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# Effect of Magnesium Sulphate on Perioperative Hemodynamic Responses in Hypertensive Patients Undergoing Laparoscopic Cholecystectomy. A Randomized Controlled Double Blinded Trial

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## Abstract

*Background:* Orotracheal intubation is one of the most invasive perioperative stimuli. Orotracheal intubation is associated with stimulation of somatic and visceral nociceptive afferents of the epiglottis, hypopharynx, peritracheal area, and vocal cords, which augment sympathetic activity. Transient tachycardia and hypertension are common cardiovascular responses to laryngoscopy and intubation.

These transient hemodynamic changes are probably of no consequence in healthy individuals, but they may be dangerous in those with hypertension as they may lead to myocardial ischemia, arrhythmias, and intracranial hemorrhage Therefore, attenuation of cardiovascular response following tracheal intubation is of particular importance in hypertensive patients, whom are more susceptible to exaggerated cardiovascular response to laryngoscopy and tracheal intubation than normotensive patients.

*Aim of Study:* The present study was designed to study the effects of pre-induction intravenous Magnesium Sulphate on hemodynamic responses to laryngoscopy, post-intubation, during pneumoperitoneum and in post-operative period in hypertensive patients undergoing laparoscopic cholecystectomy.

*Patients and Methods:* After approval of the institutional research board and getting informed written consent from the patients, this double blind randomized prospective study was conducted at the gastro-intestinal surgery center in June 2019 Patients were prepared according to ASA fasting guidelines. The day before operation, all patients were subjected to preoperative history taking, physical examination and basal laboratory investigation. Complete blood count, coagulation profile, renal and liver function test. In addition, the instruction have been given to the patient and the paramedical stuff that all antihypertensive drugs must continues till the surgery time except for ACE/ARBS must be stopped the day before surgery.

Upon arrival to the pre-operative holding area, a peripheral intravenous 18-20-gauge cannula was inserted; monitor was attached to the patients and hemodynamic parameters like heart rate, noninvasive blood pressure, oxygen saturation and ECG were recorded.

Patients were randomly allocated into two groups using computer-generated randomization and closed envelops. Study medications were prepared by an anesthesiologist who was blinded to the computer-generated randomization schedule. Patients received one of these below mentioned solution as a bolus intravenously in the pre-operative period.

(Group I, n=40): Received Magnesium Sulphate 20mg/kg in 250ml of isotonic 0.9% sodium chloride solution intravenously over 15 to 20 minutes in the preoperative room immediately before induction of anesthesia.

(Group II, N=40): Same volume of isotonic 0.9% sodium chloride solution intravenously over 15 to 20 minutes in the preoperative room just before induction of anesthesia.

*Results:* There were statistically significant difference between magnesium group and control group as regarded the hemodynamic responses to intubation and surgical stimulation during laparoscopic cholecystectomy in hypertensive patients.

*Conclusion:* Administration of magnesium sulphate immediately pre-operative can attenuate the hemodynamic response in hypertensive patient undergoing laparoscopic cholecystectomy.

***Key Words:*** *Laparoscopic cholecystectomy in hypertensive patients – Magnesium sulphate – Hemodynamic responses to intubation – Surgical stimulation.*

## Introduction

**OROTRACHEAL** intubation is one of the most invasive perioperative stimuli. Orotracheal intubation is associated with stimulation of somatic and visceral nociceptive afferents of the epiglottis, hypopharynx, peritracheal area, and vocal cords, which augment sympathetic activity **[1]**. Transient tachycardia and hypertension are common cardiovascular responses to laryngoscopy and intubation **[2]**.

These transient hemodynamic changes are probably of no consequence in healthy individuals, but

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they may be dangerous in those with hypertension as they may lead to myocardial ischemia, arrhythmias, and intracranial hemorrhage [3]. Therefore, attenuation of cardiovascular response following tracheal intubation is of particular importance in hypertensive patients, whom are more susceptible to exaggerated cardiovascular response to laryngoscopy and tracheal intubation than normotensive patients [4]. Two dynamic predictors for perioperative cardiac morbidity include tachycardia and hypertension. Acute hypertension affects both myocardial oxygen supply and demand. During systemic hypertension, peak systolic ventricular pressure increases, producing increases in ventricular wall demand, which increases myocardial oxygen consumption [1].

Many anesthesiologists agree that a skilled anesthesiologist applies only a small force to the patient's larynx when using a laryngoscope, and that reducing the force on the larynx might prevent excessive hyperdynamic responses to orotracheal intubation. The hemodynamic responses to orotracheal intubation have two components. The first is the response to laryngoscopy and the second is the response to endotracheal intubation. It is not known which component is more responsible for the reduction of the hyperdynamic response to orotracheal intubation with the administration of narcotics [5].

Pneumoperitoneum with carbon dioxide ($CO_2$) insufflation for laparoscopic surgery induces gradual elevations of heart rate and Blood pressure. These disturbances could be mediated both mechanically and humorally, mechanically by increased venous resistance, compression of the abdominal aorta contributing to the increase in cardiac afterload, partially opposed by tilting the patient to the head-up position, thus reducing venous return [6,7].

Humoral mediators attributed to Pneumoperitoneum include catecholamines, prostaglandins, the renin-angiotensin system, and vasopressin which cause an increase in systemic vascular resistance [8,9].

Magnesium has endothelium derived nitric oxide induced vasodilatory effect and produces vasodilatation by directly acting on the blood vessels by interfering with a wide range of vasoconstrictor substances [10].

Nitric oxide causes activation of guanylcyclase and increase in cyclic guanine monophosphate, which mediates the relaxation of vascular smooth muscles. Moreover, magnesium attenuates vasopressin-stimulated vasoconstriction and decrease sensitivity to vasopressin. studies have suggested that magnesium can inhibit catecholamine release in vitro and in vivo [11].

Magnesium is now regarded first as a cardiovascular drug with calcium antagonistic and antiadrenergic properties that may be accompanied by minimal myocardial depression.

