

ORIGINAL RESEARCH

BARIATRIC ANESTHESIA

A comparative study between intravenous and intraperitoneal magnesium sulphate for pain management in laparoscopic mini gastric bypass: a randomized clinical trial

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Abstract

Background: Laparoscopic bariatric surgery has become a regular procedure, and it has largely replaced traditional open surgery. Patients experience postoperative pain even after laparoscopic surgery, although the intensity is low compared to open surgery. We compared the effectiveness of intravenous (IV) vs. intraperitoneal (IP) magnesium sulphate (MgSO₄) injection in pain management in laparoscopic mini-gastric bypass surgery.

Methodology: We selected 100 patients based on convenient sampling and randomly divided into two groups; the IV group (50 patients) received MgSO₄ 50 mg/kg in 250 ml normal intravenously, and the IP group (50 patients) received MgSO₄ 50 mg/kg in 30 ml normal saline intraperitoneally. Nalbuphine was used as rescue analgesic and its total postoperative consumption during the first 24 h was recorded based on VAS score. Postoperative nausea and vomiting (PONV), sedation score and hemodynamic changes with pneumoperitoneum were also assessed.

Results: Total nalbuphine consumption postoperatively was more in IV group than IP group (12 ± 3.03 mg vs. 8.3 ± 2.8 mg; P < 0.001). Postoperative pain score was significantly lower in IP group in comparison to IV group (P < 0.001). Intraoperative hypotension and bradycardia were significantly more (P = 0.03) in IV group (21% and 17% respectively) compared to IP group (10% and 7% respectively). Postoperative sedation and nausea and vomiting scores were reduced in IP group compared to IV group, the difference being highly significant (P < 0.001).

Conclusion: Intraperitoneal MgSO₄ instillation has better results than intravenous infusion in attenuation of postoperative pain and hemodynamic response associated with pneumoperitoneum, and results in less PONV when used in laparoscopic minigastric bypass patients.

Key words: Analgesics / administration & dosage; Analgesics / pharmacology; Analgesics / therapeutic use; Bariatric; Magnesium Sulfate / administration & dosage; Magnesium Sulfate / pharmacokinetics; Magnesium Sulfate / therapeutic use; Mini-gastric bypass; Pain management; Pneumoperitoneum

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1. Introduction

Obesity is a global and rapidly rising condition with a serious impact on all aspects of healthcare especially perioperative care. The frequency of bariatric surgeries has been escalating worldwide for medically confounded obesity patients, who are unable to lose weight by various strategies.¹

Laparoscopic surgery is made possible by instillation of inert gas in the peritoneum under pressure, creating pneumoperitoneum. This condition has been found to cause a rise in systemic vascular resistance that is mostly due to the effects of the released vasopressin and catecholamines. Magnesium sulphate ($MgSO_4$) suppresses the secretion of catecholamines from the adrenal medulla in as well as from adrenergic nerve endings. A significant vasodilator action on blood vessels was observed resulting in a decrease in blood pressure. $MgSO_4$ is also able to weaken vasopressin-mediated vasoconstriction.²

Intraperitoneal instillation of $MgSO_4$ might lessen the hemodynamic stress reaction resulting from pneumoperitoneum besides enhancing patient's satisfaction by decreasing postoperative pain. Among multiple actions of Mg, the blockage of calcium channels and N-methyl-D-aspartate (NMDA) receptors has a significant importance to anesthesia. $MgSO_4$ has been observed to have a good effect in pain management besides inhibiting somatic, autonomic and endocrinal responses motivated by painful stimulus.³

We compared the outcome of early intraperitoneal instillation of $MgSO_4$ before any dissection on hemodynamic response and its analgesic effect vs. administration of IV $MgSO_4$ in laparoscopic mini-gastric bypass surgery patients.

