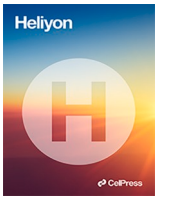
Heliyon 10 (2024) e30342

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon



Research article

Effects of intra-operative magnesium sulfate infusion on orthognathic surgery: A prospective and randomized controlled trial

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ARTICLE INFO

Keywords:
Magnesium sulfate
PONV
Postoperative pain
Inflammation
Orthognathic surgery

ABSTRACT

Purpose: To comprehensively understand the effects of intra-operative infusion of magnesium sulfate on patients who underwent orthognathic surgery, including remifentanil consumption, postoperative pain, postoperative nausea and vomiting (PONV), inflammatory response, and serum magnesium levels.

Methods: Seventy-five adult patients undergoing orthognathic surgery under general balanced anesthesia were randomly divided into two groups. One group (Group M) received 50 mg/kg of magnesium sulfate in 20 mL 0.9 % saline after intubation, followed by a continuous infusion at a rate of 15 mg/kg/h until 30 min before the anticipated end of surgery. The other group (Group C) received an equal volume of isotonic saline as a placebo. (Clinical trial registration number: chiCTR2100045981).

Results: The primary outcome was remifentanil consumption. The secondary outcomes included the pain score assessed using the verbal numerical rating scale (VNRS) and PONV assessed using a Likert scale. Remifentanil comsumption in Group M was lower than Group C (mean ± SD: 0.146 ± 0.04 μg/kg/min vs. 0.173 ± 0.04 μg/kg/min, $P = 0.003$). At 2 h after surgery, patients in Group C suffered more severe PONV than those in Group M (median [interquartile range, IQR]: 1 [3] vs. 1 [0], mean rank: 31.45 vs. 42.71, $P = 0.040$). At post-anesthesia care unit (PACU), postoperative pain in Group C was severe than Group M (3 [1] vs. 3 [0], mean rank: 31.45 vs. 42.71, $P = 0.013$). Changes in haemodynamics and surgical field scores did not differ between the groups (all $P > 0.05$). The levels of cytokines (IL-4, IL-6, IL-8, IL-10, TNF-a, and MIP-1β) were not significantly different between the groups after surgery (all $P > 0.05$). Postoperative serum magnesium levels in Group C were lower than those in Group M (0.74 ± 0.07 mmol/L vs. 0.91 ± 0.08 mmol/L, $P = 0.000$) and the preoperative level (0.74 ± 0.07 mmol/L vs. 0.83 ± 0.06 mmol/L, $P = 0.219$).

Conclusions: In orthognathic surgery, magnesium sulfate administration can reduce remifentanil requirement and relieve PONV and postoperative pain in the early postoperative phase.

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https://doi.org/10.1016/j.heliyon.2024.e30342
Received 6 March 2024; Received in revised form 20 April 2024; Accepted 24 April 2024
Available online 25 April 2024

1. Introduction

Magnesium is the second most abundant intracellular ion with an essential role to enzymatic reactions, neurotransmission, and cellular signaling [1], which is commonly thought of to be an antagonist of *N*-methyl D-aspartate (NMDA) glutamate receptors. A large number of studies have shown that magnesium seems to have antinociceptive and anesthetic effects and has been used as an adjuvant in the perioperative period to minimized postoperative pain [2–4], prevent postoperative nausea and vomiting (PONV) [5,6], diminish emergence agitation [7] and anti-inflammation [8]. Therefore, the importance of intra-operative magnesium is more pronounced in the field of pain and anesthesia [4,9,10].

Orthognathic surgery is associated with increased opioid analgesic requirements, increased blood loss, severe postoperative pain and a high incidence of PONV [11–13], which must be considered and managed by anesthesiologists. Thus, various strategies have been employed, including a multi-modal approach for pain control, hypertensive anesthesia, and prophylactic administration of antiemetic [14–16]. Among these methods, systemic magnesium as an adjuvant to general anesthesia could be a reliable option. Not only are the clinical data concerning the perioperative administration of magnesium conflicting, but there is also a lack of comprehensive evaluation regarding the effects of intra-operative magnesium sulfate infusion on surgery. The goal of perioperative anesthesia management is to improve surgical outcomes for patients by ensuring safety, pain management, and smooth surgical and recovery experience [17,18]. Thus, reevaluation of magnesium with respect to a comprehensive outcome is necessary. The present study was undertaken to evaluate the effects of systemic magnesium on opioid consumption, postoperative pain, and PONV in adult patients undergoing orthognathic surgery under sevoflurane and remifentanil anesthesia. Moreover, the serum magnesium level and the role of magnesium in the inflammatory response following surgery were evaluated.

