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COMPARATIVE EFFICASY OF MAGNESIUM SULPHATE AND CLONIDINE AS AN ADJUVANT TO LIGNOCAINE IN INTRAVENOUS REGIONAL ANAESTHESIA FOR INTRAOPERATIVE AND POSTOPERATIVE ANALGESIA

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ABSTRACT

Objectives: Intravenous regional anesthesia is used for short procedures for hand and upper limb surgeries. IVRA with adjuvants like opioids, muscle relaxants, NSAIDS increases the efficacy in terms of analgesic duration and quality of anesthesia. We conducted this comparative study for evaluating the effect of adding magnesium sulphate and clonidine with lignocaine in IVRA for upper limb surgeries. **Methodology**: Seventy five patients ASA class 1 and 2 of either sex, age 18-60 years undergoing upper limbs surgeries were enrolled. They were divided into three groups (25 each) according to drug received. Group L: 9 ml of 2% lignocaine (preservative free) diluted with normal saline to make a total volume of 36 ml of 0.5% lignocaine. Group M: 3 ml of 50% magnesium sulphate with 9 ml of 2 % lignocaine diluted with normal saline to make a total volume of 36 ml, 0.5% lignocaine. Group C: 1 µg/kg clonidine with 9 ml of 2% lignocaine diluted with normal saline to make a total volume of 36 ml of 0.5% lignocaine. Sensory and motor block (onset and recovery time), intraoperative tourniquet pain, time to first tramadol requirement and mean tramadol dosage, quality of operative conditions, hemodynamic parameters, postoperative pain (VAS) scores were recorded. **Results**: Both groups were comparable in terms of age, sex, ASA grade, baseline hemodynamic parameters, duration of surgery and tourniquet inflation time. Shortened sensory and motor block onset times were established in Group M ($p < 0.05$). Recovery from sensory and motor blockade was significantly prolonged in Group M ($p < 0.05$). Anesthesia excellence as determined by anaesthesiologist and the surgeon was significantly better in C group as compared to rest two groups ($p < 0.05$).There was statistically significant difference ($p > 0.05$) in intraoperative VAS in Group M and C as compared to Group L, throughout the procedure. Time to First analgesic requirement in Group C 43.04 ± 27.46, Group M 42.72 ± 18.06 and Group L was 27.08 ± 4.45 minutes ($p < 0.05$). Postoperative VAS scores for 24 hours were higher in Group L as compared to Group M and C ($p < 0.05$). **Conclusion**: Magnesium sulphate as an adjuvant to lignocaine hydrochloride for IVRA for upper limb surgeries shorten the onset of sensory and motor block to greater extent as compared to clonidine and lignocaine alone though postoperative analgesia was found to be of longer duration with clonidine as an adjuvant.

KEYWORDS: Biers block; IVRA; Clonidine; Magnesium sulphate; Lignocaine hydrochloride.

INTRODUCTION

Intravenous regional anaesthesia (IVRA) or Bier's block is a simple, safe, reliable and cost effective regional technique for providing anaesthesia for short duration as well as bloodless field during limb surgery.[1] It does not involve any risk of accidental central neuraxial blockade pneumothorax, phrenic nerve block or arterial hematoma as compared to different techniques of brachial plexus anaesthesia. However limitations for its use are short duration surgeries, tourniquet pain, poor muscle relaxation and inability to provide postoperative analgesia and LA toxicity.[2] In an attempt to improve block quality and post deflation analgesia, different additives have been combined with local anaesthetists such as opioids (fentanyl, meperidine, tramadol, sufentanyl), NSAIDS (Ketorolac), clonidine, muscle relaxants (pancuronium, atracurium, mivacurium) ketamine, neostigmine, dexmedetomidine lately

magnesium sulphate have also been tried.[3] However none of them proved to be ideal. Centrally acting selective partial α2 agonist Clonidine, produces analgesia by receptors activation in substantia gelatinosa of spinal cord[4] and depression of nerve fibre action potentials especially in unmyelinated C fibres.[5] Addition of clonidine to local anaesthetics in IVRA have demonstrated reduced tourniquet pain and improved post-operative analgesia.[6] Magnesium exerts its calcium channel inhibitory activity[7] and antagonism on the N-methyl-D-aspartate (NDMA) receptor.[8] In this present study we compared the efficacy of adding magnesium and clonidine to lignocaine as an adjunct for IVRA.