2. Methodology

This randomized prospective comparative study was conducted from December 2020 to December 2021 at Ain Shams University Hospitals. We enrolled 100 obese patients, ages between 21-60 y, BMI 35–59.9 Kg/m², both genders, ASA (II and III) undergoing elective laparoscopic mini-gastric bypass surgery.

The exclusion criteria were; patient refusal, pregnant or breast-feeding women, ASA > III, the need to convert laparoscopic surgery to an open one, allergy to $MgSO_4$, 1st or 2nd degree heart block, chronic treatment by beta-blockers, heart rate < 50 bpm, heart failure with LVEF < 40%, severe chronic disease, severe obstructive sleep

apnea (OSA), history of chronic pain, alcohol or drug abuse and psychiatric illness.

All candidates provided written informed consent, and were randomized to one of the two groups through a computer randomization software.

The intravenous (IV) group included 50 patients who were given $MgSO_4$ 50 mg/kg in 250 ml of normal saline. The intraperitoneal (IP) group included 50 patients who were given $MgSO_4$ 50 mg/kg in 30 ml of normal saline intraperitoneally before insufflation of CO_2 .

Medical and surgical history, physical examination, including appropriate evaluation of the airway and investigations, including complete blood count (CBC), coagulation profile, kidney and liver functions tests, and electrocardiography (ECG), echocardiography and pulmonary function tests (for patients with BMI > 40), were done in anesthesia clinic. The plan was discussed with the patients and the visual analogue scale was explained to them to describe pain perception post-surgical procedure.

At OR, an 18G IV cannula was inserted. Basic monitoring was started. All patients received famotidine (H_2 -blocker) 50 mg, metoclopramide 10 mg and dexamethasone 4 mg IV for prophylaxis from nausea and vomiting.

Inj. midazolam 2 mg was given for sedation. Pre-oxygenation with 100% was done. GA was induced with fentanyl 1 μ g/kg, propofol 1.5-2 mg/kg, and muscle relaxation by atracurium (started by 0.5 mg/Kg) later on (0.1 mg/kg) boluses as a maintenance doses. After that, Endotracheal tube (ETT) of proper size was introduced to protect airway. Anesthesia was maintained by isoflurane (1.2% mean alveolar concentration MAC) within 50/50 of oxygen and air mix, and the MAC was modified according to patient's hemodynamics, and Fentanyl was infused IV in the rate of 1 μ g /kg/h in 50 ml syringe throughout the whole procedure started prior to skin incision. Controlled ventilation in the form of intermittent positive pressure ventilation (IPPV) started; settings were accustomed to preserve end tidal CO_2 level (Et CO_2) within 35-45 mmHg.

A reference number was distinguished the $MgSO_4$ syringes, which were all identically labelled. This ensured the safety of the patients as well as the blinding of all participants, including anesthetic personnel.

Patients in Group IV received $MgSO_4$ 50 mg/kg in 250 ml normal saline intravenously. Then received 30 ml normal saline intraperitoneally before insufflation of CO_2 . Patients of Group IP received 250 ml normal saline intravenously. Then received $MgSO_4$ 50 mg/kg in 30 ml

of normal saline intraperitoneally before insufflation of CO₂.

Fentanyl infusion was withdrawn after skin closure. Inj. paracetamol 1 G and inj. diclofenac 75 mg were

Patients were transported to post anesthesia care unit (PACU) after being fully recovered.

Analgesia was maintained by inj. paracetamol 1 G IV every 6 h over subsequent 24 h, besides rescue analgesic nalbuphine 50 µg/kg, if visual analogue score (VAS) score was more than 3.

