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Effect of Magnesium Sulphate on Oxygenation and Lung Mechanics in Morbidly Obese Patients Undergoing Bariatric Surgery: A Prospective Randomized Blinded Clinical Trial.

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Running title: Mg and oxygenation in obesity

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Running title: Mg and oxygenation in obesity
Abstract

Background: Anesthesia for a morbid obese patient can be challenging due to significant changes in respiratory mechanics. Magnesium Sulphate (MgSO₄) is a promising agent in the management of several respiratory disorders. In this study, we aimed to examine the effects of magnesium sulfate infusion on oxygenation and lung mechanics in morbidly obese patients having laparoscopic bariatric surgery.

Methods: Forty morbidly obese patients aged 21–60 years, scheduled for laparoscopic bariatric surgery under general anesthesia were randomly allocated to receive either 30 mg/kg Lean body weight (LBW) of 10% MgSO₄ in 100 ml normal saline intravenously over 30 minutes as a loading dose, followed by 10 mg/kg LBW/h for 90 minutes (MgSO₄ group), or normal saline infusion (Control group). Our primary outcome was intraoperative arterial oxygenation (Δ PaO₂/FiO₂). The secondary outcomes were intraoperative static and dynamic compliance, dead space, and hemodynamic parameters.

Results: The Δ PaO₂/FiO₂ ratio at 45 and 90 minutes showed a significant decrease in the control group when compared to the MgSO₄ (P < 0.001). Δ dynamic lung compliance and Δ dead space (%) were significantly lower in the MgSO₄ group at 45 and 90 minutes intraoperatively (P < 0.001). No significant difference between the two groups was evident regarding static compliance. The means of intraoperative HR and MAP were significantly lower in MgSO₄ group (P < 0.001).

Conclusion: MgSO₄ infusion preserved arterial oxygenation and maintained the dynamic lung compliance and the dead space in morbidly obese patients.

Keywords: Obesity; Morbid; Magnesium Sulphate; Respiratory Mechanics; Bariatric Surgery; Anesthesia.
**Introduction**

Bariatric surgery is considered the most effective treatment for patients suffering from morbid obesity, as it results in maintained loss of weight and clear impact on the comorbidities related to obesity [1]. However, morbid obesity is commonly associated with a higher incidence of restrictive lung disease [2]. Significant changes in the respiratory mechanics are usually observed in obese patients that are further aggravated by general anesthesia such as decreased expiratory reserve volume (ERV) and functional residual capacity (FRC). In addition to atelectasis, insufficient oxygenation, reduction in chest and lung compliance, increased lung resistance and more breathing work [3,4].

Obesity is usually related to other respiratory diseases such as asthma, chronic obstructive pulmonary disease (COPD). According to a meta-analysis encompassing more than 300,000 adult patients, obesity and asthma were interlinked, and as BMI increased, a higher risk of asthma was noticed [5]. The mechanism behind this relation may include the mechanical consequences of long-term compression of the lung, exaggerated local and systemic inflammation, and abnormal immunological responses, which are usually altered in obesity [6]. Additionally, studies have shown that obesity was more prevalent among COPD patients than in the general population [7]. Hence, the obese patients are more prone to acute respiratory failure post-operatively [8] and have higher incidences of pneumonia, prolonged period of mechanical ventilation and weaning difficulty [9-14].

Magnesium Sulphate (MgSO\(_4\)) is a promising agent with favorable effects in managing various respiratory disturbances like asthma, COPD, and pulmonary hypertension. A crucial part is thought to be played by endogenous magnesium in sustaining the appropriate functions of the lungs and to reduce the reactivity of the airway [15,16]. Magnesium helps smooth muscle relaxation through blocking the calcium release [17]. Also, it acts through different mechanisms, like T-cells stabilization, prevention of
mast cell degranulation, inhibiting acetylcholine release, and stimulating the synthesis of nitric oxide and prostacyclin, thereby reducing the airflow obstruction [17]. Mg deficiency have been reported among asthmatic patients in several studies [18]. Furthermore, low serum magnesium was related to COPD exacerbation [19].

