Comparative Study between Magnesium Sulphate Versus Dexmedetomedine as Additives to Levobupivacaine in Ultra Sonographic Guided Supraclavicular Block in Patient Undergoing Forearm Surgeries

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ABSTRACT
Background: Supraclavicular block provides alternative way to general anesthesia for upper limb surgeries. They produce complete muscular relaxation, maintaining hemodynamic stability intraoperatively and avoidance of the risks with general anesthesia. The most important target of anesthesia is to manage the patient's pain, as we can do the surgical procedures with no discomfort, and controlling of intraoperative and postoperative pain.
Objective: Our study aimed to detect how adding Mg sulphate or dexmedetomidine can improve the effect of local anesthetic in regional block (supra clavicular block).
Patient and Methods: 90 patients aged between 20–75 years old with ASA I– II who were scheduled for forearm surgeries under supraclavicular block anesthesia were enrolled in our study. This Study was conducted in Sohag University Hospitals from May 2019 to April 2020. Patients were divided into 3 equal groups.
Results: Magnesium sulphate had a more rapid onset of both sensory and motor block onset than dexmedetomedine and control groups. Dexmedetomidine had a longer duration of both motor and sensory block than magnesium sulphate group and control groups. Dexmedetomidine had a longer analgesic effect than magnesium sulphate group and control group. As regards rate of complications, there was no significant difference between the three groups.
Conclusion: The addition of 1 ml (100 μg) dexmedetomedine or 200 mg magnesium sulphate to supraclaviculary-injected levobupivacaine improved the onset, duration and postoperative analgesia of levobupivacaine.
Keywords: Mg sulphate, Dexmedetomedine, Levobupivacine, Ultrasonographic guided, Supraclavicular block.

INTRODUCTION

Recent years' postoperative pain has a great importance in all surgeries preventing the central, peripheral and immunological stress response to tissue injury [1]. The postoperative period requires all our experiences as this period of most severe, agonizing pain that requiring our attention. So our goal is to achieve control of pain to extend to postoperative period without any side effects [2].

Various additive drugs as opioids, neostigmine, clonidine and hyaluronidase...etc have been added to local anaesthetics as adjuvants to make rapid onset, good quality, and to prolong the duration and post-operative analgesia [3]. Levobupivacaine is a long-acting local anaesthetic widely used in modern anaesthetic practice. It is well recognized that inadvertent i.v. injection or administration of toxic doses by another route can lead to severe central nervous system (CNS) toxicity and cardiovascular compromise [4]. Some authors said that the effects of opioids on regional blockade are controversial, as addition of opioids in brachial plexus block is reported to improve postoperative analgesia by one team, and another authors said that no effect was found [5].

Dexmedetomidine has many uses as in intravenous regional anesthesia (Bier's block) [5], intravenous (i.v.) sedation and analgesia for intubation. Moreover, it facilitates putting the patients on mechanical ventilation in patients admitted to intensive care units (ICUs) [6] and in minor operation in patients for surgical and other procedures not needing for intubation. In addition, it is recorded that it improves the quality of intrathecal and epidural anesthesia [7]. Its use for peripheral nerve blocks has newly observed, but its use in supraclavicular brachial plexus block is minimal [8]. In our study, we investigated whether adding dexmedetomidine to levobupivacaine for supraclavicular brachial plexus block would improve the sensory and motor blocks and duration of analgesia.

Mg sulphate is a mineral supplement given if magnesium level decreased in the blood. In addition, magnesium is very important for the normal function of cells, nerves, bones, muscles, and heart. So, we need a well-balanced diet to maintain normal blood levels of magnesium [9]. Some authors said that addition of magnesium sulfate to lidocaine leads to decreasing the postoperative pain and increasing the onset and duration of sensory and motor blocks in ultrasound guided supraclavicular brachial plexus block for upper limb surgeries [10].

Our aim of this study was to detect how adding Mg sulphate or dexmedetomidine improves the effect of local anesthetic in regional block (supra clavicular nerve block), and to compare the effect of their adding to levobupivacaine in postoperative pain management in sonar guided supraclavicular plexus block.

PATIENTS AND METHODS

A prospective randomized controlled study for 90 patients (ASA I-II) of both sex, aged 20-75 years old in the period from May 2019 to April 2020. They were scheduled for elective forearm surgeries under supraclavicular block in Sohag University Hospital.

Exclusion criteria: Patient refusal, patient with significant neurological, psychiatric or neuromuscular disease, suspected coagulopathy, morbid obesity, known allergy to some medications (levobupivacine, Mg sulphate and dexmedetomidine), septicaemia and local infection at the block site.