The primary outcome of our study was total nalbuphine consumption during the first 24 h postoperatively based on VAS score. The VAS was measured 30 min after recovery, and at 2 h, 4 h, 6 h, 12 h and 24 h

Table 1: Comparative demographic data and duration of surgery

	IV group (n=50)	IP group (n=50)	T/Z/x2	p-value
Age (years)*	44.9 ± 4.3	44.5 ± 4.2	0.5t	0.6
BMI (Kg/m ²)*	43.42 ± 3	42.98 ± 2.5	0.79t	0.43
ASA**	3 (2-3)	3 (2-3)	0.2z	0.84
Sex (Males)***	27 (54%)	24 (48%)	0.16x2	0.69
Duration of surgery*	84.2 ± 7.6	83.8 ± 6.97	0.28 t	0.78

Data defined as *mean ± SD, **median (IQR), ***proportion. t = student t test, Z= Mann-Whitney test, x2= Chi square

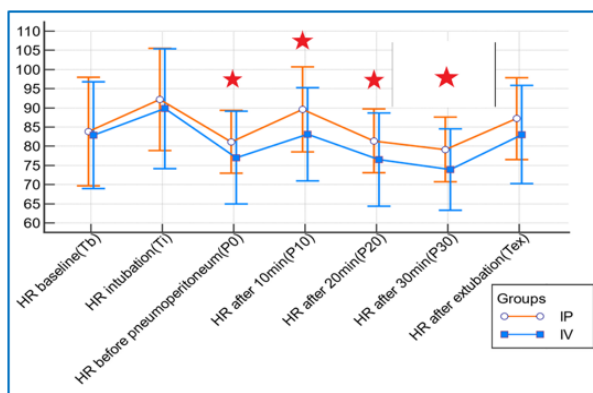


Figure 1: Comparative mean arterial blood pressure (MABP). Red star represents significant P-value

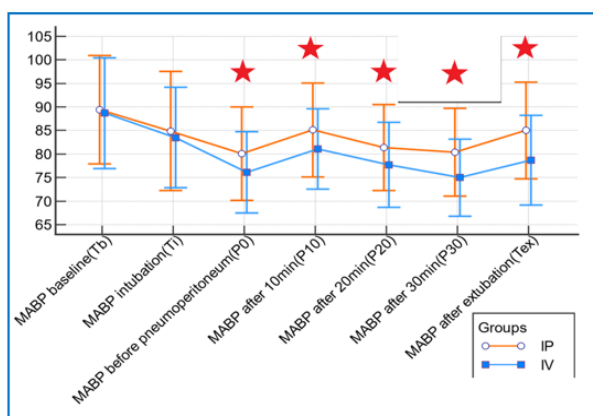


Figure 2: Comparative heart rates in two groups as regard. Red star represents significant P-value.

administrated intra-operatively to all patients. Inj. neostigmine 0.05 mg/kg and atropine 0.01 mg/kg was administrated at the end of the procedure to reverse the residual muscle relaxation. Awake extubation was done after oral suctioning.

postoperatively.

Secondary outcomes were; frequency of PONV in the first 24 h after extubation. Nausea was assessed at the same as of VAS via a scoring system (0 = none, 1 = mild, 2 = moderate, 3 = severe). Patients suffering from vomiting or who rated their nausea at level 2 or more were given inj. ondansetron 4 mg IV.

Sedation was also assessed at the same intervals of VAS by a scale (0 = alert, 1 = quietly awake, 2 = asleep but easily aroused and 3 =deep sleep).

Hemodynamic parameters; mean arterial blood pressure (MAP) and heart rate (HR) were recorded prior to induction of anesthesia as a baseline reading (Tb), immediately after intubation (Ti), before pneumoperitoneum (P0), then every 10 min till 30 min (P10, P20, and P30) and after extubation (Tex). Also, incidents of bradycardia, hypotension and hypertension were recorded. Bradycardia was described as: HR ≤ 50 bpm. Hypotension was described as a decline in systolic blood pressure less than 20% of the baseline value. Hypertension is described as a rise in systolic blood pressure more than 20% of the baseline value.

Intraoperative hypotension was managed by ephedrine 5–10 mg IV bolus, then titrated as needed. hypertension was handled by increasing isoflurane MAC to 2 or 3%, or a bolus of fentanyl 25 µg IV, then nitroglycerin infusion 1 µg /kg/min was added if still needed. Bradycardia was handled by a bolus of atropine 0.01 mg/kg, repeated as required.

