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"TWO DIFFERENT LOADING DOSES OF INTRAVENOUS MAGNESIUM SULPHATE IN ATTENUATING HAEMODYNAMIC RESPONSE TO PNEUMOPERITONEUM IN LAPAROSCOPIC SURGERIES - A PROSPECTIVE, RANDOMISED, SINGLE-BLINDED, COMPARATIVE STUDY "

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ABSTRACT **Background And Objective:** Pneumoperitoneum during laparoscopic surgeries is related with hemodynamic response due to the effects of vasopressin and catecholamine release. Magnesium has been used to counteract these hemodynamic effects. This study sought to substantiate as well as discover the best optimal dose for eliciting the desired reaction while causing the fewest negative effects. To evaluate the impact of intravenous magnesium sulphate on intraoperative hemodynamics due to pneumoperitoneum in laparoscopic surgeries under general anaesthesia. To investigate and compare the effects of two different magnesium sulphate loading doses on postoperative recovery, such as time to vocal response and time for extubation. **Methods:** This Prospective, Randomised, Single-Blinded, Comparative Study was conducted between March 2021 and September 2022. It included 80 patients of ASA grade I within age group of 18-60 years posted for laparoscopic surgeries under general anaesthesia. Patients having comorbidities, not consenting or procedures lasting under 30minutes were excluded. Patients were randomly divided into Group A and Group B. Group A patients received MgSO4 30 mg/kg intravenous loading-dose and 15 mg/kg/h maintenance infusion for 1 h. while Group B patients received MgSO4 40 mg/kg intravenous loading-dose and 15 mg/kg/h maintenance infusion for 1h. Post-pneumoperitoneum haemodynamics, extubation time and adverse effects were studied. **Results:** Increase in Systolic Blood Pressure at 5min after Pneumoperitoneum was higher in Group. A than Group. B and was statistically significant (p value 0.033). 1 case (Drowsiness) in Group. A and 6 cases (3-Bradycardia; 3- Drowsiness) in Group. B showed adverse effects and was statistically significant p<0.05. Age distribution, Mean age, Gender distribution, HR, SBP at other intervals, DBP, MAP, time to extubation and time to verbal response among the two groups were not statistically significant. **Conclusion:** Lower loading doses of intravenous magnesium sulphate - 30mg/kg - were similarly efficient in attenuating haemodynamic reaction to pneumoperitoneum as higher loading doses commonly employed in laparoscopic procedures, such as 40mg/kg. Lowering the loading dose also reduced the occurrence of adverse effects such as intra-operative Bradycardia and post-operative drowsiness.

KEYWORDS : *Pneumoperitonium, Hemodynamic changes, magnesium sulphate, loading dose.*

INTRODUCTION:

Laparoscopy is a minimally invasive treatment that allows endoscopic access to the peritoneal cavity after the anterior abdominal wall and viscera are separated by gas insufflation. The area is required for safe instrumention and organ manipulation. [1]

Extraperitoneal laparoscopic surgeries are also possible. It can also be gasless with abdominal wall retraction, and it can now be hand or robotically assisted.

Different surgical methods have increasingly improved due to the development of better surgical equipment and anaesthetic facilities, as well as enhanced knowledge and understanding of the anatomy and pathophysiology of various disorders. Thus, the concept of "minimally invasive or endoscopic surgery" decreases patient trauma by lowering morbidity, mortality, hospital stay, and, as a result, health-care costs.[1]

Endoscopic procedures were originally used for different gynaecological operations, such as diagnosis and therapy, in the early 1970s. It promptly grew popular only among gynaecologists. However, it was not widely used among general surgeons until 1987, when PHILLIPE MOURET in France described laparoscopic cholecystectomy for the first time.[2]

Pathophysiological changes caused by pneumoperitoneum, different patient positions (required during laparoscopic surgeries), long duration of some laparoscopic surgeries, risk of some unsuspected visceral injury, difficulty estimating blood loss during surgery, and other factors all contribute to the anaesthesia for laparoscopic surgery being a potentially high risk procedure.

