Zagazig University Medical Journal
www.zumj.journals.ekb.eg

DOI 10.21608/zumj.2019.13591.1253 *Anaesthesia*

ORIGINAL ARTICLE

Magnesium Sulphate versus Dexmedetomidine as an Additive to Lidocaine and Bupivacaine in Ultrasound Guided Supraclavicular Brachial Plexus Block in Upper Limb Surgeries

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Submit Date: 11-06-2019
Revise Date: 02-08-2019
Accept Date: 03-08-2019

A B S T R A C T

Background: We compared the effects of adding either dexmedetomidine or magnesium sulphate to local anesthetics in ultrasound (US) guided supraclavicular brachial plexus block (SBPB). Duration of sensory block was the primary endpoint while the secondary endpoints were the onset of sensory and motor block, duration of the motor block and the duration of the analgesia. **Methods:** Thirty patients posted for upper limb surgeries were enrolled for a comparative randomized prospective clinical study. Patients were divided into two groups, dexmedetomidine group (D) and magnesium sulphate group (M). In group D (n= 15) patients were administered 24ml volume of local anesthetics (LAs) (lidocaine 2% + bupivacaine 0.5% 1:1 mixture) +100mcg dexmedetomidine in 1ml volume. Patients in group M (n= 15) were administered 24ml volume of LAs (lidocaine 2% +bupivacaine 0.5% 1:1 mixture) + magnesium sulphate 100 mg in 1 ml volume. Onset, duration of sensory and motor blocks and the duration of analgesia were assessed. **Results:** Demographic data and surgical characteristics were comparable in both groups. The onset times for sensory and motor blocks were statistically significantly shorter in group D than group M while the duration of sensory and motor block was statistically significantly longer in group D than those of group M. The duration of analgesia in group D was statistically significant different than in group M. **Conclusion:** Dexmedetomidine is more effective than magnesium sulphate as an adjuvant to LAs in US guided Brachial plexus block. Dexmedetomidine provide more rapid onset for sensory and motor block and prolong their duration. Also, dexmedetomidine provide duration of analgesia longer than magnesium sulphate.

Keywords: Supraclavicular, Brachial plexus, Magnesium, Dexmedetomidine.

INTRODUCTION

Local anaesthetics alone for supraclavicular brachial plexus block provide good operative conditions but have shorter duration of postoperative analgesia. Hence, various adjuvants were added to local anaesthetics in brachial plexus block to achieve quick, dense and prolonged block **[1]**. Magnesium is one of the most plentiful cations in the body. Magnesium is necessary for the presynaptic release of acetylcholine from nerve endings and may produce effects similar to calcium-entry-blocking drugs **[2]**. Anti-nociceptive effects of magnesium are due to regulation of calcium influx into the cell and antagonism of the N-methyl D-aspartate (NMDA) receptors **[3]**.

Dexmedetomidine is highly selective, specific and potent α_2-adrenergic agonist having analgesic, sedative, antihypertensive, and anaesthetic sparing effects when used in systemic route. Adding dexmedetomidine to local anaesthetics during peripheral nerve blockade and regional anaesthesia procedures may also prove efficacious for the surgical patients. Dexmedetomidine has also shown to prolong the duration of the block and post-operative analgesia when added to local anaesthetic in various regional blocks **[4]**.

METHODS

The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

After the approval of the Zagazig University Institutional Review Board, this prospective, double-blind, randomized study was conducted at the orthopedic and general surgery departments at Zagazig university hospitals during a period of 6 months (July 2018– December 2018) **[Figure 1]**. The procedure was explained to the patients about the drugs and the approach, and only those who gave wellful written informed consent were included in the study. ASA physical status I and II patients aged between 18-60 years of both gender and scheduled for unilateral upper limb surgeries below level of the shoulder under supraclavicular brachial plexus block were enrolled in a comparative randomized prospective clinical study.

Patients who refused to be included in addition to those with peripheral neuropathy of the upper limb, infection at the injection site, altered mental status or had history of allergy to local anaesthetics were excluded from the study. Patients with coagulopathy or planned for receiving general anaesthesia at the same operation for any cause as (bone graft, skin graft, etc) or main site of the surgery is the medial side of the arm at axilla level (T2 distribution) were also excluded.

Sample size and randomization:

Assuming that mean±SD of duration of sensory block in both Dexmedetomidine and Ketamine groups is (413.97±238.5 min Vs 227±135 min respectively) **[5]**. So, sample size was calculated by open Epi to be 30 cases in 2 groups (15 cases in each group) with confidence level 95% and power of test is 80%.

