 180 min after giving block



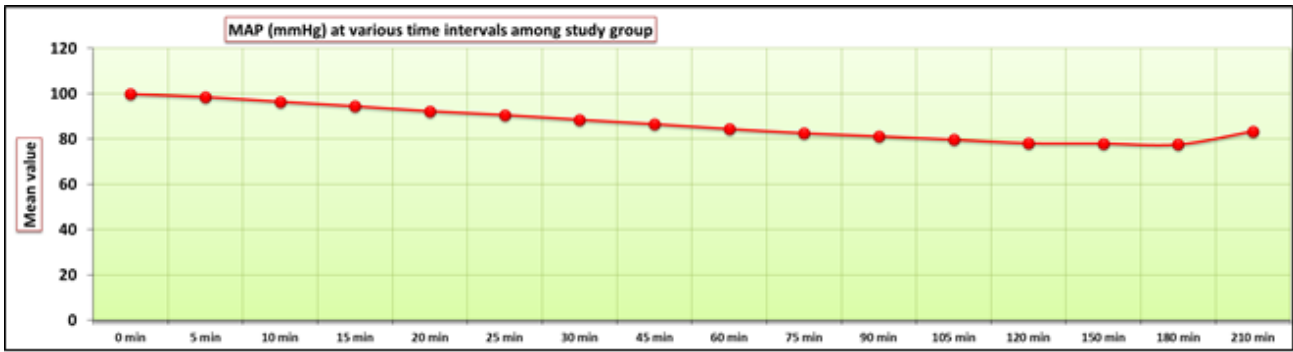
* Mean baseline diastolic blood pressure (MMHG) 85.50 ± 6.06

* The lowest mean diastolic blood pressure was 67.67 ± 3.26 mm of Hg at 180 min after giving block



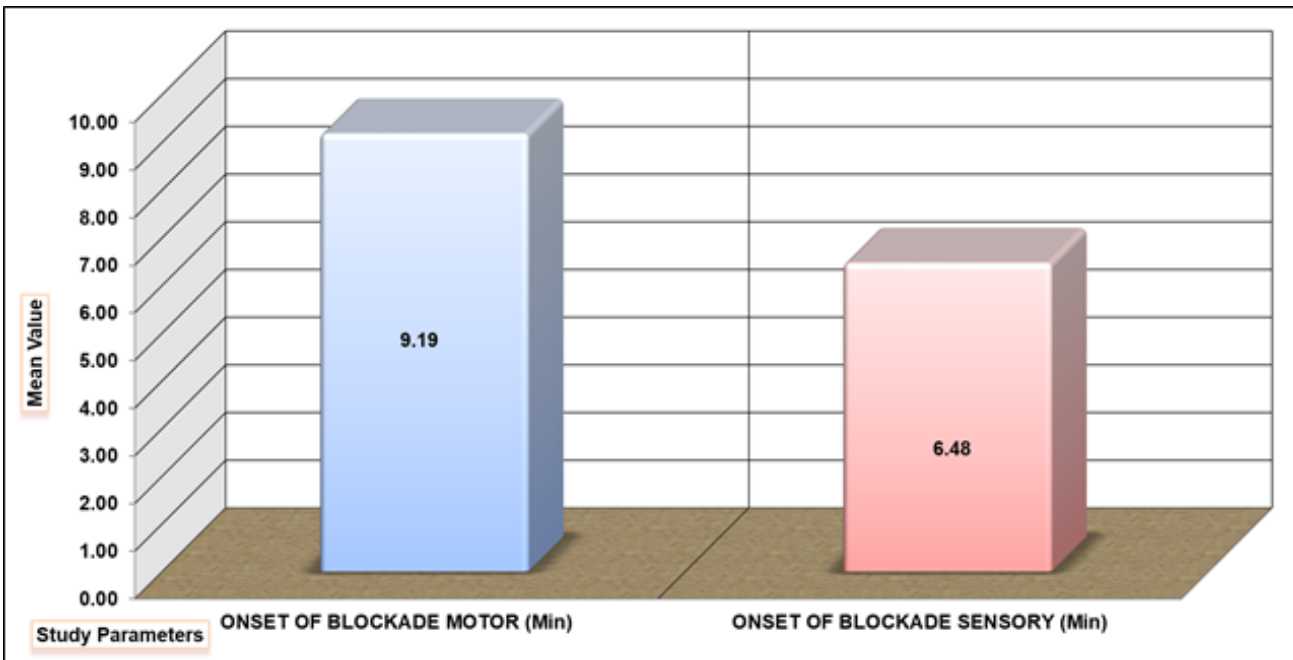
* Mean baseline mean arterial pressure (MMHG) 99.75 ± 6.37 MMHG

