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COMPARATIVE STUDY TO EVALUATE THE QUALITY OF ANESTHESIA WITH NITROGLYCERINE AND MAGNESIUM SULPHATE AS ADJUVANTS TO LIGNOCAINE IN INTRAVENOUS REGIONAL ANESTHESIA

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Abstract

Introduction: Intravenous Regional Anesthesia (IVRA) is a concise, stable, and effective treatment with a fast onset of action and speedy recovery after tourniquet release. Although lignocaine is a popular local anesthetic agent, it has the restriction of having a limited duration of anesthesia and being unable to offer postoperative analgesia; hence, other additives were added to it. This randomized control study was conducted to evaluate and compare the quality of anesthesia with Magnesium sulphate and Nitroglycerine as adjuvants to Lignocaine in intravenous regional anesthesia. **Materials and methods:** This study included upper arm surgery patients, a pneumatic tourniquet was wrapped around the arm to isolate the proximal vascular system. Totally, 60 patients, belonging to ASA 1and 2 grades posted for elective surgery of upper arm were selected and divided randomly into two groups. Patients in LM group received 10ml of 15% Magnesium sulphate with 3mg/kg 2% Lignocaine diluted up to 40ml with saline and LN group received 200mcg of Nitroglycerine with 3mg/kg 2%Lignocaine diluted up to 40ml with saline. Sensory and motor block onset time, tourniquet pain, intraoperative haemodynamics, sensory and motor recovery time and time for first rescue analgesia were noted and evaluated. **Results:** The onset time for sensory blockade was shorter in Magnesium group compared to Nitroglycerine, however onset for motor blockade was shorter in Nitroglycerine group. The intraoperative VAS score was significantly low in both the groups and no changes in haemodynamic variables observed between two groups. Sensory and motor recovery was prolonged in Magnesium group. The time for rescue analgesia was prolonged in Magnesium group. **Conclusion:** The addition of Magnesium sulphate to lignocaine in IVRA produce faster onset of anesthesia and prolonged post-operative anesthesia compared to Nitroglycerine with no serious side effects.

Keywords: Intravenous Regional Anesthesia; Analgesia; Magnesium Sulphate; Nitroglycerine.

INTRODUCTION

Relief of pain during surgery is one of the major objectives of anesthesia. Intravenous regional anesthesia is one of the useful and popular regional techniques in anesthesia practice. Intravenous regional anesthesia is a technically simple and reliable procedure, with high success rates between 94-98%.[1] IVRA was first used by August Bier in 1963, Holmes used lignocaine as local anesthetic in place of procaine and this

technique gained success and popularity, was in use for many years and used as standard local anesthetic for IVRA.[2] Intravenous regional anesthesia (IVRA) has evolved as a safe, reliable, and cost- effective technique for providing anesthesia as well as bloodless field during upper limb surgery especially in patients who are not adequately prepared for general anesthesia [3,4] and avoids polypharmacy, provides adequate postoperative analgesia and early ambulation. IVRA is a regional anesthesia technique that is executed by using pressure to the proximal extremity with the use of pneumatic tourniquet isolating limb from systemic circulation. This technique is limited to procedures lasting less than an hour because of increasing discomfort from tourniquet. Many researches are being conducted to increase the quality of analgesia in intravenous regional anesthesia by adding adjuvant to the local anesthetic solution. Ketamine, Meperidine, Morphine, Sufentanil, Ketorolac, Tramadol, Clonidine, Dexmedetomidine, Magnesium Sulphate, Pancuronium, and Nitroglycerine have all been employed as adjuvants. Clonidine is a sedative alpha-2 agonist with a central action. It enhances intraoperative stability by lowering catecholamine release and reduces the need for post-operative analgesics. It extends the duration of a peripheral nerve block. Bradycardia, hypotension, sedation, dry mouth, and respiratory depression are all possible side effects. The ideal IVRA solution should have rapid onset, reduced dose of local anesthetic, reduced tourniquet pain and prolonged post deflation analgesia. IVRA has been limited by tourniquet pain and inability to provide postoperative analgesia.[5] One of the problems with IVRA using local anesthetic alone as compared to peripheral nerve blocks is that there is no prolonged analgesic effect after tourniquet release. Lignocaine when used in lower concentration (0.5%) acts on sensory nerve endings and the small nerves whereas the higher concentration (2%) acts on both nerve trunks and nerve endings. A variety of drugs have been added as adjuvants to local anesthetics for IVRA, including opioids, clonidine, non-steroidal anti-inflammatory drugs, Dexmedetomidine, and Neostigmine, muscle relaxants in attempts to improve intraoperative anesthesia and postoperative analgesia.[6,7] The present clinical study is to compare the effects of 200µg Nitroglycerine and 15% Magnesium sulphate in combination with Lignocaine 2% in IVRA for surgeries of forearm or hand.