Statistical Analysis

PASS11 program was used for sample size calculation, setting alpha error at 5%. Elfiky M. and his colleagues (2018), showed that the total analgesic requirement during the first postoperative 24 h was (2.34 ± 1.08) for IV group versus (1.26 ± 0.78) for IP group. Based on these findings, a sample size of 50 patients per group

would reach 100% power for detecting the difference in the pain level between the two groups.

Data were analyzed using Statistical package for Social Science (SPSS) version 22.0. Mean ± standard deviation

(SD) were used for quantitative data. Frequency and percentage were used for qualitative data.

Independent-samples t-test of significance was utilized for two means comparison. Chi-square (X²) test of significance was utilized for proportions comparison between two qualitative parameters. Mann Whitney U test compared two-groups in non-parametric data. The confidence interval was set to 95% and the margin of error accepted was set to 5%. P ≤ 0.05 was considered significant.

3. Results

One hundred patients were enrolled, 50 patients in each group. The two groups were comparable in demographic data (in terms of age, sex, BMI and ASA) and duration of surgery and there were no statistically significant difference between groups (P > 0.05) (Table 1).

IV group was lesser than IP group as regard MABP, and a significant difference was observed before pneumoperitoneum, 10 min, 20 min, 30 min after pneumoperitoneum and after extubation (P = 0.03, 0.03, 0.047, 0.003 and 0.002 respectively) (Figure 1).

Regarding HR, a significant difference was observed before pneumoperitoneum, and at 10 min, 20 min and 30 min after pneumoperitoneum (P = 0.048, 0.006, 0.021, and 0.007) respectively, HR change was small in the IV group as compared to IP group (Figure 2).

Regarding HR, a significant difference was observed before pneumoperitoneum, and at 10 min, 20 min and 30 min after pneumoperitoneum (P = 0.048, 0.006,

Table 2: Assessment of groups regarding hemodynamic adverse events

Adverse event	IV group (n=50)	IP group (n=50)	X2	p- value
Hypotension	21 (42%)	10 (20%)	4.7	0.03*
Hypertension	24 (48%)	26 (52%)	0.04	0.84
Bradycardia	17 (34%)	7 (14%)	4.4	0.035*

Data expressed as proportion, x2= chi square, * significant P-value.

Table 3: Assessment of groups regarding visual analogue scale and total dose of nalbuphine consumption.

Time	IV group (n=50)	IP group (n=50)	Mann-Whitney test z	p-value
30 min	3 (1-4)	1 (0-1)	5.9	< 0.001*
2 h	3 (3-5)	1 (1-2)	7.04	< 0.001*
4 h	5 (4-6)	3 (2-4)	5.9	< 0.001*
6 h	2 (1-4)	1 (1-3)	2.6	0.01**
12 h	4 (2-4)	4 (1-4)	1.89	0.059
24 h	1 (0-1)	1 (0-1)	0.8	0.42
Postoperative nalbuphine consumption (mg)	12 ± 3.03	8.3 ± 2.8	6.4	< 0.001*

Data expressed as Median (IQR): Inter quartile range, * significant P-value, ** highly significant P-value.

0.021, and 0.007) respectively, HR change was small in the IV group as compared to IP group (Figure 2).

