The Effect of Intravenous Infusion of Magnesium Sulfate During Bimaxillary Orthognathic Surgery on Post-operative Pain: A Clinical Trial

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Abstract

Background: This prospective randomized controlled clinical study aimed to investigate the effect of magnesium sulfate (MgSO₄) on pain management post orthognathic surgery.

Methods: In this study, 52 patients undergoing orthognathic surgery were randomly allocated to receive MgSO₄ or saline intravenously. The intervention group (n = 26) received intravenous MgSO₄ (30 mg/kg bolus for 15 minutes immediately before anesthesia induction followed by 10 mg/kg/h dissolved in saline via pump infusion) and the second group (n = 26) received the placebo in the same bolus volume as a normal saline in a 15 minute intravenous infusion which was continued until the end of the operation. A visual analog scale (VAS) was used to determine the intensity of pain. Invasive arterial blood pressure and valid and invalid analgesic demand were also recorded. Side effects were recorded, as well.

Results: This study was conducted on 52 patients, 26 per group. The results showed no statistically significant differences between the two groups with respect to demographics. During the post-operative period, the patients in the control group showed larger analgesic requirement 7 (26.9%) compared to those in the magnesium group 4 (15.4%) and the difference was not statistically significant (P = 0.308). The post-operative VAS scores evaluated serially from the recovery room also showed a significant difference between the intervention 3 (11.5%) and the control group 14 (53.8%) after the surgery (P = 0.001). However, no significant difference was found between the two groups regarding VAS scores in the surgical ward [7 (26.9%) vs. 8 (30.8%) P = 0.760].

Conclusions: Intra-operative administration of intravenous MgSO₄ reduced opioid consumption for pain after bimaxillary orthognathic operations.

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Keywords: Infusions; Intravenous; Magnesium sulfate; Orthognathic surgery; Pain; Post-operative; Pain management

Introduction

A pain resulting from surgery is deleterious and can lead to post-operative complications if inadequately relieved (1). Magnesium sulfate (MgSO₄) has been used as an intravenous adjuvant to analgesics in the perioperative period (2). MgSO₄ acts as a physiologic calcium-channel blocker (3-5). Magnesium, which is a natural calcium antagonist, is an antagonist of the N-methyl-D-aspartate (NMDA) receptor that is a crucial element for enzymes function, neurotransmission, and cell signaling (6,7). NMDA receptor antagonists can prevent central sensitization because of peripheral nociceptive stimulation and abolish this hypersensitivity when it is established (7,8). Therefore, substances with calcium-channel blocker effect and NMDA antagonism can play a role in the prevention of pain, sensitization processes, and hyperalgesia in the early post-operative period (9,10). Magnesium is the fourth most common mineral salt in human body and contributes to muscle contraction, conduction of neuronal and pain impulses, and vascular tone regulation (4,5). Some studies have clearly shown that MgSO₄ reduces post-operative morphine requirement after remifentanil-based anesthesia (11). Similarly, it can reduce intra-operative and post-operative analgesic requirement in patients undergoing major lumbar orthopedic surgery (12). Opioid-induced hyperalgesia is defined as a state of nociceptive sensitization, which is characterized by a paradoxical response, whereby a
Effect of Intravenous Magnesium Sulfate during Bimaxillary Orthognathic Surgery

based on simple random number generator and using permutation numbers. The randomization was performed by the investigators and remained blinded to the participants. The samples were divided into two groups using a computer-generated table of random numbers. The patients were selected through convenience sampling and were randomly divided into two groups. The investigators hypothesized that MgSO₄ could decrease morphine consumption and provide better pain relief after orthognathic surgery.