90 patients were divided into 3 equal groups: Group (C) control group consisted of 30 patients received an ultrasound guided supraclavicular block using 25 ml of 0.375% levobupivacaine, group (M): consisted of 30 patients received an ultrasound guided supraclavicular block using 25 ml levobupivacaine 0.375% plus 200 mg Mg sulphate 20% and group (D) consisted of 30 patients received an ultrasound guided supraclavicular block using 25 ml levobupivacaine 0.375% plus 1 ml (100 μg) dexmedetomidine, after seeing investigations and examination of patients an 18 gauge iv cannula was inserted in non-operated upper limb and started lactated Ringer's solution at 5 ml/kg/hr. All patients received 0.05 mg/kg medazolam intravenously 5 minutes before the procedure. The skin of the supraclavicular fossa was disinfected with a povidone-iodine solution of 10%.

Patients were monitored for heart rate, NIBP and oxygen saturation. Patients also were observed for onset and duration of sensory and motor block in the post-anesthesia care unit (PACU). Patients were assessed for pain based on a visual analogue scale (VAS). Complications also were observed.

Ethical approval and written informed consent:
An approval of the study was obtained from **Sohag University Academic and Ethical Committee.** Every patient signed an informed written consent for acceptance of the operation.

Ultrasound guided supraclavicular brachial plexus block:

Position: After proper good positioning of the patient and under complete aseptic precautions, ultrasound guided supraclavicular brachial plexus block was performed.

The operator stood at either the head of the bed or facing the ipsilateral shoulder. The patient's head was turned to the other side between 30 and 45 away from the side to be blocked. After finishing skin sterilization and the supraclavicular fossa was visually established, noting the sternocleidomastoid muscles, clavicle and coronoid processes. A high-frequency linear probe was located in a coronal oblique axis by orienting the probe approximately parallel to the clavicle.

Technique: the Ultrasound examination started by locating the subclavian artery in the short axis view, where the artery was seen as a round pulsating, hypoechoic structure. At this moment, also the hyperechoic first rib underneath the artery and possibly, the pleura were seen. Lateral to the subclavian artery the anesthetist identifies the middle scalene, as it is characterized by its often-striated appearance. In-between the subclavian artery and middle scalene muscle the divisions of brachial plexus appear as hypoechoic grape-cluster-like structure. The block needle advances under constant visualization in an in-plane technique along the medial border of middle scalene, toward the lateral portion of the plexus. Here, a test dose shows spread of the local anesthestic in fascial layer surrounding the brachial plexus divisions.
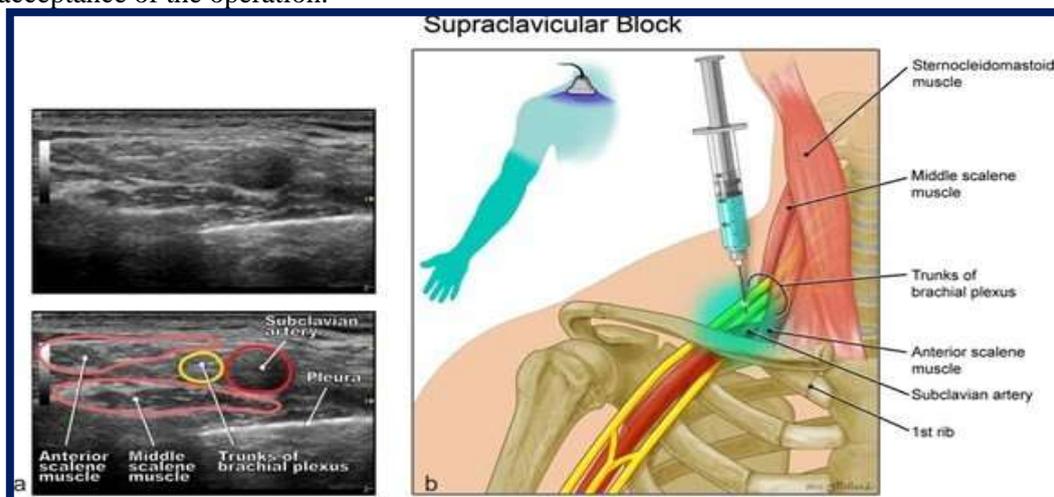

Figure (1): Supraclavicular brachial plexus block; a. Ultrasound image of the trunks of the brachial plexus sandwiched between the subclavian artery and the anterior and middle scalene muscles; b. Artist's depiction of the supraclavicular block illustrating proper needle and ultrasound probe positioning with a diagram of the upper limb representing the region that is successfully anesthetized using this approach [11].