A computer-generated randomization table divided patient into 2 equal groups randomly allocated patients into two groups, 15 patients in each of them.

Dexmedetomidine group(D) received 24 ml volume of local anaesthetics (lidocaine 2% + bupivacaine 0.5% 1:1 mixture) + 100mcg dexmedetomidine in 1ml volume.; and magnesium sulphate group M, administer 24ml volume of local anaesthetics (lidocaine 2% +bupivacaine 0.5% 1:1 mixture) + magnesium sulphate 100 mg in 1 ml volume. These drugs were given for supraclavicular brachial plexus block using the US.

In preoperative assessment the patients were enquired about any history of drug allergy, previous operations or prolonged drug treatment. General examination, systemic examinations and airway assessment were done. Preoperative fasting of minimum 6 h was ensured before operation.

On the day of surgery, standard monitors (Electrocardiography, Pulse Oximetry and non-invasive blood pressure) were applied to all the patients. An intravenous (IV) cannula secured in the non-operative limb once the patient arrived in the premedication room. Patient was positioned supine with head turned away from the limb to be operated. The injection site was cleansed with **povidone iodine 10%** and covered with sterile drapes. A high frequency adult linear ultrasound probe (Mindray M5, linear 8-14Mhz) placed over the supraclavicular region. Sterile water-based gel was used as acoustic couplant between probe and skin.

The patients were administered brachial plexus block by supraclavicular route with the patient in the proper position (supine with the head tilted to the opposite site)

The skin was disinfected and the US machine transducer was positioned in the transverse plane immediately superior to the clavicle at approximately its midpoint. The transducer was manipulated to obtain a cross-sectional view of the subclavian artery. The brachial plexus is seen as a collection of hypoechoic oval structures lateral and superficial to the artery. After negative aspiration for blood a total amount of 25 ml volume was injected slowly as planned for each group.

Data Collection:

I-Heart rate, mean arterial blood pressure, and oxygen saturation were recorded at 10 min intervals throughout the procedure and then hourly postoperative up to 12 hrs. Hypotension was defined as a decrease in MAP of more than 20% of baseline value and was planned to be treated with crystalloid infusion and 5 mg bolus of ephedrine. Bradycardia was considered if the HR went below50 b/min and was planned to be managed with atropine 0.2–0.5 mg. The patient was considered hypoxic if the oxygen saturation was less than 90% and was planned

to be managed with supplemental oxygen through nasal cannula or face mask. Nausea and vomiting if occurred was planned to be treated with metoclopramide 10 mg intravenously. Also, any intra and /or post-operative complications or side effects were recorded.

II-Sensory block: Patients were evaluated for onset of sensory block every 2 min after the end of injection till 20 minutes and then every 30 min after the end of surgery till the first 12 hours and thereafter, hourly until the block had completely worn off. The sensory block was assessed by the pinprick sensation with a blunt 25-G needle in all dermatomes innervated by the brachial plexus (C5-T1) in the distribution of median, radial, ulnar and musculocutaneous nerves. Sensory block was graded as **[6]**:

- 0: Sharp pin felt.
- 1: Dull sensation felt.
- 2: No sensation felt.

The onset time of the sensory block was taken as the time from injection of local anaesthetic into the brachial plexus to obtunding of pinprick sensation, i.e., sensory block grade 1. Duration of sensory block was defined as the time interval between the end of administration of local anaesthetic and complete recovery from anaesthesia in all dermatomes.

III- Motor block was assessed according to a 3-point scale **[7]**.

- 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 of motor block was defined as the time interval between the end of local anaesthetic administration and complete motor block, while the duration of the motor block was defined as the time interval from complete motor block (Grade 2) to complete recovery of motor function of hand and forearm (grade 0).

IV-Duration of analgesia (DOA): the time between the complete sensory block and the first analgesic request by the patient. Pain was assessed using the Visual Analogue Scale (VAS score) [8] after explaining it to the patient as an instrument used to quantify a subjective experience, such as the intensity of pain. A commonly used visual analogue scale is a 10-cm line labelled with "worst pain imaginable" on the right border and "no pain" on the left border. The patient was instructed to make a mark along the line to represent the intensity of pain currently being experienced. VAS score was assessed every hour in the first 4 hours after the end of the operation then every 4 hours for 24 hours. IV injection of 25 mcg fentanyl as a rescue analgesic was given whenVAS≥3.The amount of fentanyl used as a rescue analgesic and total number of fentanyl injections were recorded.

