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ORIGINAL ARTICLE

Intravenous Regional Anesthesia: Comparing Efficacy of Magnesium Sulfate and Clonidine as an Adjuvant to Lignocaine for Intraoperative and Postoperative Analgesia

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ABSTRACT

Objective: Intravenous regional anesthesia (IVRA) is used for short procedures for hand and upper limb surgeries. In terms of analgesia duration and quality of anesthesia, IVRA with adjuvants like opioids, muscle relaxants, nonsteroidal anti-inflammatory drugs (NSAIDs) increases the efficacy. We conducted this comparative study for evaluating the effect of adding magnesium sulfate and clonidine with lignocaine in IVRA for upper limb surgeries.

Materials and methods: Seventy-five patients with American Society of Anesthesiologists (ASA) class I and II of either sex, age 18 to 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 sulfate with 9 mL of 2% lignocaine diluted with normal saline to make 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 total volume of 36 mL of 0.5% lignocaine. Sensory and motor block (onset and recovery time), intraoperative tourniquet pain, first tramadol requirement time and mean tramadol dosage, quality of operative conditions, hemodynamic parameters, postoperative pain scores [in visual analog scale (VAS)] 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 M group ($p < 0.05$). Recovery from sensory and motor blockade was significantly prolonged in M group ($p < 0.05$). Anesthesia excellence as determined by anesthesiologist and surgeon was significantly better in C group as compared with rest of the two groups ($p < 0.05$). There was statistically significant difference ($p > 0.05$) in intraoperative VAS scores in groups M and C as compared with group L, throughout the procedure. Time to first analgesic requirement in group C was 43.04 ± 27.46 minutes, group M 42.72 ± 18.06 minutes, 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 with groups M and C ($p < 0.05$).

Conclusion: Magnesium sulfate as an adjuvant to lignocaine hydrochloride for IVRA for upper limb surgeries shortens the onset of sensory and motor block to a greater extent as compared with clonidine and lignocaine alone, though postoperative analgesia was found to be of longer duration with clonidine as an adjuvant.

Keywords: Biers block or intravenous regional anesthesia, Clonidine, Lignocaine hydrochloride, Magnesium sulfate.

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INTRODUCTION

Intravenous regional anesthesia or Bier's block is a simple, safe, reliable, and cost-effective regional technique for providing anesthesia 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 with different techniques of brachial plexus anesthesia. However, limitations for its use are short duration surgeries, tourniquet pain, poor muscle relaxation, and inability to provide postoperative analgesia and local anesthetic (LA) toxicity.[2] In an attempt to improve block quality and postdeflation analgesia, different additives have been combined with LA, such as opioids (fentanyl, meperidine, tramadol, sufentanil), NSAIDs (Ketorolac), clonidine, muscle relaxants (pancuronium, atracurium, mivacurium) ketamine, neostigmine, dexmedetomidine, and lately magnesium sulfate has also been tried.[3] However, none of them proved to be ideal. Centrally acting selective partial alpha-2 agonist clonidine produces analgesia by receptors activation in substantia gelatinosa of spinal cord[4] and depression of nerve fiber action potentials, especially in unmyelinated C fibres.[5] Addition of clonidine to LAs in IVRA has demonstrated reduced tourniquet pain and improved postoperative analgesia.[6]

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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 adjuvant 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 I and II of either sex, aged 18 to 60 years, undergoing upper limb surgery. Patients with peripheral vascular disease, sickle cell anemia, any bleeding diathesis, 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 anesthesia also excluded from the study.

These patients were randomly (lottery method) divided into three 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 36 mL and resultant concentration of lignocaine to be 0.5%.

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

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

All patients were evaluated thoroughly in preanesthesia checkup and were kept nil orally for at least 8 hours prior to the procedure. Intradermal lignocaine sensitivity test was done. The interpretation of VAS was explained 1 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 clonazepam 0.25 mg one night before surgery. No premedications were given to any patient.

