

Comparison of the Efficacy of 0.5 Percent Levobupivacaine with a Combination of 0.5 Percent Levobupivacaine and Hyaluronidase, in Ultrasound Guided Axillary Brachial Plexus Block for Forearm and Hand Surgeries

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Abstract

Introduction: Axillary block is a regional anesthesia for surgeries at and below the elbow. Complications associated with peripheral blocks using blind approaches are addressed with advent of ultrasound guidance. Hyaluronidase drug works as a spreading factor. Combination of ultrasound guidance and hyaluronidase in addition to local anesthetics in peripheral blocks will increase efficacy and reduce complications.

Objective: To compare the efficacy of 0.5% Levobupivacaine with a combination of 0.5% Levobupivacaine and hyaluronidase in USG guided axillary brachial plexus block for forearm and hand surgeries with respect to: Onset of sensory and motor block, duration of sensory block and time to rescue analgesia.

Methods: A prospective study was conducted on sixty adult patients aged 18-60 years belonging to ASA PS 1 and 2 scheduled to undergo elective upper limb below elbow orthopedic procedures. Thirty patients each in Group A and B received 20 ml of 0.5% Levobupivacaine along with 300 units of hyaluronidase and 20 ml of 0.5% levobupivacaine only respectively. Sensory and motor block onset, sensory block duration and rescue analgesia

were compared. Data were analyzed using SPSS 16.0V software. $P < 0.05$ was considered statistically significant.

Results: The sensory and motor block onset was shorter in the Group A - 10.10 minutes vs Group B 13.33 minutes; and Group A 11.73 minutes vs 14.23 minutes; respectively. Duration of sensory block was shorter in Group A compared to Group B (468 minutes vs 648 minutes). Time to rescue analgesia was also significantly reduced in Group A-594 minutes vs Group B- 732 minutes.

Conclusion: In axillary block using 20 ml of 0.5% Levobupivacaine, addition of 300 units of hyaluronidase, reduces onset of sensory and motor block time, reduces the duration of sensory block and time to rescue analgesia.

Keywords: Axillary brachial plexus block; Hyaluronidase; Levobupivacaine; sensory block; motor block.

Introduction

The popularity of peripheral nerve blocks grew because it decreases pain postoperatively, reduces incidence of nausea, decreases need for post operative analgesics, shortens post anesthesia care time, and most importantly increases patient satisfaction.^(1,2,3) Multimodal perioperative care pathways designed for enhanced recovery achieve early recovery after surgical procedures

by maintaining preoperative organ function and reducing the stress response following surgery. One key component of such enhanced recovery protocols is standardized analgesic and anesthetic regimens. Peripheral nerve blocks in particular help in enhanced recovery of the patient by the possibility of early mobilization of the patient.^(2,3,4) Early in the history of anesthesia, peripheral nerve block techniques were developed. The American surgeons Halsted and Hall described the injection of cocaine into peripheral sites for minor surgical procedures in 1884.⁽⁵⁾ Axillary block was first described by Hirschel in 1911⁽⁶⁾, but it gained popularity only after Burnham's publication in 1959⁽⁷⁾. With years of modification and development, the technique and concept of axillary block has improved. Brachial plexus (C5-T1) blockade will allow for surgical anesthesia of the upper extremity and shoulder. The Brachial plexus can be blocked at various levels from the roots to the terminal branches – Interscalene block, Supraclavicular block, Infraclavicular block, Axillary block and peripheral blocks at the Midhumeral level, elbow and wrist.⁽⁸⁾ Axillary brachial plexus block is popular because of its ease, reliability, and safety.⁽⁹⁾ Nerves blocked are the terminal nerves. Indications for axillary block include surgery at and below elbow; forearm and hand.⁽¹⁰⁾ Ultrasound imaging allows direct visualization of peripheral nerves, the block needle tip, and local anesthetic distribution. This imaging modality is highly useful for guiding targeted drug injections and catheter placement.⁽¹¹⁾ The improved accuracy of 2 needle placement using ultrasound reduces the risk of complications and their costs associated with these procedures.⁽¹²⁾ Local Anesthetics are drugs that prevent conduction of electrical impulses on the membranes of nerve and muscle.⁽¹³⁾ They are classified into – Aminoesters and Aminoamides. Levobupivacaine is