MATERIALS AND METHODS

After ethical committee approval and written informed consent, this double blind randomized prospective clinical study was carried out on 75 patients of ASA grades 1 and 2 of either sex, aged 18-60years undergoing upper limb surgery. Patients with peripheral vascular disease, sickle cell anaemia, any bleeding diasthesis, history of allergy or sensitivity to any three drugs used in this study, patients with coronary artery diseases or with deranged kidney or liver functions were excluded. Patients who were failure cases and were given general anaesthesia also excluded from study.

These patients were randomly (lottery method) divided into 3 groups of each 25 patients according to study drugs as follows: group L(Control group):patients who were to receive IVRA, with 9 ml 2% lignocaine preservative free) diluted with normal saline to make a total volume of 36ml and resultant concentration of lignocaine to be 0.5%.

Group M= patients who were to receive IVRA with 3ml 50% magnesium sulphate with 9 ml 2% lignocaine(preservative free) diluted with normal saline to make a total volume of 36ml and resultant concentration of lignocaine to be 0.5%.

Group C= patients who were to receive IVRA with 1µg/kg clonidine with 9 ml 2% lignocaine(preservative free) diluted with normal saline to make a total volume of 36ml and resultant concentration of lignocaine to be 0.5%.

All patients were evaluated thoroughly in preanesthesia check-up and were kept nil orally for at least 8 hours prior to the procedure. Intradermal lignocaine sensitivity test was done. The interpretation of visual analogue scale (VAS) was explained one day before operation to the selected patients. This was carried out with 10 cm line. The first end mark '0' means no pain and end point mark 10 means severe pain. Patients were asked to mark severity of pain experienced. All patients were given tab clonozepam 0.25mg one night before surgery. No premedications were given to any patient.

After securing intravenous access, heart rate (HR),Non-invasive systolic and diastolic blood pressure(SBP,DBP),Respiratory rate(RR), peripheral arterial saturation(SpO_2) were recorded with multipara monitor(Mindray BeneView T5). One another intravenous cannula (22gauze) was inserted on the dorsum of the operative hand. The operative arm was elevated for 3 mins then exanguinated with an Esmarch bandage. A pneumatic double cuff tourniquet was placed around the upper arm and proximal cuff was inflated to 100mmhg more than systolic blood pressure to a minimum of 250mmhg and the esmarch bandage was removed. Circulatory isolation of limb was inspected by absence radial pulse and loss of pulse oximetry tracing of the ipsilateral index finger. IVRA was established with study drugs used. Drug was then slowly injected into indwelling cannula. Parameters assessed were sensory block: onset and recovery time, motor block: onset and recovery time, intraoperative tourniquet pain, first tramadol requirement time, mean tramadol dosage, quality of operative conditions(assessed by the anaesthesiologist and assessed by the surgeon), hemodynamic monitoring(HR,SBP,DBP,RR,SpO_2), postoperative pain and any side effects. Sensory block was assessed by pin prick every 30 seconds. Patient response was evaluated in the dermatomal sensory distribution of the medial, lateral, antebrachial cutaneous, ulnar, median and radial nerves. Onset of sensory block was defined as the time elapsed from injection of drug to sensory block achieved in all dermatomes. Sensory recovery time defined as the time elapsed from tourniquet deflation to recovery of sensation in all dermatomes. Determined by pinprick test was also noted.

Motor block was assessed by asking the subject to flex and extend his or her wrist and fingers. Motor block was assessed on a three point scale (0=normal finger motility, 1= decreased motility, 2=complete blockade).[6]

Onset of motor block was defined as the time elapsed from injection of the study drug to complete motor block. Motor block recovery time defined as the time elapsed from tourniquet deflation until movement of fingers was noted.

Assessment of tourniquet pain was done on the basis of Visual Analogue Scale/VAS(0=No pain, 10=worst pain imaginable).[9] It was measured before tourniquet inflation, just after tourniquet inflation and 5min,10min,15min,20min,30min,45min,60min and at the end of surgical procedure. Patients were administered tramadol 50mg intravenously for tourniquet pain relief as and when their VAS score became greater than or equal to 4. If VAS scores were still high at the next reading tramadol dosage (50mg) was repeated again. First tramadol requirement time and mean tramadol dosages were noted among patients in all groups.

The operative conditions were independently rated by anaesthesiologist and operating surgeon, blinded to study

at the end of the operation. Quality of operative conditions as rated by the anaesthesiologist[10] at the end of procedure:
4, Excellent: no complaint from the patient.
3, Good: minor complaint with no need for supplemental analgesics.
2, Fair: complaint that needed a supplemental analgesic.
1, Poor: patient given general anaesthesia.

