

ORIGINAL ARTICLE

Comparison of Hemodynamic Response after Pneumoperitoneum with Versus without Pre-Emptive Magnesium Sulphate in Patients Undergoing Laparoscopic Cholecystectomy

TOOBA SHAFIQ¹, MAHAM AFZAL RANA², AFSHAN NISAR³, HINA⁴, MUHAMMAD ATHIF AKRAM⁵¹Anesthesia Consultant Anesthetist LGH/PINS, Lahore²Anesthesia Consultant Anesthetist Arif Memorial Hospital Lahore³Assistant Professor of Anesthesia LGH/PINS, Lahore⁴Assistant Professor, Anesthesia and Intensive Care Lahore General Hospital (LGH), Lahore⁵Associate Professor, Anesthesia Department Ali Fatima Hospital/Abu Ammara Medical CollegeCorrespondence to: Tooba Shafiq, Email: toobashafiq@hotmail.com, Cell: +92 331 4814335**ABSTRACT****Objective:** To compare the hemodynamic response after pneumoperitoneum with versus without pre-emptive magnesium sulphate in patients undergoing laparoscopic cholecystectomy.**Study Design:** It was a randomized controlled trial**Setting:** Research was conducted at Department of Anesthesiology Lahore General Hospital, Lahore.**Materials and Methods:** This study involved 104 patients of both genders aged between 18-70 years undergoing laparoscopic cholecystectomy which were randomly divided into two treatment groups. Patients in Group-A received pre-emptive magnesium sulphate while patients in Group-B were received normal saline as placebo. Outcome variable was hemodynamic response to pneumoperitoneum. It was assessed in terms of mean heart rate, mean diastolic and systolic blood pressure after 30 minutes of pneumoperitoneum which were measured and compared between the two groups.**Results:** The mean age of the patients was 44.8±9.2 years while the mean BMI was 25.3±2.7 Kg/m². There were 31 (29.8%) male and 73 (70.2%) female patients with a male to female ratio of 1:2.4. 63 (60.6%) patients belonged to ASA Class-I while 41 (39.4%) patients belonged to ASA Class-II. The mean heart rate (80.8±4.5 vs. 87.7±5.0 bpm; p-value<0.001), mean diastolic BP (77.6±6.7 vs. 84.9±6.0 mmHg; p-value<0.001) and mean systolic BP (133.3±8.2 vs. 140.6±8.9 mmHg; p-value<0.001) were significantly lower after 30 minutes of pneumoperitoneum in patients receiving magnesium sulphate as compared to normal saline.**Conclusion:** Pre-emptive magnesium sulphate attenuated the hemodynamic response of pneumoperitoneum evident from significantly lower mean heart rate and means diastolic and systolic blood pressure after 30 minutes of pneumoperitoneum as compared to controls which advocate its preferred use in future practice.**Keywords:** Pneumoperitoneum, Hemodynamic Response, Magnesium Sulphate**INTRODUCTION**

Laparoscopic surgery has replaced open surgery as the standard of care for several surgical pathologies. But the creation of pneumoperitoneum in the presence of carbon dioxide (CO₂) causes significant hemodynamic problems for patients undergoing anaesthetic treatment in hospitals.¹ Pneumoperitoneum can alter tissue perfusion due to changes in the cardiovascular system, including an increase in mean arterial pressure, a decrease in cardiac output, and an increase in systemic vascular resistance.^{1,2} Patients with ischemic heart disease (IHD), earlier crucial hypertension, or high intraocular / intracranial pressure can be at risk for severe rises in arterial pressure.³ Numerous surgical approaches e.g. use of low intra-abdominal pressure, practice of abdominal wall lift techniques, variation in nature of insufflating gas etc. have been attempts to reduce the hemodynamic changes found with pneumoperitoneum, but all with practical limitations.^{4,5,6} Use of epidural and segmental spinal anaesthesia as well as pharmaceutical therapies such as esmolol, magnesium sulphate and nitroglycerine have been utilised with mixed success in the past.^{7,8,9}

