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Original Research Article

A Comparative Study to Evaluate the Efficacy of 0.5% Levobupivacaine with Magnesium Sulphate versus 0.5% Levobupivacaine Alone in Ultrasound Guided Supraclavicular Brachial Plexus Block for Upper Limb Surgeries

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Conflict of interest: Nil

Abstract:

Introduction and Aim: Magnesium sulphate as adjuvants to local anaesthetics in brachial plexus block augments the local anaesthetic effects and reduces the analgesic requirements postoperatively. The aim of this study was to evaluate the analgesic effects of Magnesium as an adjuvant to Levobupivacaine for supraclavicular block.

Materials and Methods: In a prospective double blind study, where 60 patients of 18 to 60 years of ASA class I & II scheduled for elective upper limb surgeries were randomly divided into two groups of 30 each. Supraclavicular block was performed under ultrasound guidance. Group M received 18ml of 0.5% Levobupivacaine with 150mg Magnesium sulphate diluted to 2ml and Group N received 18ml of 0.5% Levobupivacaine and 2ml of Normal saline. Parameters observed were time of onset of sensory and motor blockade, duration of sensory and motor blockade, duration of analgesia, intraoperative hemodynamics and adverse effects.

Results: The demographic profile was comparable between the two study groups. The onset of sensory block was faster in Group M, 3.167 ± 0.9129min compared to Group N, 4.733±1.1725 min. Onset of motor blockade was faster in Group M: 5 ± 0.9469min compared to Group N: 7.100±1.0619 min. Duration of sensory block and motor block was prolonged in Group M compared to Group N. Duration of analgesia was significantly prolonged: 12.300 ± 1.7201h in Group M compared to 9.033 ± 0.9820h to Group N. No significant difference was observed in heamodynamics, side-effects and complications.

Conclusion: Addition of Magnesium sulphate to Levobupivacaine leads to early onset of sensory and motor blockade prolongs duration of sensory and motor blockade and provides good post-operative analgesia without any adverse effects.

Keywords: Magnesium sulphate; Levobupivacaine; Ultrasound; Supraclavicular Brachial plexus block.

Introduction

Supraclavicular nerve block is a good alternative to general anaesthesia in upper limb orthopaedic surgeries, as it preserves pharyngeal and laryngeal reflexes with decreased risk of aspiration, decreases post-operative complications associated with intubation and provides better post-operative pain relief without much sedation, so early mobilization and discharge [1]. With ultrasonography there is direct visualization of structures and spread of local anaesthetic agents which increases success of block and decreases its complications [2]. Levobupivacaine use in clinical anaesthesia practice has increased in past few years, which is an S-enantiomer of Bupivacaine [3]. Many evidences are present establishing the safety profile of Levobupivacaine compared to Bupivacaine when used in regional anaesthesia, as incidence of adverse effects like cardiotoxicity and neurotoxicity are more common with Bupivacaine. Hence now a days Levobupivacaine has been widely used in sub-arachnoid blocks, epidural blocks, brachial plexus block, peripheral blocks, local infiltration [4]. Magnesium is 4th most abundant cation in the body and 2nd most abundant intracellular cation. Magnesium is necessary for presynaptic release of acetylcholine from nerve

endings. Magnesium sulphate is a NMDA (N-Methyl D-Aspartate) receptor antagonist and it also regulates the calcium influx into cell [5,6]. It prevents the release of catecholamines from adrenals and peripheral nerve endings, hence catecholamine receptors are blocked and causes sympathetic block [7].

Many clinical studies have demonstrated that Magnesium sulphate, given as an adjuvant to local anaesthetics in regional anaesthesia was shown to decrease postoperative analgesics consumption. Hence this study was undertaken to see the efficacy of magnesium sulphate as an adjuvant with 0.5% Levobupivacaine in ultrasound guided supraclavicular blocks, as many studies are not conducted in combination with Levobupivacaine and Magnesium sulphate.

Methodology:

With Ethical Committee approval, a double blind, randomized prospective clinical study was planned among 60 patients. Patients providing written informed consent voluntarily, aged 18 - 60 years of either sex, belonging to American society of anaesthesiologists (ASA) Grade I and II, patients with height 150-180cms and weight 50-80kg and patients undergoing elective upper limb surgeries were included in the study.

