

ORIGINAL RESEARCH

A Hospital Based Prospective Study to Compare the Effect of Intravenously Administered Clonidine and Magnesium Sulfate on Hemodynamic Responses During Laparoscopic Surgeries at a Tertiary Care Center

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ABSTRACT

Background: Nowadays laparoscopic surgery is going to be the first choice for surgical management of various indications, especially with the well-trained laparoscopic surgeon. The benefits of minimal access techniques include less pain, early mobilization, shorter hospital stay, and better cosmetic results, which have further increased its applications. The aim of this study to compare the efficacy of intravenously administered clonidine and magnesium sulfate on hemodynamic stress response during laparoscopic surgeries.

Materials& Methods: This is a prospective randomized study done on 50 ASA physical status I and II subjects in the age group of 20-60 years planned for elective laparoscopic surgeries with CO₂ pneumoperitoneum were enrolled in department of anesthesia at American International Institute of Medical Sciences, Udaipur, Rajasthan, India during one year period. They were randomly allocated to one of the two study groups, Group C (Clonidine group) and Group M (Magnesium group). Group C Patients were given a solution containing clonidine 1.5 µg/kg (group C) in 50 ml of normal saline over a period of 15 min and Group M Patients were given a solution containing magnesium sulfate 50 mg/kg in 50 ml of normal saline over a period of 15 min. The parameters like Systolic blood pressure, Diastolic blood pressure, mean arterial Blood pressure, heart rate and SPO₂ were recorded.

Results: The mean value of age was 39.25 years in group C and 42.78 years in group M, which was statistical not significant ($P>0.05$). The comparison of mean value of body weight and duration of surgery was statistical not significant ($P>0.05$). Hemodynamic changes such as Systolic blood pressure, Diastolic blood pressure, mean arterial Blood pressure, heart rate and SPO₂ was statistical nonsignificant in different time interval. Statistically significant difference observed in the Modified Ram say sedation scale between the two groups. Clonidine found to have significantly lesser sedation than magnesium at the time of extubation.

Conclusion: We concluded that intravenous administration of clonidine 1.5µg/kg before pneumoperitoneum is as effective as intravenous magnesium sulfate 50mg/kg before pneumoperitoneum in blunting the haemodynamic stress responses during laparoscopic surgeries and clonidine has lesser sedation than magnesium at extubation.

Keywords: Laparoscopic Surgery, Clonidine Group, Magnesium Group, Pneumoperitoneum.

INTRODUCTION

Laparoscopic surgeries have become recent trend in the surgical field aim to achieve a satisfactory therapeutic result while minimizing the traumatic and metabolic stress. Advantages of Laparoscopic surgical procedures include less tissue trauma, smaller incisional sites, lower risks of wound complications, reduced postoperative pain, complications, shorter hospital stay, more rapid return to normal activities, and cost savings.

During general anesthesia laryngoscopy, tracheal intubation and extubation are the critical events provoking transient but marked sympathoadrenal response manifesting by hypertension and tachycardia. In addition, in laparoscopy requires the establishment of pneumoperitoneum in order to provide adequate surgical exposure and maintain operative freedom. This insufflation of carbon dioxide can lead to various physiological changes. An emerging body of data addresses the hemodynamic, respiratory, immunological and stress response related to the pneumoperitoneum.^{1,2}

Severe increases in arterial pressure can be a risk factor in patients with preexisting hypertension, ischaemic heart disease, or increased intracranial pressure. Opioids, alpha₂-adrenergic agonists, beta-blocking agents, or vasodilators are often used to avoid circulatory response to pneumoperitoneum.³

Clonidine, a selective α -2 adrenergic receptor agonist, has shown promising results for attenuation of hemodynamic response associated with laparoscopic surgery. Clonidine causes a fall in the heart rate and blood pressure along with decreased systemic vascular resistance and cardiac output.⁴

Magnesium blocks release of catecholamines from both adrenergic nerve terminals and adrenal gland. Magnesium also produces vasodilation by acting directly on blood vessels. In high doses, it attenuates vasopressin-mediated vasoconstriction.⁴ The aim of this study to compare the efficacy of intravenously administered clonidine and magnesium sulfate on hemodynamic stress response during laparoscopic surgeries.

MATERIALS& METHODS

This is a prospective randomized study done on 50 ASA physical status I and II subjects in the age group of 20-60 years planned for elective laparoscopic surgeries with CO₂ pneumoperitoneum were enrolled in department of anesthesia at American International Institute of Medical Sciences, Udaipur, Rajasthan, India for one year period. They were randomly allocated to one of the two study groups, Group C (Clonidine group) and Group M (Magnesium group).