Quality of operative conditions as rated by the surgeon at the end of operation:[10]
4: perfect
3: acceptable
2: poor
1: unsuccessful

Hemodynamic monitoring HR, SBP, DBP, RR, SpO_2 were monitored preoperatively, at 5,10,15,20,30,45,60 mins and at the end of surgical procedure.

Assessment of postoperative pain was done at immediate postoperative period,1,2,4,6,12 and 24 hours after surgery using VAS(0=no pain, 10= worst imaginable pain).

Side effects like nausea, vomiting, skin rashes, tachycardia, bradycardia, hypotension, hypertension, headache, dizziness, tinnitus, hypoxemia, and any other untoward complications were noted.

Statistics
Students t-test (paired and unpaired) was used for comparison of time of onset of sensory and motor blockade and recovery, intraoperative tourniquet pain scores, quality of operative conditions as assessed by anaesthesiologist and surgeon, post-operative pain scores and hemodynamic parameters among all the three groups. Epicalc 2000 software was used to compare the mean and standard deviation values from the three groups and to find out p value among them. A p value less than 0.05 were considered significant.

RESULTS
No statistical differences were found between the three study groups with respect to age, sex, weight, ASA grades, preinduction HR, SBP, DBP, RR, SpO2, duration of surgery and tourniquet inflation duration (table 1). Onset time of sensory blockade was 11.96±1.24min, 3.60±0.76min and 7.32±1.14min in group L, group M and group C respectively. The recovery time of sensory blockade was 4.08±1.19 min, 6.00±1.19 min and 4.36±1.32min in group L, group M and group C respectively. Statistically significant difference of onset of sensory blockade was found between all three groups ($p<0.05$). There was statistically significant difference of recovery time of sensory blockade between group L vs M and group M vs C($p<0.05$) but insignificant difference between groups L vs C($p>0.05$). Motor block onset and recovery was 16.04±1.27 and 2.80±0.87 in group L, 6.28±1.14 and 3.96±1.21 in group M, 15.20±1.98 and 3.20±1.00 in group C respectively. There was statistically significant difference of (mean±SD), Onset and recovery of motor blockade between group L vs M and M vs C ($p<0.05$) but statistically insignificant difference between group L vs C ($p>0.05$)(Table 2)

Table No. – 1: Table showing demographic data in all the three groups.

Variable (Mean+SD)	Group I (n=25)	Group II (n=25)	Group III (n=25)
Age (Yrs)	39.08+9.3200	39.56+9.6400	39.28+8.5200
Weight (kg)	64.36+5.7000	64.24+5.3000	64.68+3.4500
Sex (M/F)	20:5	21:4	19:6
Duration of surgery (min)	54+6.7515	54.36+5.1468	54.84+5.6839
Mean Tourniquet time (min)	66.84+5.6397	67.12+5.5024	67.56+4.8225
PR	81.92+10.10	83.04±9.56	82.60±10.40
SBP	123.28±7.50	122.36±7.22	122.32±7.97
DBP	77.24±7.33	76.40±7.70	76.64±7.74
RR	13.16±1.31	13.12±1.42	13.40±1.41
SpO_2	99.08±0.80	99.04±0.70	98.72±0.80

PR=Pulse rate, SBP=Systolic blood pressure, DBP=Diastolic blood pressure, RR=Respiratory rate, SpO_2 =Peripheral arterial saturation
No significant difference was found among three groups.

Table No. – 2: Table showing sensory & motor blockade in all three groups.

S. No.	Parameters	Group I	Group II	Group III
1	Onset time of Sensory blockade (min)	11.96±1.24	3.60±0.76	7.32±1.14
2	Recovery time of Sensory blockade (min)	4.08±1.19	6.00±1.19	4.36±1.32
3	Onset time of Complete Motor blockade (min)	16.04±1.27	6.28±1.14	15.20±1.98
4	Recovery time of Motor blockade (min)	2.80±0.87	3.96±1.21	3.20±1.00

Table 3 showing statistically significant difference of (mean±SD) Anaesthesiologist's rating of Quality of operative conditions between all three groups L vs M, M vs C, L vs M ($p<0.05$). There was statistically significant

difference of surgeon's rating of operative conditions L vs C ($p<0.05$) but statistically insignificant difference between groups L vs M and M vs C ($p>0.05$).

Table No. – 3: Table showing parameters of quality of operative conditions in all three groups.