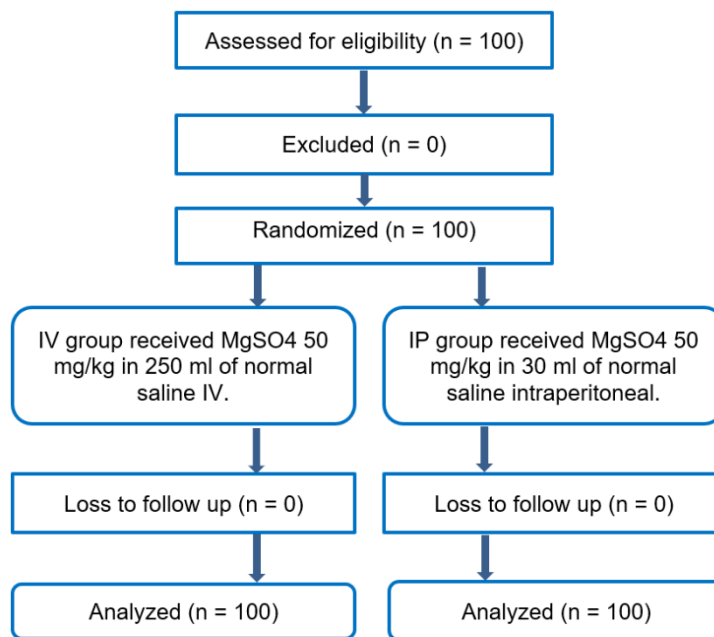


Figure 1: CONSORT diagram of the study

IV group demonstrated significantly more hypotension and bradycardia episodes (P =

0.03 and P = 0.035) respectively. Although IV group showed less hypertension episodes, but the difference was statistical not significant (Table 2).

The IP group demonstrated lower pain scores than IV group, with significant differences at 30 min, 2 h, 4 h and 6 h after surgery (P < 0.05). The total postoperative nalbuphine consumption was more in the IV group (12 ± 3.03) than IP group (8.3 ± 2.8) (Table 3).

The IP group showed less PONV with significant difference at 30 min, 2 h, 4 h and 6 h postoperatively (P < 0.05). Otherwise there was no statistical difference between two groups (Table 4).

The IP group showed less sedation than the IV group with significant difference at 30 min and 2 h postoperatively. Otherwise there was no statistical difference between two group (Table 5).

4. Discussion

Magnesium is considered the second most frequent intracellular cation with a chief function to preserve homeostasis. Magnesium is an essential factor for cell signaling, the normal function of enzymes and neurotransmission. Studies show that magnesium has an antagonist effect on NMDA receptors, which could affect pain sensitivity and extent.⁵ The usage of magnesium for perioperative analgesia was

Table 3: Assessment of groups regarding visual analogue scale and total dose of nalbuphine consumption.

Time	IV group (n=50)	IP group (n=50)	Mann-Whitney test	
			z	p-value
30 min	3 (1-4)	1 (0-1)	5.9	< 0.001*
2 h	3 (3-5)	1 (1-2)	7.04	< 0.001*
4 h	5 (4-6)	3 (2-4)	5.9	< 0.001*
6 h	2 (1-4)	1 (1-3)	2.6	0.01**
12 h	4 (2-4)	4 (1-4)	1.89	0.059
24 h	1 (0-1)	1 (0-1)	0.8	0.42
Postoperative nalbuphine consumption (mg)	12 ± 3.03	8.3 ± 2.8	6.4	< 0.001*

*Data expressed as Median (IQR): Inter quartile range, * significant P-value, ** highly significant P-value.*

Table 4: Comparative assessment of groups regarding PONV

Time	PONV score	IV group (n=50)	IP group (n=50)	X2	p-value
30 min	0	20 (40%)	40 (80%)	17.2	<0.001*
	1	18 (36%)	5 (10%)		
	2	9 (18%)	3 (6%)		
	3	3 (6%)	2 (4%)		
2 h	0	26 (52%)	40 (80%)	8.88	0.03**
	1	13 (26%)	6 (12%)		
	2	9 (18%)	3 (6%)		
	3	2 (4%)	1 (2%)		
4 h	0	27 (54%)	41 (82%)	9.48	0.02**
	1	12 (24%)	6 (12%)		
	2	8 (16%)	2 (4%)		
	3	3 (6%)	1 (2%)		
6 h	0	24 (48%)	38 (76%)	10.2	0.017**
	1	16 (32%)	6 (12%)		
	2	8 (16%)	3 (6%)		
	3	2 (4%)	3 (6%)		
12 h	0	44 (88%)	45 (90%)	1.01	0.8
	1	4 (8%)	2 (4%)		
	2	1 (2%)	2 (4%)		
	3	1 (2%)	1 (2%)		
24 h	0	49 (98%)	48 (96%)	0.34	0.56
	1	1 (2%)	2 (4%)		