METHODS

A randomized control trial was conducted on patients admitted in Orthopaedics and generalsurgery ward posted for elective surgical procedures of forearm and hand at Adichunchanagiri Hospital and Research Centre, B.G Nagara, Mandya District for a period of one year, after obtaining a permission from ethical committee of the institute. Patients who included in this study were ASA I and ASA II, 20-60years of age, Eelctive hand or forearm surgery and who gave consent. Patients who excluded were Reynaud's disease, Sickle cell anaemia, Peripheral or central neurological diseases, Cardiac comorbidities and Scleroderma. In this prospective, randomized control study all the patients were subjected to undergo thorough pre-anesthetic checkup. Informed consent was taken in writing forthe procedure. All patients were kept nil per-oral from 10pm prior to the day of surgery and Tab. Alprazolam 0.5mg was given orally. On the day of surgery IV access was taken with 18g IV cannula and crystalloid solution started. Patients were premedicated with 0.07mg/kg midazolam IV 15min before the surgical procedure. The patients were connected to monitor (ECG, NIBP, oxygen saturation (Spo2) and heart rate) and monitored throughout. A cannula was placed in a vein on the dorsum of the operative hand. The operative arm was elevated for 2 min

and then exsanguinated with an esmarch bandage. A pneumatic tourniquet was then placed around the upper arm and the proximal cuff was inflated to 250 mm Hg pressure. Circulatory isolation of the arm was verified by inspection, absence of a radial pulse, and a loss of the pulse oximetry tracing in the ipsilateral index finger. Group 1 (LN) were given 200 microgram Nitroglycerine and 3mg/kg Lignocaine 2% diluted with saline to a total of 40 ml. Group 2 (LM) were given 10 ml of 15% Magnesium sulfate (12.4 mmol) and 3mg/kg Lignocaine 2% diluted with saline to a total of 40 ml. The solution was injected over 90 seconds. Sensory block was assessed by pin prick every 30 seconds. Motor function was assessed by asking the subject to flex and extend his/her wrist and fingers. Inability to do this was considered as onset of motor block. After sensory and motor block onset, the distal cuff was inflated to 250 mmHg and the proximal tourniquet was released and surgery commenced. Assessment of tourniquet pain scores was made on the basis of the visual analogue scale (VAS) {0= no pain and 10= worst pain imaginable} measured before and after tourniquet application.

