Effect of magnesium sulfate on hemodynamic response to endotracheal intubation and carbon dioxide pneumoperitoneum in laparoscopic cholecystectomy

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Abstract: Background: Endotracheal intubation and carbon dioxide pneumoperitoneum in patients undergoing laparoscopic cholecystectomy changes hemodynamic parameters. According to magnesium effect on the inhibition of catecholamine release and attenuate vasopressin-stimulated vasoconstriction, this study was performed to reduce the hemodynamic effects during tracheal intubation and pneumoperitoneum in patients undergoing laparoscopic cholecystectomy. **Material and methods**: In prospective triple-blind clinical trial, 60 patients 18- 70 years old undergoing laparoscopic cholecystectomy were randomly assigned to one of two groups: intervention group (30 mg/kg magnesium sulfate) and control group (1.5 mg/kg lidocaine). Heart rate and mean arterial pressure were recorded before laryngoscopy (baseline value), immediately and every minute after intubation until 5 minute and before and 5, 10, 15, 30 min after pneumoperitoneum. **Results:** Mean arterial pressure was low in magnesium sulfate group than control group throughout the study period and was statistically significant at before insufflation and 5 minute after insufflation ($p=0.005$). Heart rate in magnesium sulfate group was higher than control group throughout the study period ($P>0.05$). **Conclusion**: Using magnesium sulfate 30 mg/kg in patients undergoing laparoscopic cholecystectomy can attenuate mean arterial pressure change in pneumoperitoneum than lidocaine.

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Introduction:

Laryngoscopy and tracheal intubation cause airway protective reflexes that lead to physiological changes involving various body systems. Reflex changes in the cardiovascular system is often created after Laryngoscopy and tracheal intubation and caused increasing 40-50% blood pressure and increasing 20% heart rate (1).

In Laparoscopic Cholecystectomy, CO_2 gas is used for pneumoperitoneum (PP) that blowing CO_2 gas and PP cause cardiovascular responses. Cardiovascular changes include increased arterial blood pressure and increased systemic vascular resistance and decreased cardiac output because of increased plasma catecholamine or vasopressin, or both. Increased heart rate and blood pressure can be dangerous for patients, particularly those with impaired cardiac function (2). Alpha2-adrenergic agonists, beta-blocking agents, opioids, or vasodilators are often used to avoid circulatory response to pneumoperitoneum (3,4).

For years, Intravenous Magnesium Sulfate ($MgSO_4$) was used as an antiarrhythmic agent and for prophylaxis against seizures in preeclampsia and recently importance of Magnesium has changed to be the center of attention in anesthesia and surgery (2). Magnesium sulfate inhibits the release of catecholamines from the medulla part of adrenal and peripheral nerve endings, and also causes sympathetic blocks and indirectly causes dilation of blood vessels and thus blood pressure reduction (5,6).

The effect of Magnesium Sulfate prescription to reduce the hemodynamic response during tracheal intubation and Pneumoperitoneum compared with placebo was shown in studies such as the study of Misbah Kia et.al in 2014 on CABG patients (7), the study of Paul et.al in 2013 on laparoscopic cholecystectomy surgery (2) and Dar et.al study in 2015 on abdominal laparoscopic surgery (8). Although some studies such as Dehgani Firosabadi et.al in 2014 (9) have shown that magnesium sulfate doesn't have effects on hemodynamic changes following laryngoscopy and tracheal intubation.

Given that currently in the majority of laparoscopic cholecystectomy, intravenous lidocaine is used as a premedication in order to decrease hemodynamic changes after tracheal intubation and Pneumoperitoneum, but despite these, hemodynamic changes especially after insufflation CO_2 gas are still considerable. Due to the favorable impact of magnesium sulfate on patients' hemodynamic responses (10,11,12), this study was performed in purpose of comparing magnesium sulfate with lidocaine to reduce hemodynamic responses after tracheal intubation and Pneumoperitoneum in patients undergoing laparoscopic cholecystectomy.