Kamble et al. in 2017 reported that pre-emptive magnesium sulphate attenuated the hemodynamic response after 30 minutes of pneumoperitoneum evident from significantly lower mean heart rate (67.73±7.53 bpm vs. 100.63±16.67 bpm; p-value<0.001), mean systolic blood pressure (117.03±13.89 mmHg vs. 137.03±11.28 mmHg; p-value<0.001) and mean diastolic blood pressure (69.33±11.31 mmHg vs. 85.03±9.26 mmHg; p-value<0.001) in such patients compared with controls in India.¹¹

In another similar study involving Indian population, Dar et al. in 2015 also reported similar significantly lower mean heart rate (80.52±15.86 bpm vs. 89.87±14.84 bpm; p-value<0.05), mean systolic blood pressure (101.61±9.78 mmHg vs. 109.84±18.79 mmHg; p-value=0.035) and mean diastolic blood pressure (65.32±10.35 mmHg vs. 74.42±12.77 mmHg; p-value=0.003) after

30 minutes of pneumoperitoneum in patients with pre-emptive magnesium sulphate, as compared to controls.¹²

In the light of this evidence, a pre-emptive magnesium sulphate can thus attenuate the haemodynamic response after pneumoperitoneum and should be advisable in future practice. Due to lack of local published material on this topic we repeated this study in local population and further confirm the results. If present study results show attenuation of hemodynamic response after pneumoperitoneum with pre-emptive magnesium sulphate in patients undergoing laparoscopic cholecystectomy, it will enable better anesthetic care of laparoscopic procedures in future practice.

MATERIAL AND METHODS

This randomised controlled trial (RCT) was carried out after receiving clearance from the hospital's Institutional Review Board (IRB) at Department of Anesthesiology (LGH) Lahore General Hospital, Lahore from 12/09/2018 to 11/03/2019. Sample size was calculated with an 80 percent power of the test and a 95 percent confidence interval (2-sided) while taking the expected mean SBP after 30 min of pneumoperitoneum to be 101.61±9.78 mmHg and 109.84±18.79 mmHg with pre-preemptive magnesium sulphate in patients who were undergoing a laparoscopic cholecystectomy⁶. Patients of both genders aged between 18-70 years undergoing laparoscopic cholecystectomy with CO₂ pneumoperitoneum (as per operational definition) on elective list were included in this study. Patients with known hypertensive (Blood Pressure≥140/90mmHg on at least two occasions 4 hours apart), obese (BMI≥30kg/m²) patients with known allergy to magnesium sulphate and pregnant females (as per dating scan) were excluded from our study

Using the lottery approach, 104 patients were randomly assigned to one of two groups: group A, the experimental group (magnesium sulphate), and group B, the control group (normal saline). Six hours before to surgery, all of the patients were kept nil

by mouth. Intravenous midazolam 0.02 mg/kg was given to all of the patients as a pre-medication. For analgesia, patients were administered intravenous nalbuphine 0.1 mg/kg after being pre-oxygenated with 100 percent O₂. To assist endotracheal intubation, intravenous Propofol 2 mg/kg and intravenous Atracurium 0.5 mg/kg IV were used for induction. Auscultation verified bilateral air entry, and the endotracheal tube was tightly fastened with adhesive tape. Anesthesia was maintained by a 50:50 mixture of oxygen and air, as well as isoflurane and atracurium 0.1 mg/kg boluses.

Patients in Group-A received magnesium sulphate 50 mg/kg via infusion pump for 5 minutes after intubation, diluted in 20ml normal saline 240ml/hour, but before pneumoperitoneum were formed. Patients in Group-B were given 20 mL of normal saline via infusion pump at a rate of 240 mL/hr. 5 minutes after intubation, but before pneumoperitoneum were developed throughout a 5 minute period. Pneumoperitoneum was created as per operational definition. 30 minutes after pneumoperitoneum hemodynamic response in the form of heart rate, systolic and diastolic blood pressure and demographic information were documented and entered into the provided proforma. All pre-operative evaluation, delivery of anesthesia and measurement of hemodynamic response were done by a single resident. All the collected data was entered and analyzed through SPSS version 20.0. Numerical variables have been presented by mean ±SD. Categorical variables gender has been presented by frequency and percentage. For the purpose of addressing affect modifiers, data have been stratified by BMI, gender, age and ASA class I/II. Independent sample t-test after stratification was used, with a significance level of p0.05 considered significant.