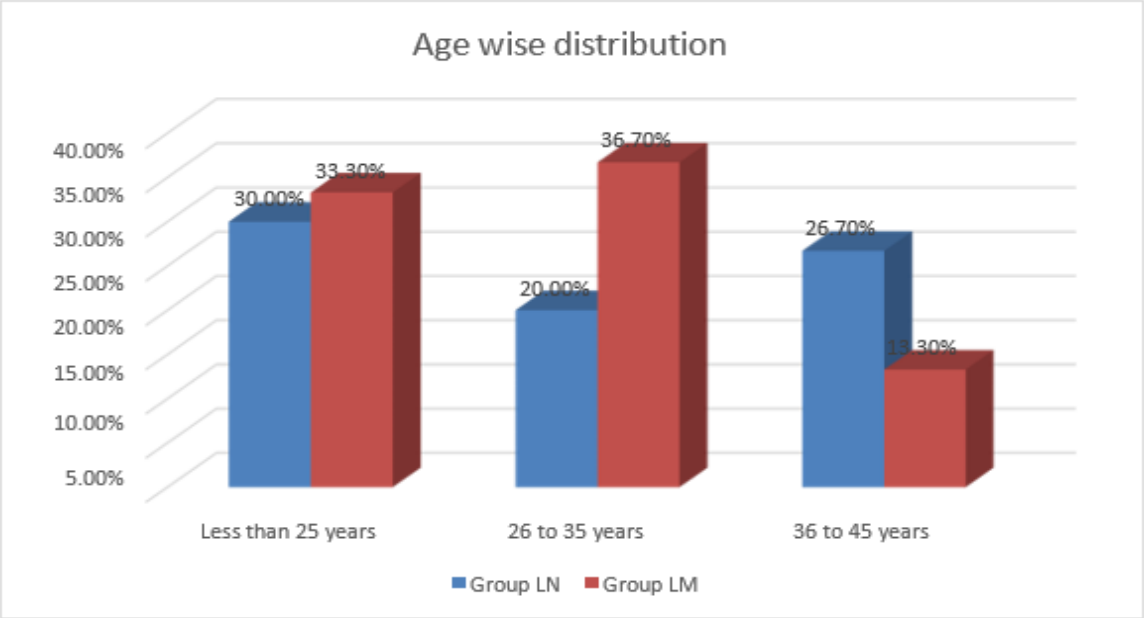
Sensory block was assessed by pinprick with a 22-gauge short-beveled needle, every 30s. Patient response was evaluated in the dermatomal sensory distribution of the medial and lateral ante-brachial cutaneous, ulnar, median, and radial nerves. Motor function was assessed by asking the subject to flex and extend his/her wrist and fingers. Absence was any voluntary movement was considered as complete motor block. Assessment of tourniquet pain scores was made on the basis of the visual analogue scale (VAS) (0-no pain and 10-worst pain imaginable) measured before and after tourniquet application and at 1, 3 5, 10, 15, 30, 45, 60, and 90 min after study drug application.

Tourniquet time in the present study was restricted between 30 and 90minutes. It was not deflated earlier to 30min after injection of the drug. At the end of surgery, the tourniquet deflation was performed by the cyclic deflation technique. Sensory recovery time was noted (the time elapsed from tourniquet deflation torecovery of sensation in all dermatomes). Motor block recovery time was noted (the time elapsed from tourniquet deflation until movement of fingers). The first analgesic requirement time was also noted (the time elapsed from tourniquet release until first patient request for analgesic). Patients were kept under observation in the post-operative unit for at least 3hours, monitored and then shifted to ward. Assessment of postoperative pain was made on the basis of the VAS. All the data were entered and analysis was done in SPSS ver-25. 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 and non-parametric test (Mann Whitney U test) was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation and p value was calculate using independent t test. p value of <0.05 was considered as statisticallysignificant after assuming all the rules of statistical tests.

RESULTS

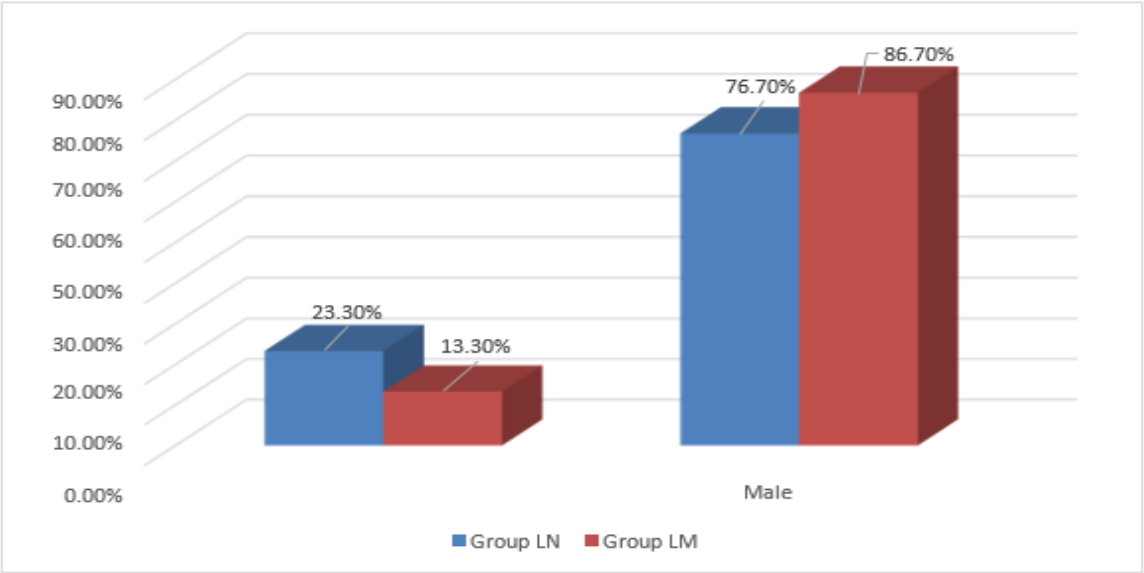
In terms of age, gender, weight, and ASA physical status, the two study groups were compared. In the present study nearly 30% of the study participants were less than 25 years of age inboth the groups. In Group LN nearly 30% were less than 25 years, 20% were between26 to 35 years, 26.7% between 36 to 45 years and 23.3% were more than 45 years of age. In group LM nearly 33.3% were less than 25 years of age, 36.7%