an aminoamide local anesthetic. Adjutants are pharmacological drugs that when co-administered with local anesthetic agents may improve speed of onset as well as the quality and duration of analgesia. Various additives can be added to local anesthetic for enhancing the peripheral nerve block⁽¹⁴⁾ like Epinephrine, Clonidine, Dexmedetomidine, Buprenorphine, Dexamethasone, Tramadol, Sodium bicarbonate and hyaluronidase. Hyaluronidase is widely used in ophthalmologic nerve blocks for better spread of the drug. It depolymerizes the mucopolysaccharide hyaluronic acid, a component of the mucoprotein substance or tissue cement. Hyaluronidase thereby renders the tissues more readily permeable to injected fluids (spreading effect) by increasing tissue membrane permeability and reducing the viscosity.⁽¹⁵⁾ The outcome is significantly improved for most techniques in peripheral regional anaesthesia when direct ultrasonographic visualization is used. With the help of ultrasonography, the anaesthetist can directly visualize relevant nerve structures for all nerve blocks at all levels. Such direct visualization improves the quality of nerve blocks and avoids complications.⁽¹⁶⁾

Objectives

To compare the efficacy of 0.5% Levobupivacaine with a combination of 0.5% Levobupivacaine and hyaluronidase in USG guided axillary brachial plexus block for forearm and hand surgeries with respect to onset of sensory block, onset of motor block, duration of sensory block and time to rescue analgesia.

Materials and Methods

An observational prospective study was carried out among 60 adult patients in the age group of 18-60 years belonging to ASA PS 1 and 2 scheduled to undergo elective upper limb orthopedic procedures in the orthopedic theatre of Dr. Somervell Memorial CSI

Medical College Hospital, Karakonam, Trivandrum after obtaining institutional approval, from January 2016 to October 2017. All the patients were assessed and those with normal clinical, hematological, biochemical and radiological parameters were selected. Informed written consent was obtained from all the patients and they were alternately assigned to two groups Group A and Group B each containing 30 patients.

GROUP A – Patients undergoing Ultrasound guided Axillary Brachial plexus block with 20 ml of 0.5% Levobupivacaine and Hyaluronidase 300 Units (15U/ml of local anesthetic)

GROUP B – Patients undergoing Ultrasound guided Axillary Brachial plexus block with 20 ml of 0.5% Levobupivacaine.

American Society of Anesthesiology Physical status Class 1 (A normal healthy patient) and Class 2 (A patient with mild systemic illness and weight 40 to 80kg alone were included in the study. Any patient with history of bleeding disorders, documented neuromuscular disorders, known allergy to Local anesthetics drugs, Psychiatric patients and if on anticoagulants were excluded from the study. Considering the mean sensory block onset time as around 13.8 minutes in the treatment group⁽¹⁷⁾ and expecting a difference of 5 to 6 minutes from the control group, using a standard error of 6 the required sample size was calculated to be 30 in each group.

Patients were assessed preoperatively and the procedure was explained to the patients. Written informed consent was obtained. Assessment of pain using Pin Prick intra operatively and VAS-Visual analogue score post operatively was explained to the patients preoperatively. All Patients were given 1mg Midazolam intravenous as premedication. On arrival of the patient in the operating room, monitors were connected and baseline vital signs

were recorded. Monitors included Pulse oximetry, Non invasive blood pressure and Electrocardiogram. An intravenous access was obtained in the opposite arm under local anesthesia. The patients were given Ultrasound guided Axillary brachial plexus block as described: The patient was made to lie supine with a small pillow below head and the upper limb to be blocked kept with the arm abducted to 90° and the elbow flexed. The anaesthetist who prepared the drug combination did not participate in the monitoring or assessment of the patient. The person assessing the axillary block as well as monitoring was blinded to the groups the patients belongs. The USG probe is cleaned and covered in a sterile cover and the patient's skin is prepared with povidone iodine and draped with sterile towel. The probe is placed perpendicular to the axis of the arm at the point where the pectoralis major muscle inserts onto the humerus and adjusted to visualize the brachial plexus around the axillary artery and 2% lignocaine solution was injected to the skin at the needle entry point. The 'IN PLANE' ultrasound technique was used^(18,19) A 50mm needle was inserted 1-2 cm away from the centre of the probe. Needle angle was maintained at 0-45 degrees to the skin. Needle was initially inserted in the superficial plane until the needle was visualized on the scan. The radial nerve is identified posterior to the artery and 5ml of the drug was injected. Similarly the median, ulnar and musculocutaneous nerves were identified and 5 ml was injected around each nerve. Immediately after injection has been stopped; the needle was withdrawn and the arm was kept adducted with the hand resting on the chest.

