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Original Article

Adding magnesium to lidocaine for intravenous regional anesthesia

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Abstract

BACKGROUND: Magnesium (Mg) has been used as an adjuvant medication in postoperative analgesia. We planed this study to assess the effects of Mg, when added to lidocaine in intravenous regional anesthesia (IVRA) on the tourniquet pain.

METHODS: Forty patients undertaking hand surgery were randomly allocated into 2 groups to be given IVRA. They received 20 ml lidocaine 1% diluted with 20 ml saline to a total of 40 ml in the group L (n = 20) or 7.5 ml magnesium sulfate 20% plus 20 ml lidocaine 1% diluted with 12.5 ml saline to a total of 40 ml in the group M (n = 20). Sensory and motor block onset and recovery times, anesthesia and operation qualities were recorded. Before and after the tourniquet use at 5, 10, 15, 20, 30, 40, and 50 minutes, hemodynamic variables, tourniquet pain, and analgesic use were noted. Subsequent to the tourniquet deflation, at 6, 12, and 24 hours, hemodynamic variables, pain, time to first analgesic requirement, analgesic use and side effects were recorded.

RESULTS: Shortened sensory and motor block onset times were established in group M ($P < 0.05$). Visual analog scale (VAS) scores were less in group M at 20, 30, 40, and 50 minutes after tourniquet inflation ($P < 0.05$). Intraoperative analgesic requirement was less in group M ($P < 0.05$). Anesthesia excellence, as determined by the anesthesiologist and surgeon, was significantly better in group M ($P < 0.05$). Time to the first analgesic requirement in group M was 53.75 ± 6.94 minutes and in group L was 40.76 ± 14.55 minutes ($P < 0.05$). Postoperative VAS scores were higher at 6, 12, and 24 hours in group L ($P < 0.05$).

CONCLUSIONS: Adding Mg to lidocaine for IVRA enhanced the quality of anesthesia and analgesia without causing side effects.

KEYWORDS: Magnesium sulfate, intravenous regional anesthesia, postoperative pain.

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Intravenous regional anesthesia (IVRA) is one of the safest and most consistent modes of regional anesthesia for short procedures on upper extremity. [1] In spite of this, it has been limited by tourniquet pain, [2] and lack of ability to offer postoperative analgesia. [3-5] The best IVRA solution should have the following characteristics: fast onset, low dose of local anesthetic, decreased tourniquet pain, and extended postdeflation analgesia. [6] Right now, this may merely be reached by adding adjuncts to local anesthetics with limited accomplishment. [6] The use of magnesium (Mg) as an adjuvant in perioperative analgesia is unique. The double blind prospective study of Tramer et al. obviously demonstrated the value of Mg as an adjuvant in postoperative analgesia. [7] Magnesium has been revealed to be doing well in reducing pain related with injection of propofol [8] and rocuronium. [9] In a different study by Turan and colleagues, [10] adding magnesium to lidocaine in IVRA revealed diminished

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intraoperative fentanyl use and pain associated with the tourniquet. Turan's study was the first one on this issue. However, the authors emphasized that more studies should be carried out to determine a relevant conclusion before its regular use. So, we designed the present study, as a second one to assess the effects of magnesium when added to lidocaine in IVRA.