2. Methods

2.1. Design and patient

Eighty patients aged 18–40 years, BMI 18–29 kg/m^2, with ASA status I and II, scheduled for orthognathic surgery under general anesthesia were eligible for participation from April 2022 to September 2022. All patients were from the same surgical team and were required to be familiar with the verbal numerical rating scale (VNRS) before surgery. Exclusion criteria were patients with liver and kidney dysfunction, atrioventricular conductance disturbance, psychiatric or neurological disorders, hypermagnesemia, drug or alcohol abuse within the last 6 months, chronic treatment with calcium channel blockers or non-steroidal anti-inflammatory drugs for more than 6 weeks, and allergy or intolerance to any of the study drugs. We also excluded patients who lost blood over 1000 ml or received blood transfusion during the surgery procedure.

2.2. Ethics and informed consent

This prospective, double-blind, randomized trial was approved by the Medical Ethics Committee of Hospital of Stomatology Sun Yat-Sen University (KQEC-2021-52-02, Chairperson Professor Chen Xiaobing, September 30, 2021) and was registered at Chinese Clinical Trial Registry (ChiCTR2100045981 , April 30, 2021). Written informed consent was obtained from all the patients.

2.3. Randomization and blinding

Patients were randomly allocated to control group (Group C) or magnesium sulfate group (Group M) in a 1:1 ratio using a computer-generated random sequence and a sealed envelope method. The study drugs were prepared in pharmacy by an independent nurse anesthetist who was not involved in the patient's care. All participants, including anesthesia providers, surgeons, patients, and nurses who took care of patient, were blinded to the group assignment.

2.4. Intervention

Patients in Group M received magnesium sulfate as intervention. A bolus injection of magnesium sulfate (10 ml:2.5 g, Hebei Tiancheng Pharmaceutical Co. Ltd, China) 50 mg/kg in 20 mL 0.9 % saline over 5min was administered immediately after intubation followed by continuous infusion at a rate of 15 mg/kg/h until 30 min before the anticipated end of surgery. Patients in Group C received an equal volume of isotonic saline as placebo. The dosage of systemic magnesium sulfate infusion was based on previous studies [6,10].

2.5. Anesthesia

No premedication was given for all patients. Upon arrival at the operating room, the patients received an intravenous access line and were connected to standard monitors. Anesthetic induction was started with intravenous propofol (Sichuan Kelun Pharmaceutical Co. Ltd, China) 2 mg/kg, remifentanil (Yichang Humanwell Pharmaceutical Co. Ltd, China) 1 μg/kg (at a rate of 0.5 μg/kg/min), and cisatracurium (Jiangsu Hengrui Pharmaceutical Co. Ltd,China) 0.2 mg/kg. Immediately after nasotracheal intubation, the dorsalis pedis artery was cannulated using 22 gauge catheters. Mechanical ventilation was maintained with a tidal volume of 6–8 ml/kg. The

respiratory rate was adjusted to maintain an end-tidal carbon dioxide concentration of 35–45 mmHg. Anesthesia was maintained with sevoflurane at end-tidal concentration of 1.6 %–2%, which was administered to keep BIS (bispectral index score) between 40 and 60 until wound closure. Dexmedetomidine (Yangtze River Pharmaceutical Group Co., Ltd, China) was constantly administered at 0.4 μg/kg/min until the end of surgery. Antiemetic prophylaxis in the form of dexamethasone 10 mg and tropisetron 4.48 mg intravenously was administered after anesthesia induction. The surgeon performed the inferior alveolar nerves block (for mandibular osteotomy), posterior superior alveolar nerve and infraorbital nerve block (for maxillary osteotomy) with 0.75 % ropivacaine 10 ml respectively. All patients were extubated in the operating room, and then transferred to post-anesthesia care unit (PACU).

In both groups, patients received continuous remifentanil infusion at an initial rate of 0.1 μg/kg/min after induction. A bolus of 0.5 μg/kg remifentanil could be administered, and the infusion rate of remifentanil was increased if there was a 20 % increase in baseline values of hypertension or tachycardia, or if controlled hypotension was required. Controlled hypotension was targeted to maintain a mean arterial pressure (MAP) of 50–65 mmHg or less than 30 % of the baseline value. If the remifentanil infusion rate reached a maximum of 0.3 μg/kg/min, urapidil could be administered if necessary. In cases of hypotension (MAP less than 50 mmHg or lower than 30 % of the baseline), the first choice was to decrease the remifentanil infusion rate. If hypotension persisted and anesthesia-related factors were ruled out, ephedrine 5 mg was administered, and a fast fluid bolus of 100 ml was allowed. In the case of bradycardia (heart rate less than 40 beats/min), atropine 0.5 mg was administered.

Patients with a verbal numeric rating scale score exceeding 3 in PACU were administered fentanyl at doses of 20–30 μg for pain management. Postoperative pain in the ward was managed with regular oral administration of celecoxib 0.2 g every 12 h and intramuscular injection of tramadol 100 mg, which was supervised by the surgeon.

