

# Effects of IV Magnesium Sulphate on Hemodynamic Response To Pneumoperitoneum In Laparoscopic Cholecystectomy; A Randomized Control Trial

Abeera Zareen<sup>1</sup>, Syed Fahim Ahmed Gardazi<sup>2</sup>, Muhammad Haroon Anwar<sup>3</sup>, Jawad Zaheer<sup>4</sup>

Assistant Professor<sup>1</sup>, Anesthesiology Trainee<sup>2</sup>, House Officer<sup>3</sup>, Professor of Anesthesiology<sup>4</sup>

(Anesthesiology Intensive Care and Pain medicine, Holy Family Hospital, Rawalpindi, Rawalpindi Medical University)

## Author's Contribution

<sup>1</sup>Conception or design of the work, data collection

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<sup>3,4</sup>Critical revision, analysis and Active Participation in active methodology

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## Address of Correspondent

Dr. Abeera Zareen

Assistant Professor

Anesthesiology, Intensive Care

and Pain medicine, Holy Family

Hospital, Rawalpindi, Rawalpindi

Medical University

abeerajsk@gmail.com

## ABSTRACT

**Objective:** To determine the effect of IV Magnesium sulphate (MgSO<sub>4</sub>) in attenuating the hemodynamic effects of pneumoperitoneum.

**Methodology:** Our single blind randomized control trial (based on computer generated randomize allocation) was carried out at Holy Family Hospital and included 60 patients, not allergic to MgSO<sub>4</sub> and belonging to the American Society of Anesthesiology (ASA) class 1 and 2. Patients were divided into two groups with Intervention group (M group) receiving 30 mg/kg of MgSO<sub>4</sub> and the control group (C group) receiving a placebo. Hemodynamic parameters were then measured at different points of time during surgery. Data was collected and analyzed by using statistical package for the social sciences (SPSS) version 25.0.

**Results:** Out of 60 patients selected 86.7% were females while 13.3% were males. Mean age was 35.78(SD=8.26). As compared to C group, patients belonging to M group had significantly lower heart rate, systolic and diastolic blood pressure at 15 minutes, after release of pneumoperitoneum and at extubation with p values less than 0.05.

**Conclusion:** Our study concludes that 30 mg/kg of MgSO<sub>4</sub> given as a bolus just before creation of pneumoperitoneum protect against its possible adverse hemodynamic effects.

**Keywords:** Intravenous, Laparoscopic Cholecystectomy, MgSO<sub>4</sub>, Pneumoperitoneum,

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## Introduction

Symptomatic cholelithiasis is one of the commonest presentations to the surgical department with laparoscopic cholecystectomy is the treatment of choice for symptomatic cholelithiasis. About 500,000 laparoscopic cholecystectomies are performed in the United States each year.<sup>1</sup> Incidence of cholelithiasis and cholecystectomy is greater among females.<sup>2,3</sup> Laparoscopic cholecystectomy offers less wound access trauma/pain, less disfigurement, reduced operating times and length of hospital stay.<sup>4</sup>

Pneumoperitoneum created during laparoscopic cholecystectomy results in the release of catecholamines and vasopressin which ultimately increases the blood pressure, heart rate and systemic vascular resistance.<sup>5</sup> Raised blood pressure increases the chance of bleeding

from surgical bed which adversely affects the view during the laparoscopic procedure.<sup>4</sup> Intraoperatively altered hemodynamic profile adversely affects the myocardium. In a study by Abbott et al intra-operative tachycardia was associated with myocardial injury after non-cardiac surgery (odds ratio 1.27 and p value <0.01).<sup>6</sup> Similarly intra-operative systolic blood pressure > 160 mm of Hg was associated with myocardial infarction (odds ratio 1.34 and p value 0.02).<sup>6</sup> Furthermore, gallstones and in particular cholesterol type of gallstones which commonly occur in females and elderly patient, are associated with a number of co morbidities such as obesity, metabolic syndrome, diabetes mellitus and hypertension.<sup>7</sup> Obesity, diabetes mellitus, metabolic syndrome and hypertension are well known risk factors for cardiovascular disease. Thus one can easily understand how the altered

hemodynamics of pneumoperitoneum can jeopardize the already stressed myocardium due to co-morbid.

Therefore, it is one of the foremost responsibilities of the anesthetist to attenuate the hemodynamic effects of pneumoperitoneum during the surgical procedure. One way to attenuate the adverse hemodynamic effects is by using Magnesium sulphate (MgSO<sub>4</sub>), a drug with wide range of actions.<sup>8</sup> Magnesium is found to have a beneficial effect on blood pressure and cardiovascular disease.<sup>9, 10</sup> MgSO<sub>4</sub> acts as a potent vasodilator, calcium antagonist, and it inhibits catecholamine release and their receptors.<sup>11</sup>

Our study aimed to evaluate the effect of intravenous magnesium sulphate on attenuating the adverse hemodynamic effects of pneumoperitoneum created during laparoscopic cholecystectomy as a primary outcome measure.