Recently, intraoperative magnesium has been investigated in COPD patients with promising results [20]. We hypothesize that magnesium can improve the perioperative oxygenation and lung mechanics parameters of morbid obese patients undergoing bariatric surgeries. So, this study was conducted to examine the usefulness of the intraoperative administration of MgSO₄ on arterial oxygenation and lung mechanics in morbidly obese patients undergoing bariatric surgery.
Materials and Methods

This double-blinded randomized study was approved by the Research Ethical Committee of the Faculty of Medicine, Ain Shams University (FMASU R07/2021) and registered at the Clinical Trials.gov (NCT04769440). In this study, forty patients were enrolled with a body mass index (BMI) greater than 40 kg/m², aged 21–60 years and suffered restrictive lung disease diagnosed by pulmonary function tests: forced vital capacity (FVC) < 70%. They had no previous abdominal surgery and were scheduled for laparoscopic bariatric surgery not exceeding three hours under general anesthesia.

Patients were excluded if they refused to take part in the study, if they had a physical status American Society of Anesthesiologists (ASA) higher than II, a history of organ failure (e.g., cardiac, hepatic, or renal), arrhythmias, those receiving antiarrhythmic drugs, beta blockers or calcium channel blockers, or patients with combined restrictive-obstructive pulmonary disease. Patients with forced expiratory volume in the first second (FEV1)/forced vital capacity (FVC) < 70%, pregnant, lactating, having a history of allergies to the study drugs, or operation time more than 3 hours were also excluded from the study.

After obtaining an informative consent from all patients fulfilling the inclusion criteria, patients were randomly allocated into two equal groups in a 1:1 ratio using computer-generated table of random numbers sealed in opaque envelopes. They were opened before the drug was given immediately. Our groups were:

1) The M (MgSO₄) group (n = 20): 15 minutes after endotracheal intubation, patients received intravenous infusion of 30 mg/kg Lean body weight (LBW) MgSO₄ of 10% in 100 ml normal saline as a loading dose over 30 minutes as a loading dose, followed by 10 mg/kg LBW/h for 90 minutes.
2) The C (Control) group (n = 20): 15 minutes after endotracheal intubation, each patient received intravenous infusion of 100 ml of normal saline over 30 minutes followed by saline infusion with the same rate as the study group for 90 minutes.

The hospital pharmacy prepared the study drugs. Moreover, a blinded anesthetist who was not participating in any part of the study, carried out the patients’ follow-up.

Preoperatively, medical history taking, and thorough physical examination were done to all patients and demographic data as; Age, BMI and ASA physical status were recorded. Preoperative investigations including complete blood picture, prothrombin time and activated partial thromboplastin time, liver and kidney function tests, serum Mg level, pulmonary function tests, Arterial Blood Gases (ABG) were done. The patients were instructed to fast for 8 hours before the operation.

On arrival to the operating theatre, an intravenous cannula was inserted. As premedication n, ranitidine 50 mg, metoclopramide 10 mg were administered. Standard monitoring in the form of non-invasive blood pressure (NIBP), electrocardiogram (ECG), pulse oximeter was attached to all patients and capnography was connected after intubation. Baseline readings were recorded for mean arterial blood pressure (MAP), heart Rate (HR) and oxygen saturation (SpO2).

The LBW -estimated by the James equation- was used to calculate drug doses except for neostigmine where total body weight was used instead. LBW was calculated as follows; For men: (1.10 weight) – (128 [weight/height]^2), while for women (1.07 weight) – (148 [weight/height]^2) [21].

Preoxygenation was done for 5 minutes then the induction of anesthesia took place with IV fentanyl 2 µg/kg LBW, and IV propofol 1.5-2 mg/kg LBW, slowly administered until the loss of response to verbal commands. IV atracurium 0.5 mg/kg LBW was given to facilitate tracheal intubation. Anesthesia was maintained with 1.0-1.5% isoflurane in oxygen at fraction of inspired oxygen (FiO2) of 0.4. If SpO2 was found to be less than 95%, the FiO2 was increased gradually by 0.1. Neuromuscular block was
maintained with incremental doses of atracurium (0.01 mg/kg LBW) every 30 minutes guided by peripheral nerve stimulator monitoring keeping train-of-four (TOF) count at 1/4. All measures were obtained while TOF count was 1/4.

Patients mechanically ventilated and we adopted volume-controlled mode of ventilation, with low tidal volume (6-8 ml/kg LBW), positive end expiratory pressure (PEEP) ranged between 8–10 cmH₂O, and the respiratory rate adjusted to keep the end-tidal CO₂ between 30 and 35 mmHg.