Materials and Methods

At first, the researchers gained the approval of the local Research Ethics Committee of Shiraz University of Medical Sciences and obtained written informed consents from the participants. Then, 52 patients with physical Status I according to the American Society of Anesthesiologists (ASA) undergoing bimaxillary orthognathic surgery were enrolled into this double-blinded, prospective, randomized trial [IRCT201307101674N7 (www.irct.ir)]. All the operations were performed by the same surgical team. The patients with hepatic, renal, or cardiovascular dysfunction, chronic obstructive pulmonary disease, asthma, heart block, myocardial damage, morbid obesity (body mass index ≥ 35), neuromuscular disease, history of neuropathy, history of using opioid or analgesics 3 days before the study, and history of using calcium channel blockers and those who were not willing to take part in the study were excluded. The study participants were required to fast for 6 hours before the surgery, and no premedication was given. The anesthetic method for surgery was similar for all the patients. Morphine 0.1 mg/kg was administered intravenously at induction of anesthesia which was achieved using 2-2.5 mg/kg propofol, 2-3 μg/kg fentanyl, and 0.5 mg/kg atracurium. Anesthesia was maintained using 6-12 mg/kg/h propofol and remifentanil by infusion. The patients were mechanically ventilated to keep EtCO₂ between 35 and 40 mm Hg and normothermia was maintained in the operation theater. The patients were selected through convenience sampling and were randomly divided into two groups via computer-generated table of random numbers. The randomization was performed by the random number generator and using permutation method. The sampling was also based on simple purposive method so if the selected person was not placed in the sample group, the another person was selected. The medications were prepared and randomly coded by nurses who were totally unaware of the nature of the study. The anesthesiologist and surgeon were also unaware of the content of injections. The patients in the intervention group received an intravenous MgSO₄ 30 mg/kg body weight bolus for 15 minutes followed by 10 mg/kg/h dissolved in saline via pump infusion. The control group, on the other hand, received the placebo in the same bolus volume as normal saline in a 15-minutes intravenous infusion continued until the end of the operation. Intra-operative monitoring included invasive-arterial blood pressure, electrocardiograph, and peripheral oxygen saturation. A visual analog scale (VAS) was used to assess the intensity of pain (0 = no pain and 10 = worst pain imaginable) and the effectiveness of the administered analgesics. At the end of the surgical procedure, all the infusions were stopped, and the residual neuromuscular block was reversed using neostigmine (0.05 mg/kg) and atropine (0.02 mg/kg). All the patients were monitored in the post-anesthesia recovery room for the first 6 hours. Post-operative monitoring included heart rate, non-invasive blood pressure, and pulse oximetry. During these 6 hours, the patients were kept in the recovery room and rescue analgesia was provided at VAS ≥ 3 in the form of intravenous morphine 0.1 mg/kg. In the surgical ward, administration of analgesics was recorded for 12 hours. Then, the patients’ post-operative complications were recorded in a questionnaire. The incidence rates of bleeding, shivering, blood pressure changes, agitation and post-operative nausea and vomiting were also recorded after the surgery.

The data have been reported as mean ± standard deviations. Continuous variables, such as demographic data (age, height, and weight) and duration of surgeries, were analyzed using independent sample t-test. Besides, the effectiveness of blood-pressure lowering drugs was assessed by repeated measures ANOVA. In addition, chi-square and Fisher’s exact tests were used to analyze VAS pain scores and morphine consumption. All the analyses were performed using the SPSS for Windows (version 10; SPSS Inc., Chicago, USA), and P < 0.050 was considered as statistically significant.

Results

This study was conducted on 52 patients, 26 per group. The study results showed no statistically significant difference between the two groups regarding age, sex, weight, and height (P > 0.050). The surgery lasted for 261.9 ± 56.0 and 234.0 ± 38.9 minutes in the MgSO₄ and control groups, respectively, the difference was statistically significant (P = 0.044) (Table 1).
Table 1. The demographic characteristics of the study patients

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Control (n = 26)</th>
<th>Mg (n = 26)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>23.4 ± 5.3</td>
<td>22.3 ± 5.2</td>
<td>0.447</td>
</tr>
<tr>
<td>Sex (F/M)</td>
<td>11/15</td>
<td>9/17</td>
<td>0.569</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>61.4 ± 11.0</td>
<td>60.4 ± 9.1</td>
<td>0.742</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>169.3 ± 9.2</td>
<td>167.0 ± 7.8</td>
<td>0.538</td>
</tr>
<tr>
<td>Duration of operation (min)</td>
<td>261.9 ± 56.0</td>
<td>234.0 ± 38.9</td>
<td>0.044</td>
</tr>
</tbody>
</table>

During the post-operative period, the patients in the control group showed larger analgesic requirement (7, 26.9%) compared to those in the magnesium group (4, 15.4%) and the difference was not statistically significant (P = 0.308). However, a significant difference was observed between the intervention and the control group regarding post-operative VAS scores evaluated serially from the recovery room (3, 11.5% vs. 14, 53.8%; P = 0.001). On the other hand, no significant difference was found between the two groups regarding VAS scores in the surgical ward (7, 26.9% vs. 8, 30.8%; P = 0.760).

