Research Article

The combination of Hyaluronidase and Magnesium Sulphate as Adjuvants to Bupivacaine in Ultrasound Guided Supraclavicular Brachial Plexus Block in Upper Limb Surgeries.

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Abstract
Background: The aim of this trial was to assess the effect of hyaluronidase and MgSo4 when added in combination to bupivacaine on the onset of sensory and motor block, quality of block and effect on duration of action. **Methods:** Fourty ASA I, II patients of either sex undergoing upper limb Surgery under ultrasound-guided supraclavicular brachial block were recruited in this in this prospective randomized double blinded controlled study and bottles numbered from 1 to 40 were prepared and divided in to two groups each group containe 20 bottles. The solutions in these bottles contain 30 ml volume. The first group contains a mixture of (28 ml 0.5% bupivacaine and 2 ml 0.9% normal saline). The second group contains a (mixture of 28 ml 0.5%bupivacaine and 2 ml of MgSo4 containing 200 mg mixed with 1000 unit hyaluronidase). **Results:** The onset of sensory and motor block was faster in group (II) than patients in group (I). Also the duration of sensory and motor block was found to be longer in group (II) than in group (I). **Conclusions:** Our study demonstrates that the combination of hyaluronidase and MgSo4 with bupivacaine for supraclavicular block decrease the onset for surgical anesthesia and increase the duration of sensory block thus it decrease analgesic requirments without significant complications.
Keywords: Anesthetic techniques, regional, brachial plexus; anaesthetics local, bupivacaine; equipment, ultrasound machines; hyaluronidase; MgSo4.

Introduction
Supraclavicular nerve block is ideal for procedures of the upper arm, from the mid humeral level down to the hand. . It has a rapid onset, with a dense and predictable level of pain control [1].

Hyaluronidase, the mucolytic enzyme which acts on the muco-polysaccharide hyalonic acid, is generally concedered to be "spreading factor". When used with local anesthetics, hyaluronidase hastens the onset of analgesia and shortens its duration of effect[2].

Magnesium sulphate can act as an adjuvant in analgesia due to its properties of calcium channel blocking and N-methyl-D-aspartate antagonism. Magnesium has been shown to decrease peripheral nerve excitability and to enhance the ability of lidocaine to raise the excitation threshold of A-beta fibers[3].

Ultrasound guidance has dramatically improved nerve localization and offers several advantages as direct visualization of nerves and anatomical structures (blood vessels) to facilitate nerve identification, increase accuracy of needle placement, facilitated visualization of local anaesthetic spread in real time and reduced incidence of complications[4].

Methods
This prospective, randomized, double blind controlled clinical study was carried out after obtaining the local ethics committee of El-Minia university hospital approval and written informed consent was taken from the patients.

It was done between September 2017 to December 2018, 90 patients of both sexes, ASA I and II, aged between 18-65 years old scheduled to undergo elective and urgent

distal arm, forearm and hand surgeries under ultrasound guided supraclavicular brachial plexus block, 40 patients were enrolled in this study and five were excluded due to block failure.

Preoperative assessment: A careful assessment of medical history was done. Routine preoperative general examination in and local examination of the site of injection for signs of infection or any other pathology were carried out. Routine investigations were done. Explanation of visual analogue pain scale was done VAPS is consisted of a straight, vertical 10-cm line; the bottom point represented "no pain"= (0 cm) and the top "the worst pain you could ever have. Two mg midazolam IV was given as a premedication 5 minutes before the block.

Equipments: The ultrasound device Sono-site, micromaxx, Lubricating gel, 21-gauge 50 mm length short bevel insulated stimulating needle, 10-ml syringes for injection, Sterile gloves, 25-gauge needle for skin infiltration, Sterile towels and sterile "4x4" gauze packs and antiseptic solution (Povidone-iodine 10%).

Preparation of the studied medications: All medications were prepared in similar sterile coated bottles and coded then passed to the anesthesiologist who is blind to its manner. In this prospective randomized double blinded controlled study 40 bottles numbered from 1 to 40 were prepared and divided in to two groups each group containe 20 bottles. Then the patients were randomly assigned to study groups.
Group (I): Received 28 ml bupivacaine (0.5%) + 2 ml saline (0.9%).