Patients were positioned in the reverse Trendelenburg position. The abdomen was insufflated with CO₂ keeping the intra-abdominal pressure at a range between (14-15) mmHg. Ringer’s acetate was used during the operation and the volume of consumed fluids was calculated. All surgical procedures were done by the same surgical team. Intravenous paracetamol (2g) and ketorolac (40 mg) were given at the end of surgery.

When the surgery ended, the surgeon carefully evacuated the carbon dioxide from the abdomen. Isoflurane was discontinued. The muscle relaxant was reversed before extubation. When the TOF count reached 2/4, neostigmine 0.05 mg/kg and atropine 0.02 mg/kg LBW were administered to counteract the remaining muscle relaxant effect. Once patients were able to follow verbal commands, they were moved to the post-anesthesia care unit (PACU), where they were closely monitored.

The following values were recorded:

1. **Intraoperative oxygenation:** 5 minutes after endotracheal intubation (baseline), 45 minutes and 90 minutes after starting the drug infusion determined by (P/F ratio: \( \text{PaO}_2/\text{FiO}_2 \)).

2. **Lung mechanics:** including lung compliance and dead space. Static lung compliance was calculated as: tidal volume/(plateau pressure - PEEP). Dynamic lung compliance was calculated as: tidal volume/(peak airway pressure - PEEP). Physiological dead space was calculated as: \( V_d / V_t = 1.14 (\text{PaCO}_2–\text{EtCO}_2) / (\text{PaCO}_2 – 0.005) \) using the Hardman and Aitkenhead equation.

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[22]; after 5 minutes of endotracheal intubation (baseline), 45 minutes and 90 minutes after the beginning of drug infusion).

3. The change in each of P/F ratio, static and dynamic lung compliance, and dead space: (Δ P/F ratio: P/F ratio at 45 minutes and at 90 minutes after the beginning of drug infusion – P/F ratio at the baseline); (Δ static compliance: static lung compliance at 45 minutes and at 90 minutes after the beginning of drug infusion – static lung compliance at the baseline), (Δ dynamic compliance: dynamic lung compliance at 45 minutes and at 90 minutes after the beginning of drug infusion – dynamic lung compliance at the baseline), (Δ dead space (%): dead space at 45 minutes and at 90 minutes after the beginning of drug infusion – dead space at the baseline/dead space by the end of the study drug infusion %).

4. Hemodynamic parameters: MAP and HR (At the baseline, then every 15 min). If the mean arterial pressure dropped by more than 20% from the starting point, vasoactive medications such as ephedrine was given, and atropine was given if the heart rate dropped to less than 50 beats per minute.

5. Sedation score: was assessed using the Ramsay Sedation Score [23] on arrival to the operating room, immediately postoperative and after one hour postoperative.

6. Serum MgSO4 level: one hour postoperatively.

7. Operative data: surgical time, intraoperative fluids, blood loss, recovery time (defined as the time interval between cessation of isoflurane and the patient complying with orders) and the need for postoperative ICU admission: criteria for admission: patients with SaO2 less than 88% on 6 L oxygen mask, individuals who showed signs of altered consciousness (agitation or drowsiness), tachypnea, and the need for postoperative mechanical ventilation. Postoperative complications such as bleeding or leakage were recorded.
The patients were moved to the ward if the modified Aldrete score ≥ 9. Our primary outcome was intraoperative arterial oxygenation assessed by Δ PaO₂/FiO₂ (%). The secondary outcomes were intraoperative lung mechanics and hemodynamic parameters.

Sample size justification

Setting the power = 0.80 and α = 0.05 with using PASS 11th release (Hintze, 2011) [24], a minimal sample size of 2 cases in each group was required to get statistically significant between assumed Δ PaO₂/FiO₂ (%) in MgSO₄ and control groups -3.1 ± 0.2 and -12.2 ± 0.5 respectively (Ahmed et al., 2020) [20]. A sample size of 40 patients (20 in each group) was used to ensure that the sample was representative to our population.