## Patients and Methods

*Patients:*

After approval of the institutional research board and getting informed written consent from the patients, this double blind randomized prospective study was conducted at the gastro-intestinal surgery center, a total number of 80 patients were included in this study equally divided in two groups (40 patients each). Hypertensive patients aged 30 to 60 years old of both gender submitted to elective Laparoscopic Cholecystectomy were included in the study under general anesthesia after preoperative evaluation according to AAGBI guidelines [12].

*The exclusion criteria were:*

- History of consumption of sedatives, Hypnotics and antidepressants preoperatively.
- Uncontrolled hypertensive patients. (Systole more than 180 MMHG or Diastole more than 110 MMHG).
- ASA grade III or greater.
- History of illicit drugs or alcohol abuse.
- Expected difficult intubation.
- Basal heart rate less than 50 beat per minute.

*Methods:*

The primary outcome is to assess the perioperative hemodynamic responses to (laryngoscopy and intubation, pneumoperitoneum, during the operative time, post-operative for 24-hour). Secondary outcomes include post-operative visual analogue scale score at (1h, 6h, 12h, 24h), Riker Sedation Agitation Score (RSAS), post-operative first time need for rescue analgesic, and total analgesic consumption.

Patients were prepared according to ASA fasting guidelines. The day before operation, all patients were subjected to preoperative history taking, physical examination and basal laboratory investigation. Complete blood count, coagulation profile, renal and liver function test. In addition, the instruction have been given to the patient and the paramedical stuff that all antihypertensive drugs

must continues till the surgery time except for ACE/ARBS must be stopped the day before surgery **[13]**.

Upon arrival to the pre-operative holding area, a peripheral intravenous 18-20-gauge cannula was inserted; monitor was attached to the patients and hemodynamic parameters like heart rate, noninvasive blood pressure, oxygen saturation and ECG were recorded.

Patients were randomly allocated into two groups using computer-generated randomization and closed envelops. Study medications were prepared by an anesthesiologist who was blinded to the computer-generated randomization schedule. Patients received one of these below mentioned solution as a bolus intravenously in the preoperative period.

(Group I, n=40): Received Magnesium Sulphate 20mg/kg in 250ml of isotonic 0.9% sodium chloride solution intravenously over 15 to 20 minutes in the preoperative room immediately before induction of anesthesia.

(Group II, N=40): Same volume of isotonic 0.9% sodium chloride solution intravenously over 15 to 20 minutes in the preoperative room just before induction of anesthesia.

During the administration of the preoperative medication patients' pulse, blood pressure, and oxygen saturation were monitored. Then patients were shifted immediately to operation room along with proper monitoring of vital signs includes 5-leads ECG, pulse oximetry and non-invasive blood pressure. Ringer lactate infusion was commenced through the intravenous 18G or 20G cannula inserted in a peripheral vein.

After 3 minutes of preoxygenation, anesthesia was induced with fentanyl 1.0mic/kg, Propofol till loss of verbal contact at 1.5-2.0mg/kg over 30 seconds and injection of Atracurium 0.5mg/kg body weight, all intubations were performed after 3 minutes, the duration of laryngoscopy and intubation was limited to minimum possible time being similar in all patients. All the patients were maintained with 40% Oxygen and sevoflurane 1.0 MAC, keeping hemodynamics at around ±20% of basal values. Atracurium 20% of intubating dose as intermittent boluses when needed. During surgery $CO_2$ pneumoperitoneum was established and maintained at a pressure below 12mmHg by an automatic insufflation unit till the completion of surgery.

Blood pressure and heart rate were measured before induction (baseline), before laryngoscopy, after intubation, before pneumoperitoneum (P0) at insufflation and at 5(P5), 10(P10), 20(P20), 30(P30) and 40(P40) min during and after commencement of procedure.

At the end of the surgery, residual neuromuscular blockade was reversed with injection of Neostigmine 0.05mg/kg and injection atropine 0.01mg/kg and patients were extubated at the operation room when the patient fulfilled Extubation criteria.

The perioperative analgesic regimen included: (Barazanchiet al., 2018).

*Surgical:*

- Limiting insufflation pressure to 12MM Hg.
- Irrigation of the field with saline 0.9%.

*Pharmacological:*

- Paracetamol infusion given 10 minutes after induction of anesthesia.
- Ketolac at 15-30mg IM/IV every 6 hours as needed, maximum dose 120Mg/day.
- Rescue analgesia: Morphine; given to keep VAS below 4, at a dose of 0.15mg/kg **[15]**.

*Sample size calculation:*

Sample size was calculated using G*Power program for windows version 3.1.9.4 (Universität Kiel, Germany, 2019) using the results published by **[16]** with the variation in both heart rate and mean arterial blood pressure during the perioperative period as a co-primary outcome. Patients was classified into two groups; Magnesium sulphate group and Control group. The null hypothesis in the absence of any difference between both groups.

Heart rate and mean arterial blood pressure were recorded at nine time points in the original study by Shamim et al., but only seven readings which were recorded after administration of Magnesium sulphate were used for calculation.

A- *Heart rate:*

The average mean heart rate in the Magnesium sulphate group across all time points was 76.111 while that of the control group was 80.587. A between factors repeated measures ANOVA model was used to calculate the effect size.

A sample of 30 patients in each group is needed to achieve 80% power (1-β or the probability of rejecting the null hypothesis when it is false) over seven measurements and detect an effect size of 0.32 (small effect size) with significance level of 0.5 (α or the probability of rejecting the null

hypothesis when it is true) and an estimated correlation co-efficient between the repeated measures 0.7 as calculated by a two-sided F test.

B- *Mean arterial blood pressure:*

The average mean arterial blood pressure in the Magnesium sulphate group across all time points were 92.353 while that of the control group was 104.183. A between factors repeated measures ANOVA model was used to calculate the effect size. A sample of 6 patients in each group is needed to achieve 80% power (1-β or the probability of rejecting the null hypothesis when it is false) over seven measurements and detect an effect size of 0.845 (large effect size) with significance level of 0.5 (α or the probability of rejecting the null hypothesis when it is true) and an estimated correlation co-efficient between the repeated measures 0.7 as calculated by a two-sided F test.