2.6. Data collection

The primary outcome was the average remifentanil consumption. Average remifentanil consumption was defined as remifentanil consumption per kilogram of weight per minute, as well as the average remifentanil rate. The remifentanil consumption was read directly from the infusion pump at the end of surgery. The secondary outcomes included pain score and PONV severity. Patients were followed up at PACU, 2 h, 6 h, 12 h and 24 h after surgery for pain and PONV assessment. Postoperative pain intensity was assessed using an 11-point verbal numeric rating scale (VNRS) scores (0 = no pain, 10 = worst imaginable pain). PONV severity was assessed using a Likert scale (0 = none, 1 = mild, 2 = moderate, and 3 = severe). The other outcomes are described as follows. MAP, heart rates (HRs) were measured at the following time points: before anesthesia induction (T0), at the beginning of the surgery (T1), at the beginning of osteotomy (T2), 5 min after osteotomy (T3), 10 min after osteotomy (T4), after extubation (T5), and 30 min after end of surgery (T6). Time to extubation was defined as the time from the end of surgery to extubation. Surgical fields were assessed by the surgeon when ostectomy began with a six-point category scale: 5-Massive uncontrollable bleeding; 4-Bleeding, heavy but controllable, that significantly interfered; 3-Moderate bleeding that moderately compromised surgical; 2-Moderate bleeding, a nuisance but without interference; 1-Bleeding, so mild it was not even a surgical nuisance; 0-No bleeding, virtually bloodless field [15].

Blood samples were obtained for laboratory examination before and 2 h after the surgery. Blood samples for cytokines were obtained before anesthesia (baseline), 0 h, and 3 h and 24 h after surgical incision, and stored on ice in vacutainer tubes (Becton Dickinson) containing the anticoagulant ethylenediaminetetraacetic acid (EDTA). Within 1 h, the tubes were centrifuged at 4 °C for 10 min at 3000 revolutions per minute, and the plasma was aliquoted and stored at −80 °C for subsequent batch analysis.

2.7. Sample size calculation

A sample size calculation was performed using PASS (Version 15.0; NCSS, USA) using a one-way analysis of variance. Based on preliminary testing and related references, we assumed that the average remifentanil comsumption in Group M, Group C, respectively was 0.14 μg/kg/min and 0.17 μg/kg/min. With a significance level of 0.05, a power of 0.80, and 1:1 allocation in each group, we aimed to recruit 40 patients per group to compensate for the lack of 20 % follow-up data.

2.8. Statistical analyses

Continuous variables were expressed as mean ± SD or median [interquartile range，IQR]. Categorical variables are reported as the numbers and the percentages. Data were assessed using the Kolmogorov-Smirnov test to determine whether they were normally distributed. T-test was used to analyze the normally distributed data between groups, whereas Mann-Whitney *U* test was used to analyze the data that were not normally distributed or ordinal data. Repeated-measures ANOVA was used to compare measurements over time (MAP and HR); however, to compare the data at each time point, a *t*-test was used. The χ^2 test for independence or the Fisher exact test was used to compare categorical variables between the two groups. The paired *t*-test was performed to evaluate the changes in laboratory variables in each group. Statistical significance was set at $P < 0.05$.

3. Results

Eighty patients diagnosed with dentofacial deformities, including bimaxillary deformity with or without micrognathia, micrognathia accompanied with maxillofacial deformity or mandibular deformity, were assessed for eligibility. Among them, 2 patients were excluded for not meeting the inclusion criteria, 1 patient underwent temporarily canceled surgery, and 2 patients underwent changes in the surgical method. Two were excluded (one in each group) after surgery due to excessive blood loss. Of these patients, 22

in Group M and 30 in Group C provided consent for cytokines testing. Therefore, we analyzed clinical data from 73 patients (36 in Group M and 37 in Group C) and cytokine data from 52 patients (Fig. 1).

The baseline characteristics and intra-operative data are depicted in Table 1. Baseline characteristics were similar between groups. In comparison to Group C, Group M showed a significant decrease in average remifentanil consumption (0.146 ± 0.04 μg/kg/min vs. 0.173 ± 0.04 μg/kg/min, $P = 0.003$). However, there was no statistically significant difference over time and at each time point for either MAP (Fig. 2a) or HR (Fig. 2b) between the two groups ($F = 0.838$, $P > 0.05$; and $F = 0.936$, $P > 0.05$, respectively). Table 1 displays the intra-operative data, and it can be seen that only one patient in Group M required intra-operative use of atropine, whereas no patients in Group C needed it. However, there was no statistically significant difference between the groups in terms of atropine, ephedrine, or urapidil dosage. Notably, no adverse events occurred in either group during the operation.