The following parameters were observed following the block.

Hemodynamic parameters like pulse rate, non invasive blood pressure, oxygen saturation were monitored. Mean

arterial blood pressure (MAP) and pulse rate (PR), oxygen saturation were recorded before application of the block as well as immediately after block & 3 min intervals until the end of the operation. Any drop in blood pressure more than 20% from the baseline signifies hypotension and was managed with Inj ephedrine 6 mg. Any decrease in pulse rate of less than 60 beats /min was managed with Inj. Atropine 0.6mg. Sensory block was tested with a 22-gauge hypodermic needle by using the pinprick test and compared with the same stimulation in the contralateral hand. Sensory block was evaluated by the pinprick method in the nerve distribution of the radial nerve (dorsum of thumb), ulnar nerve (palmar aspect of fifth finger), median nerve (palm of the hand) and musculocutaneous nerve (lateral aspect of forearm). A three-point scoring system was used: 2=normal sensation; 1=impaired sensation; 0=loss of sensation. Onset of Sensory Block⁽²⁰⁾ was defined as the time between the end of last injection and the total pinprick response score of 0 over hand and forearm. Motor block was assessed in the nerve distribution of the radial nerve (wrist extension), ulnar nerve (adduction of fourth and fifth finger), median nerve (flexion of the distal phalangeal joint on the second finger) and musculocutaneous nerve (flexion of the elbow), with the following scoring: 2=normal motor function; 1=impaired motor function; 0=no motor function. Onset of motor blockade⁽²⁰⁾ was defined as the time taken from the injection of drug to development of total block score of 0.37. Duration of sensorial block (minute) was recorded as Time interval between withdrawal of the needle and reappearance of paresthesia in the 4 nerve distribution areas. First analgesic requirement time (minute) ie, Rescue analgesia is defined as the time interval between block placement and patient's first analgesic request. Postoperatively pain scores were

recorded by using visual analogue score⁽²¹⁾ between 0 to 10(0=no pain,10= most severe pain).Rescue analgesia was given at VAS score of 4 or above.

Observation and Results

The following observations were made and data were collected using a structured questionnaire Sex, Age, Weight, Height, ASA physical status, Pulse rate, blood pressure, Oxygen saturation at 5 min intervals until 30 min, then at 1 hour, thereafter every hour till 12 hours were documented along with onset time of sensory block, onset time of motor block, duration of sensory blockade, duration of analgesia and any untoward side effects. Data were analyzed using SPSS16.0V software. Means were calculated for descriptive analysis. Two sided independent students t test was used to analyze continuous data and chi square test for categorical data. P value <0.05 was considered as statistically significant.

Demographic Data

The mean age of the participants in group A was 44.9 ± 13.6 and in group B was 43.4 ± 16.2 . The mean height in group A and B were 164.8 ± 8.7 cms and 164.5 ± 8.5 cms respectively. The mean weight in group A was 66.8 ± 6.0 Kg and in group B was 64.8 ± 6.7 Kg. 83.3% of participants in both the groups were in ASA PS grade 1. The two groups were comparable with respect to their age, height, weight, sex, and ASA physical status. There was no statistically significant difference among two groups in demographic profile. (Tables 1-5) Almost 50% of the diagnosis in study participants was fracture DER right or left (Table 6) 50% of the surgeries carried out in both groups were CMR pinning followed by other common surgeries like Implant removal and Radial head excision (Table 7).

The mean intra operative oxygen saturation was 99 ± 0.0046 for group A and 99 ± 0.0026 for Group B. This

difference observed was not statistically significant. Similarly the mean post operative oxygen saturation was also was comparable between two groups. (Table 8). The mean pulse rate in group A was 81.87 ± 1.737 and in group B was 81.43 ± 1.775 (Table 9). The mean arterial pressure in group A was 105.03 ± 2.748 (mmHg) and in group B was 105.07 ± 2.703 (mm/Hg) (Table 10). The differences observed in the mean pulse rate and the mean arterial pressure between both groups was not statistically found to be significant.