Methods

Forty ASA physical status I and II patients, aged 20-65 year old, listed for elective hand surgery gave formal, written consent to take part in this randomized double-blind study, which was approved by our local commission on human being investigation. They were planned to undertake either carpal tunnel release, removal of a ganglion cyst, or tenolysis. Patients with Raynaud's disease, sickle cell anemia, or a history of allergy to any drug were excluded from the study. A randomization list was created. Identical syringes, full of drugs were prepared by Certified Registered Nurse Anesthetist (CRNA) blinded to the study. Once the patients were transferred to the operating room, mean arterial blood pressure (MAP), peripheral oxygen saturation (Spo2), and heart rate (HR) were monitored. Before setting up the anesthetic block, two cannulae were placed; one was in a vein on the dorsum of the operative hand and the other in the contrary hand for crystalloid infusion. The operative arm was raised for 3 minutes then, exsanguinated with an Esmarch bandage. A pneumatic tourniquet was left all-around the upper arm, and the proximal cuff was inflated to 250 mmHg. Circulatory isolation of the arm was confirmed by inspection, lack of radial pulse, and failure of pulse oximetry tracing of the ipsilateral index finger. IVRA was accomplished using 20 ml lidocaine 1% diluted with 20 ml saline to a total of 40 ml in the group L (n = 20) or 7.5 ml magnesium sulfate 20% plus 20 ml lidocaine 1% diluted with 12.5 ml saline to a total of 40 ml in the group M (n = 20). The mixture was introduced in more than 90 seconds by an anesthesiologist blinded to the injected drug. The sensory block was evaluated by a pinprick executed with a 22-gauge short-beveled needle pulled out constantly each 30 seconds. Patient response was assessed in the dermatomal sensory distribution of the medial and lateral antebrachial cutaneous, ulnar, median, and radial nerves. Motor function was judged by asking the subject to flex and extend his/her wrist and fingers, and complete motor block was documented when no voluntary movement was achievable. Sensory block onset time was noted as the time passed from injection of study drug to sensory block completed the entire dermatomes. Motor block onset time was the time passed by from introduction of study drug to perfect motor block. Subsequent to accomplishment of sensory and motor blocks, the distal cuff was inflated to 250 mmHg followed by release of the proximal tourniquet; the surgery was then begun. MAP, HR, and Spo2 were monitored before and after tourniquet use, at 5, 10, 15, 20, 30, 40, and 50 minutes after the beginning of anesthesia. Hypotension (25% decrease in blood pressure from the baseline value) was treated with IV ephedrine (3 to 10 mg bolus). Bradycardia (25% decrease in HR from the baseline value) was treated with IV atropine, 0.5 mg. Arterial oxygen saturation < 91% was treated with O2 supplementation delivered through a face-mask. Evaluation of tourniquet pain scores was achieved on the basis of the visual analog scale (VAS) (0 = "no pain" and 10 = "worst pain imaginable") [10,11] determined before and after tourniquet use, at 5, 10, 15, 20, 30, 40, and 50 minutes after the injection of anesthetic medication. Intraoperatively, boluses of 1µg/kg fentanyl were supplied for tourniquet pain treatment at any necessary time (when VAS > 4), and sum of fentanyl consumptions was recorded. After the operation, the surgeon, who was not aware of given medication, was inquired to qualify the operative situation consistent with the following numeric scale: 1 = unsuccessful, 2 = poor, 3 = acceptable and 4 = perfect. At the conclusion of operation, the

quality of the operative condition was assessed along with subsequent numeric scale: 4 (excellent) = no complaint from the patient, 3 (good) = minor complaint with no need for supplemental analgesics, 2 (moderate) = complaint that required supplemental analgesics, and 1 (unsuccessful) = patient given general anesthesia. The tourniquet was not deflated earlier than 30 minutes and was not inflated for more than 1.5 hours. At the end of surgery, the tourniquet deflation was made by cyclic deflation method. Sensory recovery time was noticed (time passed by after tourniquet deflation up to the recovery of pain in all dermatomes ascertained by pinprick test). Motor block recovery time was recorded (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 the first patient demand for analgesic drug). Evaluation of postoperative pain was completed on the basis of the VAS. MAP, HR, and VAS values were recorded at 6, 12, and 24 hours. Patients received 0.1 mg IV morphine when VAS > 4. Full amounts of morphine administration to each group were recorded. Through the study period, any local or systemic complications including nausea, vomiting, skin rash, tachycardia, bradycardia, hypotension, hypertension, headache, dizziness, tinnitus, hypoxemia, sedation, respiratory depression, bradypnea, tachypnea, and other side effects were noted. The statistical evaluation was performed using SPSS version 11.0. Independent samples *t*-test was used for evaluation of the demographic data, intraoperative or postoperative hemodynamic data, the time of the onset or recovery of sensory and motor blocks, the duration of the operation and tourniquet, and intraoperative or postoperative analgesic use. Mann-Whitney *U*-test was used for intraoperative and postoperative VAS. The quality of the anesthesia was analyzed by using χ^2 and Fisher's exact tests. A P value < 0.05 was considered significant.