Patients not willing to give written informed consent, patients with any contraindications for peripheral nerve block, allergic to the study drug, with coagulation disorder, in Cardiogenic or hypovolemic shock and in Respiratory insufficiency were excluded from study. Preoperatively patients were counselled and familiarized with the use of Visual Analog Scale (VAS) pain score for the assessment of perioperative pain. After obtaining written informed consent, patients were randomly divided in to two groups using http://www.randomizer.org. Allocation concealment of the randomized groups was also done. The anaesthesiologist, surgeon and patient were blinded to patient group. The study drug was prepared by anaesthesiologist not involved in the study.

1. Group M - Inj 0.5% Levobupivacaine 18ml with 2ml of 150mg of Magnesium sulphate (total volume = 20ml)
2. Group N - Inj 0.5% Levobupivacaine 18ml with 2ml of Normal Saline (total volume = 20ml). An independent observer (senior anaesthesiologist) then observed the onset and duration of sensory and motor blockade and duration of analgesia. Blinding was opened at the end of the study.

Pre-anaesthetic examination comprising of detailed history, systemic examination and thorough airway examination was conducted on all patients. Routine investigations relevant for surgery were done. All patients were kept fasting for 8 hours. Tab Alprazolam 0.25mg and Tab Ranitidine 150mg was given night before the day of surgery. On arrival to the operating room, Non-Invasive Blood Pressure, Pulse oximetry and Electrocardiogram was connected and the baseline Systolic, Diastolic and Mean Arterial Pressures (SBP, DBP and MAP), Heart Rate (HR) and Oxygen Saturation (SpO2) was recorded. Intravenous access was secured and IV fluids were started. A scout scan was performed using a linear high frequency probe (12 MHz, Sonosite machine) over the supraclavicular area to rule out anatomical abnormalities including aberrant vasculature. Under strict aseptic precautions, ultrasound guided supraclavicular block was performed using an in-plane approach with a conventional 2.5 inch long needle with 25 G width. If longer needles were needed, a 23 G spinal needle was used.The corner pocket between the brachial plexus and subclavian artery was the target for needle tip placement. The drugs were prepared by an independent consultant and the person administering the block was unaware of the drug combinations. The following parameters were measured: **Onset of sensory block (score = 1)** - Is defined as the time taken from the end of the injection to the first dull response to pinprick in the distribution of any of the three sensory nerves in the hand by using 25G hypodermic needle. After injection, patients were assessed for sensory blockade by using pinprick by 3-point scale [8]. The pinprick was done every minute. The palmar surfaces of the index and little finger used to test the Median and Ulnar nerve in the hand, respectively. The dorsal surface of the thumb used to test the Radial nerve.

Sensory score:

0 - Normal sensations to pin prick.

1 - Dull response to pin prick.

2 - No response to pin prick.

Onset of motor block (score = 1) - From end of injection to the decreased motor strength. Motor block was assessed by asking the patient to adduct the shoulder and flex the fore-arm and hand against gravity. Motor characteristics of block were assessed using Bromage 3-point scale [8].

Motor score:

0 - Normal motor functions with full flexion and extension elbow, wrist and fingers.

1 - Decreased motor strength with ability to move fingers only.

2 - Complete motor blockade with inability to move fingers.

The end of the injection was considered time 0. Block was successful if it occurred within 30 min. Patients with inadequate blockade requiring supplementation of drugs like opioids were excluded from the study.

Duration of sensory block was defined as the time taken between injection of the drug and appearance of pin prick.

Duration of motor block was defined as the time taken between injections of the drug to complete return of motor power.

Duration of analgesia was defined as the time interval between the onsets of complete sensory block to the postoperative VAS score ≥4.

Duration of sensory, motor block and duration of analgesia was recorded. Hemodynamic parameters: Heart rate, systolic, diastolic, mean arterial pressure, respiratory rate, arterial oxygen saturation (SpO2) was measured at 0, 2, 5, 10, 20, 30 min and thereafter every 15 min till the end of surgery. Pain intensity was evaluated using 10 cm visual analogue scale (VAS) where 0 represents no pain and 10 represents worst possible pain. Rescue analgesia with Inj Paracetamol 1g I.V. was given if VAS score is ≥4. If VAS was still ≥4 after 2h, Inj Tramadol 50mg I.V. was given. VAS score was recorded postoperatively at 0, 2, 6, 12, 20 and 24 h. The time for the first rescue analgesia and analgesic consumption in first 24hrs was noted.