A total sample of 36 patients in each group is needed to achieve 80% power and significance level of 0.05 for both primary outcomes in the proposed study. A 10% drop out is expected so 40 patients will be enrolled into each group.

*Statistically analysis:*

IBM's SPSS statistics (Statistical Package for the Social Sciences) for windows (version 25, 2017) was used for statistical analysis of the collected data. Kolmogorov-Smirnov test was used to check the normality of the data distribution in continuous variables. Continuous variables were expressed as mean ± standard deviation (SD) while categorical ones were expressed as number and percentage. Independent samples *t*-test and Mann Whitney independent samples test were used to compare normally and abnormally distributed continuous variables with no follow-up readings respectively. Repeated measures ANOVA model with Bonferroni post Hoc test and 95% confidence interval to compare the follow-up values of continuous data. Fisher exact test was used for inter-group comparison of nominal and ordinal data using the crosstabs function. Comparison of follow-up and basal values (intra-group) was conducted using Wilcoxon signed ranks test and McNemar test for ordinal and nominal data respectively. All tests were conducted with 95% confidence interval. Charts were generated using SPSS' chart builder. *p* (probability) value <0.05 was considered statistically significant.

## Results

Eighty patients were randomized to receive magnesium sulphate (Mg group) and isotonic saline (control group) over 20 minutes in the pre-operative holding area before undergoing laparoscopic cholecystectomy.

All studied groups showed no statistically significant differences as regard demo-graphic data (age, sex, weight and height). (Table 1).

Regarding peri-operative heart rate in the pre injection time and post injection time there was no statistically significant differences, but inter-group comparison magnesium group showed statistically significant decrease in heart rate in pre-induction, post induction, on laryngoscopy and intubation, on insufflation (PP), 5min, 10min, 20 min, 40min. on recovery, 1hour, 6 hours, 12 hours and 24 hours post-operative in comparison to the control group. (Table 2).

When we look at basal systolic arterial blood pressure (SBP) in the pre injection time there was no statistically significant differences, but data showed significant decrease in SBP for magnesium group in post injection, pre-induction, post induction, on laryngoscopy and intubation, on insufflation (PP), 5min, 10min, 20min, 40min, on recovery and 1 hour when compared with the control group. But it shows no statistically significant differences at 6 hours, 12 hours and 24 hours post-operative. (Table 3).

The analysis of peri-operative mean arterial blood pressure (MBP) in the pre injection time showed no statistically significant differences, but show statistically significant differences in post injection, pre-induction, post induction, on laryngoscopy and intubation, on insufflation (PP), 5min, 10min, 20min, 40min, on recovery and 1 hour. But it shows no statistically significant differences at 6 hours, 12 hours and 24 hours post-operative. (Table 4).

The magnesium group showed statistically significant decrease in recovery timing presented by the Extubation time versus the time needed for Extubation in the control group. (Table 5).

When we come to analgesic requirement presented by rescue analgesia both groups showed statistically significant differences defined by the prolonged time needed by the magnesium group for the 1 st call of rescue analgesia, also as regard the total analgesic consumption there was statistically significant difference in paracetamol and ketolac consumption in comparison to the control group. (Table 6).

As regarded the Riker Sedation Agitation Score (RSAS) it shows statistically significant differences

at recovery for the magniesium group compared with the control group, but show no statistically significant differences at 10min, 20min, 40min and 60min postoperative (Table 7).

By looking at visual analogue scale (VAS) it shows no statistically significant differences at recovery, 1 hour, 12 hours and 24 hours, post-operative but only show statistically significant difference at 6 hours post-operative in magnesium group compared with the control group. (Table 8).

Table (1): Patient demographic and lesion characteristics.

| Patient characteristics | Control group (n=40) | Magnesium group (n=40) | *p*-value |
|---|---|---|---|
| Age (Years) | 48.5±10.6 | 49.4±10.6 | 0.68[1] |
| *Sex:* | | | |
| Male | 55% (18) | 45% (15) | 0.49[2] |
| Female | 47% (22) | 53% (25) | |
| Weight (Kg) | 89.5±9.3 | 91±9.2 | 0.49[1] |
| Height (cm) | 171.6±9.4 | 169±8.4 | 0.27[1] |

- Data is expressed as mean ± standard deviation or percentage and number.
[1] *p*-value was generated using independent sample *t*-test.
[2] *p*-value was generated Cramer's V Chi square test.
*p*-value is significant when <0.05.

Table (2): Perioperative and post-operative systolic heart rate (Hr.).

| Hr. (bpm) | Control group (n=40) | Magnesium group (n=40) | *p*-value |
|---|---|---|---|
| Pre-injection | 80.3±11.3 | 78.8±9.5 | 0.51 |
| Post-injection | 80.9±11.3 | 77±10.3* | 0.11 |
| Pre-induction | 79.6±11.4# | 73.5±11.4* | 0.02 |
| Post-induction | 75.5±11.4# | 69.3±9.9* | 0.01 |
| On laryngoscopy and intubation | 95.7±12.9# | 67.8±9.4* | <0.001 |
| On insufflation | 99.9±13.6# | 66.8±9.3* | <0.001 |
| 5 min. intraoperative | 86.8±14.1 | 65.6±10.3* | <0.001 |
| 10 min. intraoperative | 83.3±13.4 | 63.6±8.8* | <0.001 |
| 20 min. intraoperative | 82.8±13.5 | 63.9±9.1* | <0.001 |
| 40 min. intraoperative | 83.3±13.8 | 64.3±9.2* | <0.001 |
| RECOVERY | 85.7±1.2# | 71.5±9.5* | <0.001 |
| 1 hour postoperative | 84.5±11.4# | 70.7±7.9* | <0.001 |
| 6 hours postoperative | 81.5±9.2 | 72±9.4* | <0.001 |
| 12 hours postoperative | 77.5±10.3 | 72.6±8.9* | 0.03 |
| 24 hours postoperative | 78.1±8.3 | 71.1±7.5* | <0.001 |

Data is expressed as mean ± standard deviation.
- *p*-value was generated using a repeated measures ANOVA model.
* Significant statistical difference from basal value in Magnesium group.
# Significant statistical difference from total basal value of Control group.
- *p*-value is significant when <0.05.

