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Effect of magnesium levels on mean tissue perfusion during and after bariatric surgeries: A randomised control trial

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ABSTRACT

Background: Bariatric surgeries can be complicated by decreased perfusion of tissues, which can be caused by obesity itself or different factors during surgery. This study's primary aim was to test how magnesium affects the mean tissue perfusion and whether it can increase the perfusion or decrease the effects of hypoperfusion, while the secondary aim was to investigate its effect on decreasing postoperative pain and total analgesic consumption, sedation, and incidence of side effects

Settings and Design: This study was a prospective double blinded randomized controlled study.

Methods: Sixty patients (ASA II-III) with morbid or complicated obesity scheduled for sleeve gastrectomy (LSG) participated in this trial. Patients were divided into two groups by randomization, the M group received an IV bolus infusion of 30 mg/kg magnesium (in a volume of 50 ml) after induction and 20 mg/kg IV infusion (in a volume of 50 ml) for 8 h postoperative and C group which received a bolus of 50 ml normal saline infusion after induction and 50 ml in saline infusion for 8 h postoperative. Serum magnesium was withdrawn after induction and before starting the bolus infusion. The perfusion index together with the level of rise in liver enzymes was compared throughout the study. Also, total analgesic use and pain severity (measured by the VAS score) were compared between the two groups.

Results: In comparison to the C group, the perfusion index was significantly higher in the M group (p-value <0.001). Also, the C group consumed much more analgesics and the VAS score was significantly higher ($p < 0.01$).

Conclusion: Magnesium may have a role in increasing perfusion and consequently decreasing morbidity during bariatric surgeries with no more added complications

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1. Introduction

There is an increase in bariatric surgeries globally for people with medically complicated obesity who cannot achieve weight-loss by alternative means [1]. During bariatric surgeries, tissue perfusion is greatly affected resulting in increased morbidity and mortality in the obese population [2] Using Masimo's specific pulse oximeter, Perfusion Index (PI) can be calculated and used intra and postoperatively. The trend in PI reveals the minor changes in perfusion that can be missed by static displays. These small changes captured by this trend provide an immediate clinical evaluation of tissue perfusion and consequently the incidence of complications from bariatric surgeries.

Magnesium causes vasodilation and so more tissue perfusion. Additionally, its analgesic effect causes the tissue to be less risky for vasoconstriction and more response to ordinary analgesia, resulting in increased perfusion. Researchers [3] proved that by evaluation of factors of (the Clavien-Dindo (CD) classification) (nausea, abdominal pain, surgical side effects, decreased oral intake and consequently dehydration, hemoglobin, leukocytic count, SpO2, pulse rate, diet, CRP, and pain scores) people with VAS scores above 40 had more major complications than patients with VAS scores below 40 [3]. In addition, recovery, respiration, vital signs, mobilization, intestinal function, and hospital stay all suffer due to postoperative pain.

Early and adequate analgesia speeds up mobilization in morbidly obese patients, reduces hospital stay, lowers the risk of complications, lowers costs, and improves patient comfort [4–6]. Nevertheless, opioid-based analgesia in obese individuals is linked to dangerous side effects including drowsiness, bradypnea, hypoxemia, vomiting, ileus, delayed mobilization, and mortality. Additionally, if there is a comorbid OSA, psychiatric disorders, cardiorespiratory diseases, and chronic opioid use, these complications become worse [7,8]. Utilizing opioids in the smallest dosage possible has the benefit of minimizing those negative side effects [9,10]. Magnesium sulfate is

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being used as an adjuvant for postoperative analgesia in numerous procedures, including obstetric, orthopedic, and cardiovascular procedures [11].

The liver is one of the very sensitive organs of hypoperfusion, and also there is a percentage of morbidly obese patients have a cirrhotic liver or fatty liver disease [12] which make liver cell damage to occur if they are exposed to hypoperfusion [13].