After securing intravenous (IV) access, heart rate (HR), noninvasive systolic blood pressure (SBP) and diastolic blood pressure (DBP), respiratory rate (RR), peripheral arterial saturation (SpO_2) were recorded with multipara monitor (Mindray BeneView T5). One another IV cannula (22 gauze) was inserted on the dorsum of the operative hand. The operative arm was elevated for 3 minutes, then exanguinated with an Esmarch bandage. A pneumatic double-cuff tourniquet was placed around the upper arm and proximal cuff was inflated to 100 mm Hg more than SBP to a minimum of 250 mm Hg 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. Moreover, 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 anesthesiologist 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, antibrachial 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, and 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 based on the VAS (0 = no pain, 10 = worst pain imaginable).[9] It was measured before tourniquet inflation, just after tourniquet inflation, and 5, 10, 15, 20, 30, 45, 60 minutes, and at the end of surgical procedure. Patients were administered tramadol 50 mg 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 (50 mg) was repeated again. First tramadol requirement time and mean tramadol dosage were noted among patients in all groups.

The operative conditions were independently rated by anesthesiologist and operating surgeon, blinded to study at the end of the operation.

Quality of operative conditions as rated by the anesthesiologist[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 anesthesia.

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 minutes, 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

Student's 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 anesthesiologist and surgeon, postoperative 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 <0.05 was 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, SpO_2, duration of surgery, and tourniquet inflation duration (Table 1). Onset time of sensory blockade was 11.96 ± 1.24, 3.60 ± 0.76, and 7.32 ± 1.14 minutes in groups L, M, and C respectively. The recovery time of sensory blockade was 4.08 ± 1.19, 6.00 ± 1.19, and 4.36 ± 1.32 minutes in groups L, M, and 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 group L *vs* C ($p > 0.05$). Motor block onset and recovery were 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 ± standard deviation (SD)] onset and recovery of motor blockade between group L *vs* M and M *vs* C ($p < 0.05$) but statistically insignificant difference between groups L *vs* C ($p > 0.05$) (Table 2).

Table 3 shows statistically significant difference of (mean ± SD) anesthesiologist'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 ($p > 0.05$).

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 4).

Table 1: Demographic data in all the three groups

Variable (Mean ± SD)	*Group L (n = 25)*	*Group M (n = 25)*	*Group C (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
HR	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

No significant difference was found among the three groups.

Table 2: Sensory and motor blockade in all three groups

Parameters	*Group L*	*Group M*	*Group C*
Onset time of sensory blockade (min)	11.96 ± 1.24	3.60 ± 0.76	7.32 ± 1.14
Recovery time of sensory blockade (min)	4.08 ± 1.19	6.00 ± 1.19	4.36 ± 1.32
Onset time of complete motor blockade (min)	16.04 ± 1.27	6.28 ± 1.14	15.20 ± 1.98
Recovery time of motor blockade (min)	2.80 ± 0.87	3.96 ± 1.21	3.20 ± 1.00

Table 3: Parameters of quality of operative conditions in all three groups

Parameters	*Group L*	*Group M*	*Group C*
Anesthesiologists' rating of operative conditions	2.28 ± 0.46	2.72 ± 0.68	3.24 ± 0.52
Surgeons' rating of operative conditions	2.84 ± 0.55	3.12 ± 0.6	3.28 ± 0.54

Table 5: Postoperative VAS scoring in all three groups (mean ± SD)

Interval (hours)	*Group L*	*Group M*	*Group C*
Immediate postoperative	3.52 ± 1.71	3.08 ± 1.22	2.56 ± 1.04
1 hour	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

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

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

DISCUSSION

Intravenous regional anesthesia is a simple and rapid form of regional anesthesia which is safe, reliable, and cost-effective. The ideal IVRA solution should have the following features: Rapid onset, reduced dose of LA, reduced tourniquet pain, and prolonged postdeflation analgesia. At present, this may only be achieved by the addition of adjuncts to LAs. 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.

