Original Article

Comparative efficacy of clonidine versus magnesium sulfate as an adjunct to lignocaine in intravenous regional anesthesia for postoperative analgesia: A prospective, randomized, double-blind study

Parminder Kaur, Tanveer Singh Kundra[1], Dinesh Sood[2]

Department of Critical Care, Sir Ganga Ram Hospital, New Delhi, [1]Department of Anesthesia, Sri Jayadeva Institute of Cardiovascular Sciences and Research, Bengaluru, Karnataka, [2]Department of Anesthesia, Dayanand Medical College and Hospital, Ludhiana, Punjab, India

Abstract

Background and Aims: Intravenous regional anesthesia (IVRA) is a very good technique to be used in unstable patients. Various adjuvants have been added, but till date, there is no ideal adjuvant. Clonidine is one of the most widely used adjuvants in IVRA. However, it has many side effects. Hence, the search continues for a better adjuvant. The aim of the present study was to compare the efficacy of clonidine versus $MgSO_4$ as an adjunct to lignocaine in IVRA for postoperative analgesia and to compare their side effect profile.

Material and Methods: This prospective double-blind randomized controlled study was conducted in a tertiary care institute. Forty adult patients were included. Patients were assigned into two groups; Group 1 ($n = 20$) received 3 mg/kg of 2% lignocaine + 50% $MgSO_4$ 1.5 g diluted with normal saline to 40 ml. Group 2 ($n = 20$) received 3 mg/kg of 2% lignocaine + clonidine 150 μg diluted with normal saline to 40 ml. Pain score, time to first rescue analgesic (TTFA), total number of rescue analgesics required, and the side effects of the two drugs were compared for 24 h postoperatively.

Results: The mean TTFA was significantly longer in Group 1 (193.9 ± 38.4 min) than in Group 2 (169.5 ± 33.3 min); $P < 0.05$. The mean number of rescue analgesics required was 1.6 ± 0.7 in Group 1 as compared to 2.1 ± 0.8 in Group 2 ($P < 0.05$). More serious side effects such as hypotension and bradycardia were noted with clonidine, although all patients experienced transient pain during intravenous injection of $MgSO_4$.

Conclusion: $MgSO_4$ provides better postoperative analgesia as compared to clonidine when used as an adjunct to lignocaine in IVRA with fewer side effects.

Keywords: Clonidine, intravenous regional anesthesia, lignocaine, magnesium sulfate, postoperative analgesia

Introduction

Intravenous regional anesthesia (IVRA) is a simple method of providing anesthesia to the distal arm or leg.[1] The ideal IVRA solution should have 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 adjuvants to local anesthetic.[2] The most commonly used adjuvants in IVRA are opioids (fentanyl, meperidine, morphine, and sufentanil), tramadol, nonsteroidal anti-inflammatory drugs (NSAIDs; ketorolac, tenoxicam, and acetyl-salicylate), clonidine, muscle relaxants (atracurium, pancuronium, and mivacurium), alkalinization with sodium bicarbonate, and potassium.[2] However, till date, there is no ideal adjuvant

Address for correspondence: Dr. Tanveer Singh Kundra, Kothi No. 184, Phase 4, Mohali, Punjab, India.
E-mail: tvskundra@yahoo.co.in

Access this article online

Quick Response Code:

Website: www.joacp.org

DOI: 10.4103/joacp.JOACP_18_16

How to cite this article: Kaur P, Kundra TS, Sood D. Comparative efficacy of clonidine versus magnesium sulfate as an adjunct to lignocaine in intravenous regional anesthesia for postoperative analgesia: A prospective, randomized, double-blind study. J Anaesthesiol Clin Pharmacol 2017;33:387-90.

which has all the above properties and at the same time has minimal side effects.

Clonidine is a widely used adjuvant to lignocaine in IVRA. Choyce and Peng[2] published a systematic review of adjuncts used in IVRA, in which they concluded that using NSAIDs or clonidine as adjuncts to IVRA improved postoperative analgesia when compared to opioids and muscle relaxants. However, with NSAIDs, there is a fear of wound hematoma. Hence, clonidine appears to be the best available and most commonly used adjuvant in IVRA. Various other studies have also shown that the addition of clonidine to lignocaine provided improved analgesia in the postanesthesia care unit during the first 2 h after operation and diminished the need for analgesic supplements during the 1st day after operation.[3-5] However, clonidine has many systemic side effects such as hypotension and sedation. Hence, there is a need to find a suitable alternative to clonidine which has similar properties to provide prolonged analgesia in the postoperative period with minimal side effects.