The study's objective was to investigate magnesium sulfate's impact during bariatric surgeries, especially on tissue perfusion and postoperative pain.

1.1. Patients and methods

This double-blind randomized clinical trial was carried out on 60 patients American Society of Anesthesiologists (ASA) II-III) undergoing sleeve gastrectomy at Alexandria University Main Hospitals. The study was done after the approval of ethical committee at Alexandria University Main Hospitals, Egypt. An informed written consent was obtained from all patients.

Inclusion criteria were obese (BMI ≥ 35 kg/m^2) adult (18–65 years) scheduled for laparoscopic sleeve gastrectomy.

Exclusion criteria were patients who refused to participate in the study or had major organ failure such as renal dysfunction, known liver disease, myopathy, neuropathy or prior abdominal surgeries. Also, the patient excluded if hemoglobin less than 9, Raynaud's disease, low cardiac output status, allergy to magnesium or other products. Additionally, the patient was excluded if he had chronic pain condition, daily or chronic consumption of pain medications analgesic 24 h before surgery, opioid addiction or drug and/or alcohol abuse, calcium channel blocker consumption.

1.2. Randomization and blindness

Patients were randomly allocated into two equal groups (30 each) using the closed envelope method in a double-blind randomized controlled trial. Both investigator and participants were blinded.

Magnesium sulfate group (group M) (*n* = 30): 30 mg/kg magnesium IV infusions (in a volume of 50 ml) after induction and after withdrawal of serum magnesium sample to be completed within 1 h intraoperative and 20 mg/kg IV infusion (in a volume of 50 ml) for 8 hours postoperative.

Normal saline (group C) (*n* = 30): 50 ml normal saline infusion after induction and after withdrawal of serum magnesium sample to be completed within 1 h intraoperative and 50 ml in saline infusion for 8 hours postoperative.

1.3. Preoperative evaluation

All patients were subjected to the following: Detailed medical and surgical history taking, complete clinical examination, and routine laboratory investigations, including complete blood picture, blood urea nitrogen, serum creatinine, prothrombin time (PT), activated partial thromboplastin (aPTT) times, thrombin time, fasting blood sugar and liver enzymes (SGOT, SGPT, alkaline phosphatase). Electrocardiograph (five leads ECG) and chest x-ray were performed.

On arrival to the operative room, an intravenous 18 gauge cannula was placed, and patients were connected to Masimo perfusion index technology (MightySat® Rx Fingertip Pulse Oximeter) Figure 1 and a multichannel monitor (CARESCAPE™ Monitor B650) to demonstrate: non-invasive blood pressure (mmHg), 5-lead ECG monitor (HR beats/minutes), respiratory rate (breaths/min), end-tidal carbon dioxide (mmHg), peripheral oxygen saturation (%), and temperature (surface temperature).

Figure 1. Masimo perfusion index technology (MightySat® Rx Fingertip Pulse Oximeter).

Anesthesia induction by intravenous administration of propofol (2 mg kg^{-1} ideal body weight), fentanyl (1 µg kg^{-1} ideal body weight), lidocaine (2% 1 mg kg^{-1}) and rocuronium (0.6 mg kg^{-1} actual body weight). Trachea was intubated and mechanical ventilation was started using volume control mode, tidal volume (Vt) was tailored to 6–8 ml/kg ideal body weight, and a 5 cm H_2O of PEEP with respiratory rate modified to keep E_tCo_2 35–45 mmHg [14]. The fluids were given as usual 20 ml/kg intraoperatively [15]. Magnesium's first sample was withdrawn after induction. Morphine 5 mg IV was given.

Anesthesia was maintained by rocuronium 0.1 mg kg^{-1} intravenously every 30 min and desflurane 1 MAC (6–9%) and they were monitored for perfusion index using Masimo perfusion index technology (MightySat® Rx Fingertip Pulse Oximeter) throughout the surgery and postoperatively for 8 h.

