

Comparison of Magnesium Sulphate Vs Placebo for Hemodynamic Stability during Laparoscopic Cholecystectomy

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ABSTRACT

Background: Laparoscopic cholecystectomy is a commonly performed surgical procedure. In comparison to open cholecystectomy, there is less post-operative pain, less respiratory complications, early recovery and shorter hospital stay. In spite of all these advantages, laparoscopic cholecystectomy can have a few hemodynamic adverse effects during surgery. Carbon dioxide is used to create Pneumoperitoneum during laparoscopic surgery that can cause increase in arterial blood pressure, heart rate, and peripheral vascular resistance.

Aim: To compare the efficacy of MgSO₄ versus placebo in controlling the rise in arterial blood pressure during laparoscopic cholecystectomy after creation of CO₂ pneumoperitoneum.

Methods: This was a randomized controlled trial conducted in department of Anesthesia, Mayo Hospital, Lahore. Total 180 patients were included in the study and randomly divided in to two groups. Each group contained 90 patients. Immediately before creation of Carbon dioxide pneumoperitoneum, the placebo group (C-Group) received N/S 0.5ml/kg and Magnesium sulphate group (MS-Group) received 0.5ml/kg of 10% MgSO₄ (50mg/kg) over 2-3 mins. CO₂ pneumoperitoneum was maintained at pressure of 14mmHg. At completion of surgery, the patients were given reversal (Neostigmine 0.05mg/kg, and Atropine 0.014mg/kg) after adequate respiratory rate and tidal volume has been established. Tracheal extubation was done when patient became fully awake. Oxygen was given via face mask for ten minutes. Systolic arterial pressure and diastolic arterial pressure were noted at following intervals; before creation of PP, at 5,10,20, and 30 mins after creation of PP.

Results: The mean age of all patients was 40.08±8.31 years while mean age of patients in MgSO₄ and placebo group was 39.78±8.14 years and 40.38±8.15 years respectively. In Magnesium Sulphate group a total of 80(88.9%) cases and in placebo group 32(35.6%) cases had efficacy. The efficacy was significantly higher in MgSO₄ group as compared to placebo group, p-value < 0.05.

Conclusion: The cases who received I/V Magnesium Sulphate had higher efficacy in terms of blood pressure control after Carbon dioxide pneumoperitoneum when compared to placebo group.

Keywords: Hemodynamic, laparoscopic surgery, magnesium sulfate, pneumoperitoneum

INTRODUCTION

Cholecystectomy is a commonly performed operation in general surgery practice. It is performed both by open method and laparoscopic method. In open method the incision is bigger which results in more post-operative pain, longer hospital stay and respiratory complications. On the other hand, in laparoscopic cholecystectomy there is less post-operative pain, less pulmonary impairment, early recovery and shorter hospital stay¹. In spite of all these benefits, laparoscopic cholecystectomy is also associated with a few hemodynamic adverse effects intra-operatively. Such as decrease in cardiac output, increase in heart rate and blood pressure.

In laparoscopic cholecystectomy, CO₂ is insufflated in to the peritoneum at a pressure of 13-17mmHg to distend abdominal cavity and for better visualization of abdominal organs. This CO₂ pneumoperitoneum (PP) can lead to increase in arterial blood pressure. This increase in blood pressure is due to hypercarbia, release of catecholamine and vasopressor response. This increase in blood pressure can be hazardous in patients with hypertensions and IHD.

Different drugs like alpha-adrenergic agonists (clonidine), beta-blockers, opioids and vasodilators have been used to attenuate increase in blood pressure during pneumo-peritoneum.

Magnesium is one of major cations found in body. It also reduces the blood pressure by causing vasodilatation² and by inhibiting the release of catecholamines³.

Paul S conducted a study and showed that in laparoscopic surgery after Carbon dioxide pneumoperitoneum creation, using IV Magnesium sulphate results in better hemodynamic stability when compared with placebo⁴.

