Effectiveness of magnesium sulfate on the smoothness of extubation in patients undergoing general anesthesia with endotracheal intubation: a randomized controlled trial

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Purpose

Tracheal extubation remains a critical step in anesthetic management and is supposedly associated with coughing, bucking, laryngospasm, and agitation. Physicians should make all possible efforts to allow optimal smooth extubation and attenuate the airway and circulatory responses. Several drugs have been discovered to attenuate the aforementioned reflexes. The popularity of magnesium sulfate ($MgSO_4$) can be attributed to its sedative, analgesic, and antihypertensive properties. We aimed to study the effect of $MgSO_4$ on the smooth accomplishment of tracheal extubation.

Patients and methods

We selected 60 patients, aged 18–65 years. All patients had undergone a standardized anesthetic technique. They were randomized to either the $MgSO_4$ group (group M, 30 patients) or placebo group (control group C, 30 patients). We recorded and analyzed the smoothness of tracheal extubation, sedation score, hemodynamics, visual analog scale pain score, the time of extubation, the duration of surgery, the amount of fentanyl consumption, and postoperative morphine consumption.

Results

The aforementioned two groups were homogenized to obtain their demographic information. There were no clinically significant differences between the groups, based on the average arterial pressure, heart rate, or oxygen saturation. However, the smoothness of extubation score was lower in the $MgSO_4$ group (median=1, interquartile range: 1, 2) than in the control group (median=3, interquartile range: 2, 3) ($P<0.001$). However, the Ramsey sedation score was higher and the visual analog scale was lower in the $MgSO_4$ group compared with the control group. The $MgSO_4$ group revealed lower intraoperative fentanyl consumption than the control group. Moreover, the $MgSO_4$ group displayed lower postoperative morphine use.

Conclusion

The $MgSO_4$ group was associated with smooth extubation conditions, concomitant with less coughing, bucking, and laryngospasm than the control group.

Keywords:
endotracheal intubation, general anesthesia, magnesium sulfate, smooth extubation

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Introduction

Tracheal extubation is of great importance for the anesthetic management of patients subjected to general anesthesia with endotracheal intubation. This is because it provides an appropriate condition for smooth extubation and prevents straining, coughing, bucking, and/or laryngospasm [1]. There are different techniques for providing smooth extubation, such as intravenous lidocaine [2], short-acting remifentanil infusion [3], and dexmedetomidine or fentanyl [4,5]. Magnesium sulfate ($MgSO_4$) is considered a promising alternative because of its anti-inflammatory and analgesic properties. Moreover, it has no respiratory depressant effect. $MgSO_4$ is a widely accepted analgesic adjuvant for perioperative pain. This analgesic property is supposedly related to the regulation of calcium influx into cells or to the antagonistic activity of N-methyl D-aspartate receptors in the central nervous system [6]. Moreover, it reportedly has anti-inflammatory properties [6]. There are no reliable techniques for smooth extubation with a low incidence of coughing, agitation, movements, and/or laryngospasm [2–5].

We hypothesized that $MgSO_4$ has sedative, analgesic, and anti-inflammatory actions. Thus, we aimed to examine the extent to which $MgSO_4$ could improve extubation conditions for patients undergoing elective surgeries with endotracheal intubation.

Patients and methods

Following an approval from the ethics board of the El Fayoum University Hospital (R142), the current randomized double-blind parallel team controlled the allocation ratio (1 : 1). This research was registered at the Clinical Trial.gov registry system (NCT04617652). Written informed consent was obtained from all contributors before enrolling the participants. We conducted randomization using a computer-generated sequence. Concealment was performed once using an opaque envelope. We included 60 patients, aged 18–65 years, who had undergone a standardized anesthetic procedure. All patients had the American Society of Anesthesiologists (ASA) physical status I–II and had undergone elective noncardiac surgical procedures under general anesthesia with endotracheal intubation. We excluded patients with uncontrolled hypertension, hypersensitivity to $MgSO_4$, head and neck surgeries, cardiothoracic surgeries, cardiac disorders, bundle branch, neuromuscular diseases, and hypermagnesemia, along with those who refused to participate.