V- Degree of sedation was assessed according to Culebras and colleagues sedation score **[25]**. :0=awake and alert, 1=sleeping but easily arousable, 2=deep sleep, arousable, and 3=deep sleep, not arousable. The degree of sedation was assessed before injection of LA (T0) (base line), then at 15 min (T15), 30 min (T30), 45 min (T45), 60 min (T60),90 min (T90) after injection of LA and at the end of surgery (Tend).

Statistical analysis:

The data were compiled and subjected to statistical analysis using Statistical Package for Social Sciences (SPSS), version15. Patients and surgical data were subjected to Student's t-test to compare normally distributed quantitative data. Chi-Square was used for comparison of the qualitative data. P-value < 0.05 was considered as statistically significant, P< 0.001 as highly significant while P-value > 0.05 was considered as statistically non-significant.

RESULTS

Patients and surgical characteristics were comparable in both groups **[Table1].** The mean heart rate, mean blood pressure, and oxygen saturation did not deviate significantly from their baseline values at most of the time intervals throughout the surgery and for 12 hours in both the groups **[Figure 2,3 and 4]**.

Onset time of sensory and motor blockade was shorter while duration of sensory and motor blockade was longer in D than M group and the difference was statistically significant (P< 0.001) **[Table 2]**. The mean onset time for sensory and motor

blocks in group D was 12.1±1.9 and 14.7±2.2 min, respectively and for group M were 16±1.48 and 19.6±1.29 min, respectively. The mean duration time for sensory and motor blocks for group D were 800±44.5 and 650±40.9min, respectively; while for the group M, the mean durations were 600±13.1 and 400±32.9 min, respectively.

The mean duration of analgesia (DOA) for group D was 900±60.9min, it was 600±33.4 min for group M **(Table 3)**. DOA was significantly longer in group D than group M (P< 0.001).

The study showed that group D required less amount of fentanyl and a smaller number of patients required injections as rescue analgesic (when VAS≥3) than patients in group M in first 24 h of postoperative period, and the difference is statistically significant **[Table 4]**.

Regarding the side effects and complications encountered throughout the study, group D suffered from slightly more nausea, hypotension and bradycardia, however, it was statistically insignificant when compared with group M. No other complications had been noticed during the study **[Table 5].** In group D the median value of sedation score was 0 after injection of LAs mixture with dexmedetomidine and 1 at 15–60 min. Then, it returned to 0 at 90 min after block performance. Whereas in group M, the median value of sedation score was 0 after injection of LAs mixture with magnesium sulphate and 1 at 15 min the it returned to 0 at 30 min. Comparison of sedation scores in the two groups showed statistically significant higher score in group D at T30–60 compared with group M **[Figure 5].**

Table 1. Patients and surgical characteristics of the studied groups.

Variable	Dexmedetomidine group(D) (n=15)		Magnesium group(M) (n=15)		t test	P
Age(years): Mean ± SD Range	36.2± 3.5 29 -41		36.8 ± 2.8 30 – 44		-0.518	0.607 (NS)
Weight (Kg): Mean ± SD Range	79.5 ±4.5 60 - 88		78.5 ± 3.4 55 - 80		0.687	0.501 (NS)
BMI (kg/m2): Mean ± SD Range	27.5 ± 2.1 23 - 30		26.8 ± 3.2 21- 29		0.708	0.847 (NS)
Duration of surgery (min): Mean ± SD Range	120 ± 12.5 40 - 195		123 ± 17.2 50 - 170		-0.546	0.583 (NS)
	N	%	N	%	χ^2	P
Gender: – Female – Male	6 9	40 60	8 7	53.3 46.7	0.535	0.464 (NS)
ASA: – I – II	11 4	73.3 26.7	10 5	66.7 33.3	0.158	0.690 (NS)
Type of surgery: ORIF of Radius ORIF of Ulna ORIF of BBF Cut Wrist Repair	3 4 2 6	20 26.7 13.3 40	2 5 4 4	13.3 33.3 26.7 26.7	1.378	0.710 (NS)

n: number of patients

T test: Independent sample t test. NS: Non-significant difference (p>0.05).

Data were expressed as Mean ± standard deviation and range or Number and percentage

BMI: body mass index

ORIF:open reduction and internal fixation.

BBF:both bone forearm

Table 2. The onset and duration of both sensory and motor block in both groups.