Group (II): Received 28 ml bupivacaine (0.5%) + 2 ml MgSo4 containing 200 mg mixed with 1000 unit hyaluronidase.

Block technique: On patient arrival to the operating room, a 20 G intravenous cannula was inserted in a peripheral vein of unaffected upper limb and standard monitoring was provided in the form of Noninvasive blood pressure (NIBP), Electrocardiography (ECG), and Oxygen saturation (Spo2). Also general anesthesia and resuscitation drugs were prepared.

Patient lie down supine with head turned to the contralateral side and ipsilateral arm adducted gently by the assistant and the shoulder kept down with flexed elbow. Skin was sterilized and infiltrated with 1-2 ml of lidocaine 2% at the needle entry site.

The brachial plexus was visualized by placing ultrasound probe in the sagittal plane in the supraclavicular fossa behind the middle-third of the clavicle. It either appeared as 3 hypoechoic circles with hyperechoic outer rings or as a grape like cluster of 5 to 6 hypoechoic circles, lateral and superior to the subclavian artery between the anterior and middle scalene muscles at the lower cervical region.

Initially, the needle was placed deep to the more caudal elements of the plexus so that the brachial plexus rises closer to the skin surface with the injection of the local anesthetic. Distension of the brachial plexus sheath was regarded as an indication of correct needle placement. The multiple injection technique was used to deposit the total amount of drug.

Before injecting the drug solution, saline boluses of 0.5 mL were injected to verify the correct position of the needle. A 3-min massage was performed to facilitate an even drug distribution.

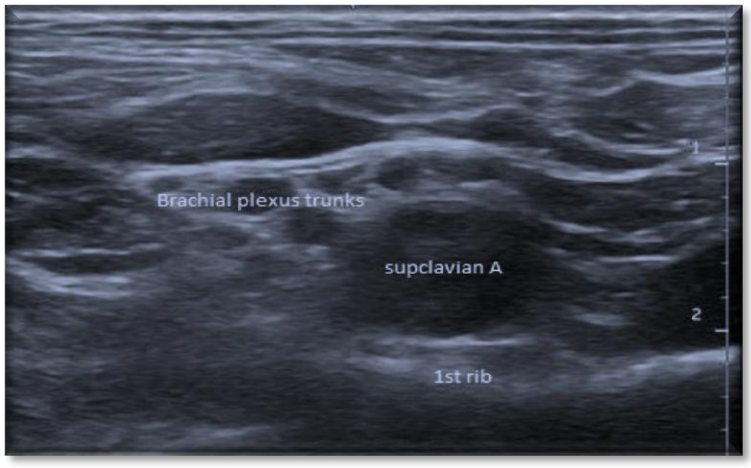

Fig (1): Ultrasonographic imaging of brachial plexus .

Parameters assessed:
The anesthesiologist who gave the block recorded the onset of sensory and motor block and recorded intraoperative data then the postoperative care physician recorded the duration of block and postoperative data.

The hemodynamic variables as Heart rate (beats/min), mean arterial blood pressure (mmHg) and peripheral arterial oxygen saturation (%) were assessed and recorded 5 minutes before the block as a baseline value, immediately after the block 0,10,20,30,60, 90 minutes during the operative time then 1,2,4,6, and 12 hours after the end of operation. Quality of sensory block was assessed by pin prick test using a 3-point scale **[5]** Grade 0 = normal sensation, Grade 1 = loss of sensation of pin prick (analgesia), and Grade 2 = loss of sensation of touch (anesthesia).

Also motor block quality 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 1997 **[6]** on a 3-point scale.
Grade 0: Normal motor function with full flexion and extension of elbow, wrist, and fingers.
Grade 1: Decreased motor strength with ability to move the fingers only.
Grade 2: Complete motor block with inability to move the fingers.