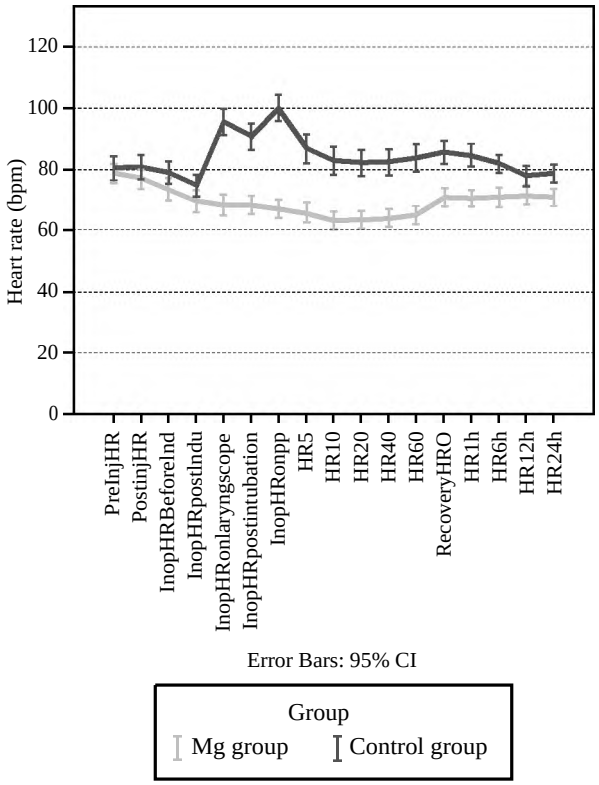
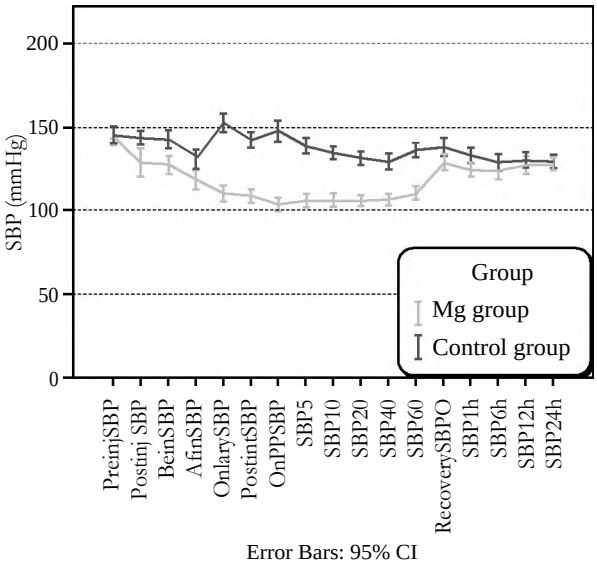



Table (3): Perioperative and postoperative systolic arterial blood pressure (SBP).

| SBP (mmHg) | Control group (n=40) | Magnesium group (n=40) | *p*-value |
|---|---|---|---|
| Pre-injection | 145.3±15.2 | 145.5±16.5 | 0.97 |
| Post-injection | 143.2±13.2 | 130.4±22.9* | 0.003 |
| Pre-induction | 142.3±15.7 | 127.7±15.5* | <0.001 |
| Post-induction | 130.7±19.1# | 117.9±17.1* | 0.002 |
| On laryngoscopy and intubation | 150.8±18.8 | 110.3±14.3* | <0.001 |
| On insufflation | 145.7±21.4 | 103.4±11.2* | <0.001 |
| 5min. post-operative | 137.1±16.6# | 105.4±10.2* | <0.001 |
| 10min. post-operative | 132.8±15# | 107.4±12.9* | <0.001 |
| 20min. post-operative | 130.7±12.9# | 105.1±11.6* | <0.001 |
| 40min. post-operative | 129.8±13.6# | 106.1±9.1* | <0.001 |
| RECOVERY | 137.9±15.9# | 128.5±16.2* | 0.01 |
| 1 hour postoperative | 132.2±14.2# | 123.5±14.1* | 0.008 |
| 6 hours postoperative | 129.7±15# | 124.5±16.5* | 0.15 |
| 12 hours postoperative | 131.1±13.8# | 127.5±14.9* | 0.26 |
| 24 hours postoperative | 128.7±13.6# | 126.7±11.7* | 0.47 |

Data is expressed as mean ± standard deviation.
- *p*-value was generated using a repeated measures ANOVA model.
* Significant statistical difference from basal value in Magnesium group.
# Significant statistical difference from total basal value of Control group.
- *p*-value is significant when <0.05.



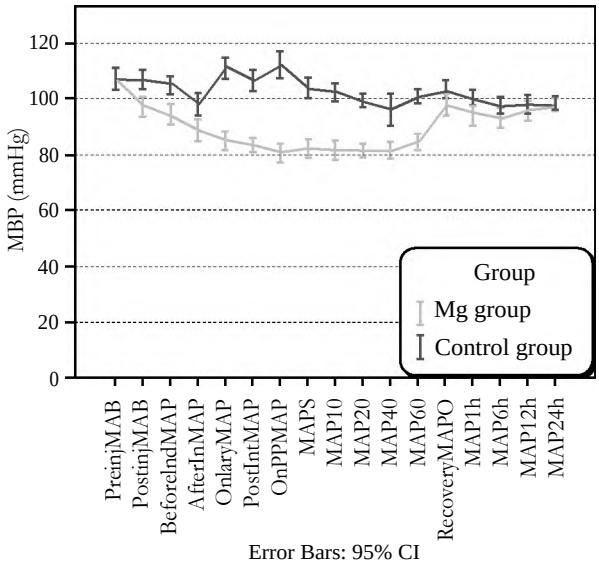




Table (4): Perioperative and post-operative mean arterial blood pressure (MBP).

