The Effect of Adding Magnesium Sulfate to Lidocaine Compared with Paracetamol in Prevention of Acute Pain in Hand Surgery Patients Under Intravenous Regional Anesthesia (IVRA)

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ABSTRACT

Introduction: This study was done to compare the analgesic effects of “magnesium plus lidocaine,” “paracetamol plus lidocaine,” and “placebo plus lidocaine” on block characteristics for intravenous regional anesthesia (IVRA) in patients undergoing upper extremity orthopedic surgery.

Methods: In a double-blind, placebo-controlled randomized clinical trial, 90 patients were selected and entered randomly into three study groups after applying the inclusion and exclusion criteria. Time to start of the sensory and motor block were measured separately and also the duration of these two block types were measured. Post-op pain assessment was measured using a numeric rating scale. Venous samples were checked and compared regarding blood gas and pH measurements.

Results: The time from drug injection to sensory block onset was the shortest in the magnesium plus lidocaine group; the time from drug injection to the time of motor block onset was the shortest in the lidocaine plus magnesium group; the duration of the motor block was the longest in the lidocaine plus magnesium group.

Discussion: Addition of magnesium lidocaine in patients undergoing upper extremity orthopedic operations using IVRA decreases significantly the time gap between drug administration and the start of the block; also, this drug combination increases the IVRA block length, while paracetamol does not have such a significant effect.

Key words: Intravenous regional anesthesia, lidocaine, magnesium, orthopedic surgery, paracetamol

INTRODUCTION

Intravenous regional anesthesia (IVRA) is one of the regional techniques which are used for surgical anesthesia in upper extremity without the need for induction of general anesthesia. In this method, usually local anesthetics are used; but at times, adjuvant drugs are used as the counterparts and adjuvants for increasing the quality of the block.
Acute postoperative pain is one of the main acute complaints affecting the quality of care and highly considered by physicians and the patients. Many therapeutic modalities, including pharmaceutical agents, have been used for its suppression. Opioids, though very effective for acute pain, are associated with a number of drawbacks.[1,2] Also nonopioid agents have been proposed to compensate for part of the complications related to the opioid agents.[3-6]

In this study three different drug combinations were used to assess the difference in their effects for IVRA, so the effects of magnesium sulfate, paracetamol, and placebo added to lidocaine for IVRA were compared regarding the quality and timing of block, venous blood gas analysis, and acute pain, in patients undergoing intravenous regional anesthesia for upper extremity surgeries.

METHODS

This study started after proposal approval by the Institutional Ethics Committee, Deputy of Research Affairs, Shahid Beheshti University of Medical Sciences, Tehran, Iran. The study proposal and its protocol were reviewed and financially supported by Anesthesiology Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

In a double-blind, placebo-controlled, randomized clinical trial, among all the patients admitted in the orthopedics operating room of a university medical center, during the period of the study (18 months), a total of 90 patients were selected and after being matched with the study criteria and applying the inclusion and exclusion criteria, they entered the study. Informed written consent was also taken from each of the patients. Inclusion criteria were adult patients undergoing elective orthopedic surgery, lasting less than 1 hour, aged 18-45 years and in American Society of Anesthesiologists classification 1 or 2 (i.e., ASA I or II). Exclusion criteria were patient refusal to enter or continue the study, lack of informed written consent, current or previous history of drug abuse or illicitly used controlled drugs or substances, and a history of renal disorders [Figure 1].

For sample size determination, a power analysis was done and after considering $\alpha = 0.05$ and $\beta = 0.2$, a sample size of 90 was calculated; then the patients were randomly assigned into three groups; IVRA using lidocaine and magnesium (Mg group), IVRA using lidocaine and paracetamol (paracetamol group), and IVRA using lidocaine and placebo (placebo group). Patients were allocated in the three groups according to a table of random numbers.

![Figure 1: Study flowchart](https://www.mui.ac.ir)
One of the study colleagues (a constant person) visited each patient at the night before the surgery. His duty was to inform the patients regarding the details of the study and also, administering the premedication drug dose. In addition, during the visit, he trained the patients regarding the method of postoperative pain assessment using a 100 mm NRS (Numerical Rating Scale). For the premedication, 0.1 mg/kg intramuscular morphine was administered, which was 1 hour before the patient transfer to the operation room. A period of 8 hours of Non Per Oss or NPO was determined before transfer of the patients to the operation room.