were between 26 to 35 years, 13.3% between 36 to 45 years and 16.7% were above the age of 45 years. In present study nearly 30% of the study participants were less than 25 years of age inboth the groups. In Group LN nearly 30% were less than 25 years, 20% were between26 to 35 years, 26.7% between 36 to 45 years and 23.3% were more than 45 years of age. In group LM nearly 33.3% were less than 25 years of age, 36.7% were between 26 to 35 years, 13.3% between 36 to 45 years and 16.7% were above the age of 45 years. The association of age between the groups was found to be statistically not significant. (p-value>0.05)



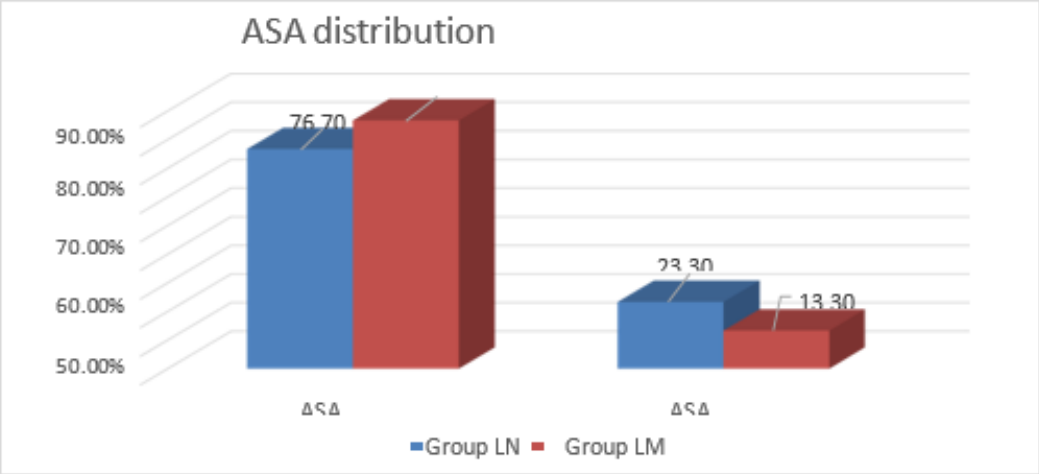
Graph 1: Distribution of study subjects by age

In present study nearly 23.3% and 13.3% of females were present in Group LN and LM respectively. Male constituted nearly 76.7% in group LN and 86.7% in group LM. There was no statistical significant difference in gender distribution among two groups.