After the end of surgery, muscle relaxant was reversed with IV sugammadex (2 mg kg^{-1}). Patients were extubated and sent to the recovery unit, where their vital signs and consciousness were observed until they were ready to be discharged. All patients received instructions preoperatively on how to use the patient-controlled analgesia device and record pain using the visual analogue scale (VAS) (0: no pain to 100: severe pain). Postoperative analgesia was provided with a patient-controlled analgesia with IV morphine (30 mg morphine in 300 ml normal saline infused at a fixed rate of 5 ml/hour and bolus dose of 5 ml with 10-min lockout interval) [16,17]. Heart rate and noninvasive blood pressure were recorded intraoperatively and for 8 h after surgery. All surgeries were performed by the same surgeon.

Serum magnesium was withdrawn again after 8 h together with liver enzymes (SGOT, SGPT, alkaline phosphatase)

Tissue perfusion was assessed intraoperatively and postoperatively using Masimo perfusion index pulse oximeter and postoperatively using liver enzymes. Pain scores were evaluated by VAS [18]. The sedation score was recorded using the Richmond Agitation Sedation Scale (RASS) [14].

1.4. Study outcomes

The primary outcome of this trial was tissue perfusion. Secondary outcomes included pain, sedation, nausea and vomiting, and incidence of other side effects.

1.4.1. Sample size calculation

The sample size calculation was performed using G power 3.1.9.2 (Universität Kiel, Germany) [19]. The sample size was calculated based on the following considerations: 0.05 α error and 90% power of the study, morphine consumption in group M was significantly lower compared to group C (14.15 ± 2.56 vs. 17.05 ± 3.38, $P = 0.001$ at 6 hr [20] and 16.98 ± 3.25 vs. 20.85 ± 4.59, $P = 0.001$ at 12 h.) according to a previous study [21]. Eight cases were added to each group to overcome dropout. Therefore, 30 patients will be allocated in each group.

1.5. Statistical analysis

Data was received by the computer and analyzed by IBM SPSS version 20.0. NY, Armonk: IBM, Inc. Qualitative information was depicted utilizing numbers and percentages. The distribution's normality was confirmed with the help of the Shapiro–Wilk test. Quantitative information was portrayed using range (minimum and maximum), mean, and standard deviation. The level of significance of the obtained results was 5%.