Reuben et al[4] revealed sensory, motor block, and postoperative analgesia improved significantly along with diminished requirement of additional analgesia till

Table 4: Intraoperative VAS scoring in all three groups

Intervals (min)	*Group L*	*Group M*	*Group C*
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

Table 6: First tramadol requirement and mean tramadol dose in all three groups (mean ± SD)

	Group L	*Group M*	*Group C*
First tramadol requirement time (min)	27.08 ± 4.49	42.72 ± 18.06	43.04 ± 27.46
Mean tramadol dose (mg)	122	52	38

24 hours postoperatively when clonidine 1 µg/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[14] obviously demonstrated the value of magnesium as an adjuvant in postoperative analgesia. In different study by Turan et al[9] adding magnesium to lidocaine in IVRA revealed diminished intraoperative fentanyl use and pain associated with tourniquet. Tramer et al[14] 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 anesthesia and analgesia in IVRA.[15] In the present study, we evaluated and compared the effects of adding either magnesium sulfate or clonidine to lignocaine in IVRA for upper limb surgeries.

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

The present study indicates that onset of sensory blockade was shortened by addition of magnesium sulfate and clonidine, though it was more significantly shortened in magnesium group. In intergroup statistical comparison, recovery time of sensory blockade was significantly prolonged in magnesium group as compared

with plain lignocaine group and clonidine group. Faster onset of sensory block using magnesium sulfate 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] found a significant shortening of the onset of sensory block from 8 minutes in lidocaine alone group to 5 minutes in lidocaine magnesium group ($p < 0.05$) and onset of motor blockade from 13 minutes in lidocaine group to 7 minutes in lidocaine magnesium group ($p < 0.05$). Alayurt et al[17] 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) were found to be consistent with the finding of Narang et al.[15] They found significant prolongation of recovery time of sensory block from 3.85 minutes in lignocaine alone and 5.71 minutes in lignocaine–magnesium group. Alayurt et al[17] found insignificant prolongation of recovery time of sensory block when clonidine was added to lignocaine for IVRA compared with lignocaine alone group but there was insignificant prolongation of recovery time of motor blockade ($p > 0.05$), which is consistent with our finding.

In our study anesthesiologist'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 with lignocaine alone group. On the contrary, addition of clonidine to lignocaine does significantly improve the operative conditions but not by addition of magnesium sulfate to lignocaine as assessed by surgeon.

Our study shows that addition of magnesium sulfate or clonidine to lignocaine as an adjuvant does not significantly alter PR, SBP, DBP, RR, SpO_2 in any groups as compared with 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 the present study, the intraoperative VAS scoring (mean ± SD) was done before tourniquet inflation, just after tourniquet inflation, at 5, 10, 15, 20, 30, 45, 60 minutes, and at the end of procedure among groups L, M, and C. This study shows both magnesium sulfate and clonidine delay the onset of intraoperative tourniquet pain as compared with lignocaine alone group, but there is greater delay and longer analgesia on using clonidine with lignocaine in IVRA as compared with magnesium sulfate with lignocaine. These findings are consistent with Gentili et al[6] and Gorgias et al.[18] Eisenach 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 are also associated with side effects like hypotension, bradycardia, and sedation. Postoperative VAS scores for 24 hours were higher in group L ($p < 0.05$). There was statistical significance at 1, 2, 6, 12 hours postoperatively between groups M and group C ($p < 0.05$). Tramer et al[14] 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 sulfate or clonidine to lignocaine hydrochloride does prolong first tramadol requirement time and decrease mean tramadol dose as compared with lignocaine alone group and are in accordance with other authors.[9,10,14]

CONCLUSION

Magnesium sulfate when added to lignocaine for IVRA significantly facilitates onset and prolongs the recovery of sensory as well as motor block as compared with clonidine and lignocaine alone. Both clonidine and magnesium sulfate as adjuvants decrease the pain associated with the inflation of pneumatic tourniquet, without any associated hemodynamic instability or other significant side effects. Block quality, total tramadol requirement (as an additional analgesic), and duration of postoperative analgesia were better with clonidine group as compared with magnesium when added to lignocaine.

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