Sr.No.	Parameters	Group I	Group II	Group III
1	Anaesthesiologists rating of operative conditions	2.28±0.46	2.72±0.68	3.24±0.52
2	Surgeons rating of operative conditions	2.84±0.55	3.12±0.6	3.28±.54

There was no statistically significant difference ($p>0.05$) in pulse rate, SBP, DBP, RR, SpO_2 among all groups at different time intervals.

Table No. – 4: Table showing intraoperative vas scoring in all three groups.

Intervals (min)	Group I	Group II	Group III
Before Tourniquet inflation	0	0	0
Just After tourniquet inflation	0.16±0.37	0	0
5 min	0.84±1.10	0.72±0.95	0.64±1.02
10 min	1.68±1.98	1.28±1.77	1.04±1.90
15 min	3.16±2.42	1.64±2.68	1.60±2.67
20 min	3.68±3.31	1.68±3.63	1.60±3.64
30 min	5.40±5.22	2.28±5.49	2.20±5.58
45 min	5.40±5.22	2.28±5.49	2.20±5.58
60 min	4.80±11.00	4.00±11.00	2.56±11.00
End of Procedure	3.52±1.71	3.08±1.22	2.56±1.04

There was no statistically significant difference in intraoperative VAS at 5,10,15,20,30,45,60 min and at the end of surgery between group M vs C ($p>0.05$).Table 5 showing statistically significant difference in post-operative VAS at immediate post-operative, 1,2,6,12 hrs postoperatively between group M vs C($p<0.05$). There was statistical significant difference in postoperative VAS at 1,2hrs postoperatively between group L vs M. Group L vs C showed statistical significant difference at immediate postoperative, 1, 2, 4, 6, 12hrs postoperatively.

Table No. – 5: Table showing postoperative vas scoring in all three groups (MEAN± SD).

Interval (Hours)	Group I	Group II	Group III
Immediate Post op	3.52±1.71	3.08±1.22	2.56±1.04
1 Hours	4.14±1.61	3.16±0.85	2.64±0.90
2 Hours	4.36±1.89	3.40±1.08	2.72±1.10
4 Hours	3.34±1.43	3.40±1.19	2.72±1.31
6 Hours	3.40±0.96	3.20±0.87	2.36±0.86
12 Hours	3.20±0.76	3.16±0.99	2.60±0.82
24 Hours	3.08±0.95	2.92±0.99	2.84±1.03

First tramadol requirement time (min) (mean±SD) 27.08±4.49 min, 42.72±18.06 min, 43.04±27.46 min among group L, M and C respectively. The mean tramadol dose consumed was 122mg, 52 mg and 38mg in group L, M and C respectively (Table 6). There were no untoward side effects noted throughout the study.

Table No. – 6: Table showing first tramadol requirement and mean tramadol dose in all three groups (mean ± sd).

	Group I	Group II	Group III
First Tramadol Requirement Time (min)	27.08±4.49	42.72±18.06	43.04±27.46
Mean Tramadol Dose (mg)	122	52	38

DISCUSSION

IVRA is a simple and rapid form of regional anaesthesia which is safe, reliable and cost effective. The ideal IVRA solution should have the following features: rapid onset, reduced dose of local anaesthestic, reduced tourniquet pain and prolonged post deflation analgesia. At present this may only be achieved by the addition of adjuncts to local anaesthetics. Holmes,[11] Janardhan and Venkata Rao[12] had advocated the use of double tourniquet method with the second tourniquet on the anesthetized portion on the extremity distal to the proximal one to prevent tourniquet pain and discomfort. Hence, in the present study, double tourniquet was used.

Ruben et al[4] revealed sensory, motor block and postoperative analgesia was improved significantly along with diminished requirement of additional analgesia till 24hrs postoperatively when clonidine 1µg/kg was added

to 0.5% lidocaine for IVRA. In our study we elected to use similar dose of clonidine. Furthermore, clonidine also reduces postoperative pain and discomfort subsequent to tourniquet inflation and deflation used in procedures like IVRA.[13] The double blind prospective study of tramer et al obviously demonstrated the value of magnesium as an adjuvant in postoperative analgesia.[14] In different study by Turan[9] and colleagues adding Mg to lidocaine in IVRA revealed diminished intraoperative fentanyl use and pain associated with tourniquet. Tramer and colleagues clearly demonstrated that patient getting magnesium as an adjuvant needed less morphine. Koinig et al[8] showed similar results with a decreasing analgesic use both intra and postoperatively. It has also been found that magnesium when added to lignocaine improves the quality of anaesthesia and analgesia in IVRA.[15] In present study we evaluated and compared the effects of adding either magnesium sulphate or clonidine to lignocaine in IVRA for upper limb surgeries.