INCLUSION CRITERIA

1. ASA I and II
2. Age group of 20-60 years
3. Patients posted for elective laparoscopic surgery

EXCLUSION CRITERIA

1. Patients with systemic disorders like hypertension, diabetes mellitus, left ventricular failure, any degree of heart block, ischemic heart disease, aortic stenosis.
2. Patients on calcium channel blockers, beta blockers, methyldopa, Tricyclic antidepressants, benzodiazepines, monamine oxidase inhibitors.
3. Hypermagnesaemia

PREANAESTHETIC EVALUATION

All patients were kept on 6 hours starvation. Patients were premedicated with intravenous ranitidine 0.25 mg/kg, metoclopramide 0.15 mg/kg and glycopyrrolate 0.02 mg/kg intramuscularly in preoperative room 60 minutes before surgery.

IN THE OPERATING ROOM

On arrival in the operation theater, monitors were connected (heart rate, NIBP, oxygen saturation, ECG) and baseline vital parameters like heart rate, systolic and diastolic blood pressure, and oxygen saturation were recorded. Fentanyl 2 µg/kg intravenous was given for analgesia. After pre-oxygenation with 100% oxygen for 3 minutes. Induction agent propofol 2- 2.5 mg/ kg and succinyl choline chloride 1- 2mg/kg given intravenously and intubated with appropriate size endotracheal tube. ETCO₂ monitor were connected.

PROCEDURE

Prefilled syringes with the test drugs was given to the anaesthesiologist with the instructions to give the test drug immediately after intubation.

Group C Patients were given a solution containing clonidine 1.5 µg/kg (group C) in 50 ml of normal saline over a period of 15 min.

Group M Patients were given a solution containing magnesium sulfate 50 mg/kg in 50 ml of normal saline over a period of 15 min.

Anesthesia was maintained with oxygen-nitrous oxide mixture (50:50) and intermittent positive pressure ventilation, Inj. vecuronium bromide 0.08mg/ kg as loading dose and thereafter vecuronium bromide 0.02mg/kg as the intermittent boluses for maintenance was given. The tidal volume and respiratory rate adjusted to maintain end tidal carbon dioxide between 35 and 45 mm Hg. During surgery, Ringer's lactate was infused in accordance with maintenance volume requirements and blood loss. CO₂ pneumoperitoneum was created and intraabdominal pressure maintained at 14 mm Hg. Trendelenburg position was used for the laparoscopic appendicectomy and Reverse trendelenburg position was used for the laparoscopic cholecystectomy.

ASSESSMENT OF PARAMETERS

The parameters like Systolic blood pressure, Diastolic blood pressure, mean arterial Blood pressure, heart rate and SPO₂ were recorded.

Patients were monitored for any adverse effects like bradycardia, and hypotension during intraoperative period.

Neuromuscular block was reversed with intravenous neostigmine 0.05 mg/kg and glycopyrrolate 0.02 mg/ kg and after adequate recovery, patient extubated.

ADVERSE EFFECTS

Immediately after the extubation the patients were monitored for nausea, vomiting, shivering and level of sedation assessed by Modified Ramsay sedation score.

STATISTICAL TEST OF SIGNIFICANCE

Comparison of parameters was done using One-Way ANOVA and categorical data was compared using Chi-square test. P Value <0.05 considered as statistically significant.