Magnesium sulphate also has potentiating effect on peri-operative analgesia and muscle relaxation. It reduces the use of intra-operative anesthetics. It can also act as antiepileptic and bronchodilator. It is also cost effective⁵.

As MgSO₄ causes vasodilatation and protects the body against catecholamines release and attenuates hemodynamic stress response. So it is assumed that Magnesium sulphate can attenuate increase in blood pressure after CO₂ pneumo-peritoneum. This study was conducted to compare the efficacy of Mg SO₄ versus placebo in attenuating the rise in blood pressure during laparoscopic cholecystectomy after creation of CO₂ pneumoperitoneum.

MATERIAL AND METHOD

This randomized controlled trial was conducted in the Department of Anesthesia Mayo Hospital, Lahore. Total 180 patients were included in the study and randomly divided in to two groups. Each group contained 90 patients.

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MgSO₄ group (MS-group) and Placebo group (C-group). Eighty percent power of test with 5% level of significance were taken to calculate the sample size and taking expected percentage of efficacy (in term of patients with rise in Diastolic Arterial pressure due to CO₂ pneumoperitoneum) in both groups i.e. 58.8% in MgSO₄ group vs. 40% in placebo group during laparoscopic cholecystectomy. Patients of ASA 1, ages 25-55 years , either gender, scheduled for laparoscopic cholecystectomy were included in this study. The patients with history of Hypertension, DM, IHD and allergy to MgSO₄ were excluded.

Data collection procedure: After approval from Hospital Ethical committee, the study was conducted in General Surgery Operation Theatres of Mayo Hospital Lahore. Informed consent was taken. Procedure was explained to all patients. The patients were shifted to operation theatre with NPO of 10 hrs patients were divided randomly into 2 groups “P and M”. Throughout the procedure, the patients were monitored for ECG, Heart Rate, Blood Pressure, Saturation of Oxygen and End-Tidal CO₂. Pre-Oxygenation was done. The induction was done with Inj. Propofol 2mg/kg, Inj. Succinylcholine 2mg/kg. Endo-Tracheal tube was passed. The muscle relaxant Inj. atracurium was given as bolus 0.5mg/kg and repeated after every 20-30 mins. The maintenance of anesthesia was done by O₂, N₂O, Isoflurane (0.5-1)%. The tidal volume and gas flow was adjusted and maintained according to weight and age of patient. Intermittent Positive Pressure Ventilation (IPPV) was given. Immediately before creation of Carbon dioxide Pneumo-peritoneum, the placebo group (P-Group) received N/S 0.5ml/kg and Magnesium group (M-Group) received 0.5ml/kg of 10% MgSO₄ (50mg/kg) over 2-3 mins. Carbon dioxide pneumo peritoneum was maintained at pressure of 14 mmHg . At completion of surgery, the patients were given revesal(Neostigmine 0.05mg/kg, and Atropine 0.014mg/kg) after adequate respiratory rate and tidal volume has been established. Tracheal extubation was done when patient became fully awake. Oxygen was given via face mask for ten mins. Systolic arterial pressure SAP and diastolic arterial pressure DAP were noted at following intervals; before creation of PP, at 5,10,20, and 30 mins after creation of PP . Efficacy was labeled as per operational definition.

Statistical analysis: After collection data was analysed by SPSS 20. Quantitative variables like age and blood pressure were presented as mean ± S.D. Qualitative variables like gender and efficacy were presented as frequency and percentage. Efficacy was compared in both groups using chi square test and p-value ≤ 0.05 was considered as significant. Data was stratified for age, gender and obesity to address the effect modifier. Post stratification chi square test was applied and p-value ≤ 0.05 was considered as significant.

RESULT

One hundred and eighty cases were scheduled for lapa4roscopic cholecystectomy. The mean age of all patients was 40.08±8.31 years while mean age of patients in MS and placebo group was 39.78±8.14 years and 40.38±8.15 years respectively(Table 1).