Statistical analysis

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for Social Sciences version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Data were tested for normal distribution using the

Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Chi square test (χ2) was used to calculate difference between two or more groups of qualitative variables. Quantitative data were expressed as mean ± SD (Standard deviation). Independent samples t-test was used to compare between two independent groups of normally distributed variables (parametric data). P value ≤ 0.05 was considered significant.

RESULTS

There was no statistically significant difference between the three study groups regarding age, sex, weight or duration of surgery (Table 1).

Table (1): Demographic characteristics of the studied groups

Demographic variable		Group C n=30	Group M n=30	Group D n=30	P- value
Age in years	Mean ± SD	35.9 ± 13.5	38.6 ± 12.3	39.9 ± 12.6	0.606
Sex	Male no (%)	13(65%)	12(60%)	14(70%)	0.803
	Female no (%)	7(35%)	8(40%)	6(30%)	
Weight in kg	Mean ± SD	68.8 ± 10.2	71.7 ± 9.8	72.8 ± 10.7	0.459
Duration of surgery in hours	Mean ± SD	3.4 ± 1.3	3.45 ± 1.3	3.1 ± 1.1	0.647

Regarding the onset of sensory block, there was no any statistically significant difference between the three groups (P = 0.052). Also, it was not significantly faster in group C than group D (P2 = 0.051), and no significant difference between group M and group D (P3 = 0.125). Also, no statistical significant difference between group M and group C (P1= 0.055). As regards onset of motor block, there was no significant difference between the three study groups (P = 0.25). Besides, there was no significant difference between group C and D (P2=0.18) & no-significant difference between group C & group M (P3 = 0.07) (Table 2).

Table (2): Onset of block (sensory and motor) of the three studied groups

Onset of Sensory block in minutes	Group C n=20	Group M n=20	Group D n=20	P1	P2	P3	P
Mean	22.75	17.20	21.50	0.055	0.051	0.125	0.055
SD	8.91	6.45	9.74				
Onset of Motor block in minutes							
Mean	22	19	21	0.43	0.18	0.07	0.25
SD	7.25	5.86	7.97				

P: p value for comparing between the three groups.   p1: p value for comparing between group C and group M.
 p2: p value for comparing between group C and group D.   p3: p value for comparing between group M and group D.

*Statistically significant at p ≤ 0.05(*mild, **moderate, *** highly). ns: non-significant.

As regards duration of sensory block, there was a statistically significant difference between the three study groups (p = 0.0001). It was mild significant longer in group M compared with group C (p1 = 0.01) & but of moderate significance between group M with group D (P3 = 0.003 both) and group C with group D (p2 = 0.0005). Concerning duration of motor block, there was significant difference between the three study groups (P = 0.0001). Also, it was mild significantly longer in group M compared to group C (P1=0.01) & more significant between group C and group D (P2 = 0.002). Moreover, there was significant difference between group M and group D (P3 = 0.03) (Table 3).

Table (3): Comparison Duration of block (sensory and motor) between the study groups

	Group C n=20	Group M n=20	Group D n=20	P1	P2	P3	P
Mean	5.30	7.90	9.20	0.01*	0.0005*	0.003	0.0001**
Sensory block duration SD	1.75	2.19	1.91				
Mean	5.90	8.50	9.80	0.01*	0.002*	0.03*	0.0001**
Motor block duration SD	1.37	2.33	1.933				

p:p value for comparing the three groups.   p1: p value for test for comparing between group C and group M.
p2: p value for comparing between group C and group D   p3: p value for comparing between group M and group D

*Statistically significant at p ≤ 0.05(*mild, **moderate, *** highly).   ns: non-significant.

Regarding heart rate, there was no significant statistical difference between the studied three groups in first 6 hours of block. The difference became significant between group C and group M (P1) and also between Group D and group C (P3) after more than 6 hours of block. There was no significant difference between group M and group D (P2) along

12 hours after block (Table 4).