* The lowest mean MAP was 77.55 ± 5.79 mm of Hg at 180 min after the block

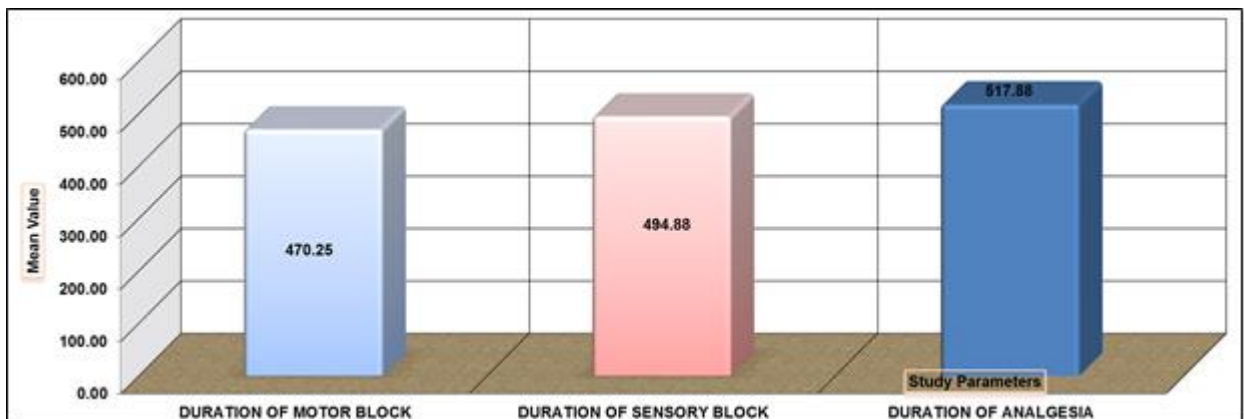


Sensory and motor block characteristics

- 1. Mean onset time for motor block (min) 9.19 ± 1.86
 * The lowest recorded time of onset of motor block in our study group was 5 min and highest was 10 min
- 2. Mean onset time for sensory block (min) 6.48 ± 2.55
 * The lowest recorded time of onset of sensory block in our study group was 2 min and highest was 10 min