Patients in both groups were subjected to an accepted anesthetic method comprising intravenous propofol (2 mg/kg), fentanyl (1–2 μg/kg), and atracurium (0.5 mg/kg) for facilitating endotracheal intubation. We adjusted the mechanical ventilation to maintain the end tidal carbon dioxide from 30 to 35 mmHg. Moreover, medications were administrated according to the ideal body weight. We administered 1.2% isoflurane in 50% oxygen, air, and atracurium (0.15 mg/kg) every 20 min to maintain anesthesia. The intraoperative oxygen saturation, mean arterial pressure (MAP), and heart rate (HR) were recorded every 30 min until the surgery was terminated. HR and MAP values were ±20% of the baseline values. We administered intravenous ondansetron (4 mg; Zofran, GlaxoSmithKline, UK) intraoperatively to prevent nausea and vomiting after surgery. Following anesthesia induction, the patients were assigned to one of either group: group C (control group, n=30) and group M ($MgSO_4$ group, n=30). The former group received 10 ml saline over 5 min, followed by the infusion of normal saline (50 ml) every hour. In contrast, group M received $MgSO_4$ (10 mg/kg) in 10 ml over 5 min, followed by the infusion of 10 mg/kg/h diluted in 50 ml hourly. The aforementioned dose was based on the ideal body weight. We administered a supplemental dose (25–50 μg) of fentanyl once for high blood pressure (MAP >20% of the value at baseline) and/or tachycardia (HR >20% of the value at baseline). Hypotension (MAP <20% of baseline value) was managed with a bolus of fluid and/or increments of ephedrine 3 mg.

Following the surgery, isoflurane was once stopped and the residual neuromuscular blockade was antagonized with neostigmine (0.05 mg/kg) and atropine (0.02 mg/kg). We removed the endotracheal tube on observing the restoration of spontaneous breathing. Moreover, the patients obeyed all instructions in a semisitting posture just before extubation and afterward. The patients were then sent to the postanesthesia care unit. We immediately assessed the smoothness of the extubation after the procedure and graded it as follows: grade 1, lack of coughing on the endotracheal tube; grade 2, coughing on the tube; grade 3, vomiting; and grade 4, laryngospasm [7]. Furthermore, we recorded the values of oxygen saturation and HR before the surgery, every 30 min during the surgery, and in the postanesthesia care unit. The visual analog scale (VAS) was used to evaluate the pain (0=lack of pain to 10=worst pain). It was administered every 2 h in the first 6 h, followed by every 6 h till 24 h. We administered supplemental doses of morphine (2 mg) in both groups when VAS score was more than 4. Furthermore, we recorded the total amount of narcotic drugs.

The sedation level was measured every 2 h in the first 6 h, followed by every 6 h until 24 h using the Ramsey sedation score [8]: 1–agitated, restless, or anxious; 2–oriented and cooperative; 3–responding the commands; 4–asleep, brisk response to the glabellar tap or loud auditory stimulus; 5–asleep, sluggish response to loud auditory stimulus or glabellar tap; and 6–asleep, no response to loud auditory stimulus or glabellar tap. Pain, sedation level, and hemodynamic parameters were measured by an experienced nurse, blinded to the medications.

Primary outcome

The degree of smoothness of extubation was the primary outcome. The smoothness of extubation was assessed immediately after the procedure.

Other outcomes

Secondary outcomes included the sedation score; hemodynamics; VAS; extubation time, which is defined as the time from discontinuing inhalational anesthetic to removal of the endotracheal tube; the duration of surgery; the amount of fentanyl consumed; and postoperative morphine consumption.

Sample size

We used the G-power software (Kiel University, Kiel, Germany) (v3.1.9) to estimate the sample size based on a pilot study with 10 patients, assuming a mean smoothness of extubation score of 1.5 and 2.5 in the intervention and control groups, respectively, with an SD of 1 in both groups. The calculated sample size was 24 in each group, with a power of 90% and α=0.05. We selected 30 patients in each group to compensate for any expected loss of follow-up or withdrawals.