Materials and methods:

In this triple blind clinical trial study, 60 patients of ASA class I and II aged between 18-70 years of either sex candidate for laparoscopic cholecystectomy surgery, were included after obtaining the approval of university ethics committee, IRCT2016022716612N6 and written consent from the patients, in Imam Khomeini Hospital in Ardebil. Exclusion criteria were allergy to magnesium sulfate, hypermagnesemia, high blood pressure, gastro esophageal reflux disease, pregnancy, lactation, heart, liver and kidney diseases, history of drug addiction and alcoholism, BMI>30 and neuromuscular disease. The patients were randomly assigned into two groups of 30each using a computer-generated block-randomized number table. Randomization was performed by a statistical expert who was blinded to the study design. Immediately before induction of anesthesia, 30 mg/kg intravenous magnesium sulfate was administered for intervention group and 1.5 mg/kg Lidocaine by adding sterile water to reach the same volume magnesium sulfate was administered for control group. Drugs were prepared in the same unlabeled syringe containing equal volume by anesthesia resident and drug injection was conducted by the anesthesiologist who was blinded to the randomization. Then patients received 1 mg Midazolam, 2 µg/kg Fentanyl, 2 mg/kg Propofol and 0.5 mg/kg Atracurium endotracheal as muscle relaxant. Tracheal intubation was done 3 minutes after drug injection. After intubation, anesthesia was kept on with 100 µg/kg/m Propofol infusion, along with the inspiratory gas mixture (50% oxygen and 50% N_2O). To maintain muscle relaxation, 0.5 mg/kg Atracurium was injected intermittent boluses and the patients were mechanically ventilated during surgery. Tidal volume and respiratory rate were adjusted to maintain end-tidal CO2 between 35-45mm Hg. After insufflation CO_2 with 12 mmHg intra-abdominal pressure (IAP) into the peritoneum, patients were placed on head up tilt position at 15º. In all patients monitoring of HR, SBP, DBP, MBP, SpO2, ETCO2 and TOF was done on a multichannel and TOF monitor. In case of hemodynamic changes such as bradycardia, hypotension or hypertension, therapeutic interventions have been done. For bradycardia (HR <50) 0.5 mg Atropine bolus was used and increased amount of intravenous fluid infusion or intravenous bolus doses of 5 mg Ephedrine were used for hypotension (MAP <60). For hypertension (MAP> 110) Nitroglycerine infusion was started. At the end of surgery all administered anesthetic drugs were interrupted and 100% oxygen about 6 L/min was given to patients. Following spontaneous respiration, muscle relaxation was reversed with injection of Neostigmine and Atropine and after establishing proper breathing; patients were extubated and transferred to the recovery room.

HR and MAP were recorded as follows:

1. Baseline vital signs
2. Before laryngoscopy
3. Immediately after laryngoscopy
4. In 1,2,3,4,5 minutes after tracheal intubation
5. Before insufflation CO_2
6. 5 minutes after insufflation CO_2
7. 10 minutes after insufflation CO_2
8. 15 minutes after insufflation CO_2
9. 30 minutes after insufflation CO_2

The sample size was calculated on the basis of previous studies (2), for detecting clinically significant reduction of %25 in hemodynamic changes, assuming a power of 80% and a significance level of 5%.

All raw data of study parameters were entered and analyzed using SPSS v21.0. Data was presented as mean and standard deviation (SD) or numbers with percentage. Independent

T-testand, repeated measure in order to compare the means (for quantitative data) and Chi-square tests (for qualitative data) were used to determine differences between the experimental and control group. P-values<0.05 were considered statistically significant.

Results:

The distribution of patients in two groups is shown as Table 1.

Table 1: Demographic characteristics and baseline vitals of patients

variable	Mg sulfate (N=30)	Control (N=30)	P value
Sex (M/F)	5/25	3/27	0.71
Age (mean ± SD)	42.73±11.61	44.17±14.7	0.68
Weight (mean ± SD)	70.87±12.76	75.53±18.68	0.26
Height (mean ± SD)	159.52±7.23	162.03±8.02	0.21
Duration of surgery (mean ± SD)	51.20±23.85	48.17±13.72	0.54
Duration of Anesthesia (mean ± SD)	74.57±26.01	78.13±19.44	0.55
MAP (mean ± SD)	102.97±14.58	107.77±16.02	0.23
Heart rate (mean ± SD)	91.67±20.99	85.30±18.63	0.22

Mean arterial pressure was low in magnesium sulfate group than control group throughout the study period (except in before and 1 minute after laryngoscopy) (Figure 1) and was statistically significant at before insufflation and 5 minute after insufflation (p=0.005).