RESULTS

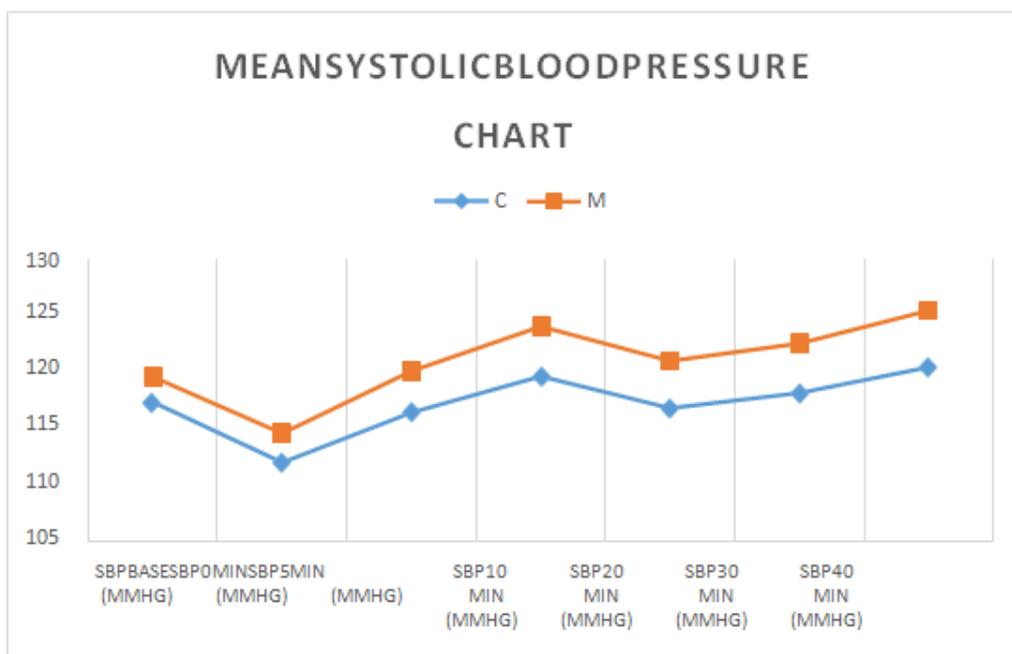
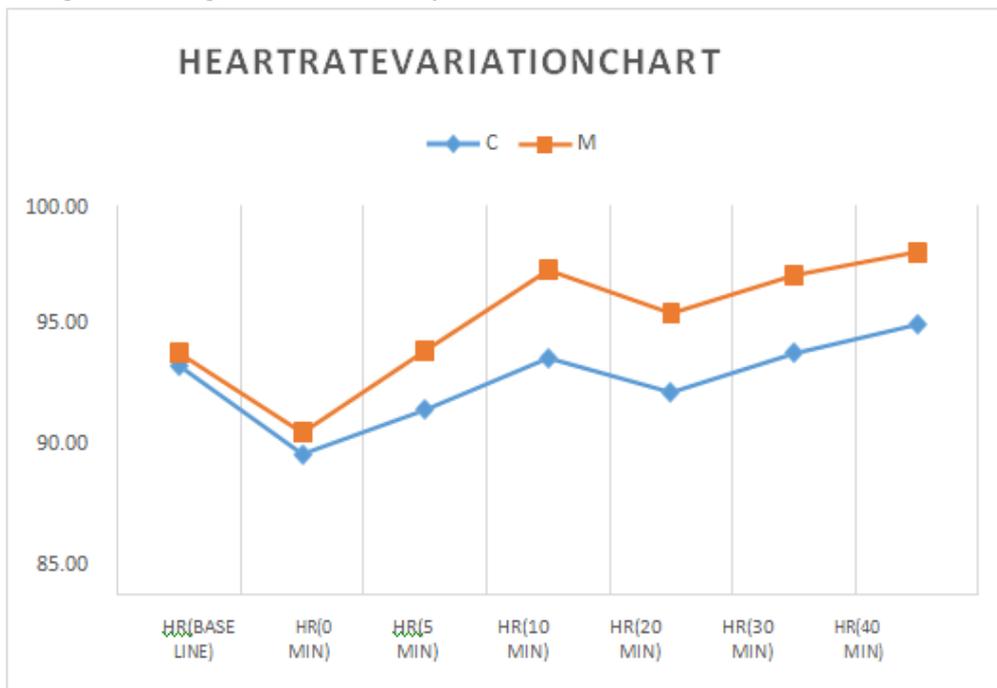
The age distribution was in the range of 20-60 years in Group C and Group M. The mean value of age was 39.25 years in group C and 42.78 years in group M, which was statistical not significant (P>0.05). The mean value of body weight was 59.23 kg in group C and 60.89 kg in

