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ORIGINAL ARTICLE

Intravenous regional anesthesia: comparing efficacy of magnesium sulphate and clonidine as an adjuvant to lignocaine 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 anesthesiologist 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 24hours 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.

Key words: Biers block; IVRA; Clonidine; Magnesium sulphate; Lignocaine hydrochloride

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INTRODUCTION

Intravenous regional anesthesia (IVRA) or Bier's block is a simple, safe, reliable and cost effective regional technique for providing anesthesia for short durations and is a preferred technique for bloodless field during limb surgery.[1] It does not involve any risk of accidental central neuraxial blockade, inadvertent pneumothorax, phrenic nerve block or arterial hematoma when compared to different approaches of brachial plexus anesthesia. However, limitations for its use are its short duration, tourniquet pain, poor muscle relaxation, inability to provide postoperative analgesia and risk of local anesthetic (LA) toxicity.[2] To improve block quality and post deflation analgesia, different additives have been combined with local anesthetics such as opioids (fentanyl, meperidine, tramadol, sufentanil), NSAIDS (ketorolac), nondepolarizing muscle relaxants (pancuronium, atracurium, mivacurium), an NMDA-receptor blocker (ketamine), neostigmine, clonidine and dexmedetomidine (alpha-2 adrenergic receptor agonist). Recently magnesium sulphate has also been tried.[3] However, none of them has been proved to be ideal. Centrally acting selective partial α2 agonist - clonidine produces analgesia by receptor 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 local anesthetics in IVRA has demonstrated reduced tourniquet pain and improved postoperative analgesia.[6] Magnesium exerts its calcium channel inhibitory activity[7] and antagonism on the N-methyl-D-aspartate (NDMA) receptor.[8] In this study, we compared the efficacy of magnesium and clonidine as adjuncts to lignocaine for IVRA.

METHODOLOGY

After ethical committee approval and written informed consent, this double blinded 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 anemia, any bleeding diathesis, history of allergy or sensitivity to any of the three drugs used in this study, patients with coronary artery diseases or with deranged kidney or liver functions were excluded.

These patients were randomly (by lottery method) divided into 3 groups of 25 patients each, according to study drugs as follows:

Group-L (Control group): patients 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 to receive IVRA with 3 ml 50% magnesium sulphate 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 preanesthetic checkup and were kept nil orally for at least 8 h 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' meant no pain and end point mark 10 meant the most severe pain. Patients were asked to mark severity of pain experienced by them. After securing intravenous access on the contralateral side, heart rate (HR), non-invasive systolic and diastolic blood pressures (SBP, DBP), respiratory rate (RR), and peripheral arterial saturation (SpO_2) were recorded with multiparameter monitor (Mindray – BeneView T5™). A second intravenous cannula (22 gauge) was inserted on the dorsum of the ipsilateral side i.e., the operative arm. The arm was then elevated for 3 min then exsanguinated with an Esmarch bandage. A pneumatic double cuff tourniquet was placed around the upper arm and the proximal cuff was inflated to 100 mmHg above systolic blood pressure to a minimum of 250 mmHg and the Esmarch bandage was removed. Circulatory isolation of limb was inspected by the absence of radial pulse and loss of pulse oximetry tracing of the ipsilateral index finger. IVRA was established with study drugs used which were then slowly injected into the indwelling cannula. Injection speed and force was totally dependent on clinical experience as no pressure monitoring device such as reported by Patil et al. was available.[9] Parameters assessed included 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 the surgeon), hemodynamic monitoring (HR, SBP, DBP, RR, SpO_2), postoperative pain and any adverse effects.

Sensory block was assessed by pin prick every 30 sec. 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 was defined as the time elapsed from tourniquet deflation to the recovery of sensation in all dermatomes.

Motor block was identified by the patients' ability to flex and extend his or her wrist and fingers. This was assessed on a three-point scale (0 = normal finger mobility 1 = decreased mobility 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 was defined as the time elapsed from tourniquet deflation until movement of fingers was noted.

Assessment of tourniquet pain was done on the basis of VAS (0 = No pain, 10 = worst pain imaginable).[10] It was measured before tourniquet inflation, just after tourniquet inflation and at 5 min, 10 min, 15 min, 20 min, 30 min, 45 min, 60 min, and at the end of surgical procedure. Patients were administered tramadol 50 mg IV 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 requirement were noted among patients in all groups.

The operative conditions were independently rated by anesthesiologist and the operating surgeon, blinded to study drug at the end of the operation. Quality of operative conditions as rated by the anesthesiologist[11] 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 needed general anesthesia.

Quality of operative conditions as rated by the surgeon at the end of operation: [11]

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 min and at the end of the surgical procedure.