*Data expressed as proportion, x2= chi square, * highly significant P-value, ** significant P-value.*

Table 5: Comparative sedation scores in the groups

Time	Sedation score	IV group (n=50)	IP group (n=50)	X2	p-value
30 min	0	3 (6%)	39 (78%)	54.4	< 0.001*
	1	15 (30%)	6 (12%)		
	2	27 (54%)	4 (8%)		
	3	5 (10%)	1 (2%)		
2 h	0	35 (70%)	49 (98%)	14.7	< 0.001*
	1	11 (22%)	1 (2%)		
	2	4 (8%)	0 (0%)		
4 h	0	48 (96%)	50 (100%)	2	0.15
	1	2 (4%)	0 (0%)		
6 h	0	50 (100%)	50 (100%)	0	1
12 h	0	50 (100%)	50 (100%)	0	1
24 h	0	50 (100%)	50 (100%)	0	1

Data expressed as proportion, x2= chi square, * highly significant P-value.

initially studied by Koinig et al. in candidates with similar degrees of surgical stimuli.⁶

Pre-emptive analgesia has been a popular practice among anesthetists and its role in the pain management has been widely discussed. It is aimed to avoid CNS sensitization to following stimuli that intensify pain signals.⁷ Postoperative pain perception has a harmful impact on recovery, hemodynamics, respiration, ambulation, and it prolongs the hospital stay. Unfortunately, it is known that opioid-based analgesia in obese patients is accompanied with critical side effects like apnea, hypoxemia, sleepiness, ileus, delayed ambulation, and so increased mortality rates.¹ Although MgSO₄ causes mild sedation, it decreases anesthetic needs; this is useful in decreasing residual anesthetic effects in bariatric patients, decreasing risk of postoperative apnea.²

In our study, MABP and HR there were significantly lower in IV group before pneumoperitoneum, 10 min, 20 min, 30 min after pneumoperitoneum and after extubation (Figure 1 and 2). IV group had more frequency of hypotension and bradycardia. We found that attenuation of the hemodynamic changes associated with pneumoperitoneum was better with IV group than IP group. IP group was better in events of bradycardia and hypotension than IV group. This might be due to rapid rise in magnesium levels and thus onset of action with IV administration.

Our results were similar to those reported by El Mourad and Arafa about the benefits of IV and IP intake of MgSO₄ in attenuating the hemodynamic alterations created due to pneumoperitoneum.² Paul et al. demonstrated a significant decline in HR and MAP throughout pneumoperitoneum for laparoscopic

cholecystectomy after administration of 30 mg/kg MgSO₄ IV.⁸ Ali et al. instilled 20 ml MgSO₄ 10% IP following pneumoperitoneum in laparoscopic cholecystectomy and reported a reduction of unwanted hemodynamic changes in comparison to the controls.⁹ The IP intake of local anesthetics with or without adjuvant was reported to be efficient in enhancing perception of pain during different laparoscopic surgeries. This might be caused by blockage of visceral afferent pain transmission.