Postoperative data are presented in Table 2. In Group M, the severity of PONV was significantly lower 2 h after surgery than in Group C (median [IQR]: 0 [1] vs. 1 [3]; mean rank: 32.45 vs. 41.68, $P < 0.05$). Similarly, the pain score in the PACU was significantly lower in Group M than in Group C (median [IQR]: 3 [1] vs. 3 [0]; mean rank: 31.45 vs. 42.71, $P < 0.05$). Postoperative adverse events were observed in five patients in Group M and one patient in Group C. However, there was no statistical difference in the occurrence rate of postoperative adverse events between the two groups ($P > 0.05$). Furthermore, no severe complications related to the surgeries and anesthesia were found in either group. As indicated in Table 3, the laboratory variables including haemoglobin, liver and renal function, and blood coagulation showed no significant differences between the groups. Although some of these variables showed variations before and after surgery, their values remained within the normal range. Notably, the post-surgery serum magnesium level in Group C was significantly lower than both the pre-surgery level (0.74 ± 0.07 mmol/L vs. 0.83 ± 0.06 mmol/L, $P < 0.01$) and the level in Group M (0.74 ± 0.07 mmol/L vs. 0.91 ± 0.08 mmol/L, $P < 0.01$). Fig. 3 illustrates that there were no significant differences between the groups in IL-4 (a), IL-6 (b), IL-8 (c), IL-10 (d), MIP-1β (e), and TNF-α (f) before anesthesia, at the start of surgical incision, and 3 h, and 24 h after surgical incision.

4. Discussion

In this study, we conducted a prospective, randomized, controlled, double-blinded trial to assess the overall impact of intravenous

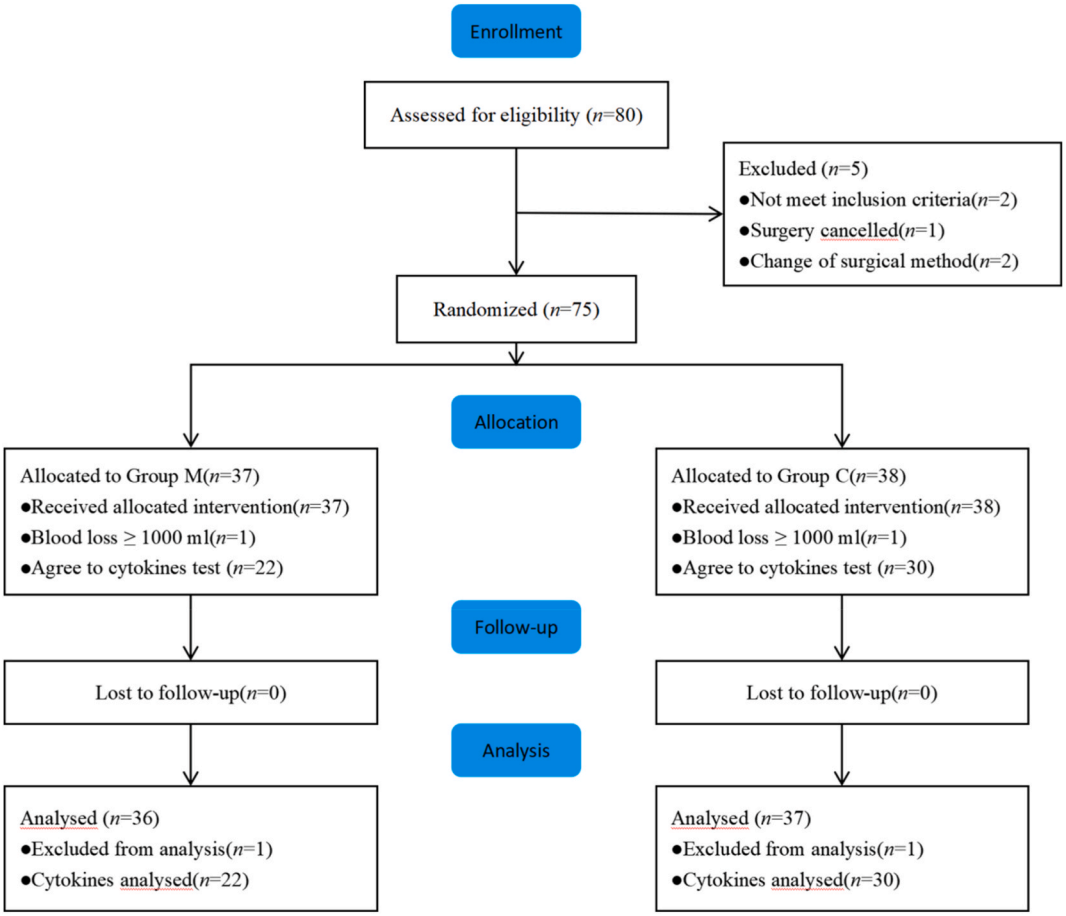

Fig. 1. CONSORT diagram of this randomized study.

Table 1
Demographic characteristics and intraoperative data.