Baseline hemodynamics, demographic datas, duration and type of surgeries, mean tourniquet time were comparable and found to be statistically insignificant ($p>0.05$) in all three groups.

Present study indicates that onset of sensory blockade was shortened by addition of magnesium sulphate and clonidine though it was more significantly shortened in magnesium group. In intergroup statistical comparison of recovery time of sensory blockade was significantly prolonged in magnesium group as compared to plain lignocaine group and clonidine group. Faster onset of sensory block using magnesium sulphate could have been due to antagonistic properties of magnesium for the NDMA receptor and its inhibitory properties for calcium channels. Clonidine by virtue of selectively blocking conduction of A delta and C fibers and causing localized vasoconstriction[16] could have led to faster sensory blockade onset.

Turan et al[9] who found a significant shortening of the onset of sensory block from 8min in lidocaine alone group to 5 min in lidocaine magnesium group($p<0.05$) and onset of motor blockade from 13 min in lidocaine group to 7 min in lidocaine magnesium group($p<0.05$). Alayurt S et al, found that addition of clonidine to lignocaine shortened the onset of sensory block significantly but did not improve the onset of motor block significantly ($p>0.05$).

Our results of recovery time of sensory blockade (mean±SD), was found to be consistent with finding of Narang S et al.[15] They found significant prolongation of recovery time of sensory block from 3.85 min in lignocaine alone and 5.71 min in lignocaine –magnesium group. Alayurt S et al[17] found insignificant prolongation of recovery time of sensory block when clonidine was added to lignocaine for IVRA compared to lignocaine alone group but there was insignificant prolongation of recovery time of motor blockade($p>0.05$) which is consistant with our finding.

In our study anaesthesiologist's rating of operative conditions on intergroup comparison addition of an adjuvant like magnesium or clonidine to lignocaine does significantly improve operative condition as compared to lignocaine alone group. On the other hand addition of clonidine to lignocaine does significantly improve the operative conditions but not by addition of magnesium sulphate to lignocaine as assessed by surgeon.

Our study shows that addition of magnesium sulphate or clonidine to lignocaine as an adjuvant dos not significantly alter pulse rate, SBP,DBP,RR,SpO_2 in any groups as compared to lignocaine alone group. Absence of hemodynamic changes might be due to the drug confined to the forearm region due to application of tourniquet thereby producing action locally rather than systemically.

In present study the (mean±SD) intraoperative VAS scoring was done before tourniquet inflation, just after tourniquet inflation, at 5,10,15,20,30,45,60 min and at the end of procedure among groups L, M and C. This study shows both magnesium sulphate and clonidine delay the onset of intraoperative tourniquet pain as compared to lignocaine alone group but there is greater delay and longer analgesia on using clonidine with lignocaine in IVRA as compared to magnesium sulphate with lignocaine. These finding is consistant with Gentili M et al[6] and Gorgias NK et al.[18] Eisenach JC et al[19] showed that clonidine clearly prolongs anesthesia and analgesia in a dose dependent manner when administered as a part of regional anesthetic technique. Larger IVRA doses also associated with side effects like hypotension, bradycardia and sedation. Postoperative VAS scores for 24hours were higher in group L($p<0.05$). There was statistical significant at 1, 2, 6, 12 hrs postoperatively between group M and group C($p<0.05$). Tramer and Schneider et al[20] had conducted a study to show that the addition of magnesium to lidocaine increases the quality of the block and decreases overall failure rate. The limitation of our study is a small sample size, but it had significantly important results.

This study showed that addition of magnesium sulphate or clonidine to lignocaine hydrochloride does prolong first tramadol requirement time and decrease mean tramadol dose as compared to lignocaine alone group are in accordance with other authors.[9,10,20]

CONCLUSION

Magnesium sulphate, when added to lignocaine for IVRA significantly facilitates onset and prolongs the recovery of sensory as well as motor block as compared to clonidine and lignocaine alone. Both clonidine and magnesium sulphate as an adjuvants decrease the pain associated with the inflation of pneumatic tourniquet, without any associated haemodynamic instability or

other significant side effects. Block quality, total tramadol requirement (as an additional analgesic) and duration of post-operative analgesia was better with clonidine group as compared to magnesium when added to lignocaine.

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