Magnesium sulfate ($MgSO_4$) has also been used as an adjuvant in IVRA. The addition of magnesium sulfate to lignocaine in IVRA has been shown to decrease intraoperative analgesic consumption and pain associated with tourniquet. It has also shortened sensory and motor block onset times, prolonged sensory and motor recovery times, and improved quality of anesthesia while prolonging the time to the first postoperative analgesic requirement.[6-9] Thus, $MgSO_4$ also appears to possess the qualities of an ideal adjuvant in IVRA. However, whether $MgSO_4$ has any significant benefit over clonidine with regard to the postoperative analgesia and whether the side effect profile is significantly better over clonidine remain unknown.

The primary aim of the present study was to compare the efficacy of clonidine and $MgSO_4$ used as adjuvants with lignocaine for the prolongation of postoperative analgesia.

The hypothesis was that $MgSO_4$ is a better adjuvant in IVRA than clonidine with regard to time to first rescue analgesic (TTFA).

Material and Methods

This prospective study was conducted after obtaining approval by the Hospital Ethics Committee.

Forty adult patients, American Society of Anesthesiologists Physical Status I or II, of either sex undergoing elective or emergency upper limb surgery were included in the study. Exclusion criteria were patient's refusal, history of allergy to any of the study drugs, Raynaud's disease, sickle cell disease, crush injury to the limb, and surgery lasting for more than 60 min.

Written informed consent was taken from all the patients. Patients were randomly allocated to Group 1 or Group 2 on the basis of a computer-generated random table. The computer-generated group number (1 or 2) was put in a closed opaque envelope. A person not related to the study (anesthesia nurse) was asked to open the closed envelope containing computer-generated group number. She prepared the drug to be administered and gave it to the attending anesthesiologist. The administering anesthesiologist did not know which drug was being given. He would fill up the study proforma noting down the various parameters and this proforma would be collected again by the anesthesia nurse who would put it back in the torn envelope. At the end of the study, these envelopes were handed over to the principal investigator.

The groups were as follows:

- Group 1 (*n* - 20): Received IVRA with 2% lignocaine 3 mg/kg and 50% $MgSO_4$ 1.5 g diluted with normal saline to 40 ml.
- Group 2 (*n* - 20): Received IVRA with 2% lignocaine 3 mg/kg and clonidine 150 μg diluted with normal saline to 40 ml.

Intraoperative monitoring included heart rate, noninvasive blood pressure, respiratory rate, ECG, and SpO_2. A 22G cannula was inserted as distal as possible in the limb to be operated upon. A second 18G cannula was inserted into the opposite arm for intravenous (IV) access.

The limb was exsanguinated by elevating the limb for 5 min. The upper part of the limb was protected with padding before placing the tourniquets. Two tourniquets were applied on the upper limb in approximation with each other. The proximal tourniquet was inflated to 50–100 mmHg above the patient's systolic blood pressure. The tourniquet was checked for any unintentional slow deflation. The drug was injected slowly via the IV cannula on the arm to be operated upon by the attending anesthesiologist, who was blinded to the nature of the drugs being administered. The IV cannula on the operating arm was removed after injecting the solution. The distal tourniquet was inflated after 5 min of giving the drug. After inflation of the distal tourniquet, the proximal tourniquet was deflated, after which the surgery proceeded. The tourniquet was kept inflated for a minimum of 30 min and a maximum of 60 min from the time of local anesthetic injection.

A 10 cm line having verbal anchors on both the ends was used to assess the postoperative pain. All the patients were

shown the visual analogue scale (VAS) preoperatively and instructed of its use as a tool for measuring postoperative pain.

