Effect of Magnesium Sulfate on Hemodynamic Response to CO_2 Pneumoperitoneum in Patients Undergoing Laparoscopic Cholecystectomy

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ABSTRACT:

BACKGROUND:

Pneumoperitoneum with CO_2 insufflation is used during laparoscopic cholecystectomy to facilitate surgical access as it is a minimally invasive procedure, and despite its benefits when compared to the open cholecystectomy, it is known that pneumoperitoneum has some adverse physiological effects including an abrupt increase in the arterial blood pressure and an increase in the heart rate due to increased catecholamines release.

OBJECTIVE:

To investigate the effect of magnesium sulfate on attenuating the hemodynamic response to carbon dioxide pneumoperitoneum in patients undergoing laparoscopic cholecystectomy.

PATIENTS AND METHODS:

This double blind prospective study was conducted in Rizgari Teaching Hospital in Erbil/Iraq on 60 patients whose ages ranges between (20-45) years to assess the effectiveness of magnesium sulfate in attenuating the hemodynamic response to cholecystectomy, after dividing the patients into two groups: group I (magnesium group) and group II control group.

RESULTS:

The increase in systolic blood pressure, diastolic blood pressure, mean arterial blood pressure and heart rate readings were less in group I (Magnesium group) when compared to group II (control group) with a statistically significant difference ($p < 0.05$).

CONCLUSION:

It can be concluded that magnesium sulfate attenuates the hemodynamic response to pneumoperitoneum in laparoscopic cholecystectomy.

KEYWORDS: Magnesium sulfate, Laparoscopic cholecystectomy, Pneumoperitoneum, Hemodynamic response

INTRODUCTION:

Laparoscopy (or peritoneoscopy) is a "minimally invasive" procedure allowing endoscopic access to the peritoneal cavity after insufflation of a gas (CO_2) to create space between the anterior abdominal wall and the viscera [1].

Laparoscopy has changed the surgical, approach to symptomatic gallstone disease. Muhe and Movret performed the first laparoscopic cholecystectomy in Europe in 1987 using a pneumoperitoneum [2,3].

Laparoscopic surgery is one of the most common surgical techniques and has several advantages over traditional surgery, including decreased postoperative pain, a shorter length of stay in the hospital, and cosmetic appeal. However, it requires a pneumoperitoneum to allow for visualization of intraabdominal structures.

Physiological changes during laparoscopy can be attributed to pneumoperitoneum, Carbon dioxide and extremes of patient positioning on the operating table [4].

Pneumoperitoneum which is the insufflation of CO_2 into the abdominal cavity is used in laparoscopic procedures. The consequences of PP are hypercapnic acidosis which can result in depressed cardiac contractility, sensitization of the myocardium to the arrhythmogenic effects of catecholamines, and systemic vasodilation [5].

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The hemodynamic changes observed during pneumoperitoneum with carbon dioxide are the result of the complex interaction of anesthesia, surgical insult the patient's position (Trendelenburg or reverse Trendelenburg), carbon dioxide, and an increase (followed by a reduction at the end of surgery) in intra-abdominal pressure as well as oxidative stress, which plays an important role in the overall response to this procedure. Fortunately, an increase in intra-abdominal pressure that does not cause it to reach 12 to 15 mm Hg is usually well tolerated by most patients [6]. Carbon dioxide is the most commonly used gas for insufflation because it is extremely soluble and diffuses easily through biological membranes [7].

CO_2 has become the gas of choice because it offers the best compromise between advantages and disadvantages [8]. CO2 is rapidly removed in the lungs, and is highly soluble because of rapid buffering in whole blood. The risk of CO_2 embolization is small. CO2 exerts widespread local and systemic effects that may manifest overall as hypertension, tachycardia, cerebral vasodilation, hypercarbia, and respiratory acidosis [9]. Insufflation of CO_2, to facilitate pneumoperitoneum, is typically associated with an elevation in catecholamine levels, resulting in an associated increase in cardiac output and BP [10].

Magnesium sulfate is a medication used to treat and prevent low blood magnesium and seizures in women with eclampsia. It is also used in the treatment of torsades de pointes, severe asthma exacerbations, constipation, and barium poisoning. It is given by injection into a vein or muscle as well as by mouth [11].

Common side effects include low blood pressure, skin flushing, and low blood calcium. Other side effects may include vomiting, muscle weakness, and decreased breathing [12].

Magnesium has been shown to dilate vascular beds and attenuate the vascular response to endogenous and exogenous vasopressors [13].