Variable		Dexmedetomidine group(D) (n=15)	Magnesium group(M) (n=15)	t test	P
Sensory Block	Onset:(min) Mean ± SD Range	12.1±1.9** 10 – 16	16 ±1.48 12 – 21	-6.272	<0.001** (HS)
	Duration:(min) Mean ± SD Range	800 ±44.5** 550-900	600±13.1 410-760	16.69	<0.001** (HS)
Motor Block	Onset:(min) Mean ± SD Range	14.7±2.25** 12 – 19	19.6±1.29 17 – 21	-7.317	<0.001** (HS)
	Duration:(min) Mean ± SD Range	650± 40.9** 520 – 760	400±32.9 260 – 480	18.44	<0.001** (HS)

**: Highly significant compared to other group (P<0.001).
Data were expressed as mean ± standard deviation and range.
Hs = highly significant

Table 3. The duration of analgesia in both groups.

Variable	Dexmedetomidine group(D) (n=15)	Magnesium group(M) (n=15)	t test	P
Duration of analgesia: (min) Mean ± SD Range	900±60.9** 700 – 1500	600±33.4 400 – 710	16.72	<0.001** (HS)

**: Highly significant compared to other group (P<0.001).
Data were expressed as mean ± standard deviationand range.
Hs = highly significant

Table 4. The amount of fentanyl injected as a rescue analgesic in both groups.

Variable	Dexmedetomidine group(D) (n=15)		Magnesium group(M) (n=15)		χ^2	P
	N	%	N	%		
Number of patients received iv fentanyl injection as a rescue analgesic in the 1st 24 hr: -No injection -One injection -Two injection	 11 2 2	 73.3 13.3 13.3	 4 9 2	 26.7 60 13.3	7.72	0.02 (S)
Variable	Dexmedetomidine group(D) (n=4)		Magnesium Group(M) (n=11)		t-test	P
Amount of fentanyl used as a rescue analgesic:(Microgram) Mean ± SD Range	29.5 ± 3.4 25 -50		37.5 ± 4.5 25 - 50		5.494	<0.001 (HS)

Each injection consisted 25Microgram of fentanyl

**: Highly significant difference (P<0.001).
Data were expressed as mean ± standard deviation.
Hs = highly significant

Table 5. The side effects among the studied groups.

Variable	Dexmedetomidine group(D) (n=15)	Magnesium group(M) (n=15)	χ^2	P
	N (%)	*N (%)*		
Nausea	1 (6.7%)	0 (0%)	1.034	0.311 (NS)
Bradycardia	3 (20%)	1 (6.7%)	1.154	0.284 (NS)
Hypotension	2 (13.3%)	0 (0%)	2.143	0.143 (NS)

Data were expressed as number (percent).
n means number of patients
NS: Non-significant difference (p>0.05).