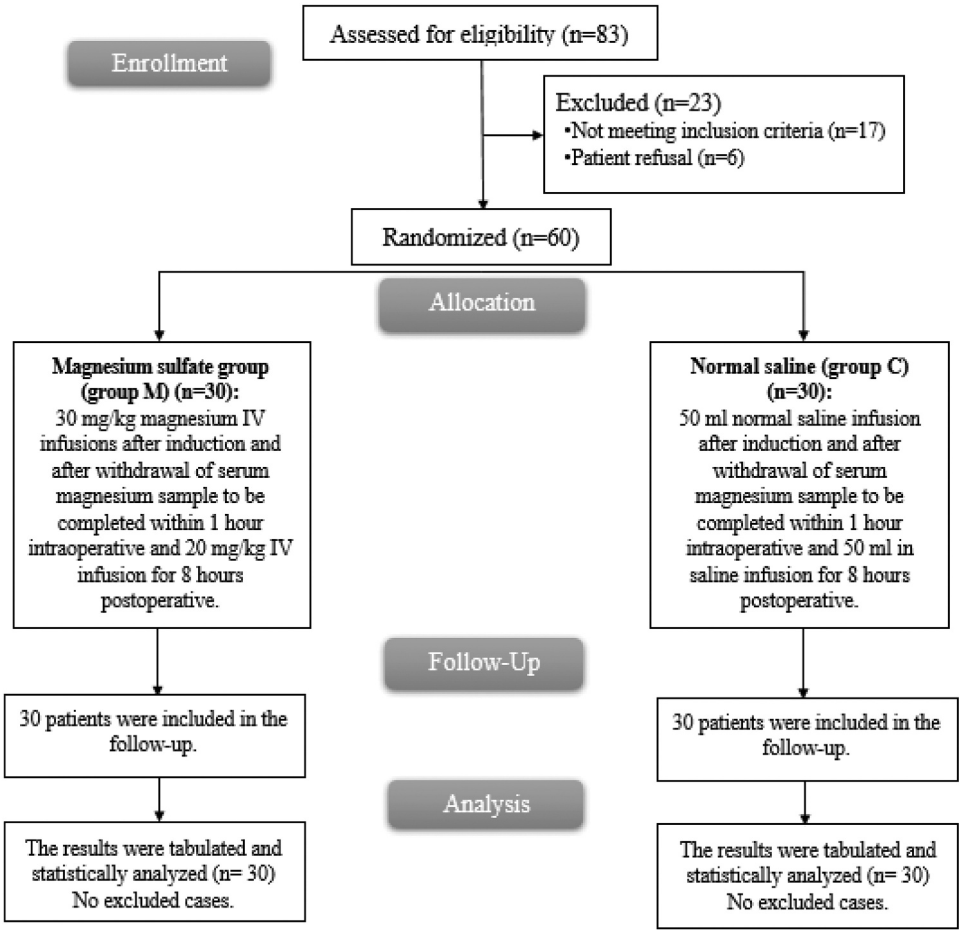
2. Results

In this study, 83 patients were assessed for eligibility, 17 patients did not meet the criteria and six patients refused to participate in the study. The remaining 60 patients were randomly allocated into two groups (30 patients in each). All the allocated patients were followed-up and then analyzed as shown in the flow chart.

2.1. CONSORT flowchart of the enrolled patients

Sixty individuals participated. Regarding sex, 29 were male and 31 were female. The patient's average age was 36.5 ± 10.9 years, ranging between 21 and 58. The demographic data, oxygen saturation, and surface temperature did not show any statistically significant differences ($p > 0.05$). Table 1

Heart rate showed a significant decrease in M group at 30 min, 1, 2, 4, 6 and 8 h in comparison with the basal recording, while in the C group there was only a significant decrease in heart rate at 1 and 2 h. Also, the heart rate was statistically significantly lower at 2, 4, and 6 hours in the M group in comparison to the C group. Mean blood pressure was slightly lower in different intervals of measurements in M group than in C group without significant differences. Regarding perfusion index, it increased significantly at 4 and 8 h (from 4.02 ± 0.90 to 4.41 ± 0.79 and 4.37 ± 0.67 at 4 and 8 h respectively) in M group while in C group PI tends to decrease to reach a significantly low level at 6 h period (from 3.70 ± 1.04 to 3.21 ± 0.83). When comparing both groups, the PI was significantly higher in the M group at 1, 4, 6, and 8 h periods. Also, liver enzymes increased postoperatively in both groups



CONSORT flowchart of the enrolled patients.

Table 1. Comparison between the two studied groups according to demographic data, analgesic consumption, time of analgesia and complications.