It blocks the release of catecholamines from adrenergic nerve terminals and adrenal glands [14].

AIM OF THE STUDY:

To investigate the effect of magnesium sulfate on attenuating the hemodynamic response to carbon dioxide pneumoperitoneum in patients undergoing laparoscopic cholecystectomy.

PATIENTS AND METHODS:

This double-blind study was conducted between October and November 2017 in Rizgary Teaching Hospital in Erbil / Iraq on (60) patients who underwent an elective laparoscopic cholecystectomy with the use of CO2 insufflation to create pneumoperitoneum under general anesthesia. The ages of the patients ranged between (20-45) years and their body weight ranged between 65-95 Kg.

The following cases were excluded from the study:

- Patient's refusal
- History of magnesium sulphate hypersensitivity
- History of smoking or alcohol use.
- Pregnant women.
- Patients taking calcium supplments.
- Difficulty in trocar insertion at the start of the operation.

The (60) patients were divided into two groups (30 patients in each) ; each patient received a bolus of solution intravenously after intubation but before the pneumoperitoneum was created.

Group I: (Magnesium group) received magnesium sulfate in dosage of 50 mg/kg diluted in 50 ml of an isotonic 0.9% normal saline over 5 mins period.

Group II: (Control group) received 50 ml isotonic 0.9% normal saline after intubation was done over a period of 5 minutes but before the creation of pneumoperitoneum.

Upon arrival to the operating theatre, patient's identity and type of surgery were confirmed. The patient's nil by mouth status was confirmed. All routine monitors to the patient including ECG, pulse oximeter, non-invasive blood pressure (NIBP) were applied.

An intravenous access through a peripheral vein was obtained. Baseline readings of hemodynamic parameters like systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) and heart rate (HR) were all recorded.

Capnometer was attached to record the level of end tidal CO_2 ($ETCO_2$) after intubation.

All patients were premedicated with 1 mg midazolam, 50ug fentany1, 1.5 mg/kg Lidocaine intravenously. Then they were preoxygenated with 100% O2 for about 3 to 5 mins before induction of anesthesia. Induction was done with an IV injection anesthetizing dose of Propofol 1.5-2.5 mg/kg body weight and an IV injection of rocuronium 0.6 mg/kg as a muscle relaxant to facilitate the endotracheal intubation. After confirming the endotracheal tube position through checking the chest air entry bilaterally by auscultation and noting the $ETCO_2$ reading on the monitor, the endotracheal tube was secured in place using an adhesive tape. Patients were mechanically ventilated thereafter where tidal volume and respiratory rate were both adjusted accordingly to keep an $ETCO_2$ of 30-35 mmHg throughout the surgery.

Anesthesia was maintained with O2 and isoflurane end-tidal of 1- 1.5%. During the surgery, ringer lactate solution was infused in accordance with each patient's deficit, maintenance and blood loss. Insufflation of CO_2 to create a pneumoperitoneum was established and the intra-abdominal pressure was kept between 12-14 mmHg. Monitoring of SBP, DBP, MAP and HR was done, and readings were taken and recorded before induction (baseline reading), after intubation(P0), 5 mins (P5), 10 mins (PI0), 15 mins (PI5), 20 mins (P20), 25 mins (P25), 30 mins (P30) and 35 min (P35), after pneumoperitoneum establishment (post-pneumoperitorieum).

At the end of the surgical procedure and after achieving good hemostasis and placement of dressing over the surgical sites, the residual neuromuscular blockade was reversed using an IV injection combination of neostigmine 0.04 mg/kg and atropine 0.02 mg/kg. Isoflurane was discontinued when last suture was done. 100% O_2 was administered and tracheal extubation was done. In recovery room, all patients were monitored for 30 mins.

Statistical Analysis

Data of all patients in both groups were entered into a database software program (Microsoft excel 2010 was used), data were checked for any error or inconsistency then analyzed by using a Minitab software version 17 for windows.

Descriptive statistics of variables were presented as mean and standard deviation (SD) for continuous variables (age, gender, systolic blood pressure, diastolic blood pressure, mean arterial blood pressure and heart rate). Comparison of means and the significance of difference in between study groups were tested by student t test (independent two groups' type) for all continuous variables. Level of significance (p value) of < 0.05 was considered as significant difference, $P< 0.001$ was considered as highly significant.

RESULTS:

In our study, the systolic blood pressures were significantly higher in the control group ($p <0.05$) which were higher at 5min,10 min, 15 min, 20 min, 25 min, 30 min post pneumoperitoneum when compared to the magnesium group in regard to baseline readings. The magnesium group showed a stable response post pneumoperitoneum with mostly lower readings when compared to baseline readings as it is shown in table (1).