| MBP (mmHg) | Control group (n=40) | Magnesium group (n=40) | *p*-value |
|---|---|---|---|
| Pre-injection | 107.2±12.1 | 107.6±12.5 | 0.87 |
| Post-injection | 106.4±11.4 | 97.6±10.2* | <0.001 |
| Pre-induction | 104.7±10.5 | 94.6±11.3* | <0.001 |
| Post-induction | 97.7±12.2# | 87.9±10.9* | <0.001 |
| On laryngoscopy and intubation | 110.1 ±12.7 | 84.7±9.1* | <0.001 |
| On insufflation | 110.5±16.3 | 80.2±9.3* | <0.001 |
| 5min. post-operative | 102.9±12.9 | 81.5±9.9* | <0.001 |
| 10min. post-operative | 101.4±11.3# | 82±10.1* | <0.001 |
| 20min. post-operative | 98.9±8.6# | 80.5±8.1* | <0.001 |
| 40min. post-operative | 95.9±16.2# | 81.2±8.2* | <0.001 |
| Recovery | 102.9±11.6# | 97.1±11.2* | 0.03 |
| 1 hour postoperative | 99.7±9.7# | 93.8±9.8* | 0.01 |
| 6 hours postoperative | 97.9±9.2# | 93.7±11.1 * | 0.06 |
| 12 hours postoperative | 98.5±9.7# | 95.7±10.1 * | 0.21 |
| 24 hours postoperative | 98.1±8.6# | 96.7±8.7* | 0.44 |

Data is expressed as mean ± standard deviation.
- *p*-value was generated using a repeated measures ANOVA model.
* Significant statistical difference from basal value in Magnesium group.
# Significant statistical difference from total basal value of Control group.
- *p*-value is significant when <0.05.

Table (5): Recovery timing.

| | Control group (n=40) | Magnesium group (n=40) | *p*-value |
|---|---|---|---|
| Extubation time (min) | 6.5±1.4 | 7.2±1.5 | 0.03 |

Data is expressed as mean ± standard deviation.
- *p*-value was generated using independent sample *t*-test.
- *p*-value is significant when <0.05.

Table (6): Analgesic requirement.

| | Control group (n=40) | Magnesium group (n=40) | *p*-value |
|---|---|---|---|
| Rescue analgesia (min) | 25.65±7.69 | 51.63±11.13 | 0.001 |
| *Analgesic:* | | | |
| Paracetamol doses | 3.31±0.72 | 2.55±0.59 | 0.001 |
| Ketolac doses | 1.5±0.64 | 0.45±0.55 | 0.001 |

Data is expressed as mean ± standard deviation.
- *p*-value was generated using independent sample *t*-test.
- *p*-value is significant when <0.05.

Table (7): Riker sedation agitation score (RSAS).

| | Control group (n=40) | Magnesium group (n=40) | *p*-value |
|---|---|---|---|
| Recovery | 3 (3-5) | 1 (3-5) | 0.01 |
| 10min postoperative | 4 (4) | 4 (4-5) | 0.16 |
| 20 min postoperative | 4 (4) | 4 (4) | 1 |
| 40 min postoperative | 4 (4) | 4 (4) | 1 |
| 60 min postoperative | 4 (4) | 4 (4) | 1 |

Data is expressed as median and range.
- *p*-value was generated using Mann Whitney U test.
- *p*-value is significant when <0.05.

Table (8): VAS.

| | Control group (n=40) | Magnesium group (n=40) | *p*-value |
|---|---|---|---|
| Recovery | 7 (4-8) | 7 (5-8) | 0.65 |
| 1 0min postoperative | 5 (3-7) | 5 (4-6) | 0.39 |
| 20 min postoperative | 4 (2-5) | 3 (2-5) | 0.04 |
| 40 min postoperative | 2 (2-3) | 2 (2-3) | 0.46 |
| 60 min postoperative | 2 (2-3) | 2 (2-3) | 0.39 |

Data is expressed as median and range.
- *p*-value was generated using Mann Whitney U test.
- *p*-value is significant when <0.05.

## Discussion

This study was designed to determine whether pre-operative intravenous magnesium sulphate could significantly modulate the peri-operative hemodynamic responses to laryngoscopy, intubation and pneumo-peritoneum represented by heart rate and blood pressure in hypertensive patients underwent laparoscopic cholecystectomy.

The results of this study showed that there was statistically significant difference between magnesium sulphate group and control group on modulation of hemodynamic responses to laryngoscopy, intubation and insufflation represented by heart rate, Systolic blood pressure and mean blood pressure.

Laryngoscopy, intubation and pneumoperitoneum (PP) for laparoscopic surgery increases arterial pressure, heart rate, and systemic vascular resistance. This issue can be solved by pre-operative administration of Magnesium sulfate which attenuates the adverse hemodynamic responses and provides hemodynamic stability during pneumoperitoneum created for laparoscopic surgery **[17]**.

The pneumoperitoneum required for laparoscopic surgery leads to several important hemodynamic alterations like Cardiac output decreases by up to 30% during laparoscopic surgery, due to a decrease in stroke volume. Pneumoperitoneum also causes an increase in systemic vascular resistance, mean arterial pressure remains increases up to 16% **[18]**.

There was a statistically significant increase in mean arterial pressure systolic blood pressure, diastolic blood pressure from control baseline values. Significant decreases in stroke volume, and cardiac index occurred within 30min of the induction of pneumoperitoneum and positioning. Laparoscopic cholecystectomy significantly and reversibly decreases cardiac performance. Hypertensive patients may be at increased risk for complications not previously recognized with this procedure **[7]**.

The infusion of magnesium sulfate is well known to reduce arterial pressure and attenuate hemodynamic response to laryngoscopy, intubation and pneumoperitoneum in patient undergoing laparoscopic gastrointestinal surgery Magnesium sulfate could safely and effectively attenuate the pneumoperitoneum-related hemodynamic instability during gastrointestinal laparoscopy **[19]**.