Scoring was accomplished by asking the patient to mark the line and measuring the length of the line till the mark in centimeters. In the scoring system, 0 mark corresponded to "no pain" and the 10 cm mark corresponded to the "worst imaginable pain." Post-deflation patients were monitored for 24 h for pain. On-demand analgesia (tramadol 50 mg IV) was given to the patients if VAS ≥4 and TTFA requirement was noted. Total analgesic consumption in 24 h was noted. Any side effect of either drug was observed. It was decided that if the patient has bradycardia or hypotension, it would be treated with injection atropine 0.6 mg IV and 250 ml fluid bolus, respectively. If hypotension does not get corrected with fluid bolus, it was decided to give injection mephentermine 6 mg IV stat.

Statistical analysis

Based on a previous study by Turan *et al.*[7] (in which they saw the TTFA = 155 ± 38 min for $MgSO_4$ group compared to 95 ± 29 min for control group) and alpha error being 0.05 and power of the study being 95%, the minimum sample size required was 12. But, we took twenty patients in each group.

The data obtained were analyzed statistically using unpaired Student's *t*-test for analysis between the two groups. Chi-square test was used for analyzing the outcomes with regard to side effects in the two groups. $P < 0.05$ was considered statistically significant.

Results

All the forty enrolled patients completed the study protocol. The demographic data including age, sex, body weight, and the duration of the surgery were comparable in both the groups [Table 1].

TTFA was significantly prolonged in Group 1 (193.9 ± 38.4 min) compared to Group 2 (169.5 ± 33.3 min) with $P = 0.046$. There was significantly less requirement of rescue analgesics in Group 1 (1.6 ± 0.7) than in Group 2 (2.1 ± 0.8 min) with $P = 0.045$ [Table 2]. Two or more rescue analgesics were required by seven patients in Group 1 whereas 11 patients required more than two rescue analgesics in Group 2.

Intraoperatively, one patient in Group 2 had an episode of hypotension while another patient had an episode of bradycardia requiring injection atropine. Postoperatively, three patients in Group 2 had hypotension, while two patients had a fall in heart rate up to 50 beats/min. No treatment was required for the fall in heart rate in the postoperative period. None of the patients in Group 1 had a fall in BP or heart rate intraoperatively or postoperatively. Patients in both the groups were not sedated. All the patients in Group 1 had transitional pain on injection of the drug, while no such complaint was observed in Group 2. On overall analysis, more side effects were noted in Group 2 as compared to Group 1 [Table 3].

Discussion

In the present study, the mean TTFA in Group 1 using $MgSO_4$ + lignocaine was significantly more than in Group 2 using clonidine + lignocaine. The mean number of rescue analgesics required in Group 1 was also less than in Group 2.

Similar results were found by Turan *et al.*[7] who concluded that $MgSO_4$ when added as an adjunct to lidocaine improved the quality of anesthesia and analgesia in IVRA. TTFA was significantly higher in the magnesium sulfate group compared to the control (saline) group. Postoperative VAS were higher for the first postoperative 6 h in the control group. The consumption of rescue analgesics was significantly less in the magnesium sulfate group.

Similarly, Bansal *et al.*[9] found that $MgSO_4$ at a dose of 1.5 g added to lignocaine prolonged postoperative analgesia, with no side effects.

In Group 2 using clonidine + lignocaine, one patient complained of transient tinnitus and another had one episode of hypotension immediately after giving the drug. Hypotension responded well to IV bolus 250 cc of normal saline. No other treatment was required. One patient, in intraoperative period, developed bradycardia up to 40 beats/min which was treated with injection atropine 0.6 mg IV successfully.

In the postoperative period, three patients in Group 2 developed hypotension, while none of the patients in Group 1 had a fall in BP. However, in all the patients, hypotension responded to fluid bolus. In addition, two patients in Group 2 had a fall in heart rate up to 50 beats/min, but no treatment was given for the same. None of the patients in Group 1 had a fall in heart rate.