Table (1): Intergroup comparison of systolic blood pressure in mmHg (2-sample t-test)

Time		Mean±SD Group II control	Mean±SD Group I mg	Group I vs. Group II t-value	Group I vs. Group II p-value
Before induction (baseline)		132.03±9.42	122.07±6.24	4.36	0.000
After intubation		117.67±9.45	112.90±6.96	2.22	0.07
pneumoperitoneum	5 minutes after pneumoperitoneum	114.9±10.1	131.83±5.77	-7.97	0.000
	10 minutes after pneumoperitoneum	114.83±8.52	133.6±4.11	-10.87	0.000
	15 minutes after pneumoperitoneum	115.63±8.46	133.4±6.05	-9.35	0.000
	20 minutes after pneumoperitoneum	115.43±8.16	131.73±6.10	-8.77	0.000
	25 minutes after pneumoperitoneum	117.13±8.68	134.73±4.32	-9.83	0.000
	30 minutes after pneumoperitoneum	119.93±8.37	137.0±6.18	-8.99	0.000
	35 minutes after pneumoperitoneum	125.47±8.72	138.70±6.47	-6.67	0.000

Regarding the diastolic blood pressures, the magnesium group had lower readings at different intervals post pneumoperitoneum when compared to baseline measurements, while the control group had significantly higher post pneumoperitoneum pressures with a statistically significant difference ($p < 0.05$) as shown in table (2).

Table (2): Intergroup comparison of diastolic blood pressure in mmHg (2-sample t-test)

Time		Mean±SD Group II control	Mean±SD Group I mg	Group I vs Group II	
				t-value	p-value
Before induction (baseline)		77.5±6.9	74.47±4.58	2.01	0.050
After intubation		69.43±8.78	69.47±5.12	-0.02	0.986
pneumoperitoneum	5 minutes after pneumoperitoneum	68.02±8.3	77.63±4.4	-5.58	0.000
	10 minutes after pneumoperitoneum	69.53±6.77	79.6±4.68	-6.7	0.000
	15 minutes after pneumoperitoneum	69.02±5.14	81.2±4.32	-9.9	0.000
	20 minutes after pneumoperitoneum	67.5±7.79	80.63±4.32	-8.03	0.000
	25 minutes after pneumoperitoneum	68.83±6.19	80.07±4.67	-7.94	0.000
	30 minutes after pneumoperitoneum	71.73±8.32	81.53±4.32	-5.72	0.000
	35 minutes after pneumoperitoneum	72.57±9.72	82.43±5.53	-4.83	0.000

The mean arterial blood pressure readings were significantly higher in the control group ($p < 0.05$) than the magnesium group at different intervals post pneumoperitoneum as shown in table (3)

Table (3): Intergroup comparison of mean arterial blood pressure in mmHg (2-sample t-test)

Time		Mean±SD Group II control	Mean±SD Group I mg	Group I vs Group II	
				t-value	p-value
Before induction (baseline)		95.0±7.34	90.07±5.09	3.03	0.004
After intubation		58.2±8.05	83.93±5.02	0.73	0.468
pneumoperitoneum	5 minutes after pneumoperitoneum	83.2±8.31	95.53±4.24	-7.24	0.000
	10 minutes after pneumoperitoneum	84.3±6.17	97.37±3.85	-9.85	0.000
	15 minutes after pneumoperitoneum	83.77±5.42	98.33±4.05	-11.78	0.000
	20 minutes after pneumoperitoneum	83.9±7.87	97.53±4.43	-8.27	0.000
	25 minutes after pneumoperitoneum	85.47±6.68	98.07±3.68	-9.05	0.000
	30 minutes after pneumoperitoneum	87.43±8.29	99.67±4.45	-7.2	0.000
	35 minutes after pneumoperitoneum	89.77±9.72	100.97±4.79	-5.95	0.000

The heart rate readings were comparable in both groups until the 5^{th} min post pneumoperitoneum; the control group had statistically significant higher heart rates at 10, 15, 20 and 25 minutes. The magnesium group showed lower heart rates at 10, 15, 20 and 25 minutes when compared with the control group, but comparable readings at 30 and 35 minutes were found as shown in table (4).