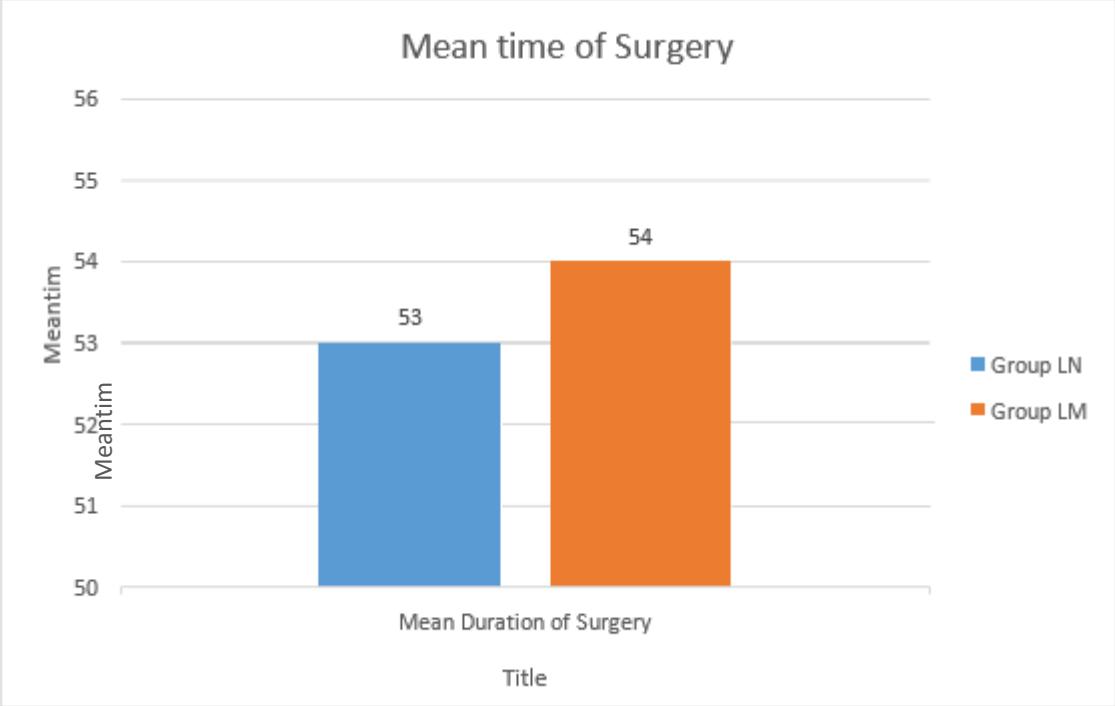
Graph 2: Gender wise distribution of subjects

Majority (76.7% in Group LN and 86.7% in group LM) were classified into ASA 1 grading and remaining 23.3% in Group LN, 13.3% in Group LM as ASA 2. There was no Statistical difference in ASA grading distribution between two groups.



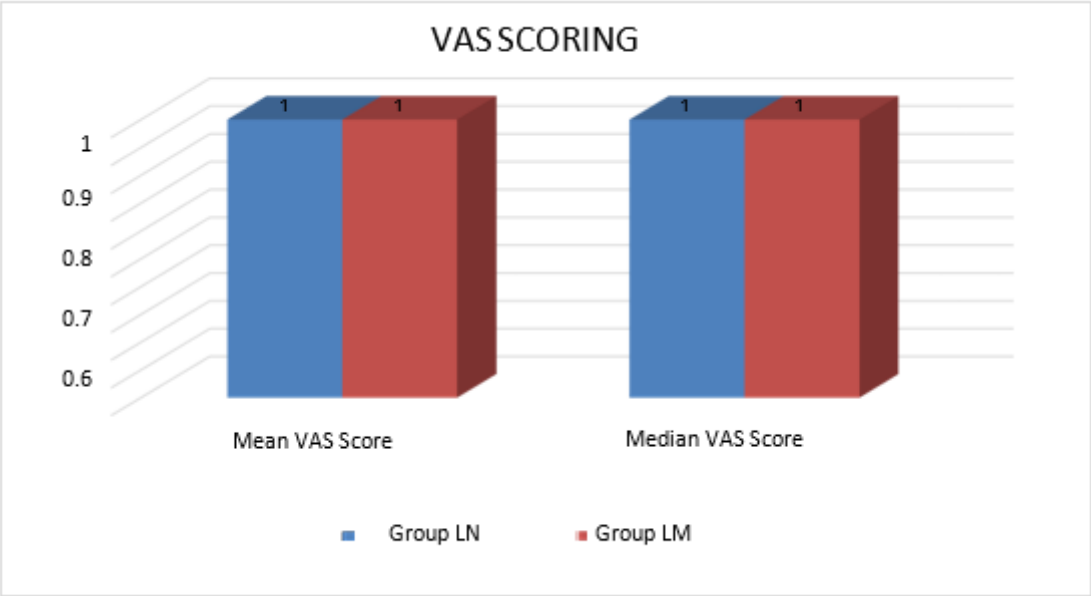
Graph 3: Distribution of Subjects based on ASA

The average duration of surgery was 53 ± 12 min in group LN and 54 ± 12 min in group LM and itwas found to be statistically not significant. (p-value>0.05)



Graph 4: Mean Duration of surgery

The pain VAS score was assessed by the VAS scale where both the groups showed similar scoring and no statistically significant difference is observed.(p-value>0.05)



Graph 5: Mean and Median VAS Scoring

Table 1: Characteristics of Sensory and Motor blockade.