	Group M n = 36	Group C n = 37	*P* value
Age (y)	24 ± 4	24 ± 5	0.93
Sex (F/M)	24/12 (66.7 %/33.3 %)	24/13 (64.9 %/35.1 %)	0.871
Weight (kg)	56.8 ± 8.8	57.2 ± 11.0	0.852
BMI (kg/m^2)	20.6 ± 2.7	20.6 ± 2.6	0.992
Duration of operation (min)	143.2 ± 38.6	128.5 ± 39.0	0.110
Duration of anesthsia (min)	181.8 ± 42.0	169.5 ± 46.8	0.240
Surgery type			
Bimaxillary	5 (13.9 %)	7 (18.9 %)	0.453
Bimaxillary + genioplasty rowhead	28 (77.8 %)	25 (67.6 %)	
Maxilla + genioplasty rowhead	2 (5.6 %)	1 (2.7 %)	
Mandible + genioplasty rowhead	1 (2.8 %)	4 (10.8 %)	
Total fluid (ml)	1250 [500]	1000 [500]	0.102
Surgical field score	3 [1]	3 [1]	0.806
Extubation time (min)	7 ± 3	6 ± 3	0.294
Average consumption of remifentanil (μg/kg/min)	0.146 ± 0.04*	0.173 ± 0.04	0.003
Average amount of atropine (mg)	0.014 ± 0.083	0	0.324
Average amount of ephedrine (mg)	0	0	–
Average amount of urapidil (mg)	7 ± 11	4 ± 9	0.152
Adverse events	0	0	–

Data are presented as the mean ± SD, median [interquartile range], or number of patients (%). Group C, control group; Group M, magnesium sulfate group. *p < 0.05 vs Group C.

magnesium sulfate on patients undergoing orthognathic surgery. Our findings reveal that the use of intravenous magnesium sulfate as an adjuvant can effectively reduce remifentanil consumption during the surgery. Furthermore, we found that, magnesium sulfate administration can relieve PONV and postoperative pain in the early postoperative phase of orthognathic surgery. Additionally, we observed that the administration of intravenous magnesium sulfate resulted in comparable surgical conditions as indicated by the surgical field score and haemodynamics stability.

Magnesium sulfate, a non-competitive NMDA receptor antagonist, has been explored as a potential adjuvant for intra-operative and postoperative pain management [2–4,19–21]. It has also been investigated for its vasodilatory properties in controlling hypertension during endoscopic sinus surgery and middle ear surgery [5,22]. Furthermore, previous studies have demonstrated the ability of magnesium sulfate to suppress haemodynamics fluctuations caused by pneumoperitoneum and reduce opioid consumption [4,23]. Our findings align with the results of these studies, providing further support for the efficacy of magnesium sulfate in various surgical settings. It is well-established that intraoperative remifentanil administration is associated with (opioid-induced hyperalgesia) OIH and tolerance, but there is still not a clear understanding of dosage and OIH and tolerance due to insufficient data and conflicting results. There is still no clear understanding of the relationship between dosage and OIH due to insufficient data and conflicting results. Recent studies suggest that high intraoperative doses of remifentanil may increase postoperative pain intensity [24,25]. According to a previous review, remifentanil infusion rates of >0.2 μg/kg/min were linked to OIH [26]. In our study, remifentanil infusion rates are were below 0.2 μg/kg/min in both groups. We think that the incidence of acute hyperalgesia may be minimal.

Orthognathic surgery is associated with high incidence of PONV [12]. Within the first 24 h, the occurrence of PONV can be as high as 40 %, with an even higher prevalence of 56 % after bimaxillary osteotomies [27]. In a study by Perrott et al. [28], PONV was identified as the most common complication following oral and maxillofacial surgery. Consistent with these findings, our study observed that over 50 % of patients in both groups experienced PONV.

Although there was no significant difference in the incidence of PONV within the first 24 h between the two groups, patients in Group M exhibited lower PONV severity at 2 h post-surgery compared to those in Group C. A similar trend was observed for the postoperative pain scores in PACU. This could be attributed to the rapid offset of remifentanil as well as the analgesic properties of magnesium. Notably significant differences in postoperative pain and PONV severity were primarily observed during the early postoperative phase, which can be attributed to the administration of analgesic and antiemetic medications in the ward setting.

Surgical injury triggers an immune response that leads to inflammation, which in turn affects pain pathways by releasing inflammatory mediators and interacting with neurotransmitters and their receptors [29,30]. Magnesium has been shown to regulate immune functions and possess anti-inflammatory properties [8,31,32]. However, in our study, we did not observe any differences in cytokine levels (IL-4, IL-6, IL-8, IL-10, TNF-a, and MIP-1β) between Groups M and C. This could be due to the small sample size or limitations of the analysis kit, as we measured only six cytokines as plasma biomarkers of systemic inflammation. It is possible that other proinflammatory cytokines were affected by magnesium but were not measured in our study. Additionally, remifentanil has been reported to have anti-inflammatory effects in various diseases [33,34]. In Group C, where remifentanil consumption was higher than in Group M, it is possible that the anti-inflammatory effects of magnesium were counteracted. Further research is required to explore the specific anti-inflammatory effects of magnesium.