Any adverse events like vomiting, pruritus, persistent paraesthesia and weakness was noted in the perioperative period. All the observations were made by the independent observer who was blinded to the group allocation.

Statistical analysis:

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square test was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. Independent t test was used as test of significance to identify the mean difference between two quantitative variables.

Graphical representation of data: MS Excel and MS word was used to obtain various types of graphs such as bar diagram and line diagram. p value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

Statistical software: MS Excel, SPSS version 22 (IBM SPSS Statistics, Somers NY, USA) was used to analyze data. Statistical software: MS Excel, SPSS version 22 (IBM SPSS Statistics, Somers NY, USA) was used to analyse data.

Results

Both the groups were comparable in the terms of demographical data, ASA Grade and duration of surgery and no statistically significant difference was found (p>0.05) (Table 1 and 2). Onset of sensory and motor blockade was faster in Group M in comparison to Group N (p <0.001) (Table 3 and figure1).

Duration of sensory and motor blockade and analgesia was prolonged in Group M in comparison to Group N (p<0.001) (Table 3and figure 2). Heart rate, Systolic and Diastolic blood pressure changes during entire intraoperative period were statistically not significant in both the groups (p>0.05).

In the study there was significant difference in mean VAS Score between two groups at 12th, 20th and 24th hr intervals of follow-up. At these intervals mean VAS Score was high in group N (figure 3). There was significant difference in mean Inj Paracetamol consumption in 24hrs between two groups. The mean 24-hour Inj Paracetamol consumption being higher in the saline group.

Table 1: Demographic parameters and duration of surgery distribution between two groups

	Group				
	M		N		
	Mean	SD	Mean	SD	p Value
Age	35.87	11.80	35.50	9.28	**.894**
Height(M)	1.67	0.06	1.66	0.07	**.813**
Weight (Kg)	68.07	10.71	64.53	8.88	**.169**
BMI(Kg/m2)	24.48	3.15	23.31	2.19	**.098**
Duration of surgery (min)	118.333	31.3856	115.167	24.4415	**.664**

Table 2: Distribution of Sex and ASA grade between two groups

		Group				Total			
		M		N					
		Count	% within group	Count	% within group	Count	% within group	Pearson Chi-Square Value	p Value
Sex	F	12	40.0%	13	43.3%	25	41.7%	.069a	**.793**
	M	18	60.0%	17	56.7%	35	58.3%		

Total		30	100.0%	30	100.0%	60	100.0%			
ASA grade	I	21	70.0%	16	53.3%	37	61.7%	1.763a	**.184**	
	II	9	30.0%	14	46.7%	23	38.3%			
Total		30	100.0%	30	100.0%	60	100.0%			

Table 3: Comparison of Mean Onset of Sensory and Motor Blockade, Duration of Sensory Block and Motor block and Analgesia between two groups

	Group						
	M			N			
	n	Mean	SD	n	Mean	SD	p Value
Onset of sensory block (min)	30	3.167	.9129	30	4.733	1.1725	**<0.001**
Onset of motor block (min)	30	5.000	.9469	30	7.100	1.0619	**<0.001**
Duration of sensory block (hrs)	30	11.133	1.5477	30	7.833	1.1472	**<0.001**
Duration of motor block (hrs)	30	9.733	1.3374	30	6.400	1.1919	**<0.001**
Duration of analgesia (hr)	30	12.300	1.7201	30	9.033	.9820	**<0.001**