Young, healthy women constitute the majority of patients receiving various gynaecological and surgical laparoscopic procedures.

They are typically linked with mild to moderate cardiopulmonary alterations that are of little significance to an anesthesiologist. However, older patients with known or latent co-existing system disorders who are waiting for laparoscopic surgery are more vulnerable, demanding meticulous care and a full understanding of the pathophysiological alterations associated with laparoscopic surgery.

Compared with open laparotomy the major advantages of laparoscopic surgery are- Reduced tissue trauma (less surgical exposure), Reduced wound size, Reduced post operative pain due to small wound, Reduced incidence of postoperative ileus, Early mobilization of patients, Shorter hospital stay , Improved post operative respiratory functions[3]

For example, following an open laparotomy, forced vital capacity (FVC) is lowered by approximately 50%, with alterations visible up to 72 hours after surgery. In contrast, following laparoscopic surgery, FVC is lowered by around 30% and returns to normal within 24 hours.

On the other hand, technically the laparoscopic surgery differs from the open laparotomy by following points- 1) Laparoscopic surgery needs gravitational displacement of abdominal viscera from the operative site by Trendelenburg or reverse Trendelenburg position.

2) It needs pneumoperitoneum which separates the abdominal wall from viscera, for pneumoperitoneum the upper limit of Intra-Abdoominal Pressure (IAP) is 13-15 mm hg. Modern pneumoperitoneum producing equipment has ability to maintain continuously this upper limit of IAP automatically

3) It needs decompression of abdominal viscera, especially the stomach by nasogastric tube and the bladder by catheter to prevent injury during insertion of trocar.

The physiologic changes associated with laparoscopy include those associated with tilting the patient to facilitate instrumentation, surgical exposure, the pressure effects of instilled gas into a closed cavity, and the systemic effects of gas, almost always Carbon-dioxide (CO2) instilled or absorbed.

Cardiovascular changes include an increase in mean arterial pressure

(MAP), heart rate (HR), systolic blood pressure (SBP), and diastolic blood pressure (DBP), a 10%-30% decrease in cardiac output (CO), and an increase in systemic vascular resistance (SVR), the release of catecholamines, vasopressin, or both.

Although pharmacological treatments such as nitroglycerin, beta blockers, and opioids can help to minimize pneumoperitoneum-induced hemodynamic changes, they have their own set of challenges. Magnesium suppresses the release of catecholamines from adrenergic nerve terminals and the adrenal gland. Magnesium also promotes vasodilation by directly acting on blood vessels. It inhibits vasopressin-mediated vasoconstriction at high doses.

This study was created with the aim of investigating whether IV Magnesium sulphate, can be used effectively to blunt the responses to pneumoperitoneum during laparoscopic surgeries.

Several studies have demonstrated that Magnesium Sulphate can reduce the hemodynamic response to direct laryngoscopy and endotracheal intubation. There have been fewer studies that show attenuation of the haemodynamic response to pneumoperitoneum. This study will work to substantiate this claim as well as determine the most appropriate dose to show the desired response with fewer side effects.

OBJECTIVES OF STUDY :

AIM:

To assess the efficacy of 30mg/kg and 40mg/kg loading doses of magnesium sulphate on the attenuation of hemodynamic response to pneumoperitoneum during laparoscopic surgeries.

OBJECTIVES:

- To evaluate the impact of intravenous magnesium sulphate on intraoperative hemodynamics due to pneumoperitoneum in laparoscopic surgeries under general anaesthesia.
- To investigate and compare the effects of two different magnesium sulphate loading doses on postoperative recovery, such as time to vocal response and time for extubation.
- To evaluate the side effects encountered, if any with two different loading doses.

METHODOLOGY:

This Prospective, Randomised, Single-Blinded, Comparative Study included 80 patients March 2021 to September 2022, of ASA grade I, within age group of 18-60 years, posted for laparoscopic surgeries under general anaesthesia attending Bapuji Hospital and Chigateri General Hospital, attached to J.J.M. Medical College, Davanagere.