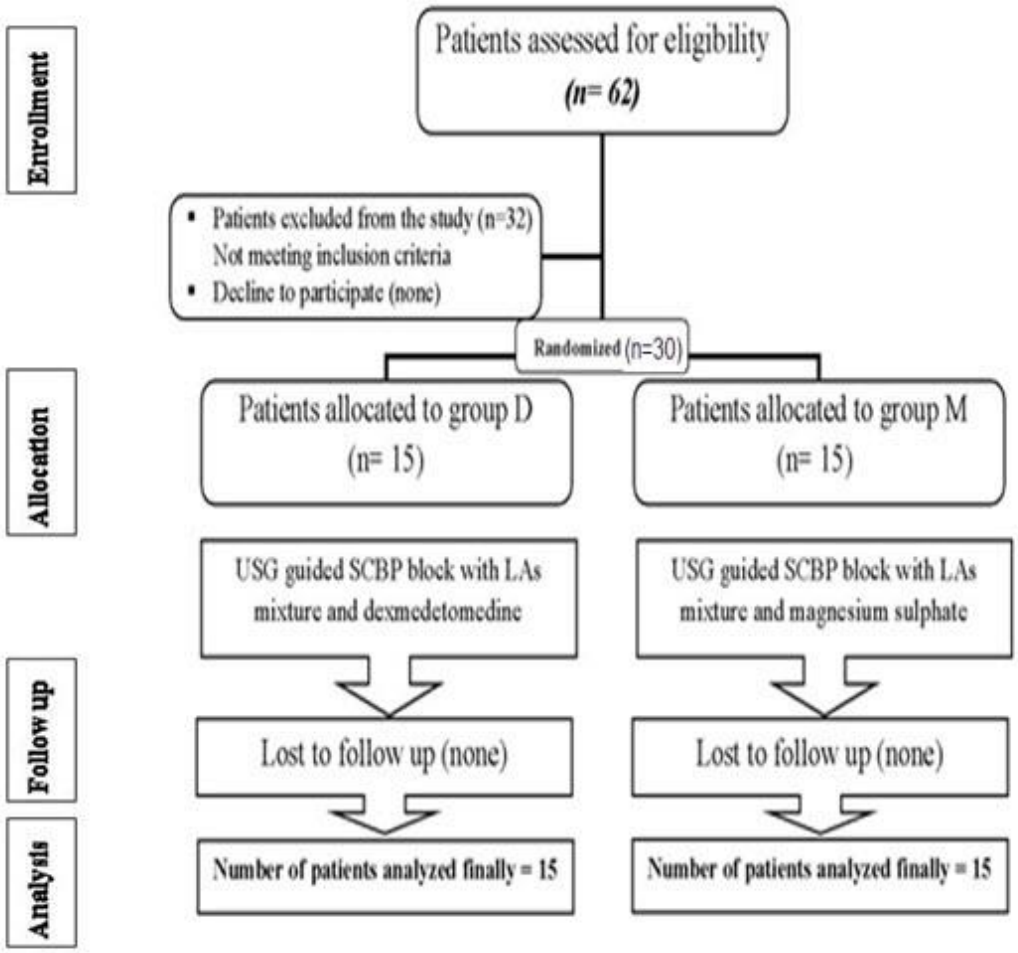

Figure 1. Consort of the study

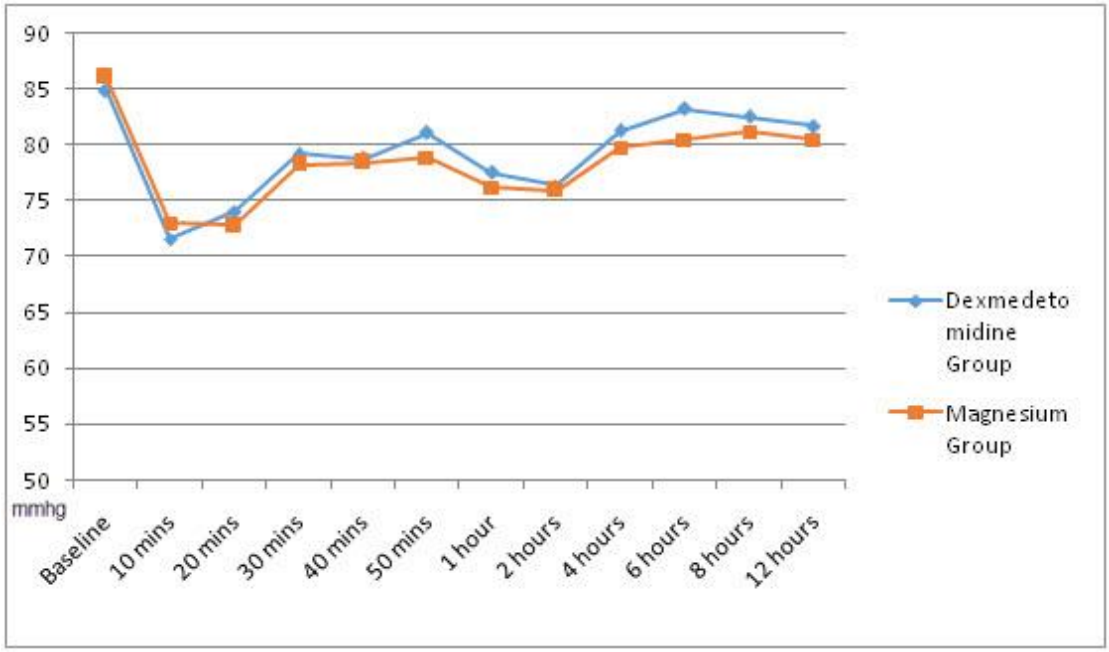

Figure2. Line graph showing mean arterial pressure measurements at different timings among the studied groups. Data were expressed as mean.