Table (4): Comparison of heart rate between the three studied groups after block

	Group C	Group M	Group D	P1	P2	P3	P
HR base line	Mean 90	88	89	0.12	0.08	0.07	0.07
	SD 0.71	0.68	0.83				
30 min	Mean 85	84	85	0.09	0.041	0.52	0.064
	SD 1.1	1.4	0.9				
1 hr	Mean 87	86	85	0.058	0.063	0.37	0.066
	SD 1.5	1.6	1.4				
3 hr	Mean 88	87	86	0.066	0.069	0.7	0.07
	SD 2.1	1.8	1.65				
6 hr	Mean 92	88	87	0.056	0.052	0.45	0.07
	SD 2.5	2.1	1.9				
12 hr	Mean 94	90	90	0.049*	0.037*	0.5	0.024*
	SD 1.9	1.7	1.85				

Regarding mean blood pressure, there was no significant statistical difference between the studied three groups (p) in first 6 hours. The difference became significant between group C and group M (P1) and also between group C and group D (P2). After more than 6 hours of block, there was no significant difference between group M and group D along (P3) 12 hours after block (Table 5).

Table (5): Comparison of mean blood pressure between the three studied groups after block

	Group C	Group M	Group D	P1	P2	P3	P
MBP base line	Mean 90	92	89	0.12	0.24	0.75	0.5
	SD 0.14	0.15	0.138				
30 min	Mean 85	83	82	0.095	0.089	0.56	0.48
	SD 0.5	0.45	0.43				
1 hr	Mean 84	82	80	0.088	0.076	0.45	0.68
	SD 1.1	0.85	0.89				
3 hr	Mean 87	85	83	0.075	0.059	0.7	0.29
	SD 0.98	0.91	0.87				
6 hr	Mean 87	84	82	0.045*	0.05*	0.65	0.06
	SD 0.85	0.80	0.81				
12 hr	Mean 89	85	83	0.025*	0.017*	0.75	0.05*
	SD 1	0.92	0.94				

P: p value for comparing between the three groups.   p1: p value for comparing between group C and group M.

 p2: p value for comparing between group C and group D.   p3: p value for comparing between group M and group D.

*Statistically significant at p ≤ 0.05 (*mild, **moderate, *** highly)

As regards first request analgesia given, there was a significant difference between the three study groups (P = 0.0001). It was highly significant smaller in group D compared to group C (P2=0.0001) & compared with group M it was mildly significant smaller (P3=0.001), while there was mild significant smaller in group M compared to group C (P1= 0.003) (Table 6).

Table (6): Comparison of first request for rescue analgesia among studied groups

First analgesic request	Group C (n=20)	Group M (n=20)	Group D (n=20)	P-value
8 hr.	5 (25%)	0 (0%)	0 (0%)	P=0.0001***
12 hr.	10 (50%)	4 (20%)	0 (0%)	P1:0.003**
18 hr.	2 (10%)	7 (35%)	0 (0%)	P2:0.0001***
24 hr.	0 (0%)	4 (20%)	5 (25%)	P3:0.001**

P1: p value for Fisher exact test for comparing between group C and group M.   P2: p value for Fisher exact test for comparing between group C and group D.   P3: p value Fisher exact test for comparing between group M and group D.

*Statistically significant at p ≤ 0.05 (*mild, **moderate, *** highly)

Regarding total analgesic dose postoperatively, there was a moderately significant difference between the three study groups (P=0.001). It was moderately significant smaller in group D compared to group C (P = 0.001) & compared to group M it was mildly significant smaller (P = 0.032). While there was mildly significant smaller in group M

compared to group C (P=0.031) (Table 7).

Table (7): Comparison of total analgesic dose postoperatively among three studied groups

Total analgesic Diclofenac Na dose in mg	Group C n=20	Group M n=20	Group D n=20	P value
Mean ± SD	176.47 ± 52.6	135.00 ± 58.09	75 ± 0.00	P=0.001**
				P1:0.031*
				P2:0.001**
				P3:0.032*

P: p value for comparing he three studied groups.   p1: p value for comparing between group C and group M.
p2: p value for comparing between group C and group D. p3: p value for comparing between group M and group D.

Postoperative pain assessment using Visual Analogue Scale (VAS) showed that when **group C** compared to base line, there was a highly significant increase in the VAS at 6 hrs, 8hrs, 18 hrs and 24 hrs postoperative. **Group (M):** There was a statistically significant rise in VAS at 8 hours postoperatively and a strongly statistically significant increase at 18 hrs and 24 hrs postoperatively relative to the base line. **Group D:** There was a large rise in VAS at 18hrs and 24 hrs postoperative relative to the base line. There was a statistically significant difference in VAS between the three groups studied at 8 hrs, 12 hrs and 18hrs postoperative and a mild statistically significant difference at 24 hrs postoperative between the three groups studied. There was a statistically significant increase in VAS between the three groups examined at 8 hours postoperatively, a statistically significant increase at 12 hours postoperatively and a less significant increase at 18 hours postoperatively between group C and M. **Between group C and M:** there was a significant difference in VAS between the three studied groups at 6 hrs, 8 hrs, 12 hrs and 18 hrs postoperative and a significant difference at 24 hrs postoperative. **Between group M, D:** there was a significant difference in VAS between the three studied groups at 12 hrs (Table 8).