Furthermore, absorption from the huge surface like peritoneum might also add to analgesia.²

In our study, the IP group patients expressed less pain perception, and less postoperative nalbuphine utilization than the IV group. Magnesium affects the influx of calcium into the cells and moreover antagonizes NMDA receptors, which affect neuronal signaling and pain processing in the central nervous system. By these receptors blockage, it causes blockage of both somatic and visceral pain fibers and so decreases postoperative pain.¹⁰ Similar results in patients undergoing laparoscopic cholecystectomy were shown by other researchers.^{1,2,5,11,12}

A systematic review by Lysakowski et al. did not identify a significant systemic impact of MgSO₄ on pain management postoperatively. That might be explained by less clinical trials in addition to fewer participants (n = 778) in comparison with meta-analysis reported by De Oliveira et al. Besides, Lysakowski et al. assessed patients undergoing dissimilar modes of anesthesia, including neuraxial blocks, while De Oliveira et al. limited their study to patients, who underwent operations under general anesthesia.^{5,13}

In our study, the IP group showed less PONV with significant difference at 30 min, 2h, 4h and 6h postoperatively. Similar results were reported by El Mourad and Arafa.² They explained that by the anesthetic / analgesic sparing actions of MgSO₄ had led to reduced frequency of PONV; another clarification was the NMDA antagonist action of MgSO₄ on receptors situated in the common pathway of nausea and vomiting. Nevertheless, there is no current information available on the direct effect of MgSO₄ on PONV.^{2,9} On the other

side, Kizilcik et al. reported that the prevalence of unfavorable side effects like PONV in addition to shivering was almost similar between the patients, who received IV MgSO₄ and control group although morphine consumption was reduced.¹

In our study, the IP group showed less sedation with significant difference at 30 min and 2 h postoperatively. In accordance to our results, Elfiky et al. reported that patients receiving IV magnesium needed more time to achieve an Alderete score of 9 to be fit for discharge from PACU; and had higher sedation score in the first 2 h postoperatively than IP group.¹¹ Ali et al. also reported that sedation score was significantly higher in patients receiving IV MgSO₄ in comparison with controls during the first 3 h postoperatively.⁹

The timing of instillation of local anesthetic and adjuvant through the procedure is still debatable. Barczynski et al. recommended early instillation of intraperitoneal local anesthetics before creation of pneumoperitoneum to provide better hemodynamic response and postoperative pain management in comparison with infusion within the closing stages of the procedure. More studies are required to establish the ideal time and the route of administration of MgSO₄ for laparoscopic procedures.

5. Conclusions

Intraperitoneal instillation of MgSO₄ is a safe technique that has better results than intravenous infusion in attenuation of hemodynamic response with pneumoperitoneum, and offers reduced postoperative pain and PONV with laparoscopic mini gastric bypass patients.

6. Limitations

It is not obvious whether magnesium has to be administered along with the actual or ideal bodyweight in obese patients due to the inadequate information on the usage of MgSO₄ in bariatric candidates. We calculated MgSO₄ dosage using actual body weight as was done in several earlier studies. Moreover, the timing of the instillation of the local anesthetic and adjuvants remains to be deduced with clear criteria.

7. Ethics approval and consent to participate

This study was approved by the research ethics committee at the faculty of medicine, Ain Shams University (FMASU M D 235/2020) and registered with Pan African Clinical Trial Registry, identifier: PACTR202111620456298. Written informed consent was obtained from all patients.

8. Availability of data

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

9. Competing interests

The authors declare no conflicts of interest.