Onset time for sensory block was defined as the time interval between the end of local anesthetic administration and complete sensory block by min. Duration of sensory block was defined as the time interval between the complete sensory block and complete resolution of anesthesia on all the nerves distribtion. Onset time for motor block was defined as the time interval between total local anesthetic administration and complete motor block (grade 2) by min. 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) by hours. Pain intensity was assessed using **VAPS**. Patients were asked to make a horizontal mark across the line at the place that indicated the amount of their pain sensation. It was measured before starting the nerve block then 15, 30, 60, 90, 120 minutes after nerve block. When it is more or equals 4 cm we gave analgesia or sedation using fentanyl and propofol during operation. Then Patients were asked to rate their pain intensity at 2, 4, 8, 12, and 24 hours postoperative and if it was more than 4 paracetamol 1 gm was given. Time of first analgesic request: The time from supraclavicular brachial plexus block administration to the patient's first request for analgesic medication by hours. Total analgesic requirments in 24 hours:

The total amount of intravenous paracetamol which was given to the patient as a rescue analgesia or maintenance during 24

hours. Adverse effects: any adverse effects such as hypotension (i.e. 20% decrease relative to baseline), bradycardia (HR <50 beats/min), nausea, vomiting, hypoxemia (SpO2 <90%), local hematoma, hemothorax, pneumothorax, recurrent laryngeal nerve block ,intravascular injection, Horner's syndrome and signs of local anesthetic toxicity were recorded during the operation and for 24 hours postoperative.

Results

During studying hemodynamic data changes among groups we found that the Mean Arterial blood pressure (mmHg.) and arterial oxygen saturation during intraoperative or postoperative period we found no statistically significant changes between the four groups. As regard the Heart rate (beat\min) we found it was lower in group (II) than group (I) at time intervals of 10,20,30 and 60 minutes intraoperative but these changes were statistically un significant. Also the onset of sensory and motor block was faster in patients in group (II) than patients in groups (I) but the duration of sensory and motor block was found to be longer in patients in group (II) than in group (I).

As regard pain measurement presented in table (1) by VASP during intraoperative period at 15 min post injection the pain score was significantly lower in patients in groups (II) than in group (I) but no significant difference was found after that during operation. In the postoperative period the VASP was significantly lower at 4, 8, 12, 24 hours in patients in groups (II) than in groups (I).

Intraoperative need for sedation and fentanyl was insignificantly different between the four groups. Also the table shows the mean time of 1st analgesic (minutes) request which was significantly longer in group (II) (540-950) minutes in comparison to group (I) (300-620) minute. And total analgesic requirement (mg) in group (II) was less than groups (I).

Surgeon satisfaction was recorded and we found no significant difference between four groups. Also patient satisfaction as regard quality and duration of block was recorded and we found high satisfaction in group (II) and less satisfaction observed in group (I).

As regard complications tachycardia was observed in 5 patients in group (I, 2 patients in group (II) treated by assurance, analgesia and anxiolytic dose of midazolam 1-2 mg. Hypotension was observed in 1 patient in group (I).Local hematoma needed only compression watched in 2 patients in group (I), 2 patients in group (II).

As regard inadvertent intravascular injection, neurological manifestations of toxicity, hemothorax, pneumothorax, nausea, vomiting, dysesthesia and neuropraxia we didn’t record any case.

Table (1): Changes in the of VAPS .Data are presented as median and Inter-Quartile Range.

VAS	Group I N=20	Group II N=20
Immediate after injection		
Median	3	3
IQR	(0.5-4)	(2-4)
intraoperative		
15 min	#	#
Median	0	0
IQR	(0-2)	(0-0)
30 min	#	#
Median	0	0
IQR	(0-1)	(0-0)
60 min	#	#
Median	0	0
IQR	(0-0.8)	(0-0)
120 min	#	#
Median	0	0
IQR	(0-2)	(0-0)
postoperative		
2 hours	#	#
Median	0	0
IQR	(0-0.8)	(0-0)
4 hours		#
Median	3	0
IQR	(2-3)	(0-0)
8 hours	#	#
Median	5	0
IQR	(4-6)	(0-2)
12 hours	#	
Median	7	3
IQR	(6-7)	(2.3-5)
24 hours	#	#
Median	7	5
IQR	(7-7.8)	(5-6)

Discussion

Brachial plexus block is a safe reliable anesthetic technique for upper limb surgery with fewer complications, especially with the introduction of ultrasound which decreased the complications dramatically.