	Group M ($n = 30$)	Group C ($n = 30$)	Test of Sig.	P
Age (years)				
Mean ± SD.	33.6 ± 7.9	37 ± 10.4	t= 1.425	0.160
Gender				
Male	15 (50%)	14 (46.7%)	χ^2= 0.067	0.796
Female	15 (50%)	16 (53.3%)		
BMI (kg/m2)				
Mean ± SD.	39.85 ± 2.3	41.1 ± 2.5	t= 1.954	0.056
VAS score (cm)				
30 min.	2.90 ± 1.37	3.90 ± 1.67	299.0*	0.022*
90 min.	2.27 ± 1.01	2.80 ± 1.10	316.5*	0.038*
2 Hr.	2.53 ± 0.82	2.70 ± 0.53	416.0	0.540
4 Hr.	2.97 ± 0.81	5.03 ± 0.67	22.50*	<0.001*
8 Hr.	3.17 ± 1.29	2.40 ± 0.77	291.0*	0.014*
Analgesic consumption (morphine) (mg) at 8 hr.				
Mean ± SD.	15.7 ± 4.55	25.25 ± 6.1	t= 6.874*	<0.001*
Time of analgesia				
30 min.	11 (36.7%)	16 (53.3%)	$\chi^2 = 1.684$	0.194
90 min.	5 (16.7%)	9 (30%)	$\chi^2 = 1.491$	0.222
2 hr.	1 (3.3%)	0 (0%)	$\chi^2 = 1.017$	$^{FE}p = 1.000$
4 hr.	7 (23.3%)	29 (96.7%)	$\chi^2 = 33.611$*	<0.001*
8 hr.	14 (46.7%)	1 (3.3%)	$\chi^2 = 15.022$*	<0.001*
Complications				
Nausea & Vomiting	9 (30%)	16 (53.3%)	$\chi^2 = 3.360$	0.067
PO hypotension	3 (10%)	1 (3.3%)	$\chi^2 = 1.071$	$^{FE}p = 0.612$
PO neurological	1 (3.3%)	0 (0%)	$\chi^2 = 1.017$	$^{FE}p = 1.000$

SD: Standard deviation t: Student t-test χ^2: Chi square test.
FE: Fisher Exact.
p: *p* value for comparing between the two studied groups.
*: Statistically significant at $p \leq 0.05$.

but were significantly higher in C group (SGOT 20.01 ± 3.53 to 59.92 ± 9.34 in M group (p-value <0.001) and 21.76 ± 3.75 to 76.21 ± 10.29 in C group (p-value <0.001)) and (SGPT 25.19 ± 4.65 to 65.13 ± 6.19 in M group (p-value <0.001) and 23.19 ± 3.30 to 72.43 ± 6.87 in C group (p-value <0.001)). While alkaline phosphatase showed no significant difference between both groups. The serum magnesium levels also showed a significant rise in M group from pre to postoperative ($p < 0.05$) and in postoperative time it was significantly higher in group M than in group C ($p = 0.05$). Table 2 , Figures 2, 3

The VAS scores were significantly higher (3.90 ± 1.67) in group C than in group M patients (2.90 ± 1.37) ($p = 0.001$; $p < 0.01$) at 30 min, 2 and 4 h while at 8 h the VAS was significantly higher in M group, while there was no significance at 90 min interval. Morphine consumption was higher in C group reaching a mean of 25.25 ± 6.14 mg morphine at 8 h period while in M group it was 15.67 ± 4.55 mg morphine. Table 1

As regards the sedation using the RASS score, group M was significantly lower than group C at 2 and 6 h. While there was no statistically significant difference at 4 and 8 h periods and at discharge. Table 3

There were no significant differences between both groups in the incidence of nausea and vomiting, hypotension, and headache. Table 1

3. Discussion

The use of bariatric surgery in severe obesity has several advantages, including improved life expectancy, sustained weight loss, and resolution of several metabolic comorbidities [12,22].

Magnesium Sulphate ($MgSO_4$) is a promising agent with favorable effects in increasing tissue perfusion through peripheral vasodilatation [15,16]. Magnesium helps smooth muscle relaxation through blocking the calcium release [23].

This study aims to assess tissue hypoperfusion during and after bariatric surgery using combined clinical and non-invasive measures and to assess if magnesium infusion can improve perfusion in these patients.

Regarding the heart rate (HR), there was a significant decrease in HR up to 8 h in the M group, while in the C group, the HR decrease was significant only up to 2 h postoperative, and there was a significant difference between both groups at 2, 4, 6, and 8 h postoperative. This may be explained by the analgesic effect of magnesium. Adequate analgesia is usually linked to a stable heart rate. Additionally, magnesium is an antiarrhythmic drug that regulates voltage-dependent sodium, potassium, and calcium channels. Therefore, magnesium can lengthen the PR interval and QRS complexes by speeding up atrioventricular nodal conduction times.