Table -1: Descriptive Statistics of age (years) in both groups

Study groups	Mean	S.D	Min.	Max.
Age (years)				
MS (n=90)	39.78	8.14	25	55
Placebo (n=90)	40.38	8.51	25	55
Total (n=180)	40.08	8.31	25	55

Table -2: Frequency distribution of gender in both groups

Gender	Study group		Total
	MS	Placebo	
Male	42(46.7%)	31(34.4%)	73(40.6%)
Female	48(53.3%)	59(65.6%)	107(59.4%)
Total	90(100%)	90(100%)	180(100%)

Table -3: Descriptive Statistics of BMI in both groups

Study groups	Mean	S.D	Min.	Max.
BMI				
MS (n=90)	28.04	5.52	18.4	37.4
Placebo (n=90)	28.44	5.95	18.5	38.1
Total (n=180)	28.24	5.73	18.4	38.1

Table 4: Descriptive Statistics of systolic blood pressure in both groups

Study groups	Mean	S.D	Min.	Max.
Diastolic BP - Baseline				
MS (n=90)	116.90	7.98	96	128
Placebo (n=90)	114.63	7.73	96	128
Total (n=180)	115.77	7.92	96	128
Diastolic BP – after 5 minutes				
MS (n=90)	116.94	7.52	97	138
Placebo (n=90)	121.62	8.42	106	139
Total (n=180)	119.28	8.30	97	139
Diastolic BP – after 10 minutes				
MS (n=90)	117.03	8.24	99	139
Placebo (n=90)	124.04	8.47	108	141
Total (n=180)	120.54	9.04	99	141
Diastolic BP – after 20 minutes				
MS (n=90)	117.11	8.33	98	141
Placebo (n=90)	125.62	8.97	105	143
Total (n=180)	121.37	9.63	98	143
Diastolic BP – after 30 minutes				
MS (n=90)	117.28	8.46	96	140
Placebo (n=90)	127.34	9.66	106	146
Total (n=180)	122.31	10.37	96	146

There were 73(40.6%) male and 107(59.4%) female patients. In MS group there were 42(46.7%) male and 48(53.3%) female while in placebo group there were 31(34.4%) male and 59(65.6%) female (Table -2).The mean BMI in MS group and placebo group was 28.04± 5.52 and 28.44 ± 5.95 respectively(Table -3).The mean systolic blood pressure (SBP)at baseline in MS group was 116.90 ±7.98 and in Placebo group was 114.63±7.73. At 5th minutes mean SBP in MS group was 116.94±7.52 and in Placebo group was 121.62 ± 8.42. The mean SBP at 10th minute in MS group was 117.03±8.24 and in Placebo group was 124.04±8.47. The mean SBP at 20th minute in MS group was 117.11±8.33 and in Placebo group was 125.62±8.97. The mean SBP at 30th minute in MS group was 117.28 ± 8.46 and in Placebo group was 127.34±9.66 (Table 4). The mean diastolic blood pressure(DBP) at baseline in MS group was 73.53±5.738 and in placebo group was 73.22± 5.548. At 5th minute the mean DBP in MS group was 74.10±5.653 and in placebo group was 78.38± 6.747. The mean DBP at 10th minute in MS group

was 74.08±5.746 and in placebo group was 79.89±6.521. The mean DBP at 20th minutes in MS group was 74.01±6.247 and in placebo group was 81.11±6.556. At 30th minute the mean DBP in MS group 73.79± 6.678 and in placebo group was 82.02±7.564 (Table -5). In MS group a total of 80(88.9%) cases and in placebo group 32(35.6%) cases had efficacy. The efficacy was significantly higher in MS group as compared to placebo group, p-value < 0.05 (Table -6). When data was stratified for age, gender and BMI, we found higher efficacy in MS group as compared to placebo group in each strata, p-value < 0.05 (Table -7,8,9).