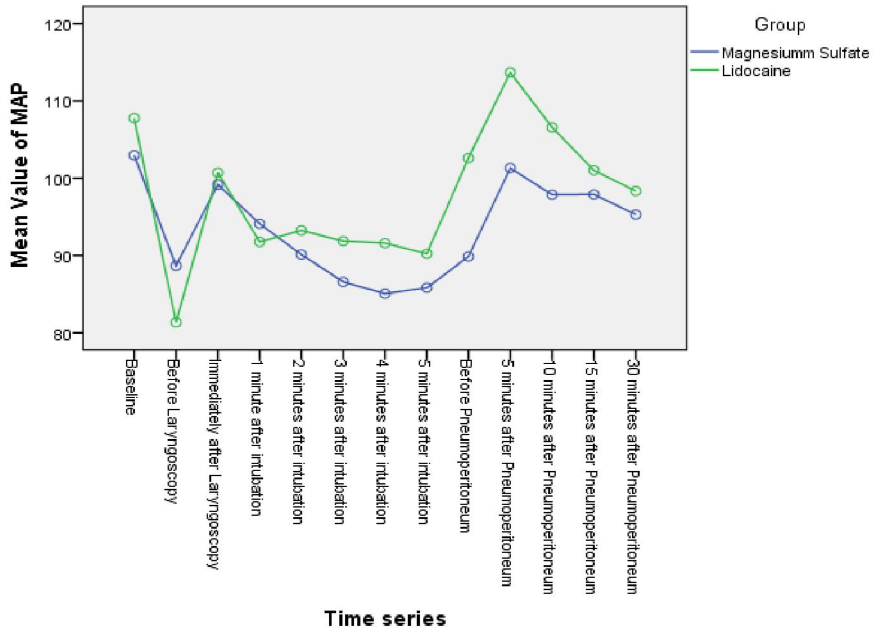

Figure1: Variations in Mean Arterial Pressure in 2 groups during the study

Heart rate in magnesium sulfate group was higher than control group throughout the study period (Figure 2) and was statistically significant at before laryngoscopy (p=0.001). Heart rate fluctuations in the magnesium sulfate group were lower than lidocaine group during surgery, especially before and after laryngoscopy, and before and after insufflation CO2 gas, but this difference was not statistically significant (P >0.05).

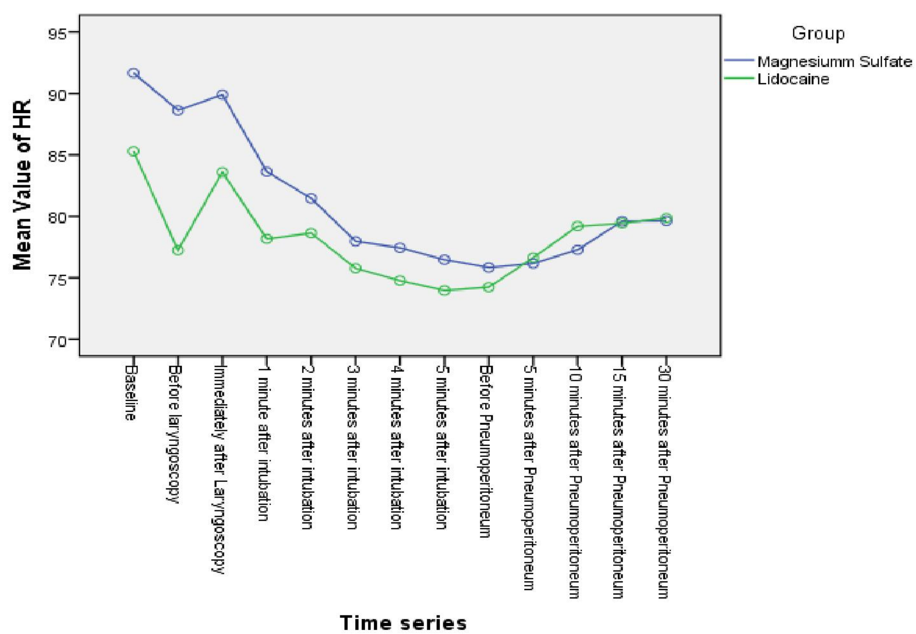

Figure 2: Variations in Heart rate in 2 groups during the study

Only one patient in magnesium sulfate group in comparison whit 3 patients in lidocaine group suffered from bradycardia (Pvalue=0.61). Hypotension occurred in one patient in each group, and one patient in lidocaien group suffered from hypertension (Pvalue=1).