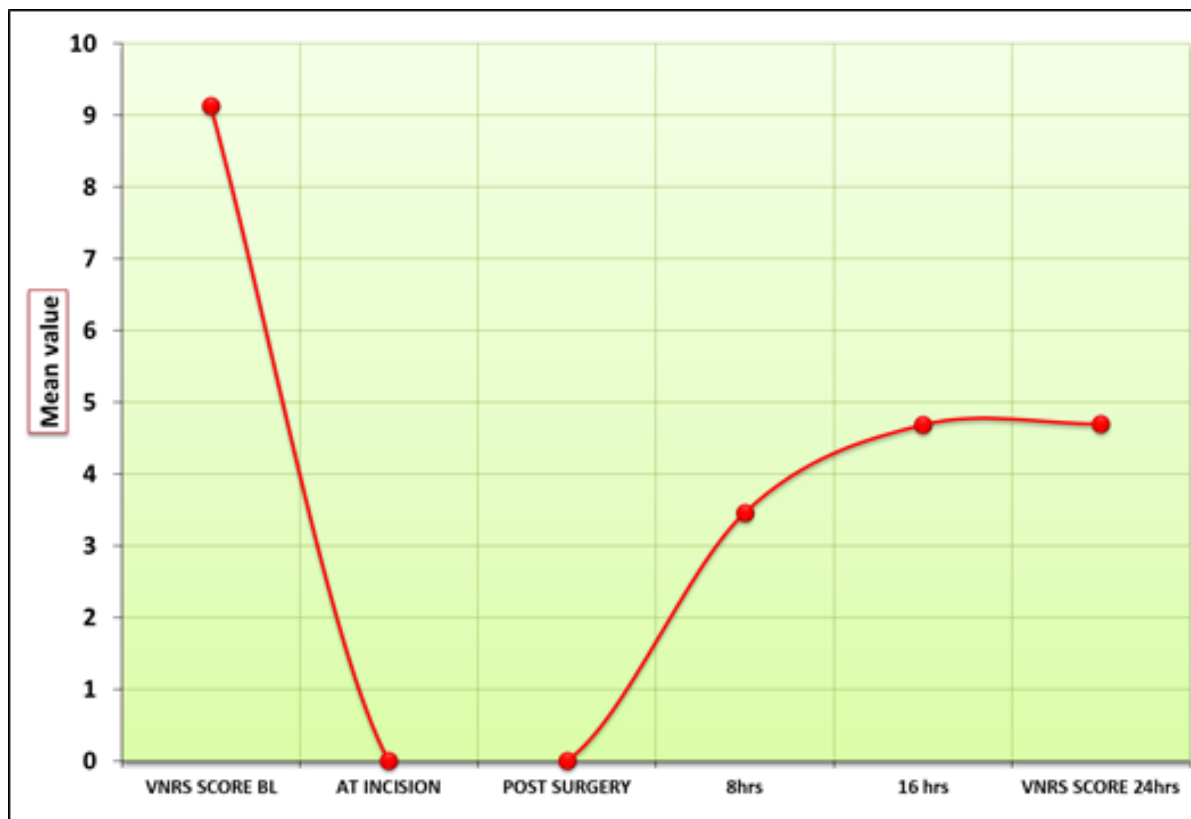


- 1. Mean duration of motor block (min) 470.25 ± 42.00
 * The lowest recorded duration of motor block in our study group was 360 mins and highest was 600 mins
- 2. Mean duration of sensory block (mins) 88 ± 37.67
 * The lowest recorded duration of sensory block in our study group was 390 mins and highest was 570 mins
- 3. Mean duration of analgesia (mins) 517.88 ± 48.24
 * The lowest recorded duration of analgesia in our study group was 420 mins and highest was 630 mins



- 4. Mean VNRS score (baseline), (mins) 9.14 ± 0.63
 * Mean VNRS score (8 hrs), (mins) 3.46 ± 1.04

* Mean VNRS score (16 hrs), (mins)	4.69 ± 0.67
* Mean VNRS score (24 hrs), (mins)	4.70 ± 0.66
Mean no. of reuse analgesia (24 hours)	3



In our present study, side effects like bradycardia, hypotension, nausea, vomiting, drowsiness, pruritus and hypoxemia etc were not observed. Also, complications like pneumothorax, hematoma, horner's syndrome, phrenic nerve palsy etc were not seen in our study group.

Discussion

Supraclavicular brachial plexus block is an excellent form of regional anesthesia for upper limb Orthopaedic surgeries as well as an effective form of analgesia for the control of post operative pain. Different studies have compared long acting local anaesthetics Levobupivacaine, ropivacaine and bupivacaine in brachial plexus block for upper limb surgery. Levobupivacaine, the pure S (-)-enantiomer of bupivacaine has been found to be equally efficacious as bupivacaine, but with a superior pharmacokinetic profile and with less cardiac and neurotoxic adverse effects [2]. The long duration of sensory block associated with good analgesia and less toxicity of Levobupivacaine makes it a better choice for upper extremity blocks [3].

Adjuncts like clonidine, dexmedetomidine, Dexamethasone, Buprenorphine, Tramadol have been successfully used in the past as adjuncts to local anaesthetics to increase the duration and efficacy of the block [4]. A variety of receptors mediate perception of pain calcium ions play an important role in analgesia mediated by local anaesthetics. Local anaesthetics reduce calcium permeability, thus calcium channel blockers potentiate the analgesic effect of local anaesthetics and act primarily by means of vasodilation and reduction of peripheral vascular resistance.

Nowycky *et al.* [5] in 1985 reported the evidence of three distinct types of calcium channels in sensory neurons