RESULTS

The patients' ages ranged from 38 to 70 years old, with a mean of 44.8±9.2 years. There were 31 (29.8%) male and 73 (70.2%)

female patients with a male to female ratio of 1:2.4. The detail of other demographics is given in Table 1. The mean heart rate (80.8±4.5 vs. 87.7±5.0 bpm; p-value<0.001), mean diastolic BP (77.6±6.7 vs. 84.9±6.0 mmHg; p-value<0.001) and mean systolic BP (133.3±8.2 vs. 140.6±8.9 mmHg; p-value<0.001) were significantly lower after 30 minutes of pneumoperitoneum in patients receiving magnesium sulphate as compared to normal saline as shown in Table 2. Tables 3 show that there was a major difference between the groups based on things like the patient's age, gender, BMI, and ASA class.

Table 1: Characteristics of included patents at baseline

Parameters	Characteristics	Participants
Age (years)	Mean ±SD	44.8±9.2
	38-54 years	78 (75.0%)
	55-70 years	26 (25.0%)
Gender	Male	31 (29.8%)
	Female	73 (70.2%)
BMI	Mean BMI	25.3±2.7
	20-25 Kg/m ²	45 (43.3%)
	25-30 Kg/m ²	59 (56.7%)
ASA Class	Class-I	63 (60.6%)
	Class-II	41 (39.4%)

Table 2: Comparison of Hemodynamic Response between the Groups

After 30 Min Pneumoperitoneum	Magnesium Sulphate n=52	Normal Saline n=52	P-value
Heart Rate (b.p.m)	80.8±4.5	87.7±5.0	<0.001*
Diastolic BP (mmHg)	77.6±6.7	84.9±6.0	<0.001*
Systolic BP (mmHg)	133.3±8.2	140.6±8.9	<0.001*

Independent sample t-test, * observed difference was statistically significant

Table 3: Stratification of mean heart rate (HR), mean diastolic blood pressure (DBP) and mean systolic blood pressure (SBP) after 30 minutes of pneumoperitoneum between the groups

Variables	Subgroups	Mean Heart Rate after 30 Minutes of Pneumoperitoneum		Mean Diastolic Blood Pressure after 30 Minutes of Pneumoperitoneum		Mean Systolic Blood Pressure after 30 Minutes of Pneumoperitoneum		P-value
		Magnesium Sulphate n=52	Normal Saline n=52	Magnesium Sulphate n=52	Normal Saline n=52	Magnesium Sulphate n=52	Normal Saline n=52	
Age	38-54 years	80.7±4.5	88.1±5.1	77.1±6.8	84.8±6.3	133.3±8.3	140.8±9.3	<0.001*
	55-70 years	81.2±4.7	86.6±4.6	79.2±6.6	85.2±5.5	133.5±8.3	140.1±7.6	0.006*
Gender	Male	80.4±5.1	87.5±4.0	77.7±6.6	84.7±6.6	133.6±7.7	140.8±9.6	<0.001*
	Female	80.9±4.3	87.8±5.4	77.6±6.9	84.9±5.8	133.2±8.6	140.5±8.7	<0.001*
BMI	20-25 Kg/m ²	79.9±5.0	88.5±4.0	77.3±6.8	85.4±5.6	131.8±8.7	139.1±8.2	<0.001*
	25-30 Kg/m ²	81.4±4.1	87.1±5.6	77.8±6.8	84.4±6.4	134.5±7.8	141.8±9.3	<0.001*
ASA Class	Class-I	79.7±4.4	87.3±5.1	77.2±6.9	85.9±5.9	134.8±7.7	140.6±9.1	<0.001*
	Class-II	82.6±4.1	88.3±4.9	78.3±6.5	83.3±6.0	131.0±8.7	140.6±8.7	<0.001*

Independent sample t-test, * observed difference was statistically significant

DISCUSSION

It is well-known that the laparoscopic cholecystectomy is one of the most frequently performed laparoscopic procedures in the world. Pneumoperitoneum utilises carbon dioxide (CO₂), which has the potential to cause severe cardiovascular effects.^{14,15} Mean arterial pressure, systemic vascular resistance, and cardiac output all fall as a result of the release of catecholamines and vasopressin. Further reducing cardiac output can be achieved by doing the surgery in reverse Trendelenburg posture.^{16,17}

In the present study, the mean heart rate (80.8±4.5 vs. 87.7±5.0 bpm; p-value<0.001), mean diastolic BP (77.6±6.7 vs. 84.9±6.0 mmHg; p-value<0.001) and mean systolic BP (133.3±8.2 vs. 140.6±8.9 mmHg; p-value<0.001) were significantly lower after 30 minutes of pneumoperitoneum in patients receiving magnesium sulphate as compared to normal saline.