Similar to these results, a meta-analysis of controlled, randomized studies on the role of magnesium in stabilizing hemodynamics following operations which were carried out by Patrice Forget and Juan Cata [24]. The results show that in quantitative analyses, magnesium vs. placebo decreased heart rate variability (−3.7 bpm; 95% CI [−6.5 to + 0.9], $P = 0.01$).

Moreover, PI was higher during magnesium infusion than the C group at all times, and the comparison was statistically significantly higher at 1, 4, 6, and 8 h periods. These results may explain by magnesium-induced vasodilatation along with an analgesic effect which increased the perfusion [25]. Similarly, a study carried out by Kamel et al. [26] compared the effect of magnesium and labetalol on tissue perfusion during hypotensive anesthesia in

Table 2. Comparison between the two studied groups according to PI (%), alkaline phosphatase, sgot, sgpt, and magnesium levels.

	Group M ($n = 30$)	Group C ($n = 30$)	T	p
PI (%)				
Immediately after induction and before surgery	4.02 ± 0.90	3.70 ± 1.04	1.261	0.212
30 min.	4.24 ± 0.81	4.01 ± 0.74	1.165	0.249
1 hr.	4.05 ± 0.83	3.64 ± 0.64	2.128*	0.038*
2 hr.	4.16 ± 0.91	3.79 ± 0.64	1.820	0.074
4 hr.	4.41# ±0.79	3.64 ± 0.76	3.827*	<0.001*
6 hr.	3.88 ± 0.71	3.21# ±0.83	3.353*	0.001*
8 hr.	4.37# ±0.67	3.72 ± 0.66	3.771*	<0.001*
Alkaline phosphatase (IU/L)				
Pre	44.69 ± 11.85	41.43 ± 12.85	1.021	0.311
Post	48.76 ± 12.19	47.51 ± 11.69	0.406	0.686
Magnesium level (mg/dL)				
Pre	2.06 ± 0.19	1.98 ± 0.17	1.826	0.073
Post	2.17# ±0.15	1.93 ± 0.15	6.452*	<0.001*
SGOT (U/L)				
Pre	20.01 ± 3.53	21.76 ± 3.75	1.865	0.067
Post	59.92 ± 9.34	76.21 ± 10.29	6.420*	<0.001*
SGPT (U/L)				
Pre	25.19 ± 4.65	23.19 ± 3.30	1.926	0.059
Post	65.13 ± 6.19	72.43 ± 6.87	4.326*	<0.001*

Data was expressed using Mean ± SD.SD: Standard deviation t: Student t-test.
p: p value for comparing between the two studied groups.
*: Statistically significant at $p \le 0.05$ #: Significant with before surgery.

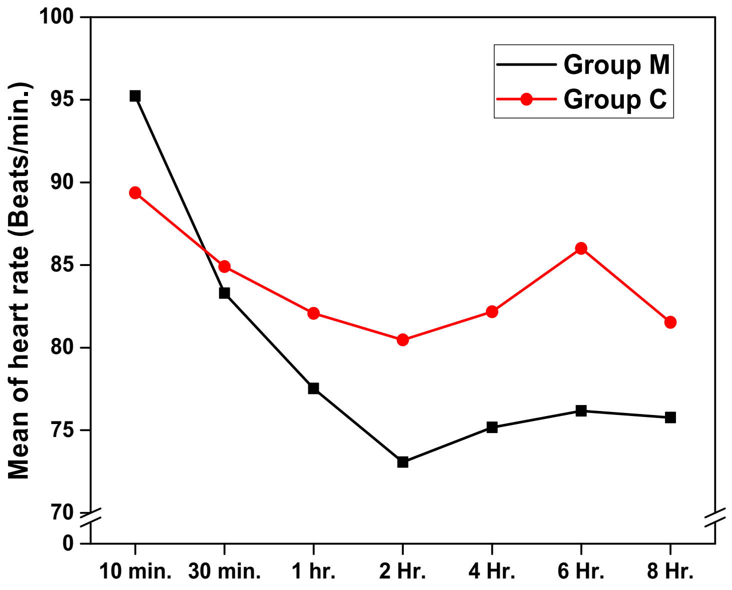


Figure 2. Comparison between the two studied groups according to HR (b/min).