In the MgSO4 and control group, systolic and diastolic blood pressure decreased during operation significantly compared to the baseline. Besides, blood pressure increased after the operation. Furthermore, the mean of systolic blood pressure was lower in the magnesium group compared to the control group. However, the trend of changes in systolic and diastolic blood pressure was not statistically significant in MgSO4 and control groups (Figures 1 and 2).

The results showed no significant difference between the two groups regarding the incidence of bleeding, shivering, blood pressure changes, agitation, nausea, and vomiting were 11.5%, 30.8%, 3.8%, 7.6%, and 3.8% in MgSO4 group and 7.6%, 23.1%, 0.0%, 11.5%, and 3.8% in control group, respectively.

![Figure 1. Trend of systolic blood pressure between two groups](image1)

![Figure 2. Trend of diastolic blood pressure between two groups](image2)
Nonetheless, no incidence of bradycardia, hypoxia or hypoventilation was recorded during the post-operative periods.

Discussion

This study assessed the possible effects of infusion of MgSO4 started before induction of anesthesia and continued throughout the procedure on reducing the analgesic requirement and post-operative pain in the patients undergoing bimaxillary orthognathic surgery. In this study, 30 mg/kg MgSO4 was administered as a bolus followed by 10 mg/kg/h infusion intra-operatively. No complications resulting from magnesium administration were evident at the used doses. Magnesium, which acts as the NMDA receptor antagonist, may play a role in prevention and treatment of perioperative pain. Some studies have indicated that MgSO4 led to a reduction in analgesic consumption during the intra-operative (14,15) and post-operative periods (12,16,17). However, Ko et al. (18) reported that intravenous MgSO4 had no analgesic efficacy and caused no reduction in post-operative analgesic requirement. In our study, on the other hand, administration of intra-operative MgSO4 resulted in superior pain relief. Similar results were also obtained by Levaux et al. (12). Mentes and colleagues (16) also revealed the efficacy of MgSO4 in reducing post-operative pain following major lumbar orthopedic surgery and laproscopic cholecystectomy. In addition, using MgSO4 was associated with significantly less analgesic requirement in the patients undergoing lower limb orthopedic surgery and abdominal hysterectomy. In the post-operative period (19,20).

The effect of magnesium on perioperative analgesic requirement was first evaluated by Koinig and colleagues (21) in patients with identical levels of surgical stimulation. Their results demonstrated that magnesium could be a per-operative analgesic management by lowering the fentanyl requirement. Tramer et al. (22) were the first to show that magnesium administration significantly reduced analgesic requirement. They found that the patients who had received magnesium required significantly less morphine compared to those in the control group during the post-operative period and this was most pronounced during the first 6 hours. Moreover, Kaur and Baghla (1) showed that administration of 30 mg/kg MgSO4 bolus before induction followed by 10 mg/kg/h by infusion intra-operatively significantly reduced post-operative pain in the patients undergoing upper limb orthopedic surgery without any significant increase in the adverse effects. Furthermore, some researchers (11) believed that MgSO4 in a 30 mg/kg bolus with 500 mg/h intra-operative continuous infusion significantly decreased post-operative morphine usage as well as early post-operative VAS.

In summary, intravenous MgSO4 following general
anesthesia reduced post-operative pain and consumption of opioids after bimaxillary orthognathic procedures. Thus, administration of 30 mg/kg MgSO₄ before induction as bolus followed by 10 mg/kg/h by intra-operative infusion significantly reduced post-operative pain in the patients undergoing bimaxillary orthognathic surgery without any significant increase in the adverse effects.

Conflict of Interests
Authors have no conflict of interests.

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References