	Group				P value
	Group LN		Group LM		
	Mean	SD	Mean	SD	
Sensory Blockade Characteristics					
Onset of Sensory Blockade (Min)	3.69	0.35	2.71	0.34	0.000
Sensory Block Recovery (Min)	6.2	0.4	7.0	0.4	0.000
Motor Blockade Characteristics					
Onset of Motor Blockade (Min)	4.98	0.56	6.13	0.28	0.000
Motor Block Recovery (Min)	7.3	0.20	6..9	0.4	0.000
Rescue Analgesia (Min)	78.4	6.2	110.7	9.4	0.000

The mean time of the onset of Sensory Blockade was found to be 3.69 $\pm$ 0.35 minutes in Group LN and 2.71 $\pm$ 0.34 minutes in group LM. The mean time for the recovery of sensory block was found to be 6.2 $\pm$ 0.4 minutes in group LN and 7 $\pm$ 0.4 minutes in Group LM. The association of the both the onset and recovery of sensory Blockade was found to be statistically significant.

The mean time of the onset of Motor Blockade was found to be 4.98 $\pm$ 0.56 minutes in Group LN and 6.13 $\pm$ 0.28 minutes in group LM. The mean time for the recovery of Motor block was found to be 7.3 $\pm$ 0.2 minutes in group LN and 6.9 $\pm$ 0.4 minutes in Group LM. The association of the both the onset and recovery of Motor Blockade was found to be statistically significant. The mean time duration of rescue Analgesia was found to be 78.4 $\pm$ 6.2 minutes in group LN and 110.7 $\pm$ 9.4 in Group LM. The association was found to be statistically significant between both the groups.

DISCUSSION

The mechanism of Magnesium sulphate as adjunct to Lignocaine in IVRA is multifactorial. The Magnesium has been proven to have an endothelium derived nitric oxide induced vasodilatory effect which mediates relaxation vascular smooth muscles. It may also block peripheral calcium channels or peripheral NMDA receptors. Magnesium also has got direct peripheral analgesic effect[8]. Tourniquet causes

ischemia distorting nerve penetration by oxidative stress and affecting blood nerve barrier[9]. Nitric oxide donors protect the vascular endothelium from ischemia and reperfusion mediated endothelial dysfunction[10]. There have been many studies to demonstrate the peripheral anesthetic activity of magnesium in Bier's block. Precautions should be taken in patients with compromisedrenal function, bradycardia and atrioventricular conduction abnormalities.

The action of Nitroglycerine in IVRA is may be because of direct short venodilating property which promotes distribution of local anesthetic to nerves. In the cell Nitroglycerine gets metabolized to nitric oxide which causes an increase in concentration of cyclic guanosine monophosphate which produces pain modulation in central nervous system and peripheral nervous system. These nitric oxide generators possess anti-inflammatory and analgesic property by which they block hyperalgesia and neurogenic component of inflammatory edema on topical application[11]. It may also produce analgesic effect through direct stimulation of peripheral nerve fibers mimicking the action of locally applied acetyl choline[12,13]. Pooja Bansal et al[14]did a randomized control trial to evaluate and compare the efficacyof Lignocaine 2% 3mg/kg with 200mcg NTG diluted to 40ml with saline and 6ml of 25% Magnesium sulphate added to 2% Lignocaine 3mg/kg diluted to 40ml with saline added to IVRA. They observed that sensory and motor block onset was faster in NTG and MgSO4 group, prolonged sensory and motor recovery times and comparable mean time of onset for tourniquet pain and prolonged duration of post-operative analgesia. In the present study LM group had mean onset of sensory blockade of 2.71 ±0.34min and in LN group it showed as 3.69±0.35min.