Results

Forty patients consented to take part in the study. The two groups were comparable with respect to demographic characteristics. There was no significant difference in tourniquet time, duration of anesthesia or surgery between the two groups (table 1). There was no statistically significant difference between the two groups for MAP, HR or Spo2 at any time during the study. The onset of sensory or motor block was significantly shorter in group M compared with group L (P < 0.05) (table 2). Sensory or motor block recovery time was more prolonged in group M compared with group L but it was not statistically significant (table 2). Intraoperative VAS scores were significantly lower in group M compared with group L at 20, 30, 40, and 50 minutes after tourniquet inflation (P < 0.05) (table 3). Fentanyl requirement was significantly lower in group M compared with group L (P < 0.05) (table 2). Number of patients who needed additional fentanyl administration was significantly less in group M compared with group L (10/20 vs. 18/20 respectively, P < 0.05). Anesthesia quality, as determined by the anesthesiologist and the surgeon, was significantly better in group M (P < 0.01) (table 4). The time to the first patients' request for morphine administration after surgery was significantly prolonged in group M compared with group L (53.75 ± 6.94 minutes vs. 40.76 ± 14.55 respectively, P < 0.05). Postoperative VAS scores were significantly lower at 6 , 12, and 24 hours after surgery in group M compared with group L (P < 0.05) (table 5). Postoperative morphine consumption (mean ± SD) was less at 6, 12, and 24 hours in group M compared with group L but it was not statistically significant (2.0 ± 0.6 vs. 3.5 ± 2.4 mg; 0.0 ± 0.0 vs. 0.5 ± 0.3 mg; 0.0 ± 0.0 vs. 0.5 ± 0.3 mg; P > 0.05). There was no significant adverse effect during the 24-hour postoperative periods in either group.

Table 1. Demographic and clinical variables (mean ± SD).

Variable	Group L (n=20)	Group M (n=20)
Age (year)	32.4 ± 12.1	31.6 ± 11.3
Weight (kg)	66.5 ± 9.1	65.2 ± 8.9
Height (cm)	167.2 ± 7.6	166.3 ± 8.2
Sex (male/female)	17/3	15 /5
Tourniquet time (minutes)	67.3 ± 2.7	66.2 ± 1.9
Duration of anesthesia (minutes)	64.2 ± 5.7	62.3 ± 4.9
Duration of surgery (minutes)	65.1 ± 4.3	63.3 ± 3.1

No significant difference was found between the two groups.

Table 2. Onset and recovery times of sensory and motor blocks and intra-operative fentanyl requirement in the two groups (mean ± SD).

Variable	Group L (n=20)	Group M (n=20)
Sensory block onset time (minutes)	6.20 ± 2.35	4.10 ± 2.22*
Motor block onset time (minutes)	10.20 ± 3.92	7.10 ± 2.61*
Sensory block recovery time (minutes)	5.00 ± 1.80	6.15 ± 2.25
Motor block recovery time (minutes)	7.55 ± 2.90	8.00 ± 2.42
Fentanyl requirement (μg)	65.00 ± 12.63	27.50 ±11.94*

* $P < 0.05$ vs. group L.

Table 3. Intraoperative VAS scores.

Variable	Group L (n=20)	Group M (n=20)
Before tourniquet	0	0
After tourniquet		
5 minutes	3 (2-4)	2 (1-4)
10 minutes	1 (0-2)	1 (0-3)
15 minutes	1 (0-2)	1(0-2)
During surgery		
20 minutes	2 (1-3)	1 (0-2)*
30 minutes	2 (1-4)	1(0-3)†
40 minutes	2 (1-4)	1 (0-3)†
50 minutes	2 (1-4)	1 (0-3)*

VAS = visual analog scale. Values are median (range).
* $P < 0.05$; † $P < 0.01$ vs. group L.

Table 4. Quality of anesthesia assessed by an anesthesiologist or a surgeon.

	Group L (n = 20)				Group M (n = 20)				
	1	2	3	4	1	2	3	4	P value
Anesthesiologist [n (%)]	0 (0)	6 (30)	9 (45)	5 (25)	0 (0)	3 (15)	0 (0)	17 (85)	0.000
Surgeon [n (%)]	0 (0)	1 (5)	12 (60)	7 (35)	0 (0)	0 (0)	2 (10)	18 (90)	0.002

Table 5. Postoperative VAS scores.

Variable	Group L (n=20)	Group M (n=20)
6 h	5 (3-6)	4 (1-5)*
12 h	3 (1-4)	2 (0-3)†
24 h	2 (0-3)	1 (0-2)†

VAS = visual analog scale. Values are median (range).
* $P < 0.05$; † $P < 0.01$ vs. group L.