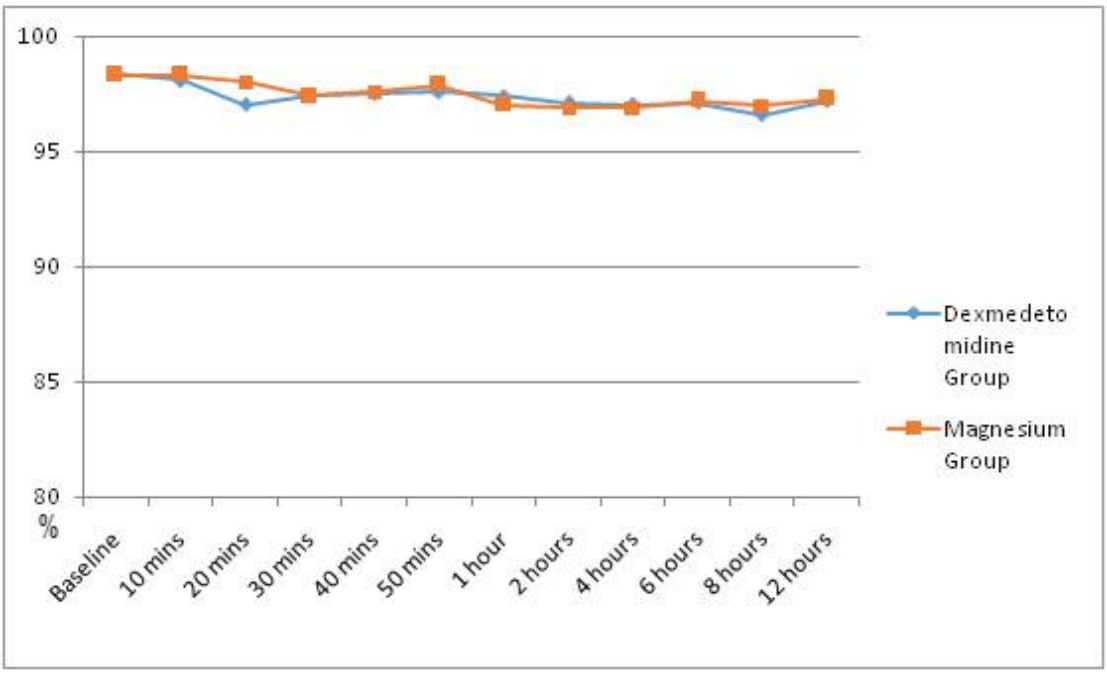

Figure 3. Line graph showing oxygen saturation at different timings among the studied groups. Data were expressed as mean

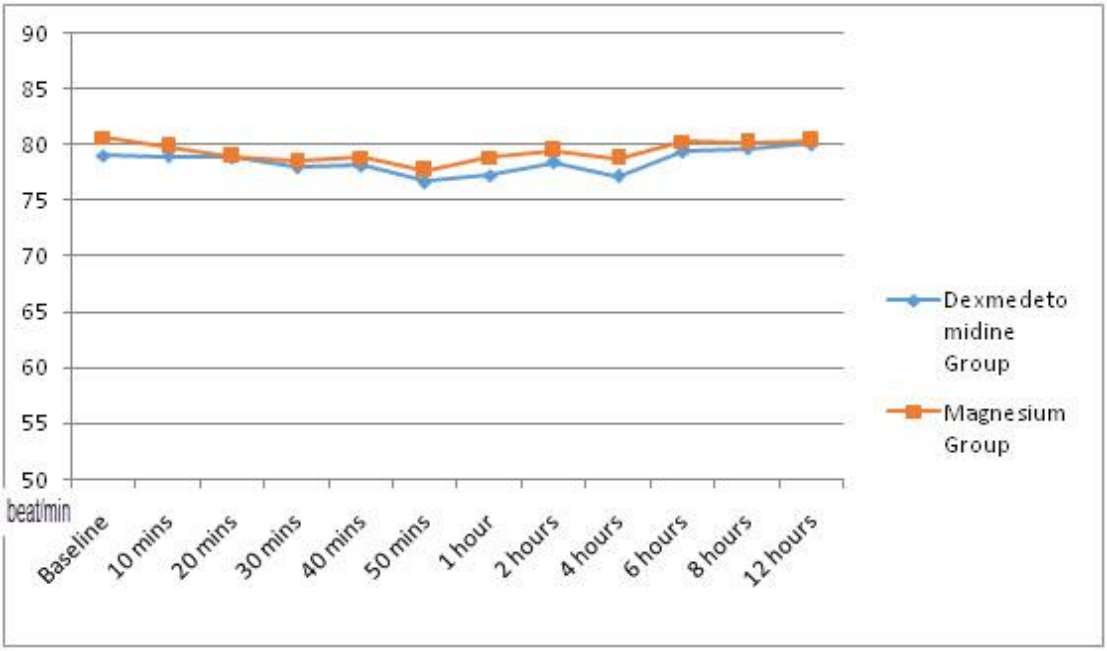

Figure 4. Line graph showing heart rate measurements at different timings among the studied groups. Data were expressed as mean