Statistical methods

IBM SPSS statistics (Statistical Package for Social Sciences) software version 22.0, IBM Corp., Chicago, USA, 2013 was used to code, tabulate and statistically analyze the collected data. Quantitative data tested for normality using Shapiro-Wilk test, quantitative normally distributed data described as mean ± SD (standard deviation), then if normally distributed compared using independent t-test (groups comparisons) and Repeated measures ANOVA (times comparisons). If not normally distributed described as Median (1st–3rd Interquartile) then compared using Mann Whitney test. Qualitative data described as number and percentage and compared using Fisher’s Exact test. The level of significance was taken at P value < 0.050 was significant, otherwise was non-significant.
Results

The study recruited 49 individuals; however, eight patients did not match the study's inclusion criteria and one patient declined to participate, therefore they were excluded. Finally, forty patients consented and completed the study. They were divided into two groups of 20 patients each (Fig. 1). There were no statistically significant differences between the studied groups regarding the baseline characteristics (Age, BMI, FVC, FEV1/FVC, intraoperative fluids, the amount of blood loss, operation duration, and the baseline MgSO4) as shown in Table 1.

Regarding the intraoperative oxygenation, the PaO2/FiO2 ratio decreased significantly at 45 and 90 minutes among patients in the control group when compared to the baseline, while no significant decrease was noticed among patients in the MgSO4 group when compared to the baseline. There was no significant difference between the MgSO4 and the control group regarding the PaO2/FiO2 ratio at 45 and 90 minutes, however the Δ PaO2/FiO2 ratio at 45 and 90 minutes showed a significant decrease in the control group when compared to the MgSO4 (P < 0.001) as shown in Table 2.

For the lung mechanics, no significant difference between the two groups was evident regarding the static compliance at baseline, 45 and 90 minutes intraoperatively. Also, no significant differences were observed when static compliance at 45 and 90 minutes was compared to the baseline in each group (Table 3).

On the other hand, the dynamic compliance was significantly higher among patients in the MgSO4 compared to patients in the control group at 45 and 90 minutes intraoperatively (P < 0.001). The dynamic compliance decreased significantly at 45 and 90 minutes in the control group compared to the baseline (P < 0.001). However, there was no significant difference found among patients in the MgSO4 group when compared to the baseline) as shown in Table 3.
No significant change was observed in the dead space in the MgSO₄ group at 45 and 90 minutes intraoperatively when compared to the baseline while a significant increase was noticed in the control group. In between-group comparison, the dead space was significantly higher in the control group compared to the MgSO₄ group at 45 and 90 minutes intraoperatively (P < 0.001) (Table 3).

Δ dynamic lung compliance and Δ dead space (%) were significantly lower in the MgSO₄ group compared to the control group at 45 and 90 minutes intraoperatively (P < 0.001) (Table 3).

Regarding the hemodynamic parameters, there were no significant differences between both groups regarding the baseline mean HR and MAP. However, the means of intraoperative HR and MAP were significantly lower in MgSO₄ group compared to the control group starting from minute 30 to minute 90 (P < 0.001) (Figs. 2, 3).

Postoperative MgSO₄ and ΔMgSO₄ were significantly higher among patients in the MgSO₄ group than the control group (P < 0.001). There was no significant difference between both groups regarding the recovery duration (P = 0.219) (Table 4).

No significant difference was found between the MgSO₄ and the control groups regarding the need to ICU admission and invasive ventilation postoperatively. Three patients (15%) in the MgSO₄ group experienced postoperative hypoxia in the PACU that needed ICU admission compared to 5 patients (25%) in the control group (relative risk [RR] = 0.60; 95% CI: 0.17–2.18; P = 0.695). In addition, two patients (10%) in the MgSO₄ group needed invasive ventilation compared to 4 patients (20%) in the control group (RR: 0.50; 95% CI: 0.10–2.43; P = 0.661). No significant differences were found between both groups regarding the sedation scores at baseline, immediately and one hour postoperatively (Table 4). No patient in the studied groups developed other postoperative complications such as bleeding or leakage.
Discussion

This study demonstrated that intraoperative MgSO₄ infusion had protective effects on arterial oxygenation and lung mechanics in morbidly obese patients with restrictive lung disease undergoing bariatric surgery under GA. MgSO₄ preserved arterial oxygenation by inhibiting the reduction of intraoperative PaO₂/FiO₂ ratio. Furthermore, MgSO₄ maintained the dynamic lung compliance without significant decrease and the dead space without significant increase during GA and mechanical ventilation.