In an Indian study, Shamim et al.¹ (2015) reported that pre-emptive magnesium sulphate attenuated the hemodynamic response and was associated with lower mean heart rate (75.5±8.5 vs. 78.6±6.9 bpm; p-value<0.001), mean diastolic BP

(77.8±8.2 vs. 87.8±7.1 mmHg; p-value<0.001) and mean systolic BP (129.3±8.2 vs. 140.7±6.4 mmHg; p-value<0.001) after 30 minutes of pneumoperitoneum as compared to controls in line with the present study.

In another similar study involving Indian population, Dar et al.⁶ in 2015 also reported similar significantly lower mean heart rate (80.52±15.86 bpm vs. 89.87±14.84 bpm; p-value<0.05), mean systolic blood pressure (101.61±9.78 mmHg vs. 109.84±18.79 mmHg; p-value=0.035) and mean diastolic blood pressure (65.32±10.35 mmHg vs. 74.42±12.77 mmHg; p-value=0.003) after 30 minutes of pneumoperitoneum in patients with pre-emptive magnesium sulphate, as compared to controls.

In a similar Korean study, Jee et al.¹⁸ (2009) also reported similar significant attenuation of hemodynamic response with pre-emptive magnesium sulphate in patients undergoing laparoscopic cholecystectomy with significantly lower mean diastolic BP (84.0±7.0 vs. 94.0±9.0 mmHg; p-value≤0.05) and mean systolic BP (123.0±10.0 vs. 135.0±13.0 mmHg; p-value≤0.05) after 30 minutes of pneumoperitoneum as compared to controls

In an Indian study, Paul et al.¹⁹ (2013) studied 10 male and 20 female patients (m:f, 1:2) with mean age of 43.7±8.6 years and reported that pre-emptive magnesium sulphate was associated with significantly reduced mean heart rate (80.4±8.4 vs. 97.8±11.4 bpm; p-value<0.001) after 30 minutes of pneumoperitoneum. In another Indian study, Kamble et al.⁵ (2017) reported comparable mean age of patients to be 42.8±13.9 years with similar female predominance (male:female, 1:1.3) as observed in the present study. They also reported similar attenuation of hemodynamic response with pre-emptive magnesium sulphate and reported significantly lower mean heart rate (67.7±7.5 vs. 100.6±16.7 bpm; p-value<0.001), mean diastolic BP (69.3±11.3 vs. 85.0±9.3 mmHg; p-value<0.001) and mean systolic BP (117.0±13.9 vs. 137.0±11.3 mmHg; p-value<0.001).

In the current study, we found that pre-emptive magnesium sulphate attenuated the hemodynamic response of pneumoperitoneum evident from significantly lower mean heart rate and means diastolic and systolic blood pressure after 30 minutes of pneumoperitoneum as compared to controls.

CONCLUSION

Pre-emptive magnesium sulphate attenuated the hemodynamic response of pneumoperitoneum evident from significantly lower mean heart rate and means diastolic and systolic blood pressure after 30 minutes of pneumoperitoneum as compared to controls which advocate its preferred use in future practice.