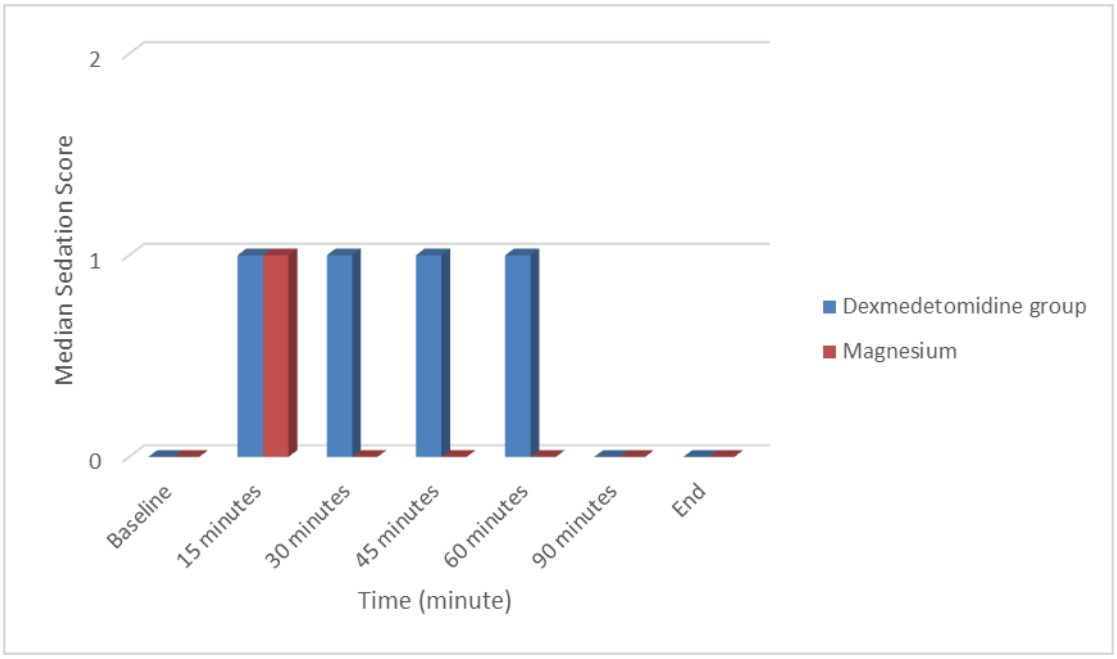

Figure 5. Bar chart showing median sedation scores at different timings between the studied groups.

DISCUSSION

This study was done to compare between the effects of administration of dexmedetomidine versus administration of magnesium sulphate as adjuvant to local anesthetics for US guided supraclavicular approach for brachial plexus block. It was found that administration of 100 mcg dexmedetomidine in 1ml volume to 24ml volume of local anesthetics (lidocaine 2% +bupivacaine 0.5% 1:1 mixture) provide more rapid onset and longer duration for sensory and motor brachial plexus block in addition to providing longer duration of analgesia to the patient in comparison to adding magnesium sulphate 100 mg in 1 ml volume to 24ml volume of local anesthetics (lidocaine 2% +bupivacaine 0.5% 1:1 mixture).

Besides its central-mediated analgesia **[9]**, the mechanism by which dexmedetomidine enhances the quality of regional anesthesia when used as an adjuvant to LAs can be explained by two peripheral mechanisms **[10-12]**. The first is the vasoconstrictor effect around the site of injection which leads to delay of the absorption of the LAs and prolong the duration of the LAs effect. The second mechanism is the direct action of dexmedetomidine on the activity of peripheral nerve. Dexmedetomidine may inhibit the compound action potentials that results in direct inhibition of nerve conduction **[11]**.

Previous studies had been investigated the use of magnesium sulfate as an adjuvant to LA solutions for peripheral nerve block (PNB) **[8, 13, 14]**. Analgesic effects of magnesium sulfate on the peripheral nerve (PN) may be explained by the NMDA receptors antagonist effect that causes prevention of central sensitization from peripheral nociceptive stimulation, as well as magnesium reduced release of acetylcholine through the competitive block of the calcium entry in presynaptic endings **[12]**. Another possible mechanism for the action of magnesium sulfate on the PN is the surface charge theory **[12]**. The modulation of the external magnesium concentration bathing a nerve bundle can enhance the PNB caused by LAs, as well as the high concentration of magnesium attracted by the negative charges of the outer membrane surface affected Na^+ channel gating and could cause hyperpolarization which results in inhibition of nerve conduction **[8]**.