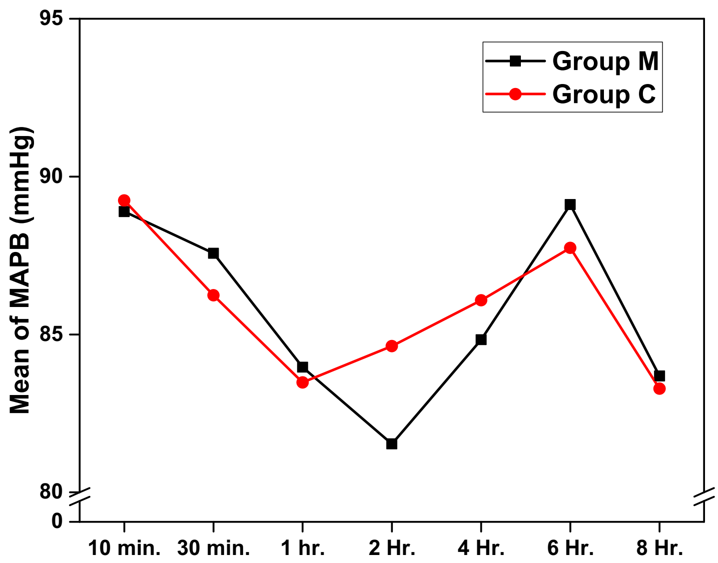


Figure 3. Comparison between the two studied groups according to MAPB (mmHg).

Table 3. Comparing the two studied groups according to RASS score.

RASS score	Group M (*n* = 30)	Group C (*n* = 30)	U	P
2 hr.				
Mean ± SD.	0.10 ± 1.30	0.80 ± 1.24	317.0*	0.038*
Median (Min. – Max.)	−0.50 (−1–2)	1 (−1–2)		
4 hr.				
Mean ± SD.	0.30 ± 0.60	0.30 ± 0.79	447.0	0.957
Median (Min. – Max.)	0 (0–2)	0 (−1–2)		
6 hr.				
Mean ± SD.	0.43 ± 0.57	1.47 ± 0.57	119.5*	<0.001*
Median (Min. – Max.)	0 (0–2)	1.50 (0–2)		
8 hr.				
Mean ± SD.	0.57 ± 0.77	0.63 ± 0.56	399.0	0.402
Median (Min. – Max.)	0 (0–2)	1 (0–2)		
At discharge				
Mean ± SD.	−0.57 ± 0.50	−0.53 ± 0.51	435.0	0. 827
Median (Min. – Max.)	−1 (−1–0)	−1 (−1–0)		

SD: Standard deviation, U: Mann Whitney test, p: p value for comparing between the two studied groups, *: Statistically significant at p ≤ 0.05.

nasal surgeries. The magnesium group showed significantly higher PPI values in comparison with labetalol. Also, there was a significant increase in liver enzymes after LSG, but the increase in the C group was significantly higher than in the M, denoting that magnesium may have a liver protective effect besides its effect on increasing tissue perfusion.

In contrast to these results, a study performed by Jeong Eun Kim et al. [27] studied the magnesium treatment of reperfusion in patients undergoing living donor liver transplantation. There was a rise in the level of enzymes, and the rise in the magnesium group was less but with no significant differences which may need a larger sample size to show a difference. Also, dissection of liver tissue makes the increase in liver enzymes inevitable, which is different from bariatric surgery where liver cell damage may occur due to steep Trendelenburg position, co2 insufflation or use of liver retractors.