Magnesium has a vasodilator action, thus contributing to the reduction of blood pressure. Magnesium sulfate at a dose of 50mg/kg over 2 to 3 minutes immediately pre-operative is reported to effectively attenuate the hemodynamic responses, without severe hypotension or bradycardia through reducing the plasma catecholamines and vasopressin levels, and the intravenous magnesium sulfate at a dose of 50mg/kg is associated with significantly reduced blood pressure at 10 and 30 minutes after pneumoperitoneum, as well as heart rate at 30 minutes during laparoscopic cholecystectomy **[20]** while in other study comparing different doses of magnesium sulphate in laparoscopic surgeries, by comparing different dose of magnesium sulfate, we found that the application of 50mg/kg magnesium sulfate not only can suppress stress response and hypertension significantly caused by laparoscopic surgery, but also has analgesia effect after surgery 19 but in another study Intravenous Magnesium at 30mg/kg as pretreatment is found to be effective in attenuating the presser response to laryngoscopy and intubation, and significantly control the hypertensive response after laryngoscopy and intubation and the effect on SBP plus safety of magnesium as a pre- treatment in comorbid patients with IHD or hypertension or decompensated systemic illness needs further investigation **[21]**.

But in our study we gave the dose of 20mg/kg to the magnesium group depending on the study done by **[22]** that show no big difference between the different doses of magnesium sulphate in Suppressing Cardiovascular Responses to Laryngoscopy & Endotracheal Intubation.

Peri-operative data in both magnesium group and control group of patients showed a heart rate on laryngoscopy and intubation of (67.8 ±9.4) for magnesium group and (95.7 ± 12.9) for control group and heart rate on insufflation of (66.8 ±9.3) for magnesium group and (99.9 ± 13.6) for control group. In the same time the peri-operative data for

the both groups showed a systolic blood pressure (SBP) on laryngoscopy and intubation (110.3±14.3) for magnesium group and (150.8±18.8) for control group and systolic blood pressure (SBP) on insufflation (103.4±11.2) for magnesium group and (145.7±21.4) for control group. And if we came to peri-operative mean blood pressure (MBP), it shows mean blood pressure (MBP) on laryngoscopy and intubation (84.7±9.1) for magnesium group and (110.1±12.7) for control group. The big difference between the two groups due to the effect of magnesium sulphate in attenuation of hemodynamics during these procedures.

When we time of recovery time there were statistically significant difference between the both groups as regarded the Extubation time presented as (7.2±1.5) for magnesium group and (6.5±1.4) for control group while clinically there were no big difference between the two groups, and this statistical difference was explained in the study done **[23]** it showed that magnesium sulfate has been shown to potentiate the neuromuscular blockade of non-depolarizing relaxants and this was evident in the study done by **[24]**, with a prolonged time to Extubation. Prolonged time to verbal response observed could be due to its central nervous system depressant action.

The same results were demonstrated by Kamble, Shruthi P Bevinaguddaiah but by comparison between magnesium sulphate and Clonidinein Attenuating Hemodynamic Response to Pneumoperitoneum in Laparoscopic Cholecystectomy **[23]**.

Also, the same results were demonstrated when magnesium sulphate used in immediately before induction 30mg/kg in 20ml normal saline. Over 2 minutes **[21]** or as a continuous infusion of 50mg/kg in 20ml saline over 5 minutes after induction but before insufflation **[25]**.

The study demonstrated statistically significant difference between the magnesium group and control group as regarded rescue analgesia (51.63 ±11.13) for magnesium group and (25.65±7.69) for control group, the total analgesic consumption for paracetamol doses (2.55 ±0.59) for magnesium group and (3.13±0.72) for the control group. Ketolac doses consumption (0.45±0.55) for magnesium group and (1.5±0.64) for control group This was similar to the study done by **[26]** which demonstrate that Per-operative 50mg/kg magnesium sulphate infusion during the surgery is effective in reducing post-operative pain in patients undergoing laparoscopic cholecystectomy.

## References


1- KOVAC A.L.: Controlling the hemodynamic response to laryngoscopy and endotracheal intubation. J. Clin. Anesth. 8 (1): 63-79. doi:10.1016/0952-8180(95)00147-6, 1996.

2- KHAN N., ASLAM M., NAZ N. and KHAN M.R.: Comparative effects of lidocaine and esmolol in modifying the hemodynamic response to laryngoscopy and intubation. Pakistan J. Med. Heal Sci., 7 (2). doi:10.3126/jssn.v17i2.17144, 2013.

3- FOX E.J., SKLAR G.S., HILL C.H., VILLANUEVA R. and KING B.D.: Complications related to the pressor response to endotracheal intubation. Anesthesiology, 47 (6): 524-525. doi:10.1097/00000542-197712000-00013, 1977.

4- PRYS-ROBERTS C., GREENE L.T., MELOCHE R. and FOËX P.: Studies of anaesthesia in relation to hypertension. II: Haemodynamic consequences of induction and endotracheal intubation. Br. J. Anaesth., 80 (1): 106-122. doi:10.1093/bja/80.1.106, 1998.

5- ADACHI Y.U., SATOMOTO M., HIGUCHI H. and WATANABE K.: Fentanyl attenuates the hemodynamic response to endotracheal intubation more than the response to laryngoscopy. Anesth. Analg., 95 (1): 233-237. doi:10.1097/00000539-200207000-00043, 2002.

6- IVANKOVICH A.D., MILETICH D.J., ALBRECHT R.F., HEYMAN H.J. and BONNET R.F.: Cardiovascular effects of intraperitoneal insufflation with carbon dioxide and nitrous oxide in the dog. Anesthesiology, 42 (3): 281-287. doi:10.1097/00000542-197503000-00008, 1975.

7- MCLAUGHLIN J.G., SCHEERES D.E., DEAN R.J. and BONNELL B.W.: The adverse hemodynamic effects of laparoscopic cholecystectomy. Surg. Endosc., 9 (2): 121-124. doi:10.1007/BF00191950, 1995.

8- ÖZDEMIR-VAN BRUNSCHOT D.M.D., VAN LAARHOVEN K.C.J.H.M., SCHEFFER G.J., POUWELS S., WEVER K.E. and WARLÉ M.C.: What is the evidence for the use of low-pressure pneumoperitoneum? A systematic review. Surg Endosc., 30 (5): 2049-2065. doi:10.1007/s00464-015-4454-9, 2016.