The mean onset of sensory block in group A was 10.10 ± 0.9 minutes and group B was 13.33 ± 0.9 minutes. The difference observed in the mean onset of sensory block between both groups was found to be statistically very highly significant $p < 0.001$. (Fig:1) The mean onset of motor block in group A was 11.73 ± 1.66 minutes and in group B was 14.23 ± 1.45 minutes. The difference observed in the mean onset of motor blocks between both

groups was found to be statistically very highly significant $p < 0.001$. (Fig:2) The mean duration of sensory block in group A was 7.8 ± 1.0 hours and in group B was 10.8 ± 2.0 hours, thus we see that there was a reduction in the duration of sensory block in patients with both levobupivacaine and hyaluronidase compared to those patients blocked with levobupivacaine alone and this difference observed was found to be statistically very highly significant. P value < 0.001 (Fig:3). The mean time to rescue analgesia in group A was 9.9 ± 1.3 hours and in group B was 12.2 ± 2.0 hours. It is observed that patients with Ultrasound guided Axillary Brachial plexus block using levobupivacaine and hyaluronidase had a lesser mean time to rescue analgesia compared to the patients with Ultrasound guided Axillary Brachial plexus block using levobupivacaine alone. This difference observed was also found to be statistically very highly significant $P < 0.001$ (Fig:4).

Table 1 :- Comparison of sex between Group A and Group B

Sex	Group A (Levobupivacaine and hyaluronidase)		Group B (Levobupivacaine)		χ^2	P
	Count	Percent	Count	Percent		
Male	15	50.0	13	43.3	0.27	0.605
Female	15	50.0	17	56.7		

Table 2 :- Comparison of age between Group A and Group B

Age	Group A (Levobupivacaine and hyaluronidase)		Group B (Levobupivacaine)	
	Count	Percent	Count	Percent
18-20	0	0.0	2	6.7
20 – 29	6	20.0	7	23.3
30 – 39	5	16.7	4	13.3

40 – 49	5	16.7	1	3.3
50 – 59	9	30.0	9	30.0
>=60	5	16.7	7	23.3
Mean ± SD	44.9 ± 13.6		43.4 ± 16.2	

Table 3 :- Comparison of height between Group A and Group B

Group	Mean Height (cm)	SD	N	t value	P
Group A (Levobupivacaine and hyaluronidase)	164.8	8.7	30	1.04	0.303
Group B (Levobupivacaine)	162.5	8.5	30		

Table 4 :- Comparison of weight between Group A and Group B

Group	Mean weight(Kg)	SD	N	t value	P
Group A (Levobupivacaine and hyaluronidase)	66.8	6.0	30	1.22	0.227
Group B (Levobupivacaine)	64.8	6.7	30		

Table 5 :- Comparison of ASA PS between Group A and Group B

ASA PS	Levobupivacaine and hyaluronidase		Levobupivacaine		χ^2	P
	Count	Percent	Count	Percent		
Grade I	25	83.3	25	83.3	0	1.000
Grade II	5	16.7	5	16.7		

Table 6 :- Comparison of diagnosis between Group A and Group B

Diagnosis	Levobupivacaine and hyaluronidase		Levobupivacaine	
	Count	Percent	Count	Percent
Fracture DER Left	7	23.3	4	13.3
Fracture DER Right	8	26.7	10	33.3
Malunited Fracture DER Left	1	3.3	0	0.0
Fracture DER Left	1	3.3	0	0.0

Fracture BB forearm left	0	0.0	3	10.0
Fracture BB forearm Right	0	0.0	1	3.3
United BB fracture left	0	0.0	2	6.7
United BB fracture right	0	0.0	1	3.3
Fracture BB forearm	6	20.0	0	0.0
United fracture BB forearm	5	16.7	0	0.0
Implant in situ left forearm	0	0.0	1	3.3
Implant in situ right radius	0	0.0	2	6.7
Fracture shaft of radius	1	3.3	1	3.3
Right forearm DCP Implant	0	0.0	1	3.3
Radial head fracture Right	0	0.0	1	3.3
Infected plate Left forearm	0	0.0	1	3.3
Ganglion wrist Right	0	0.0	1	3.3
Fracture R Little finger DIP	1	3.3	0	0.0
Fracture 5th finger	0	0.0	1	3.3

Table 7 :- Comparison of surgery between Group A and Group B

Surgery	Levobupivacaine and hyaluronidase		Levobupivacaine	
	Count	Percent	Count	Percent
CMR Pinning	15	50.0	15	50.0
Implant Removal	5	16.7	8	26.7
Closed IM nailing	2	6.7	0	0.0
Radial head excision	6	20.0	6	20.0
Osteotomy and pinning	1	3.3	0	0.0
K-Wire fix	1	3.3	0	0.0
Excision	0	0.0	1	3.3

Table 8 :- Comparison of Oxygen saturation between Group A and Group B.