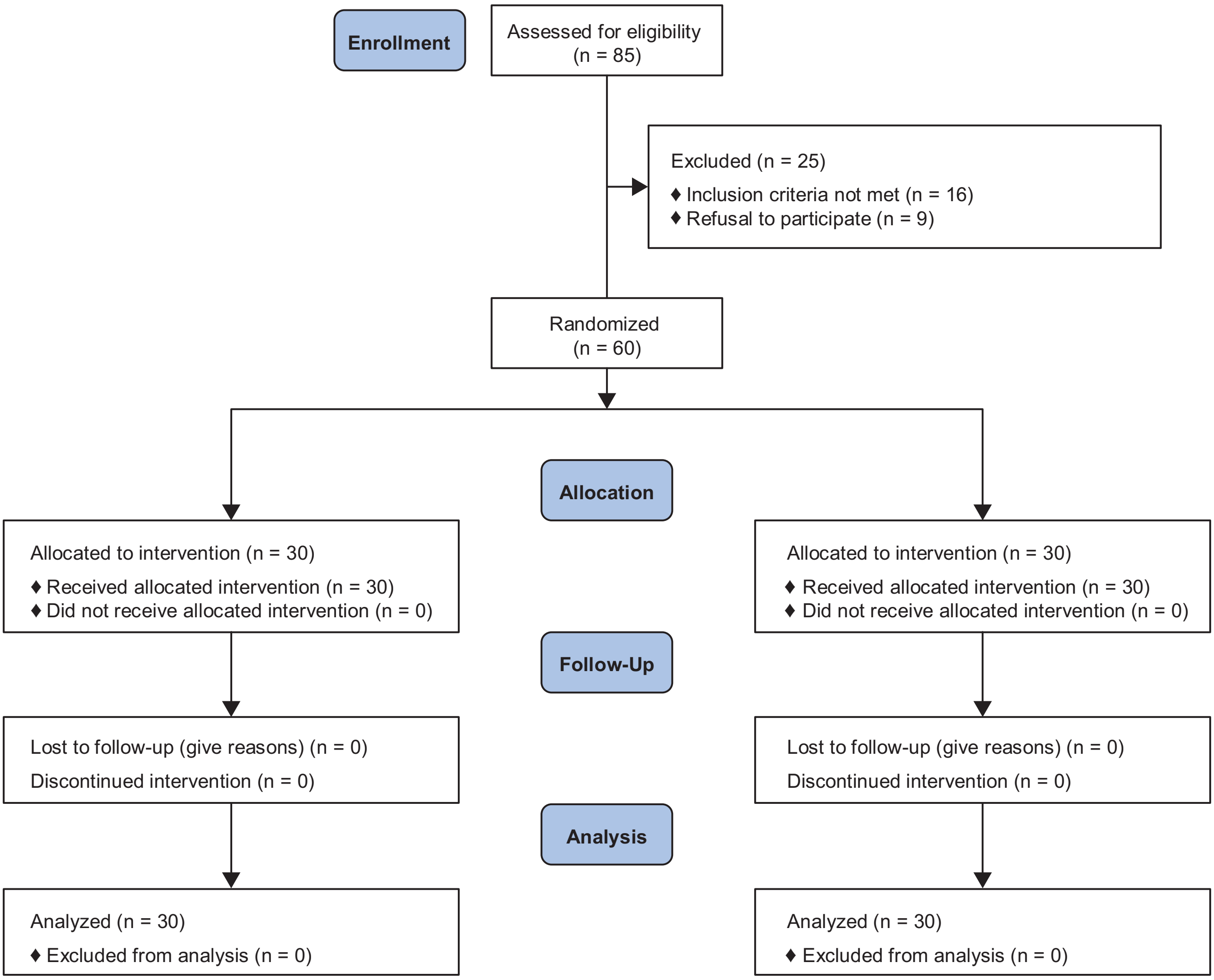
Statistical analyses

Although descriptive statistics for the categorical variables are presented in the form of frequencies and relative frequencies, those for the normally distributed numerical variables are presented as mean and SD. The nonnormally distributed numeric variables are presented as median and interquartile range (IQR). We conducted the χ^2 test to compare the sex and ASA scores between the groups. In contrast, we performed the Mann–Whitney *U* test to compare the ASA scores, the smoothness of extubation score, Ramsay sedation score, and VAS scores between the groups. An independent *t* test was performed for the remaining comparisons. We used IBM SPSS statistics software, version 26 (IBM Corp., Armonk, New York, USA) for the analysis. A *P* value less than 0.05 was considered statistically significant.