9- SUHAIL SHOUNTHOO R. and GUL S.: Effect of Magnesium Sulphate on intraoperative hemodynamic responses in laparoscopic cholecystectomy. IOSR J. Dent. Med. Sci., 14 (10): 2279-2861. doi:10.9790/0853-141067382, 2015.

10- ALTURA B.M. and ALTURA B.T.: Magnesium, Electrolyte Transport and Coronary Vascular Tone. Drugs, 28 (1): 120-142. doi:10.2165/00003495-198400281-00013, 1984.

11- WILDER-SMITH O.H.G., ARENDT-NIELSEN L., GÄUMANN D., TASSONYI E. and RIFAT K.R.: Sensory changes and pain after abdominal hysterectomy: A comparison of anesthetic supplementation with fentanyl versus magnesium or ketamine. Anesth. Analg., 86 (1): 95-101. doi:10.1097/00000539-199801000-00019, 1998.

12- WHITE L.A.: Patient information about anaesthesia. Rasing Stand a Compend Audit recipes. Published online, 67-89. https://www.rcoa.ac.uk/system/files/CSQ-ARB2012-SEC1.pdf, 2012.

13- HAZZI R. and MAYOCK R.: Perioperative management of hypertension. J. Xiangya Med., 3: 25-25. doi:10.21037/jxym.2018.05.01, 2018.

14- BARAZANCHI A.W.H., MACFATER W.S., RAHIRI J.L., et al.: Evidence-based management of pain after laparoscopic cholecystectomy: A PROSPECT review update. Br. J. Anaesth., 121 (4): 787-803. doi:10.1016/j.bja.2018.06.023, 2018.

15- BIRNBAUM A., ESSES D., BIJUR P.E., HOLDEN L. and GALLAGHER E.J.: Randomized Double-Blind Placebo-Controlled Trial of Two Intravenous Morphine Dosages (0.10mg/kg and 0.15mg/kg) in Emergency Department Patients With Moderate to Severe Acute Pain. Ann. Emerg. Med., 49 (4). doi:10.1016/j.annemergmed.2006.06.030, 2007.

16- SUHAIL SHOUNTHOO R. and GUL S.: Effect of Magnesium Sulphate on intraoperative hemodynamic responses in laparoscopic cholecystectomy. IOSR Journal of Dental and Medical Sciences. Published 2015. Accessed February 19, 2021. www.iosrjournals.org .

17- SENGUPTA J., PAUL S., BISWAS P. and BHATTACHARJEE D.: Effects of magnesium sulfate on hemodynamic response to carbon dioxide pneumoperitoneum in patients undergoing laparoscopic cholecystectomy. Anesth. Essays Res., 7 (2): 228. doi:10.4103/0259-1162.118970, 2013.

18- PERUGINI R.A. and CALLERY M.P.: Complications of laparoscopic surgery. Published online 2001. Accessed February 22. https://www.ncbi.nlm.nih.gov/books/NBK6923/, 2021.

19- TAN W., QIAN D.C., ZHENG M.M., LU X., HAN Y. and QI D.Y.: Effects of different doses of magnesium sulfate on pneumoperitoneum-related hemodynamic changes in patients undergoing gastrointestinal laparoscopy: A randomized, double-blind, controlled trial. BMC Anesthesiol., 19 (1): 1-11. doi:10.1186/s12871-019-0886-4, 2019.

20- ZHANG J., WANG Y., XU H. and YANG J.: Influence of magnesium sulfate on hemodynamic responses during laparoscopic cholecystectomy: A meta-analysis of randomized controlled studies. Med (United States), 97 (45): e12747. doi: 10. 1097/MD.00000000000 12747, 2018.

21- KOTWANI D.M., KOTWANI M.B. and HIWARKAR A.: A prospective randomised study comparing intravenous magnesium sulphate and sublingual nitroglycerine spray in attenuating haemodynamic responses to laryngoscopy and intubation. Int. J. Clin. Trials, 5 (2): 90-96. doi:10.18203/2349-3259.ijct20181396, 2018.

22- MONTAZERI K. and FALLAH M.: A dose-response study of magnesium sulfate in suppressing cardiovascular responses to laryngoscopy and endotracheal intubation. J. Res. Med. Sci., 10 (2): 82-86, 2005.

23- KAMBLE S., BEVINAGUDDAIAH Y., NAGARAJA D., PUJAR V. and ANANDASWAMY T.: Effect of magnesium sulfate and clonidine in attenuating hemodynamic response to pneumoperitoneum in laparoscopic cholecystectomy. Anesth. Essays Res., 11 (1): 67. doi:10.4103/0259-1162.200228, 2017.

24- FUCHS-BUDER T., WILDER-SMITH O.H.G., BORGEAT A. and TASSONYI E.: Interaction of magnesium sulphate with vecuronium-induced neuromuscular block. Br. J. Anaesth., 74 (4): 405-409. doi:10.1093/bja/74.4.405, 1995.

25- AHMAD DAR S. and GUPTA D. DAS: Effect of Magnesium Sulphate on Attenuation of Hemodynamic Stress Responses during Laparoscopic Abdominal Surgeries. J Anesth. Clin. Res., 06 (12). doi:10.4172/2155-6148.1000590, 2015.

26- MENTES O., HARLAK A., YIGIT T., et al.: Effect of intraoperative magnesium sulphate infusion on pain relief after laparoscopic cholecystectomy. Acta Anaesthesiol Scand, 52 (10): 1353-1359. doi:10.1111/j.1399-6576.2008.01816.x, 2008.