Magnesium sulfate is an agent that possesses analgesic, anesthetic, antihypertensive, and neuromuscular blocking effects [22,23,35]. In recent decades, there has been significant interest in exploring the role of magnesium in anesthesia. Numerous studies have indicated that intra-operative administration of magnesium sulfate can reduce opioid requirements [4,10,35,36] and alleviate postoperative pain [4,5,21,37]. Furthermore, magnesium sulfate has been investigated as a vasodilator for controlling hypertension in

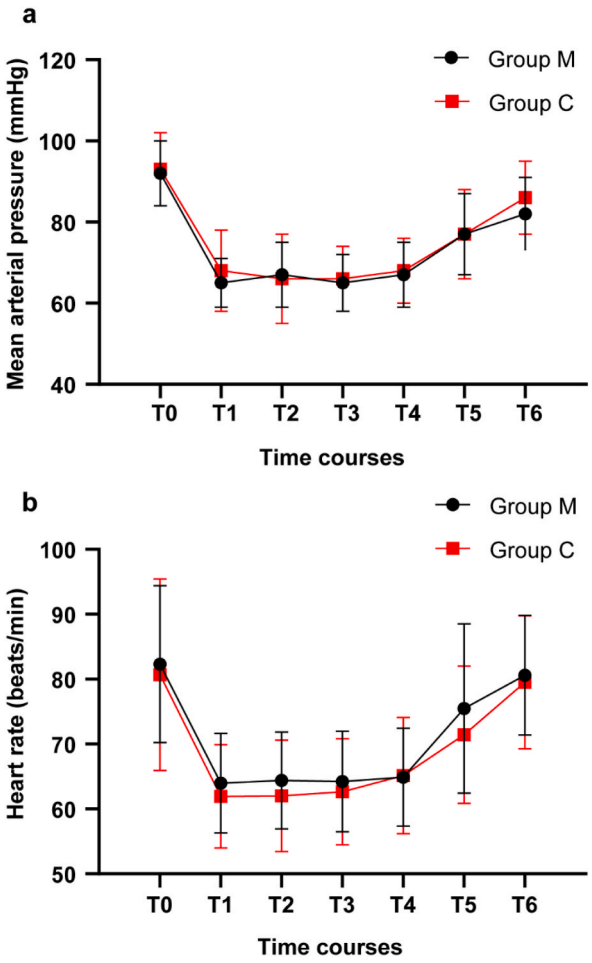

Fig. 2. Values are presented as mean ± SD. No significant differences are found over time in both MAP and HR ($F = 0.838$, $p > 0.05$ and $F = 0.936$, $p > 0.05$, respectively). No significant differences are found in each time in both MAP and HR ($p > 0.05$). Group C: control group; Group M: magnesium group. T0: before anesthetic induction; T1: at the beginning of the surgery; T2: at the beginning of osteotomy; T3: 5min after osteotomy; T4: 10min after osteotomy; T5: after extubation; T6: 30min after end of surgery. MAP: mean arterial pressure; HR: heart rate.

endoscopic sinus and middle ear surgery [5,22,38]. In gastrointestinal laparoscopy, magnesium sulfate has been shown to attenuate changes in cardiac output, systemic vascular resistance, central venous pressure, and MAP induced by pneumoperitoneum, thereby preserving intra-operative haemodynamics stability [23]. Our study yielded similar results.

However, it is important to monitor and examine the safety of magnesium sulfate in clinical practice because of its hypotensive and muscle-weakening properties. We analyzed possible side effects, including extubation time, serum magnesium concentration, liver and renal function, coagulation function, and perioperative adverse events. As for postoperative complications in 5 vs 1, fever and headache were observed in our study, both occurring within the first 48 h after surgery. Fever and headache are common complications following surgery. Early postoperative fever is a frequent complication caused by the trauma and inflammatory response from the surgery itself. Postoperative headaches can have various underlying causes. In this study, we believe that postoperative headaches may primarily be related to the surgical site and sleep disorders. Regarding dizziness and syncope, they were observed in a female patient. These symptoms occurred consecutively, without accompanying nausea, vomiting, visual symptoms, tinnitus, or headache, while she was walking 2 days post-surgery. The syncope lasted for seconds without receiving any treatment. All examinations showed normal results, including ECG, BP, blood glucose, and electrolyte tests. We discovered that this patient had a history of spontaneous unpredictable episodes of syncope. Dizziness preceding syncope is often linked to a psychological cause. It can be inferred that the episodes of dizziness and syncope are minimally connected to the treatment administered. Our findings indicate that there were no negative effects in the magnesium group, and in fact, magnesium sulfate was beneficial in correcting postoperative hypomagnesemia. These pieces of evidence demonstrate the safety of intra-operative application of magnesium sulfate at the dosage used in our study.