REFERENCES

- Shamim A, Shounthoo RS, Gul S. Effect of magnesium sulphate on intraoperative hemodynamic responses in laparoscopic cholecystectomy. *J Dent Med Sci* 2015;14(10):73-82.
- Maya G, Ramya N, Anzar S, Gangadharan S. Effect of magnesium sulphate in attenuating arterial blood pressure in elective laparoscopic abdominal surgeries. *J Evolution Med Dent Sci* 2017;6(33):2680-3.
- Zarif P, Abdelaal Ahmed MA, Abdelhaq MM, Mikhail HM, Farag A. Dexmedetomidine versus magnesium sulfate as adjunct during anesthesia for laparoscopic colectomy. *Anesthesiol Res Pract* 2016;2016:7172920.
- Bogani G, Martinelli F, Ditto A, Chiappa V, Lorusso D, Ghezzi F, et al. Pneumoperitoneum pressures during pelvic laparoscopic surgery: a systematic review and meta-analysis. *Eur J Obstet Gynecol Reprod Biol* 2015;195:1-6.
- Schietroma M, Pessia B, Stifini D, Lancione L, Carlei F, Cecilia EM, Amicucci G. Effects of low and standard intra-abdominal pressure on systemic inflammation and immune response in laparoscopic adrenalectomy: a prospective randomised study. *Journal of Minimal Access Surgery*. 2016 Apr;12(2):109.
- Hou X, Chen P, Jiang Y. How to choose a suitable intraabdominal pressure level during single-incision laparoscopic surgery in children. *Food Science and Technology*. 2020 Aug 7;41:129-32.
- Greenwood J, Nygard B, Brickey D. Effectiveness of intravenous magnesium sulfate to attenuate hemodynamic changes in laparoscopic surgery: A systematic review and meta-analysis. *JB I Evidence Synthesis*. 2021 Mar 1;19(3):578-603.
- Nygard B, Brickey D, Greenwood J. Intravenous magnesium sulfate to attenuate hemodynamic changes in laparoscopic surgery: a systematic review protocol. *JB I Evidence Synthesis*. 2019 Oct 1;17(10):2152-8.
- Liu M, Liu H, Xie A, Kang GJ, Feng F, Zhou X, Zhao Y, Dudley SC. Magnesium deficiency causes reversible diastolic and systolic cardiomyopathy. *Biophysical Journal*. 2020 Feb 7;118(3):245a.
- Nygard B, Brickey D, Greenwood J. Intravenous magnesium sulfate to attenuate hemodynamic changes in laparoscopic surgery: a systematic review protocol. *JB I Evidence Synthesis*. 2019 Oct 1;17(10):2152-8.
- Kamble SP, Bevinaguddaiah Y, Nagaraja DC, Pujar VS, Anandaswamy TC. Effect of magnesium sulphate and clonidine in attenuating hemodynamic response to pneumoperitoneum in laparoscopic cholecystectomy. *Anesth Essays Res* 2017;11(1):67-71.
- Dar SA, Gupta DD, Deopujari RC, Gomes P. Effect of magnesium sulphate on attenuation of hemodynamic stress responses during laparoscopic abdominal surgeries. *J Anesth Clin Res* 2015;6(12):590-5.
- Sheth PP, Soni B, Kapadia K. Comparative study of intravenous infusion of clonidine and/or magnesium sulphate on haemodynamic stress response to tracheal intubation and pneumoperitoneum during laparoscopic surgery. *Nat J Med Res* 2017;7(1):22-5.
- Hirvonen EA, Poikolainen EO, Pkknen ME, Nuutinen LS. The adverse hemodynamic effects of anesthesia, head-up tilt, and carbon dioxide pneumoperitoneum during laparoscopic cholecystectomy. *Surg Endosc* 2000;14(3):272-7.
- Coccolini F, Catena F, Pisano M, Gheza F, Fagioli S, Di saverio S, et al. Corrigendum to open versus laparoscopic cholecystectomy in acute cholecystitis. Systematic review and meta-analysis. *Int J Surg* 2015;24(9):196-204.
- Rist M, Hemmerling TM, Rauh R, Siebzehrnl E, Jacobi KE. Influence of pneumoperitoneum and patient positioning on preload and splanchnic blood volume in laparoscopic surgery of the lower abdomen. *J Clin Anesth* 2001;13(4):244-9.
- Branche PE, Duperret SL, Sagnard PE, Boulez JL, Petit PL, Viale J, et al. Left ventricular loading modifications induced by pneumoperitoneum. *Anesth Analg* 2008;86(3):482-7.
- Jee D, Lee D, Yun S, Lee C. Magnesium sulphate attenuates arterial pressure increase during laparoscopic cholecystectomy. *Br J Anaesth* 2009;103(4):484-9.
- 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;7(2):228-31