Inclusion Criteria:

Age group 18-60yrs**,** ASA grade I**,** Undergoing laparoscopic surgeries under General anaesthesia**,** Patient willing to give informed consent

Exclusion criteria:

Age 60 years**,** ASA II or more patients**,** hypermagnesemia. Allergy to magnesium sulphate**,** Heart block**,** Diabetes mellitus**,** Systemic hypertension**,** Cardiovascular or kidney disease**,** Endocrine or metabolic disease**,** Severe haemorrhage during the surgery.

80 patients were randomly divided into Group A and Group B after taking written informed consent for the same.

- Group A: Received magnesium sulphate 30 mg/kg intravenous loading dose and 15 mg/kg/h continuous maintenance infusion for 1 h
- Group B: Received magnesium sulphate 40 mg/kg intravenous loading dose and 15 mg/kg/h continuous maintenance infusion for 1 h

A detailed medical history, general physical examination and pre-operative investigations was done for all the patients. All the patients were kept nil per oral from 12am midnight prior to the day of surgery and were given.

1. Tab. Pantaprazole 40mg at 10pm the night before surgery
2. Tab. Alprazolam 0.5mg at 10pm the night before surgery

On the day of surgery, intravenous access was established. Standard monitors (pulse oximeter, ECG leads, NIBP) were connected. Baseline vital parameters were recorded. The patients in both groups were preoxygenated for 3 minutes and patients were given Inj. Midazolam 0.05mg/kg, Inj. Fentanyl 2mcg/kg and Inj. Glycopyrrolate 0.01mg/kg intravenously as a premedication and were induced with Inj. Propofol 2mg/kg intravenously and endotracheal intubation was facilitated by Inj. Succinyl choline 2mg/kg. After that, loading dose of Magnesium sulphate was infused over 5 min, immediately before the induction of pneumoperitoneum, followed by a common maintenance infusion of magnesium sulphate over 1 hr in both groups.

Pneumoperitoneum inflation pressure was maintained between 12 to 15mmHg using CO2 as the insufflating agent. Maintenance of Anaesthesia with O2 + N2O+ Isoflurane + Intermittent Inj. Vecuronium + IPPV was used to maintain end tidal carbon dioxide (EtCO2) between 35 and 40 mmHg.

Neuromuscular blockade reversal was achieved at the end of surgery with Inj. Neostigmine 0.05mg/kg and Inj. Glycopyrrolate 0.01mg/kg. Patients were extubated and shifted to post-operative ward at the end of the procedure.

The following parameters were recorded intra-operatively:

1. Heart rate (HR), Systolic and Diastolic blood pressure (SBP and DBP), mean arterial pressure (MAP)

a. Baseline values - before induction
b. PO at the end of loading dose of magnesium sulphate and before pneumoperitoneum
c. P5- 5min after pneumoperitoneum
d. P10-10 min after pneumoperitoneum
e. P20- 20min after pneumoperitoneum
f. P30-30 min after pneumoperitoneum
g. P40-40 min after pneumoperitoneum
h. P60-60 min after pneumoperitoneum

2. Time to tracheal extubation
3. Time to response to verbal command
4. Adverse effects during postoperative period

Statistical analysis:

Categorical data was represented in the form of frequency. Association with variables were assessed with Chi square test. Quantitative data was represented as mean and standard deviation**.** Comparison of variables has been done with unpaired t test**.** A P value of <0.05 was considered statistically significant. The statistical software namely IBM Statistical Package for Social Sciences (SPSS) Version.22 for windows was used for the analysis of the data.

RESULTS:

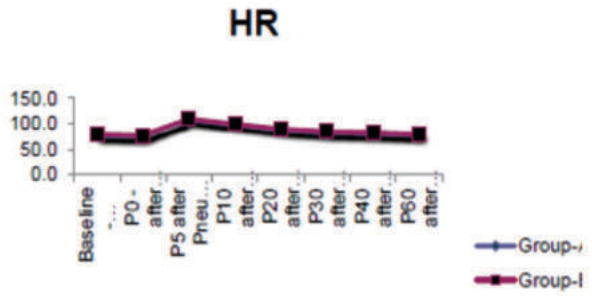
Results were reported as mean +/- standard deviation, or proportions / percentages and are presented in the form of table, graph and charts as necessary. The p value of <0.05 was taken as statistically significant difference between two groups.