Results

A total of 85 patients were assessed. We excluded 25 cases. However, 16 patients did not meet the inclusion criteria, and nine patients refused to participate. We eventually randomized 60 patients to receive either $MgSO_4$ or placebo. All patients completed the research (Fig. 1). Both groups were homogenized, in relation to their demographic information and baseline features (Table 1).

Figure 1



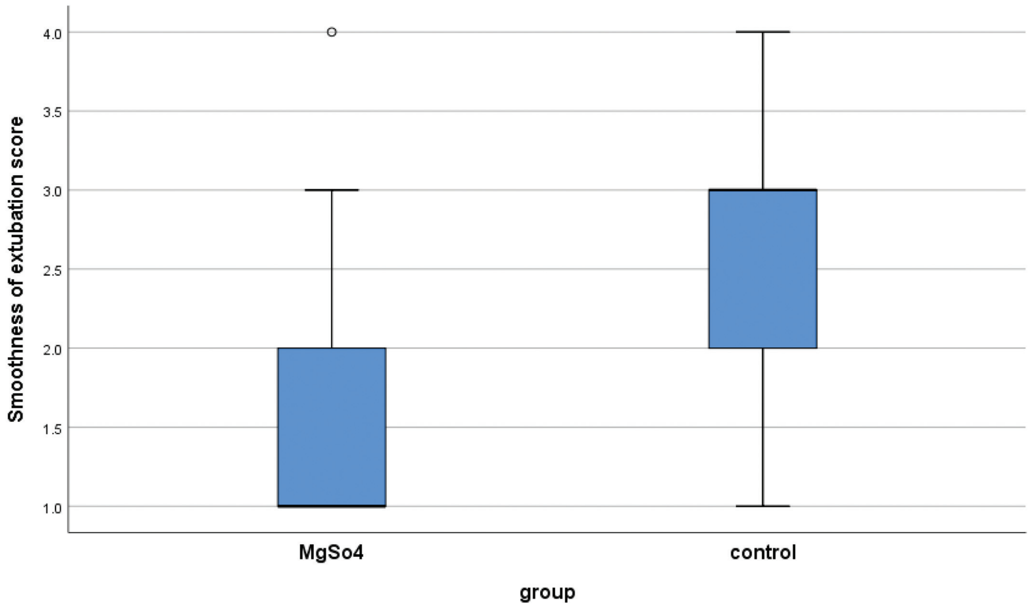
CONSORT flow diagram of participants.

Table 1 Demographic data, surgical characteristics, magnesium level, extubation time, and opioid consumption in both groups

	$MgSO_4$ group (*n*=30)	Control group (*n*=30)	*P* value
Age (years)	42.6±13.5	36.5±11.3	0.061
Sex (male : female)	15 : 15	16 : 14	0.796
BMI	22.7±2.2	23±2.2	0.565
ASA (I : II)	14 : 16	16 : 14	0.606
Duration of surgery (min)	108.1±31.0	99.6±23.3	0.231
Extubation time (min)	6.7±2.3	6.5±2.3	0.731
Preoperative Mg level (mg/dl)	1.9±0.2	2.1±0.2	0.014*
Postoperative Mg level (mg/dl)	2.4±0.2	2.1±0.2	<0.001*
Intraoperative fentanyl consumption (μg)	156.5±28.5	196.3±32.3	<0.001*
Postoperative morphine consumption (mg)	6.6±1.5	9.0±1.4	<0.001*

Data are presented as mean±SD or as *n*. ASA, American Society of Anesthesiologists; Mg, magnesium; $MgSO_4$, magnesium sulfate.
*Significance.

Figure 2



Smoothness of extubation score.

The smoothness of extubation score was significantly lower in the $MgSO_4$ group (median=1, IQR: 1, 2) than in the control group (median=3, IQR: 2, 3) (Fig. 2). The Ramsay sedation score was higher in the $MgSO_4$ group than in the control group at 0, 2, and 4 h. However, there was no substantial difference in the succeeding readings. The VAS score was lower in the $MgSO_4$ group from 0 to 12 h. Nonetheless, we observed no difference in the score at 18 and 24 h (Table 2).

The $MgSO_4$ group revealed lower intraoperative fentanyl consumption and postoperative morphine consumption, compared with the control group (Table 1).