Table -5: Descriptive Statistics diastolic blood pressure in both groups

Study groups	Mean	S.D	Min.	Max.
Diastolic BP - Baseline				
MS (n=90)	73.53	5.738	59	86
Placebo (n=90)	73.22	5.548	59	86
Total (n=180)	73.38	5.630	59	86
Diastolic BP – after 5 minutes				
MS (n=90)	74.10	5.653	60	91
Placebo (n=90)	78.38	6.747	68	91
Total (n=180)	76.24	6.567	60	91
Diastolic BP – after 10 minutes				
MS (n=90)	74.08	5.746	61	87
Placebo (n=90)	79.89	6.521	67	90
Total (n=180)	76.98	6.786	61	90
Diastolic BP – after 20 minutes				
MS (n=90)	74.01	6.247	62	89
Placebo (n=90)	81.11	6.556	68	91
Total (n=180)	77.56	7.310	62	91
Diastolic BP – after 30 minutes				
MS (n=90)	73.79	6.678	59	87
Placebo (n=90)	82.02	7.564	68	95
Total (n=180)	77.91	8.226	59	95

Table -6: Comparison of efficacy in both groups

Efficacy	Study group		Total
	MS	Placebo	
Yes	80(88.9%)	32(35.6%)	112(62.2%)
No	10(11.1%)	58(64.4%)	68(37.8%)
Total	90(100%)	90(100%)	180(100%)

p-value < 0.001

Table -7: Comparison of efficacy in both groups with respect to age groups

Efficacy	Study group		P value
	MS	Placebo	
Age group 25-35 years			
Yes	22(84.6%)	10(33.3%)	<0.001
No	4(15.4%)	20(66.7%)	
Age group 36-55			
Yes	58(90.6%)	22(36.7%)	<0.001
No	6(9.4%)	38(63.3%)	

Table 8: Comparison of efficacy in both groups with respect to gender

Efficacy	Study group		P value
	MS	Placebo	
Male			
Yes	37(88.1%)	6(19.4%)	<0.001
No	5(11.9%)	25(80.6%)	
Female			
Yes	43(89.6%)	26(44.1%)	<0.001
No	5(10.4%)	33(55.9%)	

Table -9: Comparison of efficacy in both groups with respect to BMI

Efficacy	Study group		P value
	MS	Placebo	
BMI >30			
Yes	34(91.9%)	13(34.2%)	<0.001
No	3(8.1%)	25(65.8%)	
BMI ≤ 30			
Yes	46(86.8%)	19(36.5%)	<0.001
No	7(13.2%)	33(63.5%)	

DISCUSSION

Laparoscopic cholecystectomy is considered as a surgical treatment of choice for symptomatic cholelithiasis. However, it is not completely safe in patients with comorbidities. Alterations in hemodynamics during laparoscopy and creation of PP can be potentially hazardous. Pneumoperitoneum for laparoscopic surgery increases BP,HR, and SVR⁶. Carbon dioxide PP created for laparoscopic cholecystectomy leads to alterations in cardiovascular and respiratory physiology and stress response. It may cause increase in mean arterial pressure (MAP) with no significant change in HR, decrease in cardiac output and increase in SVR. There are many factors which may result in decrease in cardiac output⁷.

There are practical limitations of various techniques used for laparoscopic surgery like change of gas for creation of PP, decrease intra abdominal pressure and use of abdominal wall lift methods⁸. Anaesthetic techniques like use of epidural anesthesia alone or combined with general anesthesia and drugs like nitroglycerine and beta adrenergic antagonist esmolol, have been used to attenuate the hemodynamic response to pp with varying success⁹.