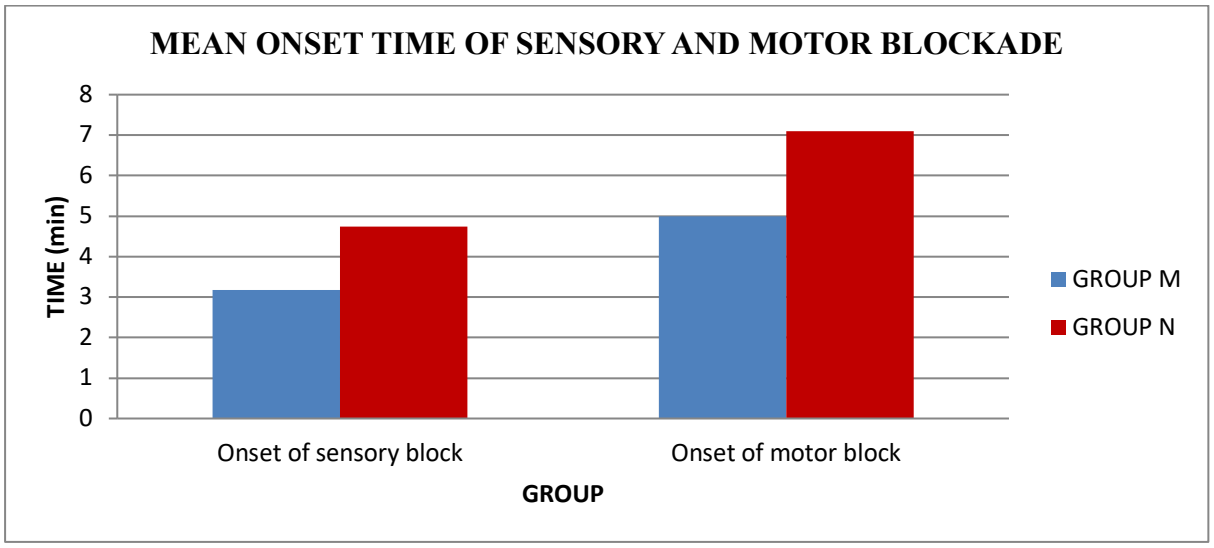

Figure 1: Bar Diagram showing Comparison of Mean Onset of Sensory and Motor Blockade between two groups

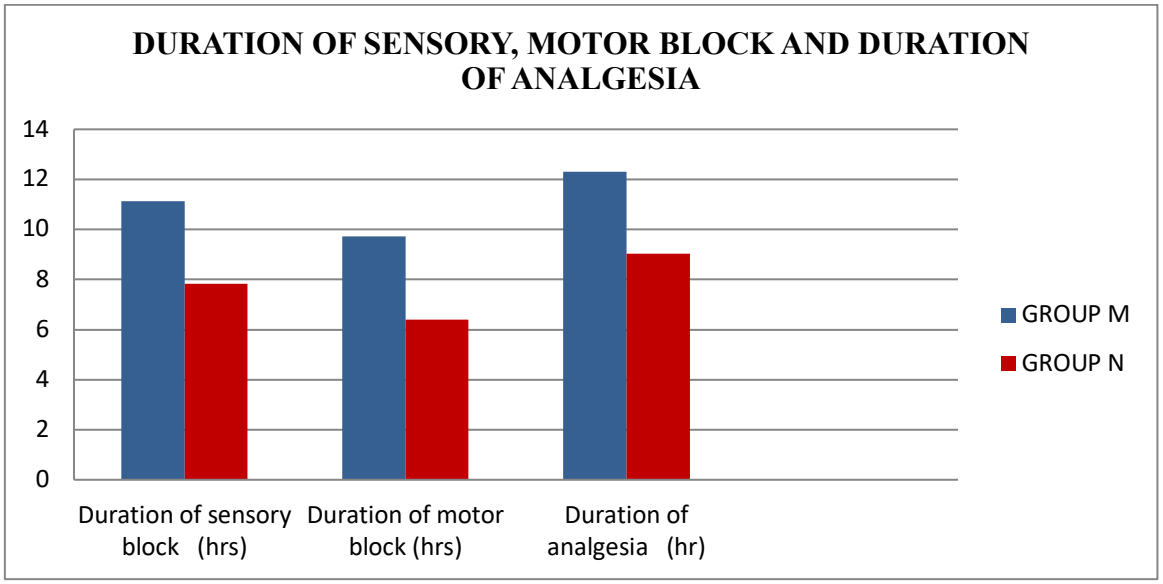

Figure 2: Bar Diagram showing Comparison of Mean Duration of Sensory Block, Motor Block and Duration of analgesia between two groups