Furthermore, the $MgSO_4$ group displayed lower intraoperative HR at the baseline, 30 min, and 120 min than the control group. The intraoperative MAP was lower in the $MgSO_4$ group at all readings from the baseline to 150 min.

The postoperative HR was lower in the $MgSO_4$ group at 4–24 h. However, there was no difference at 0 h and 2 h postoperatively. The postoperative MAP was lower in the $MgSO_4$ group at 0, 4, and 24 h. Nonetheless, there was no difference at 6, 12, or 18 h (Figs 3 and 4).

Discussion

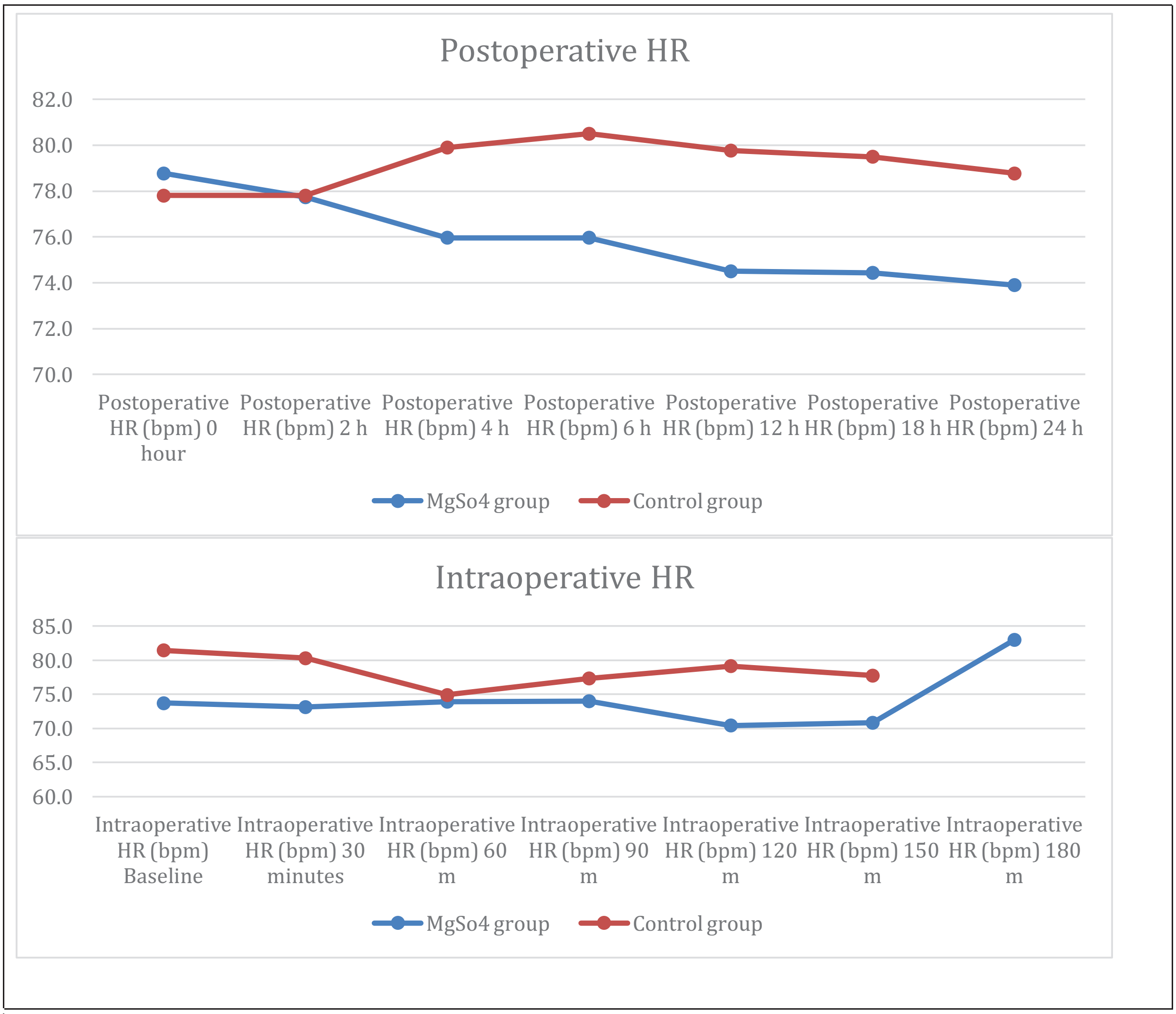
The current research reported on the efficacy of intravenous $MgSO_4$ in ensuring smooth extubation in patients undergoing surgeries that require endotracheal intubation, other than cardiac, thoracic, or head and neck surgeries.