This study has several limitations. First, it is important to note that this study was conducted at a single center, which may limit the generalizability of the findings to other settings or populations. Second, we investigated only a single dosage of magnesium sulfate and did not explore the effects of different dosages. It would be valuable for future studies to examine the potential dose-response relationship of magnesium sulfate administration. Lastly, we did not monitor urine volume in this study due to the relatively short duration

Table 2
Postoperative data.

	Group M $n = 36$	Group C $n = 37$	*P* value
PONV			
In PACU	0 [1]/33.18	0 [2]/40.93	0.070
At 2 h after surgery	0 [1]*/32.45	1 [3]/41.68	0.040
At 6 h after surgery	0 [2]/36.73	0 [2]/37.28	0.900
At 12 h after surgery	0 [2]/36.76	0 [2]/37.25	0.908
At 24 h after surgery	0 [1]/35.89	0 [1]/38.14	0.570
Incidence of PONV in 24 h after surgery	20 (54.1 %)	19 (52.8 %)	0.913
VNRS			
In PACU	3 [1]*/31.45	3 [0]/42.71	0.013
At 2 h after surgery	3 [2]/33.31	3 [1]/40.79	0.116
At 6 h after surgery	3 [2]/37.88	3 [0]/36.10	0.699
At 12 h after surgery	3 [2]/37.57	3 [0.75]/36.42	0.804
At 24 h after surgery	3 [1]/35.51	3 [1]/38.53	0.507
Other adverse event	5 (13.5 %)	1 (2.8 %)	0.095
Fever	2	1	–
Headache	1	0	
Dizziness	1	0	
Syncope	1	0	

Data are presented as median [interquartile range]/mean rank, and number of patients (proportion). PONV: postoperative nausea and vomiting; VNRS: verbal numerical rating scale. Group C: control group; Group M: magnesium sulfate group. *$p \leq 0.05$ versus Group C.

Table 3
Laboratory variables data.

		Group M n = 36	Group C n = 37	*p1* value
Hemoglobin (g/L)	before	136 ± 15	135 ± 13	0.781
	after	117 ± 15$^{\#}$	119 ± 14$^{\#}$	0.603
p2 value		0.000	0.000	
ALT (U/L)	before	13 ± 7	14 ± 7	0.241
	after	12 ± 6$^{\#}$	13 ± 5	0.271
p2 value		0.045	0.110	
AST ((U/L)	before	16 ± 3	16 ± 3	0.669
	after	17 ± 3$^{\#}$	18 ± 4	0.940
p2 value		0.006	0.111	
Cr (mmol/L)	before	72 ± 14	69 ± 13	0.424
	after	63 ± 13$^{\#}$	59 ± 11$^{\#}$	0.126
p2 value		0.000	0.000	
BUN(mmol/L)	before	4.39 ± 1.07	4.55 ± 0.98	0.506
	after	4.69 ± 1.10	4.68 ± 1.02	0.952
p2 value		0.118	0.477	
PLT (10^9/L)	before	265 ± 51	268 ± 46	0.798
	after	249 ± 48$^{\#}$	249 ± 47$^{\#}$	0.943
p2 value		0.002	0.000	
APTT(s)	before	29.7 ± 3.9	29.2 ± 3.0	0.401
	after	28.2 ± 3.2$^{\#}$	27.3 ± 2.1$^{\#}$	0.147
p2 value		0.000	0.000	
PT(s)	before	11.6 ± 0.8	11.5 ± 0.9	0.612
	after	12.7 ± 0.9$^{\#}$	12.7 ± 0.7$^{\#}$	0.872
p2 value		0.000	0.000	
INR	before	1.01 ± 0.08	1.00 ± 0.08	0.565
	after	1.11 ± 0.08$^{\#}$	1.11 ± 0.07$^{\#}$	0.863
p2 value		0.000	0.000	
Mg^{2+}(mmol/L)	before	0.85 ± 0.05	0.83 ± 0.06	0.219
	after	0.91 ± 0.08$^{\#}$	0.74 ± 0.07$^{*\#}$	0.000
p2 value		0.000	0.000	
Ca^{2+}(mmol/L)	before	2.32 ± 0.18	2.35 ± 0.18	0.452
	after	2.14 ± 0.15$^{\#}$	2.21 ± 0.11$^{\#*}$	0.028
p2 value		0.000	0.000	

Data are shown as means ± SD.The normal range at our institution is: Mg^{2+}:0.75–1.02 mmol/L, Ca^{2+}:2.11–2.52 mmol/L. Group C: control group; Group M: magnesium sulfate group. ALT: alanine aminotransferase; AST: aspartate aminotransferase; APTT: activated partial thromboplastin time; BUN: blood urea nitrogen; Cr: serum creatinine; INR: international normalized ratio; PT: prothrombin time; PLT: blood platelet count. Mg^{2+}: concentration of serum magnesium; Ca^{2+}: concentration of calcium; *p*1: difference between groups; *p*2:difference within group between before and after surgery. $^{\#}p \leq 0.05$vs before, *$p \leq 0.05$ vs Group C.