Regarding postoperative pain, there was a significantly higher VAS score in group C than in group M at 30 min, 2, 4, and 8 h with no significant difference at 90 min. Also, total morphine usage at 8 h was significantly less in group M than in group C indicating that magnesium is important in decreasing opioids consumption and the number of patients requesting analgesia was significant at 4 h where almost all group C requested analgesia (29 patients) with only significant high number of patients (14 patients) requested analgesia in group M at 8 h period and these results denote that magnesium prolonged the analgesia postoperatively and increasing the actions of opioids. Numerous studies have been conducted on the analgesic effects of magnesium, which are described by a non-competitive NMDA receptor blocking action and by reducing the intracellular calcium influx.

Similarly, a study performed by Nurcan Kizilcik [21] who used the same dosage of magnesium in 80 patients discovered that the non-magnesium group's VAS score was significantly higher. Also, morphine consumption in group C at intervals of 30, 60, and 90 min and 2, 4, 6, 12, and 24 h was more than in group M. Also, a study by Hicham Jabbour et al. [28] investigated the effect of magnesium and ketamine in reducing early morphine usage after bariatric surgeries. When compared to the other two groups, patients in the PACU Group (K) had a higher VAS at rest ($p = 0.049$), with movement ($p = 0.048$), and cough ($p = 0.043$) after 3 h. Additionally, compared to group (P) patients, patients in the groups (Mg + K) and (K) used considerably less morphine in the PACU (4.85 ± 4.51 mg). Patients in the group (Mg + K) consumed much less morphine in the first 24 h following surgery than those in groups (K) and (P), with relative decreases of 87% and 21%, respectively.

As regards RASS score, group M was significantly lower than group C at 2 and 6 h (p-value 0.038)) and (p-value <0.001)), respectively. Similarly, a trial performed by H. Elseresy et al. [29]) studied magnesium's effect on the management of postoperative agitation after sinus surgery (FESS). They found that magnesium infusion intraoperatively decreased the agitation at intervals of (0, 5, 10, 15, and 30 min) postoperatively together with agitation total score [3 (0 to 6) versus 9 (0 to 12)]. This may be due to increased analgesia and increased sedative effects of opioids

Regarding adverse effects between the two groups, there was no significant distinction in the frequency of complications, only one patient experienced a headache, and he was excluded from the study. Similar to this, C. H. Wilder-Smith et al. [30] examined 24 patients receiving conventional general anesthesia for elective hysterectomies who received a 5-h infusion of magnesium sulphate (first bolus, 8 mmol; then, 8 mmol/h) or a placebo commencing with anesthesia induction. They found that nausea and vomiting were similar in both groups.

4. Conclusion

Magnesium sulphate infusion during and after bariatric surgeries decreases the effect of hypoperfusion, improves pain management, and reduces the need for more analgesia without having more negative side effects.

4.1. *Study limitations*

It is unknown if magnesium can be administered to obese people based on their actual or ideal body weight. In several earlier investigations, the MgSO4 dosage was calculated per kilogram using actual body weight [31–35]. Also, the liver enzymes effects may need more time and a bigger sample size to show differences.

Abbreviations

ASA	American Society of Anesthesiology
LSG	Laparoscopic sleeve gastrectomy
VAS	visual analogue scale
RASS	Richmond Agitation Severity Score
IV	intravenous, PI: perfusion index
CD	Clavien-Dindo classification
BMI	body mass index
V_t	Tidal volume
E_tCo_2	end-tidal carbon dioxide
SGOT	Serum Glutamic Oxaloacetic Transaminase
SGPT	Serum Glutamate Pyruvate Transaminase
HR	heart rate
NMDA	N-methyl-d-aspartate

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Disclosure statement

There are no declared conflicting interests, according to the author(s).

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