## Methodology

After obtaining approval from the Institutional Ethical Forum, this randomized, single blind control trial was conducted at the department of anesthesiology, Holy Family Hospital over a period of 6 months. 60 patients undergoing elective cholecystectomy and fulfilling the inclusion criteria (25-45 years of age with no known allergy to MgSO<sub>4</sub> and belonging ASA class 1 and 2) were allocated to either M or C group with the help of computer-generated random number. The sample size was calculated using Open-Epi calculator and two-sided significance level (1-alpha) was 95, power (1-beta, % chance of detecting) was 80, Ratio of sample size Unexposed/Exposed was 1, percent of Unexposed with Outcome was 5, percent of exposed with outcome was 59, Odds Ratio was 27, Risk/Prevalence Ratio was 12, Risk/Prevalence difference was 54 and Sample Size: 30 in each group so 30+30=60.

Patients excluded from the study were those belonging to either ASA grade III & IV, who refused, were on calcium channel blockers, or had hepatic, renal or cardiovascular dysfunction, who received antihypertensive during surgery due to acute severe hemodynamic fluctuations and in whom laparoscopy was converted to open procedure. Included patients had their pre-anesthetic checkup done, one day before surgery. Detailed history, baseline HR, BP, respiratory rate (RR), and systemic examination was done during pre-anesthetic workup. Routine investigations including Complete blood picture (Blood CP), liver function tests (LFT), renal function tests (RFT), prothrombin time (PT), activated partial thromboplastin

time (aPTT), complete urine examination, random blood sugar (RBS), electrocardiography (ECG) and chest x-ray were performed. Informed and valid written consent were obtained for conduct of the study as well as for the administration of general anesthesia. All patients were kept fasting overnight. Upon arrival to operation theatre ECG, pulse oximetry, noninvasive blood pressure (NIBP) and baseline vital parameters like heart rate, mean arterial pressure (MAP), and arterial oxygen saturation with help of pulse oximeter (SpO<sub>2</sub>) were recorded. An intravenous line was maintained. Patients were induced with 0.1 mg/kg of nalbuphine and propofol 2 mg/kg. Endotracheal intubation was facilitated by muscle relaxant atracurium 0.5mg/kg. Just before the generation of pneumoperitoneum group M patients received magnesium sulfate 30 mg/kg intravenously as a bolus and group C received placebo (0.9% saline). The study medication was prepared in identical 20 ml syringe: 8 ml sterile water was added to 12 ml magnesium sulfate (6000 mg) for group M patients (1 ml = 300 mg). Study medication was prepared by an anesthesiologist who was blinded to the computer-generated randomization schedule. Patients received one of the above said solutions as a bolus intravenously; immediately before pneumoperitoneum. Anesthesia was maintained with 50% O<sub>2</sub>, 50% air, 1 MAC Isoflurane and Atracurium. CO<sub>2</sub> was insufflated into the peritoneal cavity to create pneumoperitoneum. Intra-abdominal pressure (IAP) was maintained to 12 mmHg throughout the laparoscopic procedure. All the patients were positioned in a head-up tilt for about 15°. The patients were mechanically ventilated to keep ETCO<sub>2</sub> between 35-40 mmHg. Vital monitoring was done at 15 minutes interval, till end of the operation.

In case of acute severe hemodynamic fluctuations, the following medical interventions were given: For bradycardia (heart rate < 60 beats/min), i.v. bolus dose of 0.6 mg inj. atropine; for hypotension (MAP < 60 mmHg) increased rate of infusion of i.v. fluid and/or i.v. bolus dose of inj. phenylephrine, and for hypertension (MAP > 110 mmHg) i.v. bolus dose of inj. labetalol.

At the end of the operation, ondansetron 4 mg was administered for prophylaxis against nausea and vomiting. Residual neuromuscular blockade was reversed by an appropriate dose of neostigmine along with glycopyrrolate and tracheal extubation was performed. Patients were observed for any adverse events like bradycardia, hypotension and hypertension during the postoperative period in post anesthesia care unit.

During the study, data was collected according to a self structured questionnaire having 2 parts. Collected data was entered onto statistical package for the social sciences (SPSS) version 25.0 and analysis was done at Holy Family Hospital, Rawalpindi. Mean age and weight were calculated. Frequencies of qualitative variables were calculated. Kolmogorov smirnov test was utilized to check the normality of the quantitative variables. Mann Whitney U test was applied to find association between hemodynamic parameters and the group of patients. A p-value of less than 0.05 was considered to be significant.

## Results

Our single blind randomized control trial compared the efficacy of Magnesium sulphate with placebo, in controlling the hemodynamic alterations caused by pneumoperitoneum.

Out of 60 patients, 86.7% of the patients were females while 13.3% were male. The mean age was 35.78 years (SD=8.26) and the mean weight was 64.75 kg (SD=8.56).