After patient entry to the operation room, all the patients were anesthetized only by a constant colleague (the three groups), while he was not aware of the drug composition he used for IVRA. He also did not have any contribution to data collection process in the postoperative period and did not have any kind of contribution in the process of blinding or the process of patient allocation into the study groups. The measured variables included the following items: the duration of the operation; time from drug injection to the onset of sensory block; time from drug injection to the onset of motor block; the duration of the sensory block; the duration of the motor block; and NRS scores for pain assessment for three times using a 100 mm pain assessment scale (i.e., before tourniquet closure, after tourniquet removal at the end of the surgery and in the postanesthesia care unit; PACU). Also, two venous samples were taken to check for pH, PCO2, and PO2; these two samples were taken at the beginning of anesthesia, i.e., before tourniquet closure and at the end of anesthesia, i.e., before removal of the tourniquet.

Those colleagues who were caring for the patients in order to assess the study outcomes during the course of anesthesia and in the postoperative period were blinded regarding the specific group each patient belonged to.

Also, the patients did not know which group they belonged to, although they were fully informed regarding the study. After entering the operation room, electrocardiography monitoring, pulse oxymetry, noninvasive blood pressure, and heart rate monitoring were initiated plus 0.05 mg/kg of intravenous midazolam. A number 18 intravenous catheter was used as the site of drug injection and exactly after catheter entrance to the vein, 1 ml venous blood was taken from the patients for checking the blood gas variables before IVRA. Then the proximal tourniquet was inflated to 100 mmHg above the systolic blood pressure and the patients received the drug for IVRA in a 50 ml syringe. In the first group, i.e., IVRA using lidocaine and magnesium, 3 mg/kg of lidocaine plus 1 g of magnesium sulfate (5 ml of 20% solution), in the second group, i.e., IVRA using lidocaine and paracetamol, 3 mg/kg of lidocaine plus 300 mg of paracetamol, and in the third group, i.e., IVRA using lidocaine and placebo. In the three groups the drug combination was increased to 50 ml using normal saline.

Throughout the study, the patients’ personal data were kept fully confidential. Also, the grouping of the patients was not revealed and the patients left the study whenever they decided, as was allowed, just by informing one of the researchers; then they received their standard care.

Data entry and analysis was performed by SPSS software (version 11.5). For data analysis, analysis of variance (ANOVA) with a post hoc Bonferroni test was used. Mean ± SEM was used for demonstrating the findings and a P value < 0.05 was considered as statistically significant.

RESULTS
There was no difference between the three groups regarding basic variables [Tables 1 and 2]. Also, duration of the operation was not different in the three groups.

Regarding the times for sensory block, the time from drug injection to sensory block onset was the shortest in the magnesium plus lidocaine group (the first group), while there was no difference regarding the duration of sensory block between the three groups.

Regarding the times for motor block, the time from drug injection to the time of motor block onset was the shortest in the first group (lidocaine plus magnesium), while there was no statistically significant difference between the second (paracetamol plus magnesium) and third (placebo plus lidocaine) groups. Also, regarding the duration of the motor block, it was the longest in the first group, while there was no difference between the second and the third group.

The values related to the pH before the block were the same between the three groups while
Table 1: Basic variables in the three groups*

| Group                  | Lidocaine and MgSO4 | Lidocaine and paracetamol | Lidocaine and placebo | P value |
|------------------------|---------------------|---------------------------|-----------------------|---------|
| Weight                 | 73.9 ± 12.5         | 74.9 ± 12.9               | 75.5 ± 11.2           | 0.9     |
| Age                    | 43 ± 15.9           | 45 ± 13.5                 | 45 ± 13.2             | 0.8     |
| Duration of operation  | 72.8 ± 21.8         | 83.5 ± 20.5               | 78.7 ± 22             | 0.16    |
| Injection-to-sensory block onset | 7.2 ± 2.8<sup>a</sup> | 10.8 ± 4.1               | 11.1 ± 3.7            | 0.000   |
| Duration of the sensory block | 87.2 ± 24.3         | 79.3 ± 22.8               | 75.5 ± 15.5           | 0.1     |
| Injection-to-motor block onset | 12.6 ± 4.9<sup>b</sup> | 15.8 ± 5.7               | 16.6 ± 5.6            | 0.01    |
| Duration of the motor block | 90.7 ± 23.5<sup>c</sup> | 80.9 ± 18.2               | 74.1 ± 14             | 0.003   |
| pH before the block    | 7.39 ± 0.03         | 7.4 ± 0.02                | 7.39 ± 0.01           | 0.3     |
| pH after the block     | 7.32 ± 0.1          | 7.38 ± 0.03<sup>d</sup>  | 7.34 ± 0.07           | 0.001   |
| pO2 before the block   | 48.5 ± 12           | 51.7 ± 15                 | 50.6 ± 13             | 0.6     |
| pCO2 before the block  | 45.7 ± 16.8         | 48.4 ± 19                 | 46.2 ± 17.6           | 0.8     |
| pO2 after the block    | 43 ± 9              | 40.8 ± 6.2                | 42 ± 8.6              | 0.6     |
| pCO2 after the block   | 50.1 ± 13.6         | 44.4 ± 14.2               | 47 ± 13               | 0.3     |