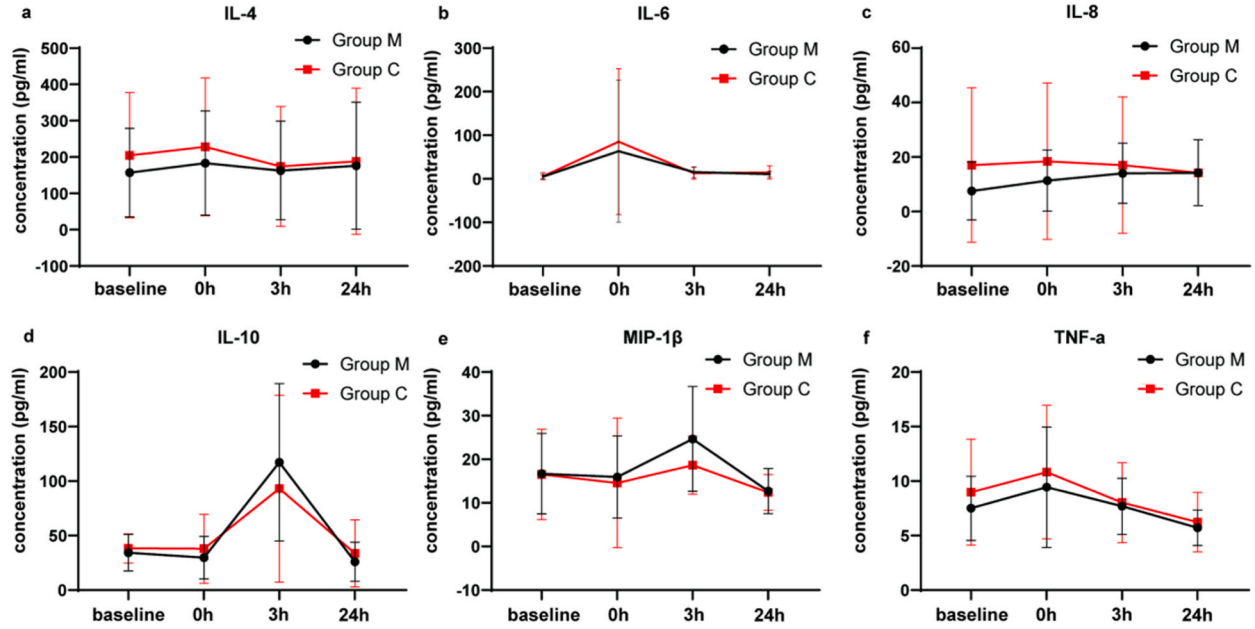

Fig. 3. Values are shown as mean (SD). There was no differences between groups in IL-4(a), IL-6(b), IL-8(c), IL-10(d), MIP-1β(e) and TNF-α(f). Group C: control group; Group M: magnesium group. Baseline:before anesthesia; 0 h: at the beginning of surgical incision; 3 h: 3 hour after surgical incision; 24 h: 24 h after surgical incision.

of surgery. Magnesium sulfate is primarily excreted by the kidneys, so monitoring urine output can provide a more accurate assessment of the impact of magnesium sulfate on renal function. As the duration of surgery was not expected to be prolonged, the impact of urine volume monitoring on the evaluation of magnesium sulfate administration was considered minimal. However, future studies with longer surgical durations should consider incorporating urine volume monitoring to provide a more comprehensive assessment of the effects of magnesium sulfate administration.

In summary, our study findings indicate that the addition of magnesium sulfate as an adjunct to orthognathic surgery in patients undergoing remifentanil-sevoflurane basal general anesthesia can significantly reduce the consumption of remifentanil. Furthermore, the use of magnesium sulfate offers additional advantages in terms of improved recovery profiles, including reduced postoperative pain and less severe PONV, compared with remifentanil alone during the early postoperative period. However, further research is needed to explore the potential anti-inflammatory effects of magnesium sulfate in this context.

Funding

This research was supported by Young Clinical Research Fund of the Chinese Stomatological Association (CSA-A2021-06) and the National Natural Science Foundation of China (No.82270997).

Data availability statement

The data that support the findings of this study are available from the corresponding author (Wenguo Fan), upon reasonable request.

CRediT authorship contribution statement

Xiaoxiao Hua: Writing – original draft, Methodology, Funding acquisition. **Yanling Chen:** Data curation. **Zhi Wu:** Supervision. **Guangsen Zheng:** Resources. **Dongye Yang:** Investigation. **Jing Li:** Project administration, Investigation. **Qiaomei Wu:** Data curation. **Wenguo Fan:** Writing – review & editing, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:Xiaoxiao Hua reports financial support was provided by Chinese Stomatological Association. Wenguo Fan reports financial support was provided by National Natural Science Foundation of China. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

Assistance with the study: we would like to thank all the study participants, and the clinical staff for their support and cooperation.

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