Table (8): Comparison of VAS among the three studied groups

Postoperative period	Mean + SD			P-value
	Group C (n=20)	Group M (n=20)	Group D (n=20)	
1hr	0.00 ± 0	0.00 ± 0	0.00 ± 0	1.000
2hrs	0.00 ± 0	0.00 ± 0	0.00 ±0	1.000
4hrs	0.05 ± 0.22	0.00 ± 0	0.00 ±0	0.374
6hrs	0.95 ± 0.82[###]	0.00 ± 0	0.00 ± 0	<0.001***
8hrs	2.35 ± 1.6[###]	0.65 ± 1.04[#]	0.10 ± 0.44	<0.001***
12hrs	4.35 ± 1.9	2.80 ± 2.09	0.65 ±1.04	<0.001***
18hrs	4.80 ± 2.2[###]	3.60 ± 1.7[###]	1.55 ± 1.14[###]	<0.001***
24hrs	4.75 ± 3.1[###]	3.65 ± 2.05[###]	2.45 ± 1.82[###]	0.015*
One way ANOVA test				
	P1	P2		P3
1hr	1.000	1.000		1.000
2hrs	1.000	1.000		1.000
4hrs	0.226	0.226		1.000
6hrs	<0.001***	<0.001***		1.000
8hrs	<0.001***	<0.001***		0.145
12hrs	0.008**	<0.001***		<0.001***
18hrs	0.037*	<0.001***		0.001***
24hrs	0.155	0.004**		0.121

p- value for one-way ANOVA test.   p1: p value for comparing between group C and group M.
p2: p value for comparing between group C and group D.   p3: p value for comparing between group M and group D.
   *Statistically significant at p ≤ 0.05(*mild, **moderate, *** highly). n.s: non-significant.
#: significant difference from basal value among each group individually at <0.05(#mild, ##moderate, ### highly).

DISCUSSION

In our study we found that Mg sulphate as an additive to local anesthetic made the onset of block faster (sensory block 17.20 ± 6.45 in min) (motor block 19 ± 5.86 min) than control group (sensory block 20.75 ± 8.91 min) (motor block 20 ± 7.25) who received local anesthetic only, while dexmedetomidine as an additive to local anesthetic made the onset of block slower (sensory block 21.50 ± 9.74 min) (motor block 21 ± 7.97) than control group but difference between the three groups is insignificant. **Abdelfatah and Elshaer[12]** found in their studies that addition of Mg sulphate made the onset of block faster when it is added to lidocaine and epinephrine than to lidocaine and epinephrine only but no significant difference. In agreement with our study, **Verma et al.** [13] also found in their study that Mg Sulphate as adjuvant in brachial plexus block made onset of block faster and it was dose-dependent when compared to other groups. In contrast to our study **Haghighi et al.** [14] found in their study that adding Mg

sulfate to lidocaine delayed the onset of block when it is compared to lidocaine alone to block the axillary plexus using the trans-arterial technique. **Rao _et al._** [15] in Andhra Pradesh, India, concluded in one study that the addition of magnesium sulfate to 0.5% bupivacaine in supraclavicular brachial plexus block for upper limb surgeries increased the duration of sensory and motor blocks in comparison with the use of 0.5% bupivacaine, although the change was not statistically significant. **Haghighi** _et al._ [14] observed that the effect of magnesium in the axillary brachial plexus block when applied to lidocaine in upper limb surgeries in contrast to the use of lidocaine alone, significantly increased the length of sensory and motor blocks. In Cairo, Egypt, **Abdelfatah and Elshaer** [12] observed that the addition of magnesium sulphate to lidocaine in the interscalal brachial plexus block increased statistically significantly analgesic length and decreased postoperative pain and opioid requirements for shoulder arthroscopic acromioplasty. In Seoul, Korea, **Lee _et al._** [16] noted when applied to bupivacaine for interscalene brachial plexus block, magnesium sulphate induced a reduction in postoperative pain in arthroscopic rotator cuff repair.