Intraoperative	No of cases	Mean ±S.D(%)	P value
Group A	30	99±0.0046	
Group B	30	99±0.0026	
Postoperative	No of cases	Mean±S.D	

Group A	30	100±0.001	0.9602
Group B	30	99±0.00111	

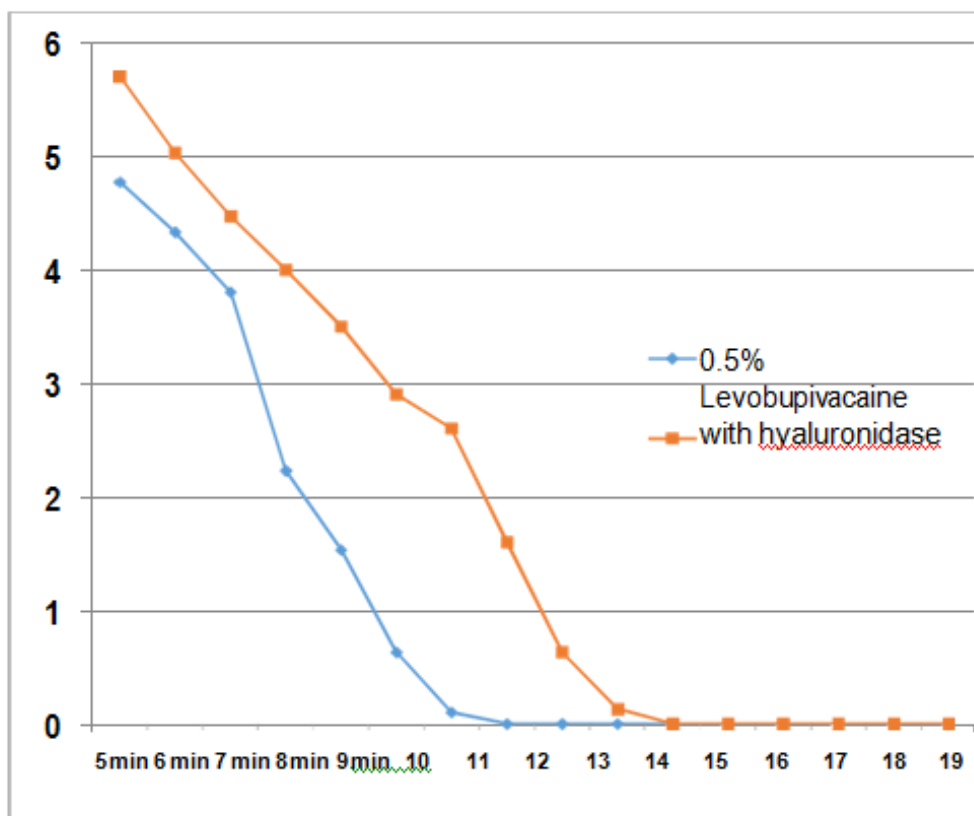
Table 9 :- Comparison of pulse between Group A and Group B