Assessment of postoperative pain was done at immediate postoperative period, at 1, 2, 4, 6, 12 and 24 h after surgery using VAS.

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

Statistical analysis:

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 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 less than 0.05 was considered significant.

RESULTS

No statistical differences were found between the three study groups with respect to age, sex, weight, ASA grades, pre-induction 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 min, 3.60 ± 0.76 min and 7.32 ± 1.14 min 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 ± 1.32 min

Table 1: Demographic data

Variable (Mean ± SD)	Group-L (n = 25)	Group-M (n = 25)	Group-C (n = 25)
Age (years)	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

Table 2: Table showing sensory & motor blockade in the groups

Parameters	Group-L	Group-M	Group-C
Onset time of Sensory blockade (min)	11.96 ± 1.24	3.60 ± 0.76	3.60 ± 0.76
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: Quality of operative conditions in the 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 ± .54

Table 4: Intraoperative VAS in the 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 5: Postoperative VAS scoring in all three groups (mean ± SD)

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

in Group-L, Group-M and Group-C respectively. Statistically significant difference of onset of sensory blockade was found between the three groups ($p < 0.05$). There was statistically significant difference in 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 min and 2.80 ± 0.87 min in Group-L, 6.28 ± 1.14 min and 3.96 ± 1.21 min in Group-M, 15.20 ± 1.98 min and 3.20 ± 1.00 min in Group-C. There was statistically significant difference of 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).

PR = Pulse rate, SBP = Systolic blood pressure, DBP = Diastolic blood pressure, RR = Respiratory rate, SpO2 = Peripheral arterial saturation

No significant difference was found among three groups.

Table 3 showing statistically significant difference of (mean ± SD) Anesthesiologist's rating of quality of operative conditions between 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 in 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, SpO2 among all groups at different time intervals.

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 postoperative VAS at immediate postoperative, 1, 2, 6, and 12 h postoperatively between Group-M vs. C ($p < 0.05$). There was statistically significant difference in postoperative VAS at 1, 2 h postoperatively between Group-L vs. M and Group-L vs. C showed

statistically significant difference at immediate postoperative, 1, 2, 4, 6, and 12 h postoperatively.

First tramadol requirement time was 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 122 mg, 52 mg and 38 mg in Group-L, M and C respectively (Table 6). There were no untoward side effects noted throughout the study.

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

DISCUSSION

IVRA 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 local anesthetic, reduced tourniquet pain and prolonged post deflation analgesia. At present this may only be achieved by the addition of adjuncts to local anesthetics. Holmes[12], Janardhan and Venkata Rao[13] 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 24 h 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.[14] The double blind prospective study of Tramer et al. demonstrated the value of magnesium as an adjuvant in postoperative analgesia.[15] In a 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 used both intra and postoperatively. It has also been found that magnesium when added to lignocaine improves the quality of anesthesia and analgesia in IVRA.[16] In this study we have evaluated and compared the effects of adding either magnesium sulphate or clonidine to lignocaine in IVRA for surgery to the upper limbs.

Baseline hemodynamics, demographic data, duration and type of surgery and 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 Group M. In intergroup statistical comparison of recovery time, sensory blockade was significantly prolonged in Group M 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 onset of sensory blockade.

Turan et al.[10] found a significant shortening of the onset of sensory block from 8 min in lidocaine alone group to 5 min in Group M ($p < 0.05$) and onset of motor blockade from 13 min in lidocaine group to 7 min in Group M ($p < 0.05$). 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, were found to be consistent with finding of Narang S et al.[16] They found significant prolongation of recovery time of sensory block from 3.85 min in lignocaine alone and 5.71 min in Group M. Alayurt S et al.[18] 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 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 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 does 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.

Our 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. This finding is consistent with Gentili M et al.[6] and Gorgias NK et al.[19] Eisenach JC et al.[20] showed that clonidine clearly prolongs anesthesia and analgesia in a dose dependent manner when administered as a part of regional anesthesia technique. Larger IVRA doses also associated with side effects like hypotension, bradycardia and sedation. Postoperative VAS scores for 24 h were higher in Group-L ($p < 0.05$). There was statistically significant difference at 1, 2, 6, 12 h. postoperatively between Group-M and Group-C ($p < 0.05$). Tramer and Schneider etal[21]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 decreases mean tramadol dose requirement as compared to lignocaine alone group are in accordance with other authors.[10,11,21]

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 plus lignocaine or lignocaine alone. Both clonidine and magnesium sulphate, as adjuvant, 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 was better in clonidine group as compared to magnesium when added to lignocaine.

Conflict of interest: nil

Authors' contribution:

DS: Concept, Conduction of study, literature search, statistical analysis

MS: Concept, literature search, statistical analysis, manuscript editing

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