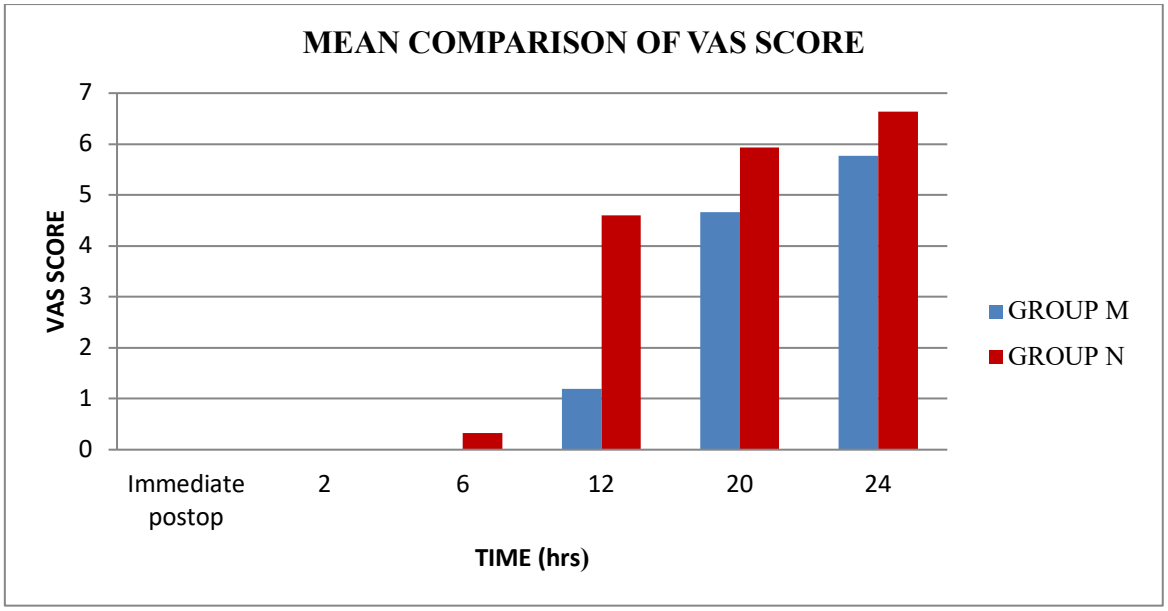

Figure 3: Bar Diagram for Mean comparison of VAS Score between two groups at different periods of follow-up

Discussion

Brachial plexus block has been considered as a better technique for providing anaesthesia for upper limbs surgeries. Regional nerve blocks are found to be better than general anaesthesia in account of untoward complications related to airway instrumentation and also effective in terms of safety, cost effectiveness, easy to perform and lesser polypharmacy. It provides good post-operative analgesia. Among the various approaches of brachial plexus block, supraclavicular block is the relatively easiest mode and most effective for surgical anaesthesia and to provide post-operative analgesia The advantages of performing upper limb surgeries under brachial plexus block are many but the lesser duration of action in prolonged surgeries is a significant downside. When continuous catheter techniques are not available, adjuvants help by potentiating the action of local anaesthetics. [9]

Levobupivacaine is comparatively a new long acting local anaesthetic, it is been produced in order to address the complications resulting due to incidental intravascular injections like cardiovascular and neurological toxicity. It is S (-) isomer of bupivacaine. Bupivacaine is commercially available as a mixture of its two enantiomers levobupivacaine, S (-) and dextrobupivacaine, R (+) as a racemic mixture (50:50). The levo-rotatory isomers are known for safer pharmacological profile with lesser cardiotoxic and neurological side effects [4]

Levobupivacaine is a relatively new local anaesthetic that has not been tested with other additives like magnesium sulphate. Since the introduction of MgSO4 as NMDA receptors antagonist, its role has been evaluated for the analgesic properties in anaesthesia practice. The NMDA receptors play an important role in central nociceptive transmission, modulation and sensitisation of acute pain states. In addition to central location, NMDA receptors are found in the muscle and skin, knee joint and play a role in sensory transmission of noxious signal.[10,11,12]

Many clinical studies have demonstrated that Magnesium Sulphate given as an adjuvant to local anaesthetics in regional anaesthesia shown to decrease post-operative analgesics consumption. Hence this study is undertaken to see the efficacy of magnesium Sulphate as an adjuvant with 0.5% Levobupivacaine in ultrasound guided supraclavicular blocks as many studies are not conducted with Levobupivacaine and Magnesium Sulphate

A randomized double blinded study was undertaken among 60 patients posted for upper limb surgery who were aged between 18 to 60 years. Patients were divided into two groups of 30 each (Group M and Group N). Group M received supraclavicular brachial plexus block with 18 ml of 0.5% Levobupivacaine and 2ml of 150mg Magnesium Sulphate. Group N received supraclavicular brachial plexus block with 18ml of 0.5% Levobupivacaine with 2ml of normal saline. Parameters observed are onset of sensory-motor blockade, duration of sensory motor blockade and duration of analgesia, hemodynamic parameters and safety profile of drug.