Discussion

Our study showed that adding magnesium to lidocaine for IVRA enhances the speed of onset and the quality of anesthesia, decreases tourniquet pain and intraoperative analgesic use, lengthens the time to the first patients' demand for morphine administration after surgery, and finally, does not produce significant side effects. This claim is based on the antagonist properties of Mg for the NMDA receptor and its inhibitory properties for calcium channels. [7] Calcium channel blockers have revealed antinociceptive effects in animals and morphine potentiation in patients with chronic pain. NMDA receptor antagonists can inhibit the induction of central sensitization owing to peripheral nociceptive stimulation and eliminate hypersensitivity [7]. Tramer and Glynn [12] used magnesium for the treatment of chronic limb pain in IVRA and showed that the addition of magnesium to lidocaine increases the quality of the block, lengthens the analgesia, and decreases the overall failure rate. The double blind prospective study of Tramer et al clearly showed the value of Mg as an adjuvant in postoperative analgesia. Tramer and colleagues demonstrated that patients getting Mg as an adjuvant in postoperative analgesia, needed less morphine, had fewer distresses and slept better through the first 48 hours than those receiving morphine alone. The quality of postoperative analgesia was, certainly, the same. Three respiratory depressions occurred in the controlled analgesia group receiving morphine only vs. no one in the group treated by morphine and Mg. [7] Koinig et al described similar results with a decreasing analgesic use both intra- and post-operatively in the group receiving Mg pre- and intra-operatively. [13] In both studies, plasma Mg concentration was markedly diminished postoperatively in the control group (values close to hypomagnesemia), but was significantly raised in the treatment group. [7,13] Wilder-Smith et al [14] carried out a comparative study of pain intensity and postoperative use of morphine in three groups. In each group, patients received ketamine, Mg or fentanyl pre- and intraoperatively. No differences were demonstrated between groups for the effects of these products. In an additional statement, Mg infusion after anesthesia induction decreased intraoperative consumption of remifentanil. [15] In two other studies, the tendency in the direction of reduced use of fentanyl intraoperatively [16] and morphine postoperatively [16,17] was verified, but showed no statistically significant difference. In the study of Wilder-Smith et al, [17] lack of significance was most likely owing to the small numbers of patients in the groups. Moreover, magnesium possesses an endothelium-derived nitric oxide-induced vasodilatory effect. [18,19] The pneumatic tourniquet produces ischemia, which interferes with nerve dissemination by oxidative stress and influences the blood-nerve barrier. [20] Nitric oxide donors have been demonstrated to defend vascular endothelium from ischemia/reperfusion-mediated endothelial dysfunction. [21]

In the present study, in contrast to Turan et al [10] study in which postoperative VAS scores were significantly higher for only the first 6 hours postoperatively in control group compared with magnesium group, postoperative VAS scores were significantly lower at 6, 12, and 24 hours after surgery in group M compared with group L. This difference between the two studies may be due to dissimilarity in severity of insults to the hand and techniques of surgery. Also, in our study, we used 20 ml lidocaine 1% in both groups regardless of the precise body weight and it is probable that we overestimated the lidocaine dosage in some patients. This was a limitation of our study. In our study, the sensory and motor block recovery times were not different in the two groups

while in Turan et al study, these variables were statistically prolonged in group receiving magnesium and lidocaine. This difference between the results of the two studies may also be due to over- or under-estimation of lidocaine dosage in both groups. In summary, adding magnesium to lidocaine in IVRA demonstrated reduced intraoperative fentanyl use and pain associated with the tourniquet. It also shortened sensory and motor block onset times and made better the quality of anesthesia while prolonged the time to the first postoperative analgesic requirement. The addition of magnesium to a local anesthetic in IVRA was effective; nevertheless, more studies must be carried out with further peripheral techniques and several doses to establish an appropriate conclusion before its regular use.