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11. References

1. Kizilcik N, Koner O. Magnesium sulfate reduced opioid consumption in obese patients undergoing sleeve gastrectomy: a prospective, randomized clinical trial. *Obes Surg*. 2018 Sep;28(9):2783-2788. [PubMed] DOI: [10.1007/s11695-018-3243-7](https://doi.org/10.1007/s11695-018-3243-7)
2. El Mourad MB, Arafa SK. Effect of intravenous versus intraperitoneal magnesium sulfate on hemodynamic parameters and postoperative analgesia during laparoscopic sleeve gastrectomy-A prospective randomized study. *J Anaesthesiol Clin Pharmacol*. 2019 Apr-Jun;35(2):242-247. [PubMed] DOI: [10.4103/joacp.JOACP_208_18](https://doi.org/10.4103/joacp.JOACP_208_18)
3. Do SH. Magnesium: a versatile drug for anesthesiologists. *Korean J Anesthesiol*. 2013 Jul;65(1):4-8. [PubMed] DOI: [10.4097/kjae.2013.65.1.4](https://doi.org/10.4097/kjae.2013.65.1.4)
4. Aldrete JA. The post-anaesthesia recovery score revisited. *J Clin Anesth*. 1995;7(1):89-91. [PubMed] DOI: [10.1016/0952-8180\(94\)00001-k](https://doi.org/10.1016/0952-8180(94)00001-k)
5. De Oliveira GS Jr, Castro-Alves LJ, Khan JH, McCarthy RJ. Perioperative systemic magnesium to minimize postoperative pain: a meta-analysis of randomized controlled trials. *Anesthesiology*. 2013 Jul;119(1):178-90. [PubMed] DOI: [10.1097/ALN.0b013e318297630d](https://doi.org/10.1097/ALN.0b013e318297630d)
6. Koinig H, Wallner T, Marhofer P, Andel H, Hörauf K, Mayer N. Magnesium sulfate reduces intra- and postoperative analgesic requirements. *Anesth Analg*. 1998 Jul;87(1):206-10. [PubMed] DOI: [10.1097/00005539-199807000-00042](https://doi.org/10.1097/00005539-199807000-00042)
7. Shamim A, Salman W, Gul S. Effect of magnesium sulphate on postoperative pain in laparoscopic cholecystectomy. *Int J Adv Res*. 2015;3(10):813-818. [FreeFullText]
8. Paul S, Biswas P, Bhattacharjee DP, Sengupta J. Effects of magnesium sulfate on hemodynamic response to carbon dioxide pneumoperitoneum in patients undergoing laparoscopic cholecystectomy. *Anesth Essays Res*. 2013 May-Aug;7(2):228-31. [PubMed] DOI: [10.4103/0259-1162.118970](https://doi.org/10.4103/0259-1162.118970)
9. Ali RM, Rabiea AH, Elshalakany NA, El Gindy TM. Effect of intraperitoneal magnesium sulfate on hemodynamic changes and its analgesic and antiemetic effect in laparoscopic cholecystectomy. *Ain-Shams J Anaesthesiol*. 2015;8:153-159. DOI: [10.4103/1687-7934.156661](https://doi.org/10.4103/1687-7934.156661)
10. Marks JL, Ata B, Tulandi T. Systematic review and metaanalysis of intraperitoneal instillation of local anesthetics for reduction of pain after gynecologic laparoscopy. *J Minim Invasive Gynecol*. 2012 Sep-Oct;19(5):545-53. [PubMed] DOI: [10.1016/j.jmig.2012.04.002](https://doi.org/10.1016/j.jmig.2012.04.002)
11. Elfiky M, Stohy A, Ibrahim W, Ibrahim A. Comparative study between intravenous and intraperitoneal magnesium sulphate as adjuvant to general anesthesia for pain management in

- laparoscopic cholecystectomy. *Egyptian J Hosp Med.* 2018;72(11):5695-5704. DOI: [10.21608/ejhm.2018.11553](https://doi.org/10.21608/ejhm.2018.11553)
12. Yadava A, Rajput SK, Katiyar S, Jain RK. A comparison of intraperitoneal bupivacaine-tramadol with bupivacaine-magnesium sulphate for pain relief after laparoscopic cholecystectomy: A prospective, randomised study. *Indian J Anaesth.* 2016 Oct;60(10):757-762. [[PubMed](#)] DOI:
 13. Lysakowski C, Dumont L, Czarnetzki C and Tramèr MR: Magnesium as an adjuvant to postoperative analgesia: A systematic review of randomized trials. *Anesth Analg* 2007;104:1532-9. [[PubMed](#)] DOI: [10.1213/01.ane.0000261250.59984.cd](https://doi.org/10.1213/01.ane.0000261250.59984.cd)