Before generation of pneumoperitoneum, no statistical difference was found between hemodynamic profiles of the two groups (p value > 0.05). However, after generation of pneumoperitoneum, the hemodynamic parameters of patients who were pre-medicated with Magnesium sulphate were significantly lower than the patients belonging to the control group with p values at different point of times being less than 0.05. The results are elaborated in table I.

## Discussion

During the generation of pneumoperitoneum, carbon dioxide insufflation lead to catecholamine release resulting in tachycardia and hypertension.<sup>5</sup> Various pharmacological agents can be used to manage the possible hemodynamic alterations caused by

pneumoperitoneum. Our study employs the use MgSO<sub>4</sub> in attenuating the possible adverse hemodynamic effects of pneumoperitoneum.

In our study before a generation of pneumoperitoneum there was no statistically significant difference among the two groups (p value > 0.05). However, after generation of pneumoperitoneum, as compared to the control group the M group had significantly lower values of heart rate, systolic and diastolic blood pressure. Our findings are supported by several studies.<sup>12-14</sup> In our study the systolic and diastolic blood pressures of the M group were significantly lower than C group at 15 minutes after generation pneumoperitoneum till extubation (p value <0.05). Bansal et al found a significant fall in both systolic and diastolic blood pressure 10 minutes after generation of pneumoperitoneum till extubation, among patients belonging to M (MgSO<sub>4</sub>) group as compared to C (Normal saline) group (p value <0.05).<sup>12</sup> Similarly, MgSO<sub>4</sub> was found to have a beneficial effect on controlling the possible adverse hemodynamic effects of pneumoperitoneum.<sup>13</sup>

Paul et al found significant fall in MAP at 15 minutes after generation of pneumoperitoneum till extubation, among MgSO<sub>4</sub> group patients as compared to control group (p value <0.05).<sup>14</sup>

In our study, statistically significant fall in heart rate of M group patients were seen at 15 minutes after generation of pneumoperitoneum, after release of pneumoperitoneum and at extubation (p value < 0.05). Kamble et al in their study compared the effect of pneumoperitoneum on heart rate in three different groups with NS group receiving placebo i.e. Normal saline, M group receiving MgSO<sub>4</sub> and C group receiving Clonidine.<sup>15</sup> Kamble et al found that Heart rate was significantly higher in NS group than M and C groups (p value <0.05) at 5 to 40 minutes after pneumoperitoneum and after release of pneumoperitoneum (p value <0.001) and heart rate was

**Table I: Comparison of hemodynamic parameters during laparoscopic cholecystectomy**

Time	Group	SBP	P value for SBP	DBP	P value for DBP	Heart rate	P value for Heart rate
Before pneumoperitoneum	M	125.71(6.81)	0.21	72.56(4.91)	0.37	81.56(7.25)	0.079
	C	128.94(5.82)		78.24(6.24)		87.92 (6.57)	
15 minutes after pneumoperitoneum	M	121.63 (6.18)	0.000	76.47(7.65)	0.000	79.60(9.13)	0.014
	C	133.47 (8.29)		85.10(4.89)		85.70(8.10)	
After release of pneumoperitoneum	M	119.67(5.94)	0.000	76.77 (5.72)	0.000	78.80(6.94)	0.000
	C	128.50(5.94)		80.33(7.67)		88.13(9.21)	
At extubation	M	125.47(9.18)	0.000	79.80(7.08)	0.002	81.50(7.27)	0.000
	C						

SBP= Systolic Blood pressure DBP= Diastolic Blood pressure M group= MgSO<sub>4</sub> group C group= Control group

more significantly reduced in M group as compared to C group (p value <0.001).<sup>15</sup>

Ishrat et al and Kamble et al in their studies used 50mg/kg of MgSO<sub>4</sub> in attenuating the hemodynamic response to pneumoperitoneum.<sup>12, 15</sup> However we found 30 mg/kg of MgSO<sub>4</sub> to be equally effective. 30 mg/kg of MgSO<sub>4</sub> was found to be effective in attenuating hemodynamic response to pneumoperitoneum by Bansal et al and Paul et al.<sup>11, 12</sup> In a meta-analysis done by Zhang J et al, 50mg/kg of MgSO<sub>4</sub> was found to be effective in reducing systolic and diastolic blood pressure at 10 and 30 minutes while it reduced heart rate at 30 minutes only.<sup>16</sup> However our analysis revealed that a lower dose of MgSO<sub>4</sub> (30 mg/kg) was as effective as higher dose of MgSO<sub>4</sub> (50 mg/kg) at attenuating hemodynamic response of pneumoperitoneum from 15 minutes after generation of pneumoperitoneum till extubation.

## Conclusion

Our study recommends the use of 30mg/kg of MgSO<sub>4</sub>, given as a bolus just before generation of pneumoperitoneum to effectively counteract its possible hemodynamic alterations.

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