In our study we found that the mean onset of sensory block was faster in Magnesium sulphate group which was 3.167 ± 0.9129 min and was 4.733 ± 1.1725 min in Levobupivacaine with saline

group, which is statistically significant ($p \leq 0.001$). This observation well matches with study by Ahmed Hamody Hassan et al [13] on the addition of 200mg of Magnesium sulphate with 0.375% Levobupivacaine (group M) decreases the time of onset of sensory block when compared to control group (group C) and dexmedetomidine group(group D) in supraclavicular block. The mean duration of onset of sensory block was 22.75min, 17.20min and 21.50min in group C, group M and group D respectively.

In our study we observed that onset of motor block was faster in study group of Magnesium sulphate having the mean value of 5 ± 0.9469 min and was 7.100 ± 1.0619 min in levobupivacaine with saline group. Dogru K et al [14] showed that onset of motor block was earlier with addition of magnesium sulphate to Levobupivacaine compared to control group. The time of onset of motor block was 13.25±1.74min and 11.5±1.5min in saline and Magnesium group respectively, and was statistically significant.

The Mean duration of sensory block in Magnesium sulphate group was 11.133 ± 1.5477hrs and 7.833 ± 1.147 hrs in saline group .The mean duration of motor block in Magnesium sulphate group was 9.733 ± 1.3374 hrs and 6.400 ± 1.1919 hrs in Saline group .There was statistically significant differences in duration of action between Magnesium sulphate and saline group ($p<0.005$). Similar findings were noted in the study done by Taneja P et al [15], comparison of 0.5% Ropivacaine with 150mg of Magnesium sulphate in supraclavicular brachial plexus block. The mean sensory duration was 420±30.25min in Magnesium group and 290±26.95min in normal saline group. Whereas motor duration was 350±15.25min and 236±20.06min in Magnesium group and control group respectively

In our study we found that, the mean duration of Analgesia was 12.300 ± 1.7201hr in Magnesium sulphate group and was 9.033± 0.9820hr in Saline group. There was significant difference in mean Duration of Analgesia between two groups ($p<0.005$). This matches well with a study conducted by Kasturi Mukherjee et al [6] noted adding Magnesium sulphate to Ropivacaine in supraclavicular brachial plexus block increase the sensory and motor block duration and time to first analgesic use. The duration of analgesia was 461.71±152min in magnesium group and 379.79±145.52min in control group. In our study it was found that the total dose of Inj Paracetamol required in post-operative period was significantly high in the group receiving Levobupivacaine alone 1400.00 ± 498.27 mg compared to the group receiving Levobupivacaine with Magnesium sulphate 1033.33 ± 182 .57 mg ($p < 0.05$). Additional rescue analgesic requirement was higher in control group compared to Magnesium sulphate group. Hemodynamic parameters were well maintained with in normal range in both groups. No side effects like bradycardia, ECG changes, hypotension or urinary retention were observed. There was no incidence of sedation and respiratory depression with respect to Magnesium sulphate.

Conclusion

Ultrasonography guided supraclavicular brachial plexus block is a well-accepted and safer technique in delivery of anaesthesia in patients undergoing elective upper limb surgeries. Visualizing and drug administering under ultrasonogram make it safe, provide prolonged analgesia with a lesser volume of local anaesthetic and prevents the side effects of general anaesthesia. Adjuvants are commonly used along with local anaesthetics to prolong the duration of analgesia. From our study we conclude that, the addition of Magnesium sulphate (150mg) with Levobupivacaine 0.5% has following effects:

- Faster onset of sensory block
- Faster onset of motor block
- Longer duration of analgesia
- Lesser volume of local anaesthetic drug requirement
- Minimal hemodynamic variability and no side effects.

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