Release of catecholamine from adrenergic nerve endings and adrenal medulla is blocked by MgSO₄. Intravenous MgSO₄ attenuate presser response associated with laryngoscopy and endotracheal intubation. When given intravenously it also causes vasodilatation by its direct action on blood vessels, and in high doses it counteracts vasopressin mediated vasoconstriction¹⁰. Magnesium sulphate blocks N-methyl d-aspartate (NMDA) receptors and prevents calcium entry into the cell. At different voltage-gated channels Magnesium acts as an antagonist to calcium¹¹. Administration of MgSO₄ through different routes has been used in anesthetic practice for its analgesic effects. Magnesium sulphate has been used to attenuate the hemodynamic response associated with pneumoperitoneum and improve the quality of patient recovery¹².

Recently a randomized, placebo controlled study was designed to find the effect of intravenous MgSO₄ on hemodynamic changes induced by PP in patients undergoing laparoscopic cholecystectomy. The study was performed on 52 patients of ASA I or II aged 20-70 years scheduled for laparoscopic cholecystectomy¹³. In this study we included patients of ASA-I with average age 40.08±8.31 years while mean age of patients in MgSO₄ and placebo group was 39.78±8.14 years and 40.38±8.15 years respectively. Overall there were 73(40.6%) male and 107(59.4%) female patients.

In another randomized, double-blinded study ninety patients of ASA I and II were scheduled for elective laparoscopic cholecystectomy to investigate the hemodynamic response in three different regimes. Patients were divided into three groups of thirty patients each. Patients in Group C were given clonidine 1µg/kg diluted in 10 ml normal saline over 10 min, Group M received injection MgSO₄, 50 mg/kg diluted in 10 ml normal saline over 10 min, Group NS received 10 ml normal saline intravenously over 10 min, prior to creation of pneumoperitoneum. Hemodynamic parameters were recorded before induction of anaesthesia, at the end of magnesium sulfate/clonidine/saline administration and before and after creation of pneumoperitoneum at 5 min, 10 min, 20 min, 30 min, and 40 min. The study showed that systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and heart rate (HR) were all significantly higher in NS group compared to M and C group. The DBP, MAP, and HR were significantly lower in M group when compared with C Group. However mean extubation time and time to respond to vocal commands were significantly prolonged in the M group. The study has concluded that both magnesium and clonidine attenuate the hemodynamic response to pneumoperitoneum. However, magnesium 50 mg/kg is superior to clonidine 1µg/kg in suppressing hemodynamic response to pneumoperitoneum¹⁴. In current study our objective was to compare efficacy of magnesium Sulphate in terms of control in blood pressure so we found that in M group a total of 80(88.9%) cases and in placebo group 32(35.6%) cases had efficacy. When compared to placebo group the efficacy was significantly higher in M group, p-value < 0.05. Another study conducted by Paul S, Biswas P, Bhattacharjee DP and Sangupta J, in 2013, showed that in laparoscopic surgery after Carbon dioxide PP using IV MgSO₄ i.e. efficacy (41.2%) 58.8% patients had more than 20% rise in systolic blood pressure than baseline and 41.2% (58.8% efficacy) had more than 20% rise in diastolic blood pressure than baseline value compared when placebo is used value are higher i.e., 86.7% and 60% efficacy 13.3% and 40%⁴.

Likewise another randomized, double-blind, prospective study was undertaken to evaluate the effect of MgSO₄ in attenuating the stress responses associated with laparoscopic abdominal surgeries. Sixty two patients who underwent laparoscopic abdominal surgery were randomly divided in to two groups, group I and group II. Five minutes after intubation but before creation of PP, the magnesium group (group I) received MgSO₄, 50 mg/kg diluted in normal saline to total volume of 20 ml at 240 ml/hour over 5 minutes. The control group (group II) received same amount of normal saline. The result of the study has showed that heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure were significantly less in group I with p< 0.05. Extubation time was more in Group I but had no statistical significance. Hence the study stated that the MgSO₄ attenuates hemodynamic stress response in laparoscopic abdominal surgeries¹⁵.