Hyaluronidase, the mucolytic enzyme which acts on the muco-polysaccharide hyalonic acid, is generally concedered to be "spreading factor". When used with local anesthetics, hyaluronidase hastens the onset of analgesia and shortens its duration of effect[7].

In a study done by Koh et al., investigated the hypothesis that addition of hyaluro-nidase to ropivacaine may reduce the time to achieve complete sensory block after axillary brachial plexus block. The patients

were randomly assigned into a hyaluronidase group (n = 24) and a control group (n = 24). The hyaluronidase group received ropivacaine 0.5% with 100 IU.ml_1 of hyaluronidase, and the control group received ropivacaine alone. The primary endpoint was the time to achieve complete sensory block. The hyaluronidase group demonstrated significantly shorter mean (SD) sensory block onset time (13.8 (6.0) min) compared with the control group (22.5 (6.3) min), p < 0.0001). Addition of hyaluronidase to ropivacaine resulted in a reduction in the time needed to achieve complete sensory block[8].

However, the study performed pinprick tests only twice, at 15 and 30 min after the block placement, so the exact time of complete sensory block was not measured. Furthermore, the block was conducted via the landmark-guided technique without the use of a nerve stimulator or ultrasound guidance, which may have led to the relatively lower block success rate for radial nerve compared with that in our study.

Mgso4 can act as an adjuvant in analgesia due to its properties of calcium channel blocking and N-methyl-D-aspartate antagonism. Magnesium has been shown to decrease peripheral nerve excitability and to enhance the ability of lidocaine to raise the excitation threshold of A-beta fibers[9].

Haghighi et al., in Guilan, Iran, in 2014, investigated the effect of Mgso4 in axillary brachial plexus block when added to lidocaine in upper limb surgeries, and reported that the addition of Mgso4to lidocaine significantly increased the duration of sensory and motor blocks in comparison with the use of lidocaine alone[10].

Rao et al., found that The addition of MgSo4 to 0.5% bupivacaine increased the duration of motor and sensory supraclavicular brachial block in the upper extremities during surgeries when compared to the use of 0.5% bupivacaine alone, The mean sensory block duration in the group MgsSo4 was 249±9.36 and in control Group was (160±5.62) (p<0.39). The mean motor block duration in the group MgsSo4 was (232±9.64) and in control group was (147±26.52) (both p<0.32). The mean onset of sensory block in group MgsSo4 was (15.5±2.16) and the onset of block in control group was (12.73±1.18) (p<0.4) statistically not significant). Also the mean onset of motor block in group Mgso4 was (23.5±1.1) and the onset block in control Group P was 41±3 (p<0.53; statistically not significant)[11].

In our study is the addition of both MgSo4 and hyaluronidase to bupivacaine 0.5 % which resulted in significant decrease in the onset of motor and sensory block and also significant increase in the duration of the block which produced rapid surgical anesthesia, reduced postoperative pain and decrease postoperative analgesic requirement, the mean sensory block onset was (8.7±2.7), the mean motor block onset was (14.5±4).mean VAPS at 4, 8, 12, 24 hours was (0-0), (0-2), (2.3-5), (5-6) which was significant in comparison with control and MgSo4 groups with p value < 0.001. Mean sensory duration was (660.3±94.9), Mean motor duration was (546.6±99.8) both was significantly increased than control and hyaluronidase groups with p value < 0.001. Mean total postoperative analgesic request was (1-1.8) also it was significantly less than control and hyaluronidase groups.

Conclusion

The present study shows that the compination of both MgSo4 with hyaluronidase as adjuvants to bupivacaine in supraclavicular brachial plexus blocks produces significant effect on reducing the time to reach complete sensory and motor block and therefore shortens the total anesthetic time before operation, increases the duration of motor and sensory block, increases the analgesic duration and reduces the postoperative analgesic consumption.

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