As far as we know, this is the first clinical study that has been conducted to examine the impacts of the intraoperative MgSO₄ infusion on both arterial oxygenation and lung mechanics in morbidly obese patients undergoing bariatric surgery.

Obesity has been shown to create altered changes in the lung physiology including increased respiratory rates, reduced lung volume, diminished chest and lung compliance, higher airway resistance (referred to decreased lung volume, small airway closure, and airway remodeling by the proinflammatory adipokines), and increased oxygen consumption. Furthermore, obesity has been related to an increased alveolar-arterial oxygen gradient caused by a ventilation-perfusion mismatch due to microatelectasis which is getting worse by the supine position [25]. Obesity-related increases in adipose tissue mass are also associated with enhanced mast cell proliferation. As primary mediators of allergies, mast cells raise the possibility that obesity-induced mast cell proliferation may represent a potential pathway for airway illness in obese individuals [26].

A morbidly obese patient is at danger for rapid oxygen desaturation upon the induction of general anesthesia because of the reduction of FRC which is decreased by about 50% compared to the preoperative values [4]. The impacts of general anesthesia are further intensified with mechanical
ventilation and the usage of muscle relaxant that may lead to compromise of pulmonary functions, lung compliance, and gas exchange due to the development of atelectasis. Also, the use of pneumoperitoneum and the patient position may lead to more impairment [27, 28].

In our study, MgSO₄ maintained the arterial oxygenation by preventing the reduction of intraoperative PaO₂/FiO₂ ratio. MgSO₄ may preserve intraoperative arterial oxygenation in obese patients by promoting both pulmonary vasodilation and bronchodilatation which lead to improvements in both perfusion and ventilation. In general, the therapeutic effects of magnesium may be attributed to its effect as a calcium antagonist [29, 30].

MgSO₄ can enhance vasodilation by relaxing the tone of the vascular smooth muscles. Moreover, MgSO₄ promotes the local synthesis of vasodilator substances such as nitric oxide and prostaglandins (e.g., prostacyclin) [31]. In terms of the magnesium-induced bronchodilation, various experimental data suggest that there are several pathways involved such as suppression of cholinergic neuro-muscular transmission, inhibition of calcium-induced muscle contractions, attenuation of the release of histamine, reversal of magnesium depletion following β-adrenergic therapy, and the enhancement of the effects of β-agonists on adenylyl cyclase [32-35]. Magnesium also has sedative properties that help people relax and achieve anxiolysis particularly during acute bronchoconstriction [31].

It has been demonstrated that magnesium relaxes rabbit bronchial smooth muscle in a dose-dependent manner when exposed to histamine, bethanechol, or electrical impulses [32]. Similarly, magnesium raised the percentage of the bronchial cross-sectional area in dogs following histamine-elicited bronchoconstriction in vivo and relaxed histamine-induced contraction of guinea pig tracheal strips in vitro [36].

MgSO₄ revealed to cause bronchodilator impacts regardless of the serum magnesium baseline level and even with drug infusion for short periods [28]. The previous effects could also interpret the positive
impacts of MgSO₄ infusion on dynamic compliance and dead space in this study. Our results were similar to previous study by Ahmed et al. [20] that showed that MgSO₄ intraoperative infusion demonstrated mild perioperative protective effects on both arterial oxygenation and lung mechanics in patients with moderate COPD following laryngectomy surgery under general anesthesia.

In the current study, in the Mg group the post-infusion serum magnesium level was 2.9 ± 0.3 mg/dl this level is less than those that have been associated with magnesium toxicity. The loss of the patellar reflex happens with plasma levels 9.6-12 mg/dl, while respiratory depression happens at levels 12-18 mg/dl [37].

MgSO₄ is readily accessible, affordable, with few side effects when used at the recommended doses [38]. It has a rapid onset of action when administered intravenously, which is necessary in emergency situations. Besides, intravenous MgSO₄ is rapidly eliminated by the kidneys. This considered a therapeutic opportunity and a challenge at the same time. As renal tubular reabsorption of magnesium is at its maximum at normal serum levels and renal clearance increases linearly with the higher concentrations, achieving a sustained spasmolytic effect is not so easy [39]. As a result, the rate of infusion rather than the overall dosage or infusion time has a greater impact on the maximum serum level throughout treatment. Since it was first described in 1936, the ideal dose of IV MgSO₄ as a bolus has not been identified. Consequently, a wide dose range, from 25 to > 100 mg/kg, is used [39-43].