*Data are presented as mean ± SEM; total 90 cases in three groups, P value for ANOVA (with a post hoc Bonferroni test),
<sup>a</sup>The difference is statistically significant only for this group with the others.

Table 2: Gender distribution in the study group

|        | lidocaine and magnesium | lidocaine and paracetamol | lidocaine and placebo |
|--------|-------------------------|---------------------------|-----------------------|
| Male   | 15                      | 13                        | 12                    |
| Female | 15                      | 17                        | 18                    |

P value for the chi square test = 0.7.

the pH after the block was significantly higher in the second group, while there was no difference between the first and the third groups.

There was no statistically significant difference between the three groups regarding these variables: partial venous pressure of oxygen before the block; partial venous pressure of carbon dioxide before the block; partial venous pressure of oxygen after the block; partial venous pressure of carbon dioxide after the block.

Also, the three groups had no significant difference regarding NRS scores for acute pain (i.e., before tourniquet closure, after tourniquet removal at the end of the surgery, and in the postanesthesia care unit; PACU) [Table 3].

**DISCUSSION**

The results of this study demonstrated that adding magnesium to lidocaine in patients undergoing upper extremity orthopedic operations using IVRA decreases significantly the time gap between drug administration and the start of the block; also, this drug combination increases the IVRA block length. This effect is the most prominent in patients receiving magnesium plus lidocaine, but not so much seen after adding paracetamol to lidocaine.

However, regarding the duration of the motor block, only the combination of magnesium plus lidocaine was effective compared with placebo, which demonstrated the effect of this drug combination. But this study did not demonstrate any difference between the groups regarding the results of acute pain assessments using the NRS scores, though there are studies insisting on the effects of magnesium in suppressing acute pain.[3-7]

Paracetamol can suppress the acute postoperative pain effectively.[8-10] Also, there are many studies describing the analgesic effects of intravenous paracetamol: a considerable number denoting its mechanism.[11-13] However, the analgesic effects of magnesium sulfate have been described in patients receiving this drug, especially when administered as an adjuvant.[7,14,15] Magnesium is proposed to antagonize N-methyl-D-aspartate receptor to antagonize pain and these studies usually consider its effects as an antagonist for the NMDA receptors.[6,7,16-18]

Of course, there is not such a study comparing the effects of these two combinations with each other and also, with placebo; considering the block properties and the venous blood gas parameters in patients undergoing hand surgery with IVRA.

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The results of this study did not demonstrate any difference between the magnesium group and the placebo group regarding venous pH. However, the paracetamol plus lidocaine group had the most normal pH values after the operation which was significantly higher than the two other groups; this may be due to the chemical effects of the drug combination. The similarity of the oxygen and carbon dioxide values after the block between the three groups could be explained by the lack of difference between the three groups regarding their metabolic effects.

Although there are studies assessing the effects of pH on the quality of block in IVRA,[19-21] there has been nearly no study so far, assessing the block effect on venous pH. So there is a novelty in this issue that has not been previously considered.

There are a number of limitations for this study. First of all, the blood gas samples were taken from the venous blood which could be more exact if they were from the arterial blood. But it would be more invasive and at the same time, would induce untoward arterial puncturing to the patients while the venous sampling of this study was done just from the venous catheter used for drug administration, without any extra punctures. Second, the drug combinations were not compared regarding their pH before their injection. Maybe their differences before injection could be a source of difference for postblock differences in venous pH. Also, we had only one pH measurement after the block. Maybe it would be possible to trace more changes with performing more venous samplings.

Finally, this study demonstrated that addition of magnesium to lidocaine in patients undergoing upper extremity orthopedic operations using IVRA decreases significantly the time gap between drug administration and the start of the block; also, this drug combination increases the IVRA block length, while paracetamol does not have such a significant effect.

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