Table (4): intergroup comparison of heart rates (2-sample t-test)

Time		Mean±SD Group II control	Mean±SD Group I mg	Group I vs Group II	
				t-value	p-value
Before induction (baseline)		88.3±6.94	85.83±6.43	5.45	0.016
After intubation		84.53±5.34	80.73±4.93	2.86	0.006
pneumoperitoneum	5 minutes after pneumoperitoneum	83.43±5.2	85.43±4.39	-1.61	0.113
	10 minutes after pneumoperitoneum	83.4±4.65	86.13±3.79	-2.49	0.016
	15 minutes after pneumoperitoneum	83.13±4.64	85.57±4.64	-2.03	0.047
	20 minutes after pneumoperitoneum	82.3±4.18	84.53±5.06	-1.86	0.067
	25 minutes after pneumoperitoneum	82.77±4.69	85.83±4.11	-2.69	0.009
	30 minutes after pneumoperitoneum	84.33±5.92	85.73±3.89	-1.08	0.284
	35 minutes after pneumoperitoneum	85.8±4.81	86.67±3.82	-0.77	0.443

DISCUSSION

Laparoscopic surgery induces complex physiologic changes that impact multiple organ systems. Direct mechanical stress placed on the patient, as well as neuroendocrine stimulation during laparoscopy are the primary forces responsible for much of the physiologic derangement observed [15].

The role of magnesium sulfate regarding its effect on attenuating the hemodynamic response to pneumoperitoneum has been studied before. Our study was done to further investigate its effect.

The hallmark of laparoscopy is the creation of a pneumoperitoneum with pressurized CO_2. The result is an increase in intraabdominal pressure. The high solubility of CO_2, increases systemic absorption by the vasculature of the peritoneum[16]. Carbon dioxide gas is highly soluble and, during insufflation, rapidly moves from the peritoneal cavity into the circulation [17].

Jee *et al.* found that giving magnesium sulfate at a dose of 50 mg/kg over 2-3 min before the creation of pneumoperitoneum attenuated the hemodynamic responses, without any adverse episodes of bradycardia or severe hypotension[18]. We did not have any patient suffering from hypotension or bradycardia in our study as well with the given dose in our study. In our study, we used a similar dose of magnesium sulfate and compared it to normal saline and we found that giving such a dose before pneumoperitoneum reduced the SBP, DBP and MAP more than the control group which was statistically significant. It is shown that bolus dose of Mg (50 mg/kg) increases the serum concentration of Mg, in this range and this serum level of Mg, blunts the increase of catecholamines level of the plasma, during pneumoperitoneum, and effectively, prevents the sympathoadrenal hemodynamic stress responses emerging form carbon dioxide pneumoperitoneum[20].

Ghodraty et al. found that giving magnesium sulfate at a dose of 50 mg /kg before the induction of anesthesia decreased pneumoperitoneum induced hypertension caused by the pneumoperitoneum by CO_2, in patients undergoing laparoscopic cholecystectomy. Their results showed that magnesium sulfate, could induce significant hemodynamic stability during pneumoperitoneum in laparoscopic operations, although they found that there are no significant changes in heart rates or mean arterial blood pressure readings between the two group[21], unlike our study where the difference was significant in mean arterial blood pressure and regarding heart-rate-it was- significant-only at 10^{th} ,15^{th} ,20^{th} ,25^{th} post pneumoperitoneum. They found also that Propofol requirements are less when compared to the control group; however, this was not investigated in our study.

Paul et al. used 30 mg/kg magnesium sulfate given as a bolus prior to pneumoperitoneum and investigated its effect on the mean arterial, blood pressure and the heart rate, and their results were significant with this dose when compared to the control group [20].

Magnesium is a vasodilator in both the systemic and pulmonary circulations [22]. Thus, attributing its action in blood pressure reduction.

A study of patients with American Society of Anesthesiologists (ASA) physical status I and II showed that an increase in intra-abdominal pressure to 15 mm Hg was associated with Increases in left and right ventricular end-diastolic area by 65% and 45%, respectively. The ejection fraction of both ventricles decreased by approximately 18% [23]. Patients in our study who received magnesium sulfate had significantly lower heart rates in comparison to the control group at 10min, 15 min, 20 min and 25 mins. But no statistical difference at 5 min, 30 min and 35 mins post pneumoperitoneum. Earlier studies showed no difference in heart rates between patients who receiver magnesium sulfate (Magnesium group) and patients who received normal saline only (control group).

Magnesium infusions have been shown useful in managing hypertension by inhibiting catecholamine release and by altering adrenergic receptor response Other studies tried giving magnesium sulfate as bolus before the induction of anesthesia then to be followed by a low dose infusion throughout the surgical procedure but this was associated with high rate of complications in terms of severe hypotension and severe bradycardia.

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