Discussion:

The findings of our study on the effect of magnesium sulfate premedication on heart rate in comparison with lidocaine showed that heart rate fluctuations in the magnesium sulfate group were lower than lidocaine group during surgery, especially before and after laryngoscopy, and before and after insufflation CO2 gas, but this difference was not statistically significant ($P > 0.05$). The study on the mean blood pressure showed that mean blood pressure in the magnesium sulfate group was significantly lower than that for lidocaine group ($P < 0.001$), and mean blood pressure during the period before and after insufflation CO2 gas in magnesium sulfate group was statistically significant ($P < 0.005$) lower than that in the lidocaine group.

In Panda et.al (13) study was performed in patients with high blood pressure who were undergoing surgery and intubation, MAP was maintained in the normal range during the surgery in a group that was received 30mg/kg Magnesium sulfate, but in lidocaine group, 3 and 4 min after intubation had a significant decrease compared to the baseline. Also in our study, blood pressure in magnesium sulfate group which was somewhat lower than that in lidocaine group is consistent with the results of this study.

In shamim et.al. (14) and in Zarif et.al (15) studies were performed on hemodynamic changes during laparoscopic cholecystectomy after infusion of magnesium sulfate and placebo, the results showed that magnesium sulfate effectively attenuates hemodynamic responses during intubation and pneumoperitoneum in laparoscopic cholecystectomy than placebo compared to the baseline which was consistent with our study.

In a study by Paul et.al. (2), effects of magnesium sulfate on hemodynamic response to carbon dioxide pneumoperitoneum in patients undergoing laparoscopic cholecystectomy, MAP in the group who received magnesium sulfate during PP was significantly less than placebo group and had less fluctuations than baseline ($P < 0.05$). The heart rate in patients who received magnesium sulfate during PP was significantly lower than placebo group ($P < 0.05$). In Ahmad Dar et. al. study (8), on the effect of magnesium sulfate on reducing hemodynamics stress responses during abdominal laparoscopic surgery, mean heart rate in magnesium sulfate group was lower than in the placebo group during surgery, after intubation, especially 10 minutes after creating pneumoperitoneum ($P < 0.05$) and Systolic blood pressure, Diastolic blood pressure, Mean arterial pressure was low in magnesium sulfate group than placebo group throughout the study period and were statistically significant ($p<0.05$). In both above mentioned studies, placebo is used in comparison with Magnesium sulfate that justifies the significance of obtained results. Our results revealed that, increasing blood pressure after insufflation CO_2 in magnesium sulfate group compared to lidocaine group was low.

In a study by Jee et.al. (4) " Magnesium sulphate attenuates arterial pressure increase during laparoscopic cholecystectomy", Systolic and diastolic blood pressure significantly ($p<0.05$) were greater in the placebo group than in the magnesium sulfate group at 10,20, and 30 min post pneumoperitoneum. But there were no significant differences in patients' heart rate in duration of surgery between two groups ($P > 0.05$). In our study, there was not a significant difference in patients' heart rate during surgery in both groups but heart rate fluctuations were significantly lower in magnesium sulfate group.

In our study only one patient in magnesium sulfate group in comparison whit 3 patients in lidocaine group suffered from bradycardia (Pvalue=0.61). Hypotension occurred in one patient in each group, and one patient in lidocaien group suffered from hypertension (Pvalue=1). This shows that magnesium sulfate provides more hemodynamic stability than lidocaine during surgery.

In the study of Paul et.al. (2) none of the patients required atropine but just only one hypotension case in magnesium sulfate group required medical interventions. Hypertension occurred in 12 patient of control group whereas no patients of magnesium sulfate group suffered from hypertension.

In study conducted by Ahmad Dar et.al (8) was about the effect of magnesium sulfate on reducing hemodynamics stress during abdominal laparoscopic surgery, none of the patients required medical interventions.

The limitations of this study are not study of different dosage of magnesium sulphat and lack of patients adequate follow-up for the side effects occurrence in both groups.

Conclusion:

Using magnesium sulfate 30 mg/kg in patients undergoing laparoscopic cholecystectomy can attenuate mean arterial pressure change in pneumoperitoneum and provides more hemodynamic stability than lidocaine during surgery.

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