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Hyaluronidase Versus Magnesium Sulphate as Adjuvants to Bupivacaine in Ultrasound Guided Supraclavicular Brachial Plexus Block in Upper Limb Surgeries

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Abstract

Background: Aim of this trial was to assess the effect of hyaluronidase and MgSo4 when added separately or in combination to bupivacaine on the onset of sensory and motor block, quality of block and effect on duration of action.

Method: Eighty ASA I, II patients of either sex undergoing upper limb Surgery under ultrasound-guided supraclavicular brachial block were recruited in this prospective randomized double blinded controlled study and divided in to four groups each group contain 20 patients. First group received (28 ml 0.5% bupivacaine and 2 ml 0.9% normal saline). Second group received (28 ml 0.5% bupivacaine and 1000 unit hyaluronidase dissolved in 2 ml 0.9% normal saline). Third group received (28 ml 0.5% bupivacaine and 2 ml of MgSo4 containing 200 mg). Fourth group received (28 ml 0.5% bupivacaine and 2 ml of MgSo4 containing 200 mg mixed with 500 unit hyaluronidase).

Results: Hyaluronidase fastened the onset but didn't affect the duration however MgSo4 prolonged the duration of postoperative analgesia without effect on the onset of block

Keywords: *Regional, brachial plexus; local anesthetics, 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 hyaloronic acid, is generally considered to be "spreading factor". When used with local anesthetics, hyaluronidase hastens the onset of analgesia and shortens its duration of effect[2].

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Magnesium sulphate acts 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, facilitated visualization of local anesthetic spread in real time, produced good compensation for anatomical variation, reduced incidence of complications[4].

Method

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, 80 patients were enrolled in this study and ten were excluded due to block failure.

Preoperative assessment and preparation: A careful assessment of medical history was done. Routine preoperative general examination 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.

Equipment: The ultrasound device Sonosite, micromaxx, Lubricating gel, 21-gauge 50 mm length short bevel insulated stimulating needl, 10-ml syringes for injection, Sterile gloves, 25-gauge needle for skin infiltration, Sterile towels and sterile antiseptic solution (Povidone-iodine 10%).

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 80 bottles numbered from 1 to 80 were prepared and divided in to four 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%) + 1000 unit hyaluronidase dissolved in 2 ml saline (0.9%).

Group (III): Received 28 ml bupivacaine (0.5%) + 2 ml MgSo4 containing 200 mg.

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

Block Technique: A 20 G intravenous cannula was inserted in a peripheral vein of unaffected upper limb and standard monitoring was provided. Patient lie down supine with head turned to the contralateral side and ipsilateral arm adducted gently by the assistant. 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 clavicleas 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.

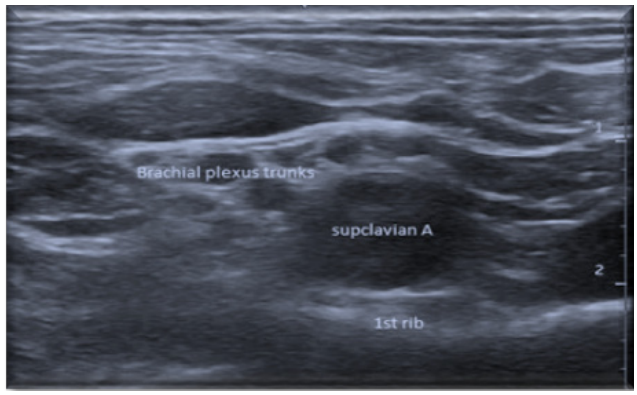

Fig (1): Ultrasonographic imaging of brachial plexus

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 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. **Grade2:** Complete motor block with inability to move the fingers.

Pain intensity was assessed using **VAPS**. 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 four paracetamol 1000 mg bottle 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 requirements 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, The Mean Arterial blood pressure (mmHg) and arterial oxygen saturation changes during intraoperative or postoperative period were statistically insignificant between the four groups. As regard the Heart rate (beat\ min) we found it was lower in group (II, IV) than the other two groups (I, III) at time intervals of 10,20,30 and 60 minutes intraoperative but these changes were statistically insignificant.

Sensory, motor block onset and density of block were faster in groups (II & IV) than in groups (I & III) but the duration of sensory and motor block was found to be longer in groups (III & IV) than in groups (I & II) as presented in fig (2, 3, 4).