# تأثير كبريتات المغنيسيوم على استجابات الدورة الدموية المحيطة بالجراحة فى مرضى ارتفاع ضغط الدم الخاضعين لاستئصال المرارة بالمنظار. دراسة عشوائية محكمة ثنائية التعمية

تنظير الحنجرة والتنبيب الرغامى يحفز العناصر المصلية الجسدية والحشوية من لسان المزمار، والبلعوم، ومنطقة الصفاق، والحبال الصوتية، مما يزيد من النشاط الودى لعنق الرحم. المرضى الذين يعانون من ارتفاع ضغط الدم أكثر عرضة لاستجابة القلب والأوعية الدموية المبالغ فيها لتنظير الحنجرة والتنبيب الرغامى من المرضى الذين يعانون من ضغط الدم المعتاد من المحتمل أن تكون هذه التغييرات فى الدورة الدموية العابرة عديمة الفائدة عند الأشخاص الأصحاء، ولكنها قد تكون خطيرة فى الأشخاص الذين يعانون من ارتفاع ضغط الدم لأنها قد تؤدى إلى نقص تروية عضلة القلب، وعدم انتظام ضربات القلب، ونزيف داخل الجمجمة. لذلك، فإن الوقاية من تحفيز القلب والأوعية الدموية بعد التنبيب الرغامى لها أهمية خاصة فى مرضى ارتفاع ضغط الدم.

بسبب نفخ الصفاقب ثانى أكسيد الكربون أثناء الجراحة بالمنظار ارتفاعات مفاجئة من الضغط الشريانى ومقاومة الأوعية الدموية الجهازية مع عدم حدوث تغيير كبير فى معدل ضربات القلب ربما بسبب زيادة الضغط داخل الصفاق وتنشيط الصفاق بواسطة ثانى أكسيد الكربون. الكاتيكولامياتو البروستاجلاندين ونظام الرينين أنجيوتنسينو الفاسوبريسين الذى يسبب زيادة فى مقاومة الأوعية الدموية الجهازية. يمكن التوسط فى هذه الاضطرابات ميكانيكيا وروحياً، ميكانيكيا عن طريق زيادة المقاومة الوريدية، وضغط الشريان الأورطى البطنى مما يساهم فى زيادة الحمل القلبى المائل وإمالة المريض إلى وضع الرأس، مما يقلل من العودة الوريدية.

منع المغنيسيوم إطلاق الكاتيكولامينات من كلا طرفى الأعصاب الأدرينالية والغدة الكظرية وعلى سبيل المثال كبريتات المغنيسيوم تحول دون إطلاق الكاتيكولامين المرتبط بالتنبيب الرغامى. علاوة على ذلك، ينتج المغنيسيوم توسع الأوعية عن طريق العمل مباشرة على الأوعية الدموية وتخفيف المغنيسيوم بجرعة عالية من الفاسوبريسين ويحفز الحساسية للفاسوبريسين. وقد أشارت الدراسات إلى أن المغنيسيوم يمكن أن يحول دون إطلاق الكاتيكولامين فى المختبر وفى الجسم الحى المغنيسيوم له تأثير توسع الأوعية المستحث بواسطة أكسيد النيتريك ويؤدى إلى توسع الأوعية عن طريق العمل مباشرة على الأوعية الدموية عن طريق التداخل مع مجمو عة واسعة من مواد مضيق الأوعية. يتسبب أكسيد النيتريك فى تنشيط غوانييلكلاز ويزيد من أحادى فوسفات جوانين الدورى، الذى يتوسط فى استرخاء العضلات الملساء الوعائية. يعتبر المغنيسيوم الآن أولاً وقبل كل شىء دواء القلب والأوعية الدموية مع خصائص الكالسيوم المضادة ومضادة للحساسية التى قد تكون مصحوبة بأقل قدر ممكن من الأكتئاب عضلة القلب.

الهدف من العمل: صممت هذه الدراسة لدراسة آثار كبريتات المغنيسيوم على استجابات الدورة الدموية قبل الحث وبعد التنبيب أيضاً خلال نفخ الصفاق وفى فترة ما بعد الجراحة فى مرضى ارتفاع الدم الخاضعين لاستئصال المرارة بالمنظار. والنتيجة الأولية هى تقييم الاستجابات الديناميكية الدموية للتنبيب تشمل نتائج الخروج الثانية، الاستجابات الديناميكية الدموية عقب نفخ الصفاق وخلال فترة العملية الجراحية وديناميكا الدم اللاحقة للعمليات الجراحية لمدة ٢٤ ساعة ، ودرجة مقياس التناظرية المرئية اللاحقة للعمليات الجراحية، والإثارة، والمرة الأولى للحاجة المسكنة، والاستهلاك المسكن.

الطريقة والمرضى: سيتم إجراء هذه الدراسة الاستطلاعية مزدوجة التعمية العشوائية فى غرفة عمليات الجهاز الهضمى على عدد مريض بعد موافقة مجلس البحوث المؤسسية والحصول على موافقة كتابية وشفوية من المرضى. سيتم تضمين المرضى الذين تتراوح أعمارهم من ٤٠ إلى ٦٠ عاماً من كلا الجنسين والمعروف أنهم مرضى ارتفاع ضغط الدم المتحكم به فى الدراسة والذين سيكونون مرشحين لاستئصال المرارة بالمنظار اختيارياً تحت التخدير العام مع التنبيب الرغامى بعد فحص مسبق للمريض اليوم السابق للجراحة.

تلقت المجموعتان من المرضى العلاج التالى فى غرفة ما قبل الجراحة، وتم ربط المراقبين بالمرضى وتم تسجيل جميع المعلمات مثل معدل ضربات القلب وضغط الدم غير الموسع وتشبع الأكسجين وتخطيط القلب.

(المجموعة الأولى) سلفات المغنيزيوم ٥٠ ملغ/كغ فى ٢٥٠ مل من محلول كلوريد الصوديوم متساوى التوتر ٠.٩٪ تدار عن طريق الوريد على مدى ١٥ إلى ٢٠ دقيقة فى غرفة قبل الجراحة مباشرة قبل تحريض التخدير. (المجموعة الثانية) نفس الحجم من محلول كلوريد الصوديوم ٠.٩٪ متساوى التوتر عن طريق الوريد خلال ١٥ إلى ٢٠ دقيقة فى غرفة ما قبل الجراحة مباشرة قبل التخدير.