Table 2 Visual analog scale and Ramsey sedation score in two groups

	Control group (*n*=30)	$MgSO_4$ group (*n*=30)	*P* value
VAS	Median (IQR)	Median (IQR)	
0 h	3 (3, 4)	3 (2, 3)	0.003*
2 h	3 (2, 3)	2 (2, 2)	<0.001*
4 h	3 (2, 3)	2 (2, 2)	<0.001*
6 h	2 (2, 2)	2 (2, 2)	>0.999
12 h	2 (2, 2)	2 (2, 2)	>0.999
18 h	2 (2, 2)	2 (2, 2)	>0.999
24 h	2 (2, 2)	2 (2, 2)	>0.999
RSS			
0 h	3 (3, 3)	4 (3, 5)	<0.001*
2 h	2 (2, 2)	3 (2, 3)	<0.001*
4 h	1 (1, 1)	2 (1, 3)	<0.001*
6 h	0 (0, 1)	1 (1, 2)	<0.001*
12 h	0	0 (0, 1)	<0.001*
18 h	0	0	0.317
24 h	0	0	>0.999

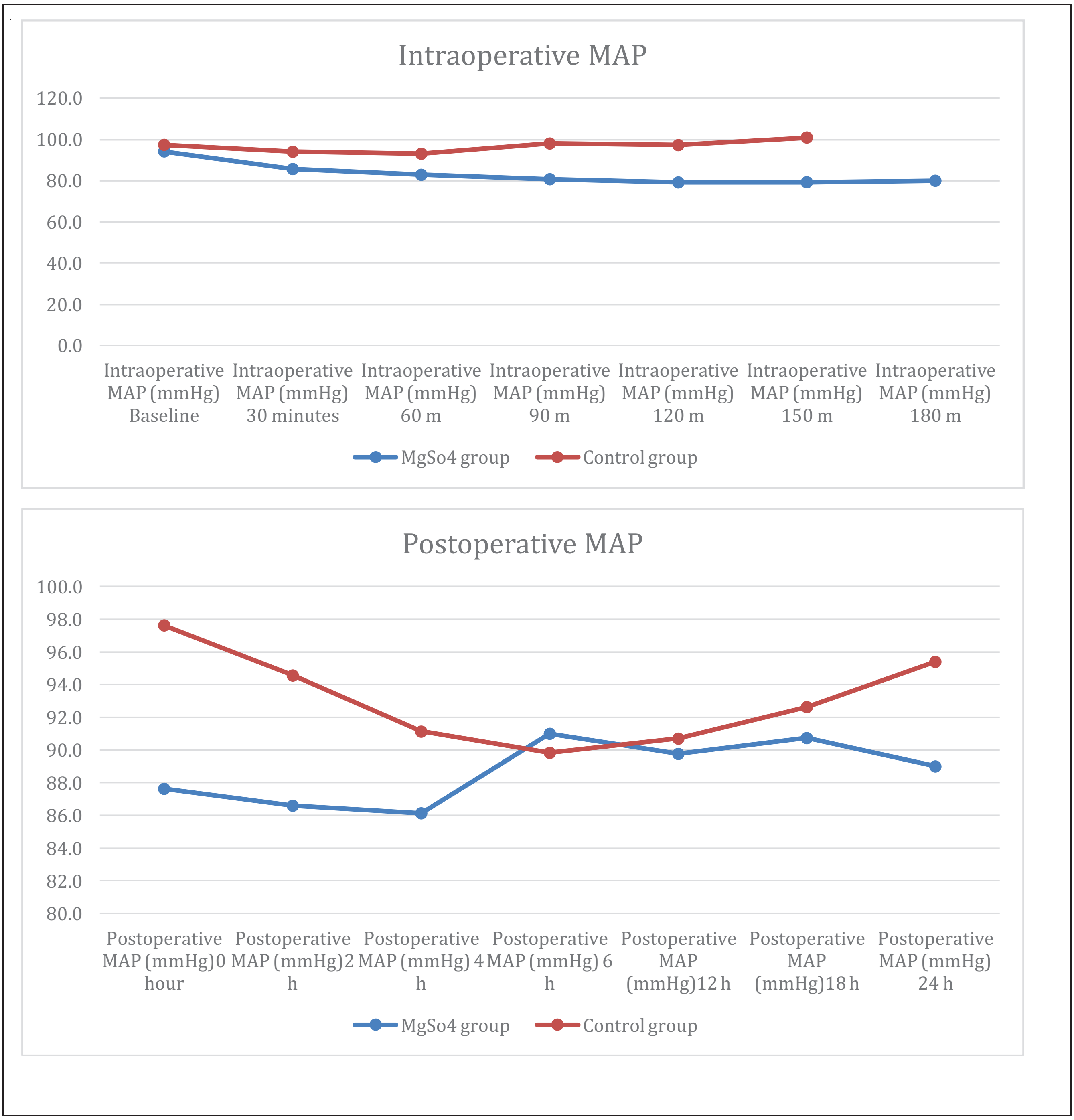
Data are presented as median (IQR). IQR, interquartile range; $MgSO_4$, magnesium sulfate; RSS, Ramsey sedation score; VAS, visual analog scale. *Significance.