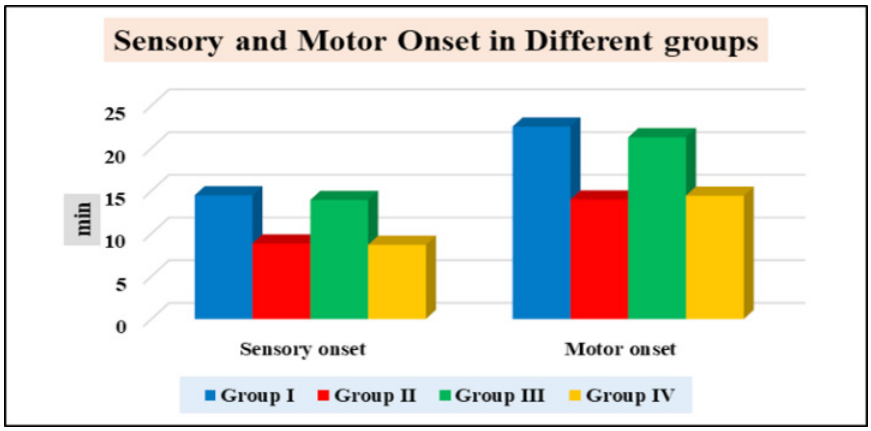

Fig (2)

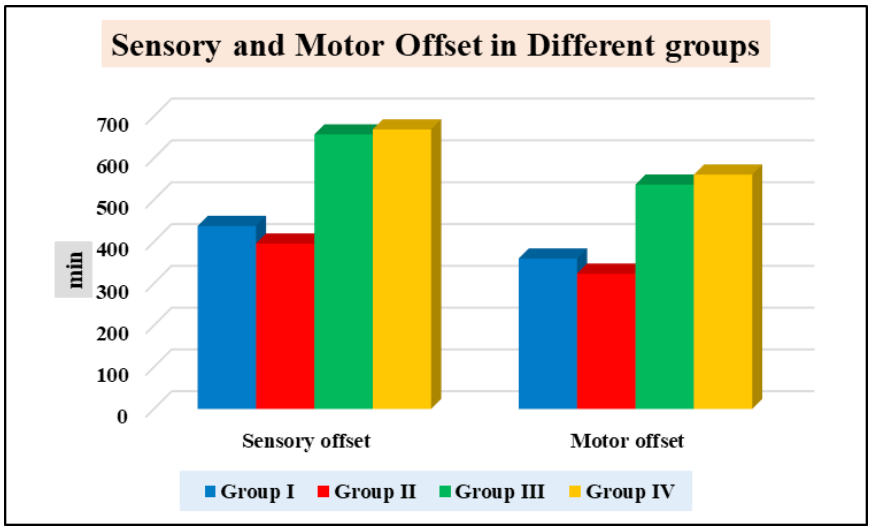

Fig (3)

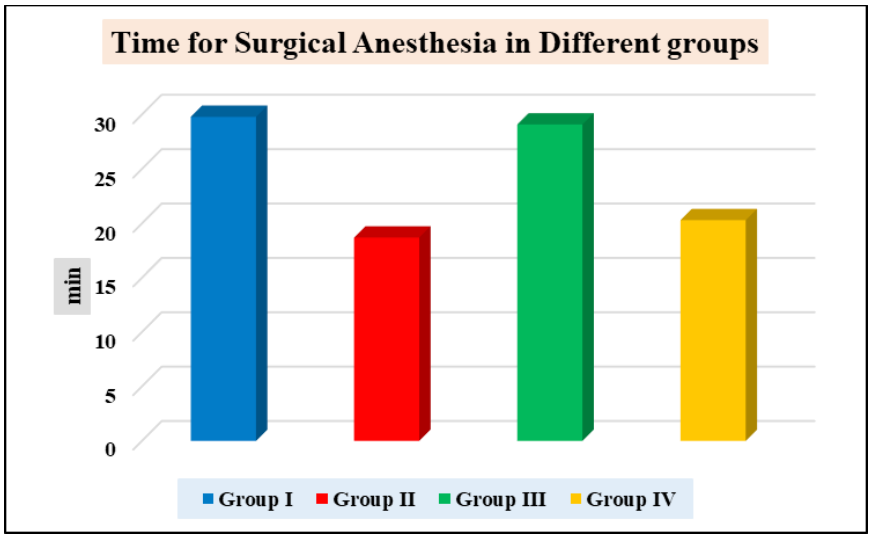

Fig (4)

Pain measurement presented by VASP during intraoperative period at 15 min post injection the pain score was significantly lower in patients received hyaluronidase in groups (II & IV) than in groups (I & III) 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 received MgSo4 in groups (III & IV) than in groups (I & II).