namely L, T and N type of these L and N type of channels have a significant role in regulating neurotransmitter release from neurons. The N type has much more potent anti-nociceptive effects than L type. Studies in rats have shown that application of morphine and N type calcium channel blockers attenuate pain mediated by A delta and C fibre [6]. N type channel blockers were not clinically suitable for use because of their severe neurotoxicity. In a series of in vitro experiments on rats, Hara *et al.* [7] showed that L type channel blockers verapamil and diltiazem produced both somatic and visceral pain relief in a dose dependent manner suggesting the relevance of L type channel blockers in pain management. Verapamil, a synthetic palaverine derivative, is an L type calcium channel blocker. Chemically, it belongs to phenylalkylamine group. Verapamil inhibits various ionic processes and its analgesic effects are complete. Verapamil blocks the slow inward transmembrane ionic current carried by calcium and/or sodium in cardiac and vascular smooth muscle [8]. Verapamil has been shown to have potent local anaesthetic activity, reflecting inhibition of fast sodium channels. Verapamil is supplied as a racemic mixture. The Dextro isomer is devoid of activity at slow calcium channels and induces fast channel blocking effects similar to local anaesthetics. Its anaesthetic potency is 1.6 times that of procaine [9]. Keeping these facts in mind, we decided to study the effects of adding verapamil as an adjuvant to Levobupivacaine in supraclavicular brachial plexus block to determine if there is an increase in the onset and duration of block and whether it increases the duration of postoperative analgesia. Kim *et al.* [10] opined that verapamil, when added to epidural bupivacaine, decreased the postoperative pain through central desensitization.

Sidharth Sraban Routray, *et al.* [11] in their study concluded that Verapamil, when added to Levobupivacaine in supraclavicular brachial plexus block reduced the onset time of sensory and motor block.

Dr. Md. Arman Ali, *et al.* [12] found similar results in a similar study and concluded that verapamil can be used as an adjuvant to decrease the onset time of sensory and motor blocks of bupivacaine in supraclavicular block.

Sidharth sraban routray, *et al.* [11] in their study also concluded that Verapamil, when added to Levobupivacaine in supraclavicular brachial plexus, increased the duration of sensory and motor block.

F. Mosaffa, *et al.* [13] in their study concluded that using bupivacaine in combination with verapamil significantly decreases the onset time of sensory and motor block as well as the initiating time of complete analgesia. There was no significant difference between 2 doses of 2.5 and 5mg of verapamil.

Amir Ibrahim Mohamed Salah, *et al.* [14] conducted a study on Verapamil as An Adjunct to Local Anaesthetic for Brachial Plexus block. they concluded that adding 2.5 mg verapamil with 0.25% bupivacaine solution (20ml) with 1% lignocaine (20 ml) to brachial plexus block can prolong sensory anesthesia without significant effect on duration of motor block, onset of sensory and motor block, Dr. Murali Krishna Chava, *et al.* [8] in their study concluded that addition of verapamil to levobupivacaine solution for brachial plexus block prolongs the duration of sensory blockade. Although the dosage used in the study did not significantly modify the duration of Reuben, Scott S, *et al.* [15] examined the analgesic effects of administering morphine, verapamil or its combination into the brachial plexus sheath with lidocaine. They concluded that the addition of verapamil to lidocaine in brachial plexus block has no effect on the analgesic duration or 24 hour analgesic use analgesia, onset and duration of motor blockade Also, Reuben and Reuben in his study concluded that the addition of verapamil to brachial plexus block had no effect on analgesic duration or 24 h analgesic requirement. Multiple other investigations by Hasegawa and Zacny [16]; Miranda *et al.* [17] and Carta *et al.* [18] suggested that calcium channel blockers combined with local anesthetics could increase analgesic effects, Ved prakash pandey, *et al.* [19] compared the effect of dexmedetomidine and verapamil as an adjuvant to local anaesthetic solution. they observed that there is no statistically significant difference in the quality of block in group which received bupivacaine alone in comparison to group which received verapamil in combination with bupivacaine

Mohammad Salah, *et al.* [20] in their study recorded and observed any significant difference in between the groups regarding systolic, diastolic and mean blood pressure as well as pulse rate and oxygen saturation for every 5 min interval during procedure and every half an hr post operatively till 6 hrs but did not note any significant difference. Amir Ibrahim Mohamed Salah, *et al.* [14] encountered two patients in their study who developed Horner's syndrome and one patient developed phrenic nerve paralysis and all three patients improved spontaneously.

Conclusion

On the basis of the observations in our study we conclude that the addition of verapamil to local anaesthetics for supraclavicular brachial plexus block can modify the action

of local anaesthetics. Thus, Verapamil can be effectively and safely used as an adjuvant to Levobupivacaine in Supraclavicular Brachial Plexus Block. However, due to paucity of studies in literature, there is still scope for further study using different calcium channel blocking drugs or in different dosage strengths.

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