Age distribution of patients

Majority of patients in group A were between 31-40 (n= 30%) while those in group B were between 21-30 (n=37.5%). The age distribution in both groups was considered to be statistically insignificant since p> 0.05 as per chi square test

Gender distribution of patients :

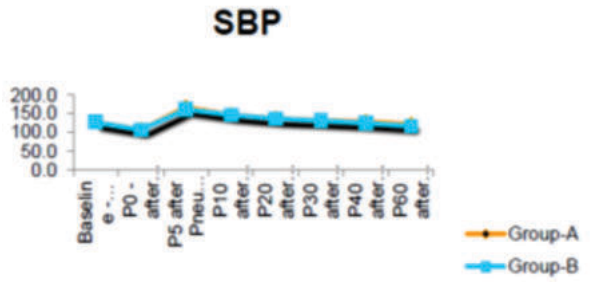
Number of male patients in group A were 15 and female patients were 25. Number of male patients in group B were 14 and female patients were 26. the gender distribution in both groups was considered to be statistically insignificant > 0.05 as per chi square test.



Graph 1 : Comparision of heart rate between two different groups

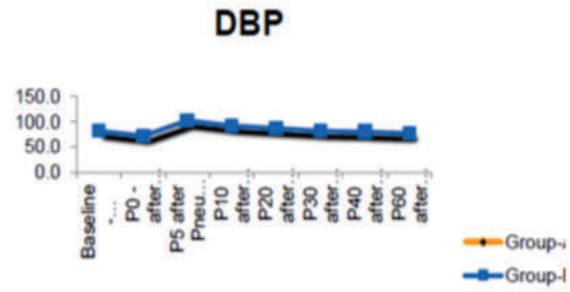
The mean heart rate in Group A before induction (baseline) was 78.4+/- 10.3, while in Group B was 79.6 +/- 10.6, and it was not

statistically significant.



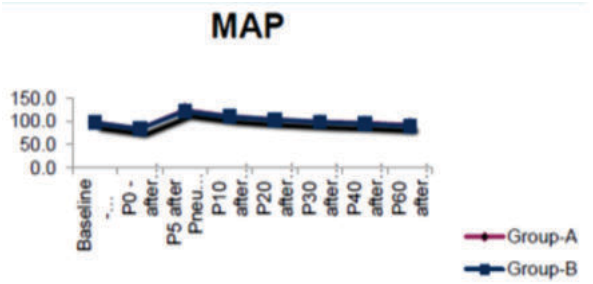
Graph 2: Comparision of systolic blood pressure between two groups

Increase in Systolic Blood Pressure at 5min after Pneumoperitoneum was higher in Group. A than Group. B and was statistically significant (p value 0.033).



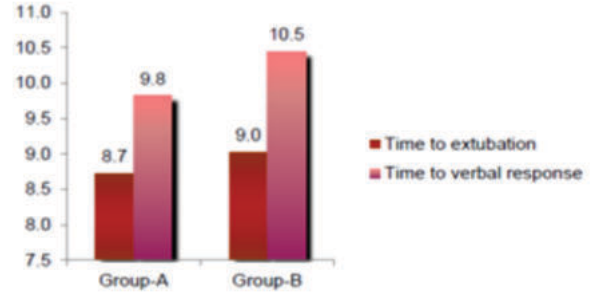
Graph 3 : Comparison of Diastolic Blood Pressure

The Diastolic blood pressure in Group A before induction (baseline) was 82.7+/- 6.6, while in Group B was 82.3 +/- 6.4, and it was not statistically significant.