Figure 3



Intraoperative and postoperative heart rate.

Figure 4



Intraoperative and postoperative MAP. MAP, mean arterial pressure.

There are limited reports on the effect of $MgSO_4$ on a smooth emergence and reliable recovery, without coughing. Clinicians have administered several adjuvants to attenuate the extubation response and enable smooth emergence from anesthesia, such as fentanyl and dexmedetomidine [7]. However, the techniques are not completely reliable and do not provide smooth recovery under extubation conditions [2–5].

$MgSO_4$ is an abundant intracellular cation, with adjuvant analgesic properties associated with calcium influx [9] and N-methyl D-aspartate antagonism [10,11]. Moreover, it has an anti-inflammatory effect [12].

Hur *et al.* [13] investigated the effect of an antitussive on magnesium infusion in the anesthetic emergence in patients with a double-lumen endotracheal tube (DLT), which is largely worrying and irritant to the trachea. They conducted a prospective, randomized, double-blinded trial that comprised 140 patients undergoing one lung ventilation (OLV) anesthesia with a DLT. In aggregate, with a low dose of remifentanil, patients were randomly distributed to hold either $MgSO_4$ (infusion of 15 mg/kg/h after a single bolus of 30 mg/kg) or saline infusion. Primary outcomes comprised the severity and incidence of coughing at some factor of emergence. They mentioned that magnesium attenuated the severity of cough following OLV anesthesia and the utilization of a DLT. Therefore, we recommend the use of $MgSO_4$ in OLV anesthesia with DLT to avoid coughing, which might lead to unfavorable outcomes, such as leakage from the surgical site, bleeding, and/or surgical emphysema. With regard to cardiac surgeries, magnesium might promote enhanced recovery programs, fast track recovery, and reduced stay in the ICU.Agrawal and Khadke [14] investigated and compared the effects of intravenous $MgSO_4$ and intravenous esmolol on reducing hemodynamic extubation response, following general anesthesia in a prospective, randomized, double-blind trial. They randomly allocated 60 adults subjected to major operations into two groups, where group M was administered 40 mg/kg $MgSO_4$, and group E was administered intravenous esmolol (0.6 mg/kg) infusion over 5 min, before the extubation. They did not directly measure the smoothness of extubation. However, the $MgSO_4$ group had a higher sedation score and lower VAS score.

Our study has few limitations. First, we conducted a single-center trial. Second, we did not investigate the effect of magnesium in the head and neck, cardiothoracic, or shared airway surgeries, considering its association with coughing, emergence agitation, and bucking. Third, we did not study the magnesium effects in chronic heavy smoker patients, which may be beneficial in these patients.

In conclusion, $MgSO_4$ is effective in providing smooth extubation circumstances. Thus, we recommend its use under possible circumstances.

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Nil.

Conflicts of interest
There are no conflicts of interest.

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