A prospective randomized, double-blind study was conducted in 60 patients scheduled for laparoscopic cholecystectomy to find the attenuating response on hemodynamic parameters, analgesic and antiemetic

properties of MgSO₄. Patients were randomly divided into two groups: group M and group C. Patients in group M received 20 ml of 10% MgSO₄ intraperitoneally after creation of PP, whereas patients in group C were given 20ml of 0.9% sodium chloride intraperitoneally. The result showed that hemodynamic parameters were significantly higher in group C compared with group M at 10, 20, and 30 min after PP, and at the time of extubation. Recovery characteristics in terms of extubation time (9.70±1.12 vs. 6.77 ± 0.73), emergence time (19.83±1.44 vs. 15.93±1.60), and time to reach full Aldrete score (43.03±8 vs. 21.4± 4.7) were significantly longer in group M compared with group C. Mean pain scores (visual analog scale) were significantly lower in group M compared with group C during the first 6 postoperative hours, and the time to first analgesic request was longer in group M (9.2±3 h) compared with group C (2.4±1.3 h). Postoperative nausea was significantly higher in group C (63.3%) compared with group M (36.6%). There was no incidence of vomiting in group M compared with 13.3% in group C. The study concluded that intraperitoneal instillation of MgSO₄ attenuated the hemodynamic stress response to PP, as well as reduced postoperative pain, nausea, and vomiting in patients undergoing laparoscopic cholecystectomy¹⁶.

In 2013, Paul et al conducted a randomized, double blind study in patients undergoing laparoscopic cholecystectomy to find the efficacy of Magnesium sulphate to attenuate adverse hemodynamic response to creation of pneumoperitoneum. Two groups consisting of 30 patients in each group (18-65 years of age), planned for laparoscopic cholecystectomy were included in the study. Patients in Group M received MgSO₄ 30 mg/kg intravenously whereas patients in Group C were given same volume of 0.9% saline before creation of PP. Their study has shown that MAP and HR remained significantly lower during pneumoperitoneum in patients of group M as compared to patients in group C. Intravenous labetalol was required in 40% (12 out of 30) of the patients in group C to control intraoperative hypertension. The study suggested that MgSO₄ given before creation of pneumoperitoneum decreased the undesirable hemodynamic response and resulted in hemodynamic stability during laparoscopic surgery¹⁷.

A study was conducted to find haemodynamic stress response attenuating affect of MgSO₄ when given intravenously before creation of PP during laparoscopic cholecystectomy. The study was conducted on thirty two patients scheduled for laparoscopic cholecystectomy. Patients were randomly allocated to one of the two groups; Patients in C group were given saline, and in M group received MgSO₄, 50 mg/kg immediately before creation of PP. Blood pressure, HR, serum magnesium, plasma renin activity (PRA), catecholamine, cortisol, and vasopressin levels were measured. The result of the study has shown that Systolic and diastolic arterial pressures were greater in the control group (P,0.05) than in the magnesium group at 10, 20, and 30 min after creation of PP. Norepinephrine or epinephrine levels were higher in the control group than in the magnesium group at 5 [211 (37) vs 138 (18)] or 10 min [59 (19) vs 39 (9)] post PP, respectively (P,0.05). In the control group, vasopressin levels were higher compared with the magnesium group at 5 [64 (18) vs 35 (9), P,0.01]

and 10 min [65 (18) vs 47 (11), P,0.05] after creation of PP. There were no significant differences between the groups in PRA and cortisol levels. Hence it can be concluded that I.V. MgSO₄ administered before creation of PP attenuates arterial pressure increases during laparoscopic cholecystectomy. This attenuation is apparently related to reductions in the release of catecholamine, vasopressin, or both⁶.

CONCLUSION

The cases who received intravenous MgSO₄ had higher efficacy in terms of blood pressure controls after Carbon dioxide pneumoperitoneum during laparoscopic cholecystectomy when compared to placebo group. In future we can prevent hypertension due to Carbon dioxide pneumoperitoneum in laparoscopic surgeries by giving preoperative MgSO₄.

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