Magnesium sulphate has been found to offer several therapeutic effects in clinical anesthesia, including enhancement of postoperative analgesia and reduced consumption of other anesthetics, opioids, and hypnotics [38]. Adverse effects, on the other hand, were generally moderate, including intravenous injection pain, residual neuromuscular blockade, and hypotension. Hypermagnesemia is an uncommon complication that usually affects people who have renal failure and are receiving magnesium-containing
medicines [44]. However, close monitoring still needed to detect any adverse event and deal with it promptly. No complications to magnesium were detected during the study [45].

There are some limitations to this study. Since we only enrolled morbidly obese patients with restrictive lung disease, our findings cannot be generalized to other patient categories. Additionally, this study included only bariatric surgery patients; therefore, we need to evaluate our results with other surgical procedure. Lastly, because the intraoperative MgSO₄ infusion was not continued until the end of the procedure, the outcomes may vary with longer periods of infusion or greater plasma concentrations.

**Conclusion:**

Intraoperative administration of MgSO₄ infusion preserved arterial oxygenation and maintained the dynamic lung compliance and the dead space in in morbid obese patients undergoing bariatric surgery.
References


Table 1. Comparison between the studied groups regarding baseline characteristics

<table>
<thead>
<tr>
<th>Variables</th>
<th>MgSO₄ (N = 20)</th>
<th>Control (N = 20)</th>
<th>*P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>32.4 ± 4.5</td>
<td>33.7 ± 4.2</td>
<td>0.334</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>49.2 ± 2.2</td>
<td>48.5 ± 2.7</td>
<td>0.367</td>
</tr>
<tr>
<td>FVC</td>
<td>62.8 ± 1.3</td>
<td>63.3 ± 1.4</td>
<td>0.304</td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td>78.5 ± 1.5</td>
<td>79.1 ± 2.0</td>
<td>0.292</td>
</tr>
<tr>
<td>Intraoperative fluids (ml)</td>
<td>872.0 ± 39.1</td>
<td>884.0 ± 42.4</td>
<td>0.358</td>
</tr>
<tr>
<td>Blood loss (ml)</td>
<td>243.5 ± 49.0</td>
<td>257.5 ± 49.7</td>
<td>0.376</td>
</tr>
<tr>
<td>Operation duration (min)</td>
<td>121.8 ± 11.0</td>
<td>118.4 ± 11.0</td>
<td>0.334</td>
</tr>
<tr>
<td>Baseline MgSO₄ (mg/dl)</td>
<td>1.6 ± 0.3</td>
<td>1.5 ± 0.3</td>
<td>0.622</td>
</tr>
</tbody>
</table>

Data presented as mean ± SD. *Independent t-test. BMI: body Mass Index; FVC: forced vital capacity; FEV1: forced expiratory volume in the first second.
Table 2. Comparison between the studied groups regarding intraoperative oxygenation.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Time</th>
<th>MgSO\textsubscript{4} (N = 20)</th>
<th>Control (N = 20)</th>
<th>*P value</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean ± SE</td>
<td>95% CI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intraoperative oxygenation (PaO\textsubscript{2}/FiO\textsubscript{2} ratio)</td>
<td>Baseline</td>
<td>317.7 ± 24.1</td>
<td>315.5 ± 40.2</td>
<td>0.832</td>
<td>2.3 ± 10.5</td>
</tr>
<tr>
<td></td>
<td>Minute-45</td>
<td>317.0 ± 23.7</td>
<td>307.4 ± 40.4</td>
<td>0.364</td>
<td>9.6 ± 10.5</td>
</tr>
<tr>
<td></td>
<td>Minute-90</td>
<td>316.9 ± 23.5</td>
<td>298.6 ± 41.1</td>
<td>0.093</td>
<td>18.4 ± 10.6</td>
</tr>
<tr>
<td>$P$ value</td>
<td></td>
<td>0.067</td>
<td>&lt; 0.001$^{\text{II}}$</td>
<td></td>
<td></td>
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<tr>
<td>$\Delta$ Minute-45</td>
<td></td>
<td>-0.7 ± 1.8</td>
<td>-8.1 ± 2.0</td>
<td>&lt; 0.001$^{\text{II}}$</td>
<td>7.4 ± 0.6</td>
</tr>
<tr>
<td>$\Delta$ Minute-90</td>
<td></td>
<td>-0.8 ± 1.8</td>
<td>-16.9 ± 3.9</td>
<td>&lt; 0.001$^{\text{II}}$</td>
<td>16.1 ± 1.0</td>
</tr>
</tbody>
</table>