The results of the current study are in agreement with the results of **Agarwal et al.**

[15] compared the effects of adding dexmedetomidine to bupivacaine in supraclavicular brachial plexus block in fifty patients. They concluded that dexmedetomidine added as an adjuvant to bupivacaine for supraclavicular brachial plexus block significantly shortens the onset time and prolongs the duration of sensory and motor blocks and duration of analgesia.

Also, **Dar et al. [16]** evaluated the effect of adding dexmedetomidine to ropivacaine for axillary brachial plexus blockade in eighty patients scheduled for elective forearm and hand surgeries. Sensory and motor block onset times were shorter when dexmedetomidine was added, also sensory and motor blockade durations were longer along with duration of analgesia.

On the same line, **Biswas et al. [17]** evaluated the effect of combining dexmedetomidine with levobupivacaine in patients scheduled for elective forearm and hand surgeries under SBPB with respect to duration of motor and sensory block and duration of analgesia. They found sensory and motor block durations were longer when dexmedetomidine was added as adjuvant. Duration of analgesia was also significantly longer with addition of dexmedetomidine.

However, **Das et al. [18]** noticed that when dexmedetomidine was added to 0.5% ropivacaine in supraclavicular brachial plexus block, there was no clinically significant difference in the onset of block. Similar findings to **Das et al. [18]** were reported by **Rancourt et al. [19]** when evaluated the effect of dexmedetomidine (1µg/kg) when added to 10ml of 0.5% ropivacaine for posterior tibial nerve block.

The superiority of dexmedetomidine over magnesium in our study is in accordance with **Elyazed and Mogahed [20]** in their comparative study between magnesium Sulfate and dexmedetomidine as an adjuvant to 0.5% ropivacaine in infraclavicular brachial plexus block. Also, our study`s results goes with **Mohamed and Genidy [21]** in their study of magnesium sulphate versus dexmedetomidine as an adjuvant to local anesthetic mixture in peribulbar anesthesia.

The results of the current study are also consistent with the results of **Kassem et al. [22]** who showed in a compartive study between dexmedetomidine and magnesium sulphate addition to LAs for peribulbar block the superiority of dexmedetomidine over magnesium sulphate.

Our results showed a significant increase in the duration of analgesia , this findings could be explained by the peripherally effect of dexmedetomidine by blocking the hyperpolarization-activated cation current in the peripheral nerves as supposed by **Brummett et al. [23]** or through the systemic absorption of dexmedetomidine as reported by **Kaygusuz [24]**.

The patients of both groups D and M showed mild sedation but with shorter duration in group M and this finding is in line with the results of **Agarwal et al. [15]** and **Mukherjee et al. [8]**. Sedation is desirable during surgery and it could be due to partial vascular uptake of dexmedetomedine or magnesium sulphate and their effects on the central nervous system where dexmedetomedine act as agonist on α2 adrenergic receptors **[4]** and magnesium sulphate regulates calcium entry and antagonizes the NMDA receptors **[3]**.

CONCLUSION

Adding 100mcg of dexmedetomidine in 1 ml volume to 24ml volume of (lidocaine 2% +bupivacaine 0.5% 1:1 mixture) is more effective in various aspects than adding 1ml volume of 100 mg magnesium sulphate to the same LAs mixture for US guided Brachial plexus block. Dexmedetomidine provide more rapid onset for sensory and motor block and prolong their duration. Also, Dexmedetomidine provide duration of analgesia longer than magnesium sulphate. Moreover, it provides a favorably mild degree of sedation.

Limitations of the study:

The main obstacle during our research was the availability of dexmedetomidine in our Zagazig university hospitals along with its high cost in private drugs market.

Conflict of Interest: None.

Financial Disclosures: Nothing to declare.

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Hassan, M., Abaza, K., Fawzy, E., Kamel, A. MAGNESIUM SULPHATE VERSUS DEXMEDETOMIDINE AS AN ADDITIVE TO LIDOCAINE AND BUPIVACAINE IN ULTRASOUND GUIDED SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK IN UPPER LIMB SURGERIES. *Zagazig University Medical Journal*, 2020; (1066-1077): -. doi: 10.21608/zumj.2019.13591.1253