References

1. Chilvers CR, Kinahan A, Vaghadia H, Merrick PM. **Pharmacoeconomics of intravenous regional anaesthesia vs general anaesthesia for outpatient hand surgery.** *Can J Anaesth* 1997; 44**:** 1152-1156.
2. Crews JC, Hilgenhurst G, Leavitt B, Denson DD, Bridenbaugh PO, Stuebing RC. **Tourniquet pain: the response to the maintenance of tourniquet inflation on the upper extremity of volunteers.** *Reg Anesth* 1991; 16**:** 314-317.
3. Reuben SS, Steinberg RB, Kreitzer JM, Duprat KM. **Intravenous regional anesthesia using lidocaine and ketorolac.** *Anesth Analg* 1995; 81**:** 110-113.
4. Reuben SS, Steinberg RB, Lurie SD, Gibson CS. **A dose-response study of intravenous regional anesthesia with meperidine.** *Anesth Analg* 1999; 88**:** 831-835.
5. Reuben SS, Steinberg RB, Klatt JL, Klatt ML. **Intravenous regional anesthesia using lidocaine and clonidine.** *Anesthesiology* 1999; 91**:** 654-658.
6. Choyce A, Peng P. **A systematic review of adjuncts for intravenous regional anesthesia for surgical procedures.** *Can J Anaesth* 2002; 49**:** 32-45.
7. Tramer MR, Schneider J, Marti RA, Rifat K. **Role of magnesium sulfate in postoperative analgesia.** *Anesthesiology* 1996; 84**:** 340-347.
8. Memis D, Turan A, Karamanlioglu B, Sut N, Pamukcu Z. **The use of magnesium sulfate to prevent pain on injection of propofol.** *Anesth Analg* 2002; 95**:** 606-8, table.
9. 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**:** 277-281.
10. Turan A, Memis D, Karamanlioglu B, Guler T, Pamukcu Z. **Intravenous regional anesthesia using lidocaine and magnesium.** *Anesth Analg* 2005; 100**:** 1189-1192.
11. Gentili M, Bernard JM, Bonnet F. **Adding clonidine to lidocaine for intravenous regional anesthesia prevents tourniquet pain.** *Anesth Analg* 1999; 88**:** 1327-1330.
12. Tramer MR, Glynn CJ. **Magnesium Bier's block for treatment of chronic limb pain: a randomised, double-blind, cross-over study.** *Pain* 2002; 99**:** 235-241.
13. Koinig H, Wallner T, Marhofer P, Andel H, Horauf K, Mayer N. **Magnesium sulfate reduces intra- and postoperative analgesic requirements.** *Anesth Analg* 1998; 87**:** 206-210.
14. Wilder-Smith OH, rendt-Nielsen L, Gaumann D, Tassonyi E, Rifat KR. **Sensory changes and pain after abdominal hysterectomy: a comparison of anesthetic supplementation with fentanyl versus magnesium or ketamine.** *Anesth Analg* 1998; 86**:** 95-101.
15. Schulz-Stubner S, Wettmann G, Reyle-Hahn SM, Rossaint R. **Magnesium as part of balanced general anaesthesia with propofol, remifentanil and mivacurium: a double-blind, randomized prospective study in 50 patients.** *Eur J Anaesthesiol* 2001; 18**:** 723-729.
16. Zarauza R, Saez-Fernandez AN, Iribarren MJ, Carrascosa F, Adame M, Fidalgo I *et al*. **A comparative study with oral nifedipine, intravenous nimodipine, and magnesium sulfate in postoperative analgesia.** *Anesth Analg* 2000; 91**:** 938-943.
17. Wilder-Smith CH, Knopfli R, Wilder-Smith OH. **Perioperative magnesium infusion and postoperative pain.** *Acta Anaesthesiol Scand* 1997; 41**:** 1023-1027.

18. Mallet RT, Sun J, Fan WL, Kang YH, Bunger R. **Magnesium activated adenosine formation in intact perfused heart: predominance of ecto 5'-nucleotidase during hypermagnesemia.** *Biochim Biophys Acta* 1996; 1290**:** 165-176.
19. Altura BT, Altura BM. **Endothelium-dependent relaxation in coronary arteries requires magnesium ions.** *Br J Pharmacol* 1987; 91**:** 449-451.
20. Saray A, Can B, Akbiyik F, Askar I. **Ischaemia-reperfusion injury of the peripheral nerve: An experimental study.** *Microsurgery* 1999; 19**:** 374-380.
21. Katzung BG, Chatterjee K. **Vasodilators and the treatment of angina pectoris.** In: Katzung BG, ed. *Basic and clinical pharmacology*. Stamford, CT: Appleton & Lange; 1998: 179-304.