	Mean(min)	S.D	P value
Group A	81.87	1.737	0.343
Group B	81.43	1.775	

Table 10 :- Comparison of Mean arterial pressure between Group A and Group B

	Mean(mm/Hg)	S.D	P value
Group A	105.3	2.748	0.962
Group B	105.07	2.703	

Figure 1. – Comparison of onset of sensory block between Group A and Group B



t=12.59, p<0.001

Figure 2. – Comparison of onset of motor block between Group A and Group B

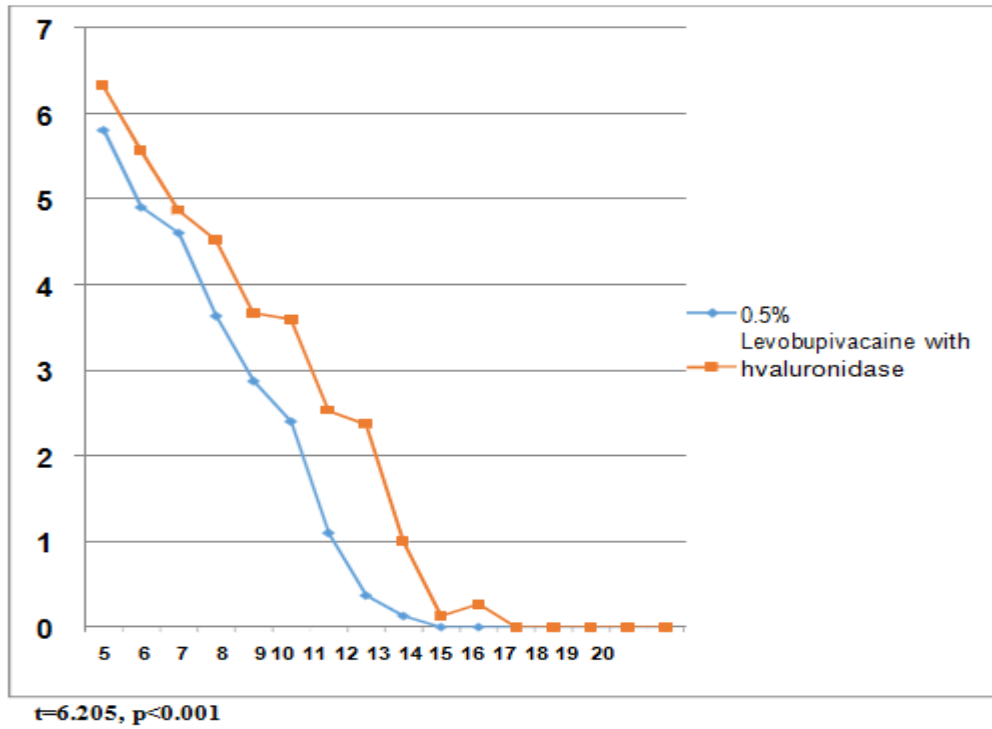


Figure 3. Comparison of duration of sensory block between Group A and Group B

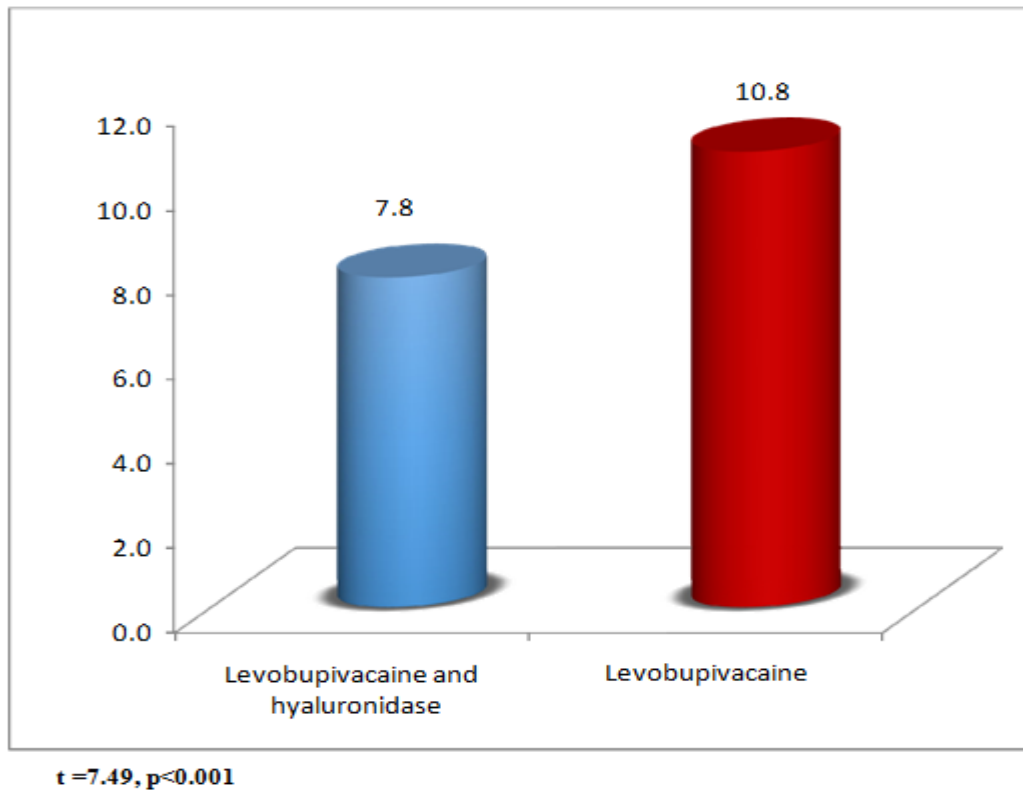
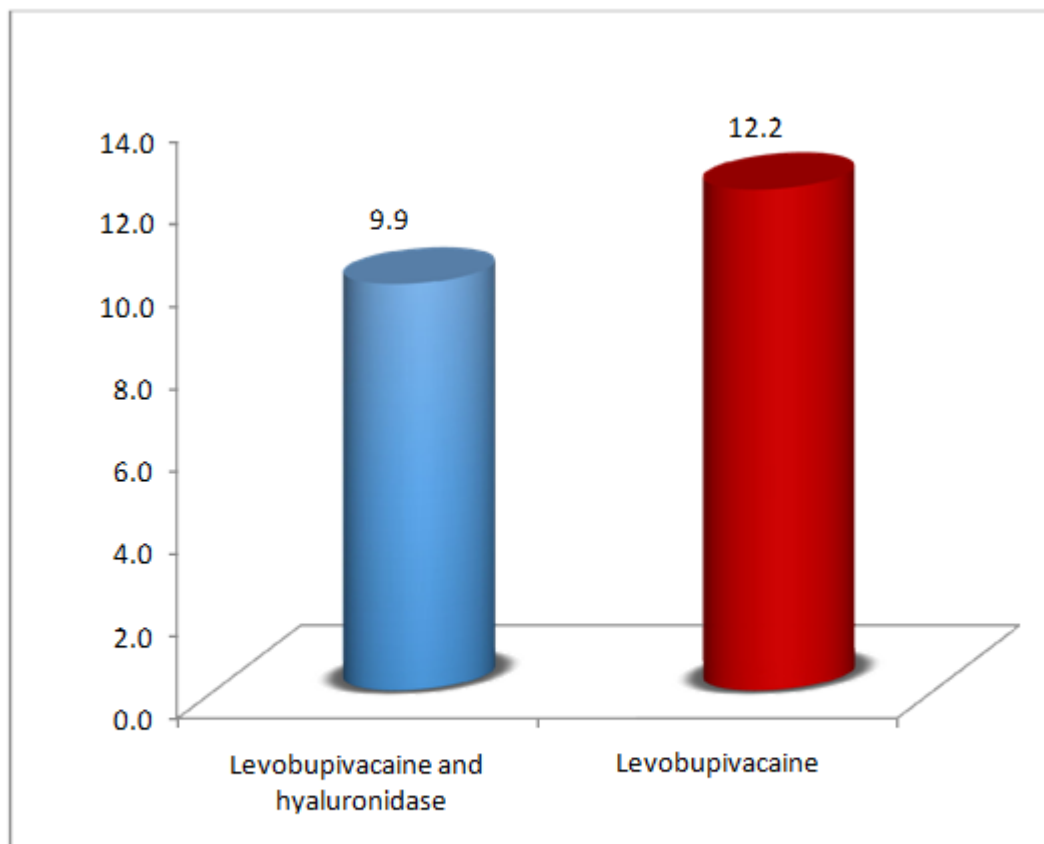


Figure 4. Comparison of time of rescue analgesia between Group A and Group B



$t=5.4, p<0.001$

Discussion

The hypothesis of this study was addition of hyaluronidase (15U/ml) to 0.5% levobupivacaine in axillary brachial plexus block under ultrasound guidance, reduces the onset time of sensory and motor block. In my present study, addition of 300 units of hyaluronidase to 20ml of 0.5% levobupivacaine has resulted in faster onset of sensory and motor block, thus reducing the anesthetic time prior to surgery. The study also demonstrated a reduction in duration of sensory block and earlier use of rescue analgesia in the hyaluronidase group, which was statistically significant. The earlier onset of block is advantageous in places where the number of surgeries being performed is more and thus the reduction in time