Data presented as mean ± SD unless mentioned otherwise. Effect size: value of MgSO\textsubscript{4} relative to control. $\Delta$: Change = time-baseline. *Independent t-test (comparison between groups). $^{\text{II}}$Repeated measures ANOVA (Comparison within groups). $^{\text{II}}$Significant. CI: Confidence interval. Abbreviations: PaO\textsubscript{2}, partial pressure of oxygen in arterial blood; FiO\textsubscript{2}, fraction of inspired oxygen concentration; $\Delta$, delta.
Table 3. Comparison between the studied groups regarding lung mechanics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Time</th>
<th>MgSO₄ (N = 20)</th>
<th>Control (N = 20)</th>
<th>*P value</th>
<th>Effect size</th>
<th>Mean ± SE</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Static compliance</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(ml/cmH₂O)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td></td>
<td>42.9 ± 5.0</td>
<td>41.2 ± 3.8</td>
<td>0.235</td>
<td>1.7 ± 1.4</td>
<td>-1.2, 4.6</td>
<td></td>
</tr>
<tr>
<td>Minute-45</td>
<td></td>
<td>42.7 ± 5.0</td>
<td>40.9 ± 3.6</td>
<td>0.198</td>
<td>1.8 ± 1.4</td>
<td>-1.0, 4.6</td>
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<tr>
<td>Minute-90</td>
<td></td>
<td>42.7 ± 4.8</td>
<td>40.9 ± 3.4</td>
<td>0.181</td>
<td>1.8 ± 1.3</td>
<td>-0.9, 4.5</td>
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<tr>
<td>§P value</td>
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<td>0.095</td>
<td>0.074</td>
</tr>
<tr>
<td>Δ Minute-45</td>
<td></td>
<td>-0.2 ± 0.5</td>
<td>-0.3 ± 0.7</td>
<td>0.622</td>
<td>0.1 ± 0.2</td>
<td>-0.3, 0.5</td>
<td></td>
</tr>
<tr>
<td>Δ Minute-90</td>
<td></td>
<td>-0.2 ± 0.6</td>
<td>-0.4 ± 0.8</td>
<td>0.515</td>
<td>0.2 ± 0.2</td>
<td>-0.3, 0.6</td>
<td></td>
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<tr>
<td>Dynamic compliance</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>(ml/cmH₂O)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Baseline</td>
<td></td>
<td>41.6 ± 6.1</td>
<td>39.7 ± 4.9</td>
<td>0.297</td>
<td>1.8 ± 1.7</td>
<td>-1.7, 5.4</td>
<td></td>
</tr>
<tr>
<td>Minute-45</td>
<td></td>
<td>41.5 ± 6.0</td>
<td>35.5 ± 4.6</td>
<td>0.001ⅱ</td>
<td>6.0 ± 1.7</td>
<td>2.6, 9.4</td>
<td></td>
</tr>
<tr>
<td>Minute-90</td>
<td></td>
<td>41.3 ± 6.0</td>
<td>31.1 ± 5.5</td>
<td>&lt;0.001ⅱ</td>
<td>10.3 ± 1.8</td>
<td>6.6, 13.9</td>
<td></td>
</tr>
<tr>
<td>§P value</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.063</td>
<td>&lt;0.001ⅱ</td>
</tr>
<tr>
<td>Δ Minute-45</td>
<td></td>
<td>-0.1 ± 0.4</td>
<td>-4.3 ± 0.9</td>
<td>&lt;0.001ⅱ</td>
<td>4.2 ± 0.2</td>
<td>3.7, 4.6</td>
<td></td>
</tr>
<tr>
<td>Δ Minute-90</td>
<td></td>
<td>-0.3 ± 0.6</td>
<td>-8.7 ± 2.1</td>
<td>&lt;0.001ⅱ</td>
<td>8.4 ± 0.5</td>
<td>7.4, 9.4</td>
<td></td>
</tr>
<tr>
<td>Dead space (%)</td>
<td></td>
<td></td>
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<tr>
<td>Baseline</td>
<td></td>
<td>18.4 ± 3.6</td>
<td>17.3 ± 3.3</td>
<td>0.321</td>
<td>1.1 ± 1.1</td>
<td>-1.1, 3.3</td>
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</tr>
<tr>
<td>Minute-45</td>
<td></td>
<td>18.5 ± 3.6</td>
<td>22.1 ± 3.5</td>
<td>0.003ⅱ</td>
<td>-3.6 ± 1.1</td>
<td>-5.8, -1.3</td>
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</tr>
<tr>
<td>Minute-90</td>
<td></td>
<td>18.2 ± 3.8</td>
<td>25.1 ± 3.3</td>
<td>&lt;0.001ⅱ</td>
<td>-6.9 ± 1.1</td>
<td>-9.2, -4.6</td>
<td></td>
</tr>
<tr>
<td>§P value</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.200</td>
<td>&lt;0.001ⅱ</td>
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<tr>
<td>Δ Minute-45</td>
<td></td>
<td>0.1 ± 1.0</td>
<td>4.8 ± 0.9</td>
<td>&lt;0.001ⅱ</td>
<td>-4.7 ± 0.3</td>
<td>-5.3, -4.0</td>
<td></td>
</tr>
<tr>
<td>Δ Minute-90</td>
<td></td>
<td>-0.3 ± 0.9</td>
<td>7.8 ± 1.1</td>
<td>&lt;0.001ⅱ</td>
<td>-8.0 ± 0.3</td>
<td>-8.6, -7.4</td>
<td></td>
</tr>
</tbody>
</table>