A study conducted by Deepak Solanki et al[15] also showed similar values in which they administered 9ml of 2% Lignocaine with 3ml of 50% Magnesium sulphate diluted to total volume of 36 ml in IVRA, where mean onset time for sensory block was 3.60±0.76 min. It was also comparable with that of study by Turan et al[16] where IVRA was achieved with 0.5% Lignocaine 3mg/kg with 15% Magnesium sulphate 10ml diluted with saline to 40ml, they observed mean onset for sensory blockade as 5±2min. Mirkheshti et al[17] in their study conducted using 3mg/kg Lignocaine with 5ml of 20% Magnesium sulphate diluted to 50ml with saline observed longer mean onset time for sensory blockade as 7.2±2.8min, possibly because of lower dose of Magnesium used in the study. However, a study conducted by Mohammed Ali Sahmeddini et al[18] where they administered 0.5% Lignocaine 3mg/kg diluted to 40ml first, followed by injection of 1.5g of Magnesium sulphate (7.5ml 20% Magnesium sulphate) showed mean onset time for sensory blockade as 3.18±1.79min,possibly because of Magnesium being injected separately after injecting local anesthetic agent.

Asadi et al[19] in their randomized double blinded study with 3mg/kg Lignocaine with 200mcg Nitroglycerine observed mean onset time for sensory blockade of 2.94±1.02min which was comparable with our present study. In the present study the mean onset for motor blockade was observed to be 6.13±0.28min LM group and the LN group in study showed mean onset of motor blockade as 4.98±0.56min. It was comparable with that of Deepak Solanki et al[15] where they observed mean onset of motor blockade of 6.28±1.14min and 7±2min respectively with Magnesium as adjuvant to Lignocaine in IVRA.

Mean onset time for LN group was similar to that of Selda Sen et al where they found mean onset of motor blockade to be 3.3±1.6min. In study by Honarmand et al[20] with

200mcg, 300mcg, 400mcg Nitroglycerine in IVRA with 3mg/kg Lignocaine showed mean onset of motor blockade as 5.4±0.7min, 4.8±0.6 min and 3.8±0.7min which was comparable with that of present study. In the present study, the mean sensory recovery time in LM group was 7 ±0.4min and LN group showed mean recovery of sensory blockade as 6.2±0.4min. The mean onset time of sensory recovery of LN group was similar to that of Selda Sen et al[21] where they found the mean time for sensory recovery of 6.8±1.6min. Asadi et al[19] observed as 10.69±3.97min in their study which was comparable with that of present study. Honarmand et al[20] in their study with different dosage of Nitroglycerine observed mean time for sensory recovery of 6.6±0.7min, 7.9±0.9min and 8.4±0.8min with 200mcg,300mcg and 400mcg respectively which was comparable with that of our present study. In the present study the mean motor recovery time in LM group was 6.9± 0.4min. The mean recovery time in LN group observed was 7.3±0.20min. The values of LM group were comparable with that of Deepak Solanki et al[15]where they observed mean motor recovery time of 3.96±1.21 min and 6±2min. The mean time for rescue analgesia following deflation of tourniquet in LM group was 110.7±9.4min. Mean time for first analgesic requirement in LN group was 78.4±6.2min. The time for rescue analgesia in LN group was comparable with that of study done by Selda Sen et al[21] but in their study time for first rescue analgesia being 225±74min. However, a study conducted by Pooja Bansal et al[14] where patients received 2% Lignocaine 3mg with 200mcg of NTG diluted with normal saline to 40ml showed mean time for rescue analgesia of 52.56±4.48min duration, which was comparable with our present study. There was no significant difference with respect to Visual analogue score in both the study groups at different time intervals during the study period. Similar findings were observed by Turan et al[16] in his study. Two of the patients in magnesium study group experienced flushing and burning sensation after injection of study drug, which got relieved by itself after 3-5min. The pain during injection of magnesium sulphate has been attributed to acidity of the solution. Similar observations have been reported by Narang et al[22] in their study. No other problematic effects were observed in the present study.

CONCLUSION

Addition of Magnesium sulphate to IVRA as adjuvant to Lignocaine provides faster onset of anesthesia and prolonged post-operative analgesia compared to Nitroglycerine without any significant untoward effects.

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