Intraoperative need for sedation and fentanyl was insignificantly different between the four groups. But the mean time of for postoperative 1st analgesic (minutes) request was significantly longer in groups (III & IV) (360-900) and (540-950) minutes in comparison to groups (I & II) (300-620) and (300-700) minute. And total analgesic requirement (mg) in groups (III & IV) was less than groups (I & II).

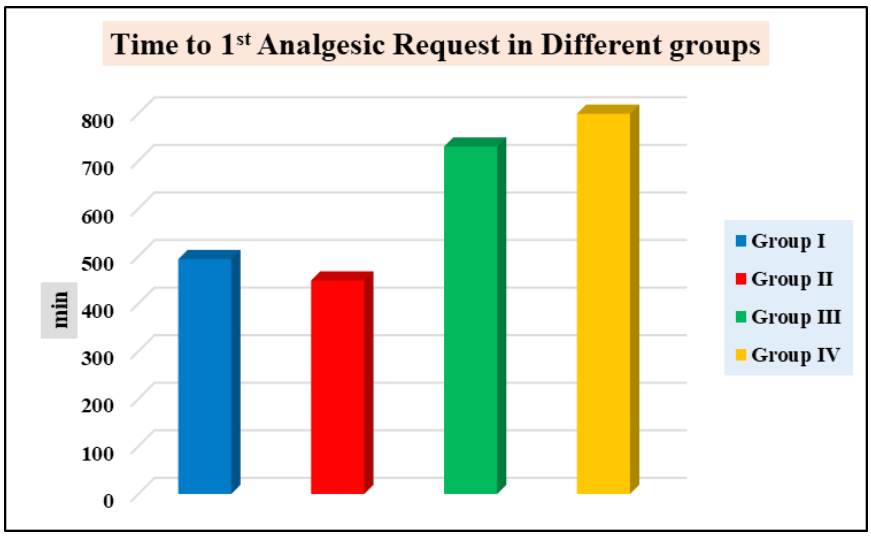

Fig (5)

As regard complications happened during the study no significant differences were found between the four groups.

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 hyaloronic acid, is generally considered to be "spreading factor". When used with local anesthetics, hyaluronidase hastens the onset of analgesia and shortens its duration of effect [7].

A number of studies have shown that addition of hyaluronidase during ocular blocks has beneficial effects including higher quality of anaesthesia and improved success rates.

In a study done by **Koh et al** investigated the hypothesis that addition of hyaluronidase 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].

Another previous study by **Keeler et al** reported the effect of the addition of hyaluronidase to bupivacaine 0.5% for axillary brachial plexus blocks. In that study, 3000 IU hyaluronidase mixed with bupivacaine significantly reduced the duration of the sensory and motor block, and had no effect on the number of patients experiencing a complete sensory block after 30 min while the duration of sensory anesthesia was significantly shorter in the hyaluronidase group and the duration of motor block showed a shorter trend [9].

In our study hyaluronidase had obvious effect on decreasing the sensory onset that recorded by pinprick test at 5 min interval after performing the block till complete sensory block occurred and motor onset detected by detection of complete thumb block also detected at 5 min interval after the block in comparison with control group and Mgso4 group. The mean sensory onset was (8.9 ± 3.3) minutes in hyaluronidase group in comparison to the mean sensory onset (14.5±4.5), (14± 3.8) minutes in control and Mgso4 groups respectively. The mean motor onset was (14±5.1) minutes in hyaluronidase group in comparison to the mean motor onset (22.5±4.9), (21.3±5) minutes in control and Mgso4 groups respectively, and both results were significant with p value < 0.001. However it didn't affect the duration of sensory or motor block or the postoperative analgesic requirement in comparison with other groups.

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 [10].

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 [11].