Data presented as mean ± SD unless mentioned otherwise. Effect size: value of MgSO₄ relative to control.

Δ: Change = time-baseline. *Independent t-test (comparison between groups). §Repeated measures ANOVA (Comparison within groups) ⅱSignificant. CI: Confidence interval
Table 4. Comparison between the studied groups regarding the postoperative events

<table>
<thead>
<tr>
<th>Variables</th>
<th>MgSO₄ (N = 20)</th>
<th>Control (N = 20)</th>
<th>*P value</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postoperative MgSO₄ (mg/dl)</td>
<td>2.9 ± 0.3</td>
<td>1.5 ± 0.3</td>
<td>&lt; 0.001§</td>
<td>1.3 ± 0.1</td>
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<tr>
<td>Δ MgSO₄ (mg/dl)</td>
<td>1.3 ± 0.1</td>
<td>0.0 ± 0.1</td>
<td>&lt; 0.001§</td>
<td>1.3 ± 0.0</td>
</tr>
<tr>
<td>Recovery duration (min)</td>
<td>19.9 ± 1.9</td>
<td>19.1 ± 2.1</td>
<td>0.219</td>
<td>0.8 ± 0.6</td>
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<tr>
<td>Sedation score</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>1.6 ± 0.5</td>
<td>1.6 ± 0.5</td>
<td>0.757</td>
<td>-0.1 ± 0.2</td>
</tr>
<tr>
<td>Immediate postoperative</td>
<td>3.2 ± 0.8</td>
<td>3.1 ± 0.7</td>
<td>0.838</td>
<td>0.0 ± 0.2</td>
</tr>
<tr>
<td>Hour-1 postoperative</td>
<td>2.6 ± 0.5</td>
<td>2.7 ± 0.5</td>
<td>0.531</td>
<td>-0.1 ± 0.2</td>
</tr>
</tbody>
</table>

Data presented as mean ± SD. Effect size: value of MgSO₄ relative to control. Δ: Change = time-baseline.

*Independent t-test. §Significant. CI: Confidence interval
Fig. 1. Consort flow chart for the studied cases
Fig. 2. The intraoperative heart rate among the studied groups (beats/min). Lines are the mean data and error bars are SD. *P < 0.001 compared to control group.
Fig. 3. The intraoperative mean arterial pressure (MAP) among the studied groups (mmHg). Lines are the mean data and error bars are SD. *P < 0.001 compared to control group.