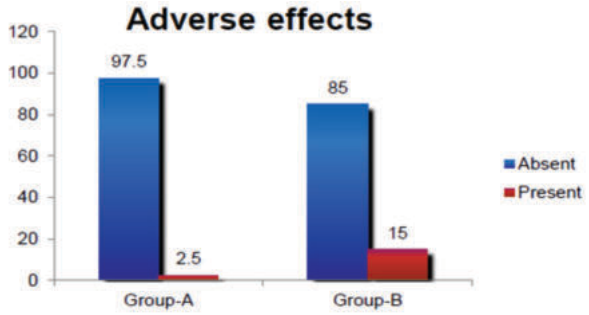
Graph 4: Comparision of mean arterial pressure between two groups

The MAP in Group A at end of administration of drug and before pneumoperitoneum (P0) is 84.5 +/- 8.6, while in Group B was 83.9+/- 7.2 and it was statistically not significant.



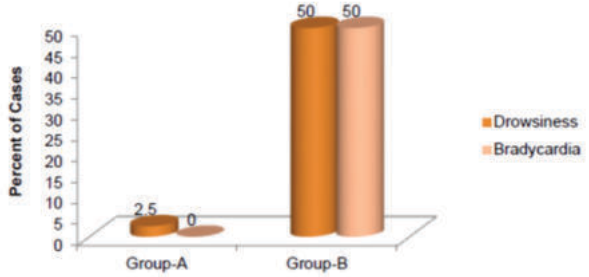
Graph 5 : Comparision of time to extubation and time to verbal response between the two groups

Mean time to verbal response in Group A is 9.80 with S.D of 2.3 Mean time to extubation in Group B is 10.50 with S.D of 2.0. Statistical evaluation showed verbal response times between the two groups statistically insignificant.



Graph 6 : Comparison of Adverse effects:

1 case (Drowsiness) in Group. A and 6 cases (3-Bradycardia; 3-Drowsiness) in Group. B showed adverse effects and was statistically significant p<0.05."



Graph 7: Pattern of Adverse effects

Adverse effect were significantly higher (p<0.010) in Group.B compared to Group. A. 97.5% cases (n=39) in Group.A and 85% cases (n=34) in Group. B showed no adverse effects.

DISCUSSION

Stress response to pneumoperitoneum can lead to complications especially in patients with systemic hypertension or ischemic heart disease. This response should be attenuated in order to maintain normal intraoperative haemodynamics in patients.

Magnesium sulphate is a safe, inexpensive drug for treating hypertension. In recent years, it has been found to have many other effects during perioperative applications, such as its role in alleviating post-operative pain and treating Intubation induced hypertension.

Paul S stated that Magnesium sulfate administered before PP attenuates adverse hemodynamic response and provides hemodynamic stability during PP created for laparoscopic surgery which is similar to our study.[4]

Tan Wei stated that application of 50 mg/kg magnesium sulfate not only significantly suppress stress response and hypertension which is caused by laparoscopic surgery, but also has analgesia effect after surgery. Another advantage of this trial is provided the direct evidence for the role of magnesium sulfate in suppressing the increased SVR induced by pneumoperitoneum.[5]

In the present study, by comparing different dose of magnesium sulfate, we found that the application of 30 mg/kg magnesium sulfate not only can suppress stress response and hypertension significantly caused by laparoscopic surgery, but also has lesser adverse effects than a higher loading dose (40mg/kg magnesium sulphate) group. The use of Magnesium sulphate also did not affect neuromuscular blockade reversal and extubation time.

CONCLUSION :

Both 30mg/kg and 40mg/kg intravenous Magnesium sulphate loading doses showed comparable attenuation of hemodynamic response to pneumoperitoneum in laparoscopic surgeries.

Lower loading dose - 30mg/kg intravenous Magnesium sulphate was associated with significantly lesser incidences of adverse effects like intra-operative Bradycardia and post-operative Drowsiness.

Hence, Lower loading dose of Magnesium Sulphate (30mg/kg) is

preferred to be used during Laparoscopic surgery to attenuate the haemodynamic response induced by pneumoperitoneum

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