Rao et al, found thatThe 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). Alsothe 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) [12]

In our study the addition of Mgso4 to 0.5% bupivacaine in supraclavicular brachial plexus block for upper limb surgeries increased the duration of sensory and motor blocks with mean sensory block duration (643.1±144.8) in Mgso4 group vs (423.5±89.4) in control group or (387.2±78.3) in hyaloronidase group and mean motor block duration (546.6±99.8) vs (337.5±77.6) in control group or (310±84.9) in hyaloronidase group with (p value <0.001) for both. Also Mgso4 decreased the postoperative pain with mean VAPS at 4, 8, 12, 24 (0-2.8), (0-3), (2-6), (5-6) vs (2-3), (4-6), (6-7), (7-7.8) in control group vs (2-3), (3.3-6), (6-7), (6-7.8) with (p value <0.001) for all. Also Mgso4 reduced total

analgesic requirements in comparison with the use of 0.5% bupivacaine or bupivacaine plus hyaluronidase with mean total analgesic requirement (1-2) in Mgso4 vs (2-3) in both control and hyaluronidase groups and the change was statistically significant with (p value <0.001). However MgSo4 didn't affect the onset of sensory or motor block when compared to the control and hyaluronidase group.

The most recent 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 use of hyaluronidase reduces the time to reach complete sensory and motor block and therefore shortens the total anesthetic time before operation, hyaluronidase has no influence on the total analgesic duration or the consumption of postoperative analgesics.

Also the study shows that the use of Mgso4 increases the duration of motor and sensory block, increases the analgesic duration and reduces the postoperative analgesic consumption. However MgSo4 has no effect on the sensory or motor onset of block.

Last conclusion was that the combination of both MgSo4 with hyaluronidase as adjuvants to bupivacaine 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.

The Institutional Ethics Committee approved this study of the School of Medicine, Minia University, Egypt, and all patients gave informed consent before participation in this study. The study conducted in accordance with the ethical guidelines of the 1975 Declaration of Helsinki and International Conference on Harmonization Guidelines for Good Clinical Practice.

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Conflict of Interest: The authors declare that there is no conflict of interests.

References

1. Sadowski M, Tułaza B and Łysenko L. Renaissance of supraclavicular brachial plexus block.Anaesthesiology intensive therapy. 2014; 46 (1):37-41.
2. Bailard NS, Ortiz J and Flores RA, Additives to local anesthetics for peripheral nerve blocks: Evidence, limitations, and recommendations. American Journal of Health-System Pharmacy, 2014. 71(5): p. 373-85.
3. Vastani N, Seifert B, Spahn DR, et al., Sensitivities of rat primary sensory afferent nerves to magnesium: implications for differential nerve blocks, European Journal of Anesthesiology(EJA). 2013. 30(1): P. 21–28.
4. Price A, Walker KJ, McGrattan K, et al. Ultrasound guidance for upper and lower limb blocks. The Cochrane of Systematic Reviews. 2015; (9).
5. Lee I. O., Kim W. K., Kong M. H., et al., No enhancement of sensory and motor blockade by ketamine added to ropivacaine interscalene brachial plexus blockade. Acta anaesthesiologicascandinavica. 2002. 46, 821-6.
6. Bromage P, Epidural analgesia. st Ed. Philadelphia, WB Saunders; 1997:144.
7. Wohlrab J, Finke R, Franke WG, et al. Efficacy study of hyaluronidase as a diffusion promoter for lidocaine in infiltration analgesia of skin. Plastic and reconstructive surgery. 2012; 129 (4):771-772.
8. Koh W. U, Min H. G, Park H. S. et al.Department of: Hyaluronidase for axillary block. Anesthesiology and Pain. 2015, 70, 282–289.|
9. Keeler JF, Simpson KH, Ellis FR, et al.,Effect of addition of hyaluronidase to bupivacaine during axillary brachial plexus block. British Journal of Anaesthesia 1992; 68: 68 –71.

10. Vastani N, Seifert B, Spahn DR, et al., Sensitivities of rat primary sensory afferent nerves to magnesium: implications for differential nerve blocks. Eur J Anaesthesiology. 2013; 30(1):21–8. P mid: 23138572.
11. Haghighi M, Soleymanha M, Sedighinejad A, et al.The effect of magnesium sulfate on motor and sensory axillary plexus blockade. Anesth Pain Med. 2015; 5(1).
12. Rao LN, Jeyalakshmi V, Nagaraju M, Anitha S. The effect of magnesium sulfate as an adjuvant to 0.5% bupivacaine on motor and sensory supraclavicular brachial plexus blockade. Int J Basic Clin Pharmacol. 2015; 4(2):317–21.