All patients in Group 1 complained of pain while injecting lignocaine with $MgSO_4$. However, this pain was transient and got relieved by itself. A similar side effect was noted in the study conducted by Narang *et al.*,[8] in which there was an increased incidence of transient pain on addition of $MgSO_4$. The exact etiology of pain on IV injection of $MgSO_4$ is unknown but has been attributed to acidity of the solution.[10,11]

Table 1: Demographic profile

Parameters	Group 1 (*n*=20)	Group 2 (*n*=20)	*P*
Age (years)	48.8±17.9	49.7±15.8	0.867
Sex (male:female)	11:9	9:11	0.527
Weight (kg)	67.0±8.2	68.5±7.8	0.570
Duration of surgery (min)	31.0±11.4	26.8±10.2	0.133

Table 2: Total number of rescue analgesics in 24 h

Number of rescue analgesics	Group 1, *n* (%)	Group 2, *n* (%)
0	2 (10.0)	1 (5.0)
1	9 (45.0)	8 (40.0)
2	5 (25.0)	7 (35.0)
3	2 (10.0)	4 (20.0)
Mean ± SD	1.6±0.7	2.1±0.8
P	0.045	

SD=Standard deviation

Table 3: Comparison of side effect profile of the two drugs

Side Effect	Group 1 (%)	Group 2 (%)	*P*
Hypotension	0	3 (15)	0.000
Bradycardia	0	3 (15)	0.000
Sedation	0	0	1.00
Pain on injection	20 (100)	0	0.000

On overall analysis, patients in Group 2 experienced more severe side effects as compared to patients in Group 1.

A limitation of the present study was that the type of surgery performed under IVRA was not standardized in the study design. All surgeries performed under IVRA were taken in the present study which included some surgeries such as Carpal Tunnel release and, on the other hand, surgeries such as fracture of the forearm. On retrospective analysis, we found the distribution of the surgeries as comparable in the two groups. However, a further study with only one type of surgery under IVRA would increase the robustness of the results.

Conclusion

From our study, we conclude that $MgSO_4$ provides better postoperative analgesia with regard to TTFA and the total number of rescue analgesics needed. Lesser side effects were noted as compared to clonidine when used as an adjunct to lignocaine in IVRA. Although $MgSO_4$ is also not an ideal adjuvant, it may be suggested as a better choice over clonidine as an adjuvant in IVRA.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Brown BL, Fink BR. The history of neural blockade and pain management. In: Cousins MJ, Bridenbaugh PO, editors. Neural Blockade in Clinical Anesthesia and Management of Pain. 3rd ed. Philadelphia, PA: Lippincott-Raven; 1998. p. 3-34.
2. Choyce A, Peng P. A systematic review of adjuncts for intravenous regional anesthesia for surgical procedures. Can J Anaesth 2002;49:32-45.
3. Reuben SS, Steinberg RB, Klatt JL, Klatt ML. Intravenous regional anesthesia using lidocaine and clonidine. Anesthesiology 1999;91:654-8.
4. Gentili M, Bernard JM, Bonnet F. Adding clonidine to lidocaine for intravenous regional anesthesia prevents tourniquet pain. Anesth Analg 1999;88:1327-30.
5. Lurie SD, Reuben SS, Gibson CS, DeLuca PA, Maciolek HA. Effect of clonidine on upper extremity tourniquet pain in healthy volunteers. Reg Anesth Pain Med 2000;25:502-5.
6. Tramèr MR, Glynn CJ. Magnesium Bier's block for treatment of chronic limb pain: A randomised, double-blind, cross-over study. Pain 2002;99:235-41.
7. Turan A, Memis D, Karamanlioglu B, Güler T, Pamukçu Z. Intravenous regional anesthesia using lidocaine and magnesium. Anesth Analg 2005;100:1189-92.
8. Narang S, Dali JS, Agarwal M, Garg R. Evaluation of the efficacy of magnesium sulphate as an adjuvant to lignocaine for intravenous regional anaesthesia for upper limb surgery. Anaesth Intensive Care 2008;36:840-4.
9. Bansal P, Baduni N, Bhalla J, Mahawar B. A comparative evaluation of magnesium sulphate and nitroglycerine as potential adjuncts to lidocaine in intravenous regional anaesthesia. Int J Crit Illn Inj Sci 2015;5:27-31.
10. Memis D, Turan A, Karamanlioglu B, Süt N, Pamukçu Z. The use of magnesium sulfate to prevent pain on injection of propofol. Anesth Analg 2002;95:606-8.
11. Turan A, Memis D, Karamanlioglu B, Sut N, Pamukcu Z. The prevention of pain from injection of rocuronium by magnesium sulphate, lignocaine, sodium bicarbonate and alfentanil. Anaesth Intensive Care 2003;31:277-81.