between surgeries, including the anesthetic time, is valuable. It is also useful in places where a separate setup for performing peripheral nerve blocks is not available and the block procedure and wait time occurs within the operating room. The spreading factor of hyaluronidase helps in the faster onset of the block. In this study, ultrasound guidance which increases the precision of better needle placement further augmented the rapidity of onset. In ophthalmology it is widely used to cause spread of the drug, thus helping in minimizing total drug volume. Sarvela et al (1992)(18) demonstrated that addition of hyaluronidase to local anesthetics helps reduce the total volume of drug required for the block. WU Koh et al (2015)(17) in their study used hyaluronidase 100

units/ml of local anesthetic. But in this study, only 15 units/ml of local anesthetic was used which was in accordance with the BNF (10- 15units/ml of drug) and the FDA (50-300 units). The total drug volume was standardized to 20 ml of 0.5% levobupivacaine for all patients. The maximum dose of levobupivacaine for peripheral nerve blocks is 150 mg.(19) So the volume used in this study is within the reference range. Adjuvants are used along with local anaesthetics to improve the quality of block. An ideal adjuvant should provide a faster onset, longer duration of analgesia and better hemodynamic stability. Hyaluronidase has no effect on the hemodynamic, unlike other agents (adrenaline, dexmedetomidine, clonidine). It has a good safety profile. No significant hemodynamic changes were noted between both the groups in this study preoperatively, intra operatively and postoperatively. The patients in both groups of this study did not show any statistically significant difference with respect to age, sex, height, weight and ASA physical status.

Onset of sensory and motor block

This study has shown that addition of 300 units of hyaluronidase to 20 ml of 0.5% levobupivacaine in group A reduced the onset time for sensory block when compared to 0.5% levobupivacaine in the group B. In group A the onset of sensory block was 10.10 ± 0.9 minutes which was shorter than group B which was 13.33 ± 0.9 minutes. This result was concurrent with Koh WU (2015)(17) where they concluded sensory block onset times were shorter in the group that was given hyaluronidase with local anesthetic (13.8 minutes) than in group that was given local anesthetic alone (22.5 minutes). Our study is different from this study in the aspect of block technique. We used an Ultrasound guided approach which has further reduced the onset time in both

the groups. This is in correlation to Chan et al (2007) (20) study which clearly depicts the advantages of ultrasound in the success of peripheral nerve blocks.

Onset of motor block

This study has shown that group A had reduced onset time for motor block when compared to group B. In group A the onset of motor block was 11.73 ± 1.66 minutes, which was shorter than group B which was 14.23 ± 1.45 minutes. This is also in correlation to Koh WU (2015)⁽¹⁷⁾ where the time to achieve surgical anesthesia was reduced in the group that used hyaluronidase.

Sensory block duration and Time to Rescue analgesia

Current study has shown Group A had reduced duration of sensory block when compared to Group B. In group A the duration of sensory block was 468 ± 60 minutes compared to group B which was 648 ± 120 minutes. This is similar to what was suggested in Koh WU (2015) study(17). In their study also there was reduction in sensory block duration time. In the hyaluronidase group the duration was 610 minutes and in the control group it was 759 minutes. There was a more significant reduction in sensory block in this study. There are multiple studies (21) that suggest the addition of hyaluronidase causes reduction in sensory block duration.

Corresponding to the reduction in duration of sensory block, this study has shown that Group A patients received rescue analgesia earlier when compared to Group B patients. In group A the time to rescue analgesia was 594 ± 78 minutes compared to group B which was 732 ± 120 minutes.

Hemodynamic Stability

The Pulse, Mean arterial pressure and oxygen saturation remained stable both during intraoperative and postoperative period. The blood pressure never decreased

below 20% of baseline values. No significant hypotension and bradycardia were observed.

Side -Effects

Side effects like bradycardia, hypotension, hypoxemia, nausea, vomiting, features of local anesthetic toxicity and any other side effects were not seen in any patients.

Conclusion

In ultrasound guided axillary brachial plexus block using 0.5% levobupivacaine, addition of 15 units of hyaluronidase per milliliter of levobupivacaine (300 units in 20 ml) reduces onset of sensory and motor block time therefore shortens the total anaesthetic time before the operation. It also reduces the duration of post operative sensory block time and time to requirement of rescue analgesia.

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