We performed this study with a magnesium dose of 200 mg, but in previous studies, they used magnesium sulphate in doses of 150, 300, 450, and 600 mg.

Swami _et al._ [17] noted that dexmedetomidine (1 μg/kg) plus local anaesthetic (35 cc, 0.25 percent bupivacaine) for supraclavicular brachial plexus block improved sensory and motor block length, as well as analgesia duration. In patients receiving dexmedetomidine, the time for rescue analgesia was extended. It also increased block consistency compared to clonidine (1 μg/kg). **Zhang _et al._** [18] also reported that there was prolonged sensory and motor blockade length in patients who obtained dexmedetomidine (50 μg) in 40 ml of 0.33 percent ropivacaine compared to the control group for axillary brachial plexus blockade. However, dexmedetomidine was also followed by an increased occurrence of complications such as bradycardia, hypertension, and hypotension. In contrast to our study **Elyazed and Mogahed** [19] stated that Mg sulphate made the onset of block slower than block with local anesthetic alone when they used it as an additive to infraclavicular nerve block in comparison with dexmedetomidine.

In our study we found that both Mg sulphate (sensory duration 7.90 ± 2.19 hours) (motor block duration 8.50 ± 2.33 hours) and dexmedetomedine (sensory block duration 9.20 ± 1.91 hours) (motor duration 9.80±1.933 hour) increased the duration of block and analgesia, but dexmedetomidine increased the duration more than Mg sulphate. Also, both dexmedetomidine and Mg sulphate delayed time of first analgesia requirement and also the total analgesic doses required than local anesthetic alone, but dexmedetomidine was better than Mg sulphate in this. In agreement with our study, **El-Morabaa _et al._** [20] found that Mg sulphate prolongs sensory block and analgesia with increasing the dose when added to local anesthesia

perineurally when they compared between different groups with different dosses and routes of Mg Sulpahte. In accordance with our research **Akhondzade _et al._** [21] reported that the addition of Mg sulphate to lidocaine reduced postoperative pain and increased the length of sensory and motor blocks in the supraclavicular brachial plexus block in upper limb surgery under ultrasound guidance.

Regarding first request analgesia given, there was a significant difference between the three study groups (P = 0.0001). It was highly significant smaller in group D compared to group C (P2 = 0.0001) & compared to group M, it was mildly significant smaller (P3 = 0.001), while there was mildly significant smaller in group M compared to group C (P1 = 0.003).

Concerning total analgesic dose postoperatively, there was a moderately significant difference between the three study groups (P = 0.001). It was moderately significant smaller in group D compared to group C (P = 0.001) & compared to group M, it was mildly significant smaller (P = 0.032), while there was mildly significant smaller in group M compared to group C (P = 0.031). **ELShamaa _et al._** [22] found that diclofenac sodium (35.6 mg vs. 113.6 mg) was statistically substantially less as a rescue analgesic in the bupivacaine plus magnesium group, compared to bupivacaine plus regular saline group during the femoral nerve block. Other authors also found that less patients in the magnesium sulphate group requested rescue analgesia (9 vs. 30).

In our study as regards complication in comparison between three studied groups, only one patient of each group developed attack of nausea with or without vomiting managed by metoclopramide i.v., only one patient of group C developed transient attack of hypotension managed by ephedrine i.v. The incidence of complications and side effects were not affected by addition of Mg and a less significant difference at 18 hrs postoperatively. In accordance with the research by **Swami _et al._** [17] **and Esmaoglu _et al._** [23], no major serious side effects were identified in any group in their study with the exception of lower pulse rates and blood pressure found in conservatively controlled dexmedetomidine groups.

CONCLUSION

In our study, we concluded that supraclavicular block is a safe technique and has many advantages. Our study demonstrated that both Mg sulphate and dexmedetomidine as additives for supraclavicular brachial plexus block hastens most of properties of block like onset of sensory block, motor block and provided a longer duration of motor blockade and postoperative analgesia as compared to control group in which patients received local anesthetic only. As comparison between Mg sulphate and dexmedetomidine, Mg sulphate as additive to local anesthetic in block made the onset of block faster than dexmedetomidine which made the onset even slower than block with local anesthetic alone. As regards duration of block, both Mg sulphate and

dexmedetomidine increased duration of block than block with only local anesthetic but Mg sulphate made the duration longer than dexmedetomidine. As regards analgesia, both of them increased time of analgesia postoperatively but dexmedetomidine increased time of analgesia more than Mg sulphate. As regards complications and side effects, both of them as additive had no effect on incidence of complications or side effects of block.

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