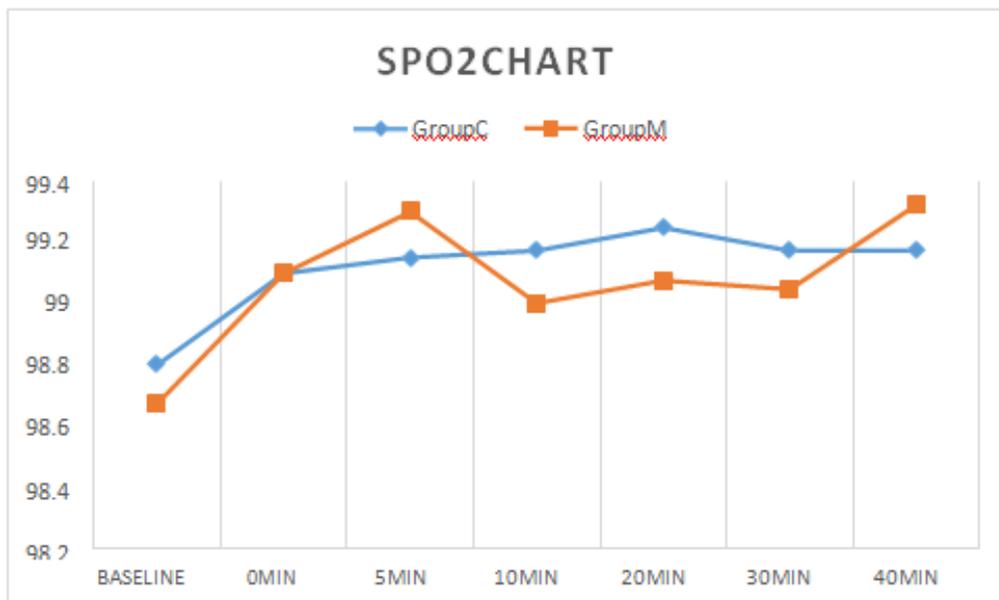
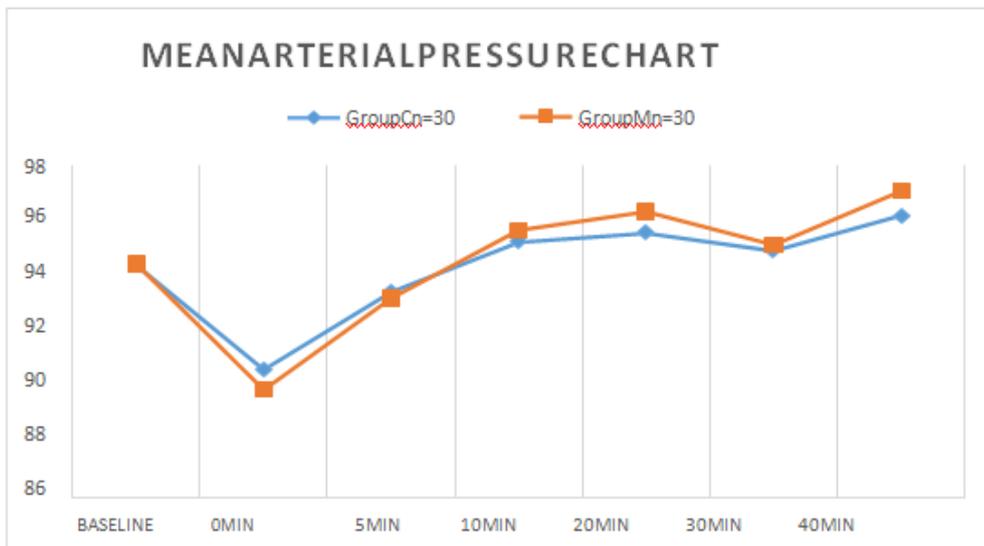
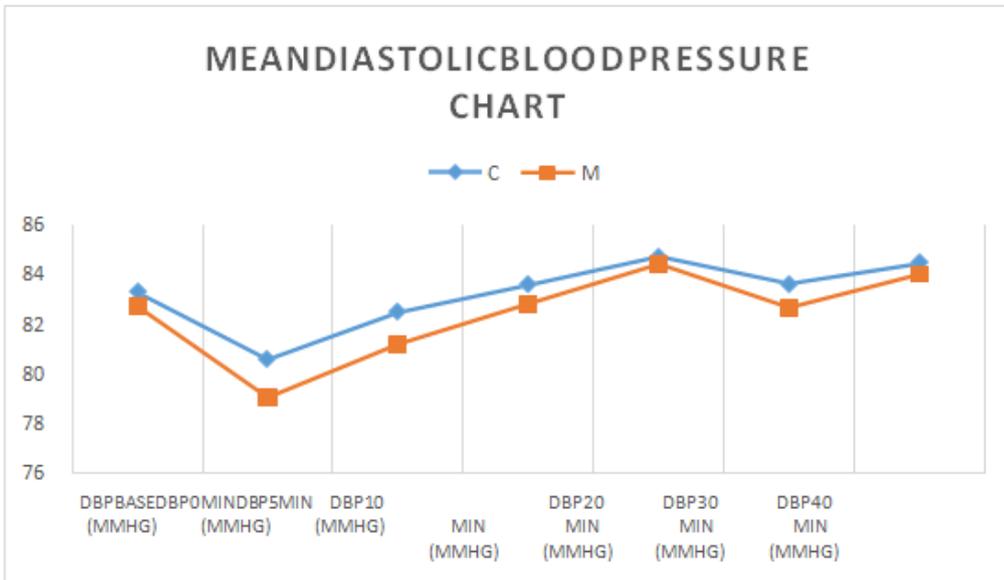
group M, which was statistical not significant ($P>0.05$). The mean duration of the surgery in the group C was 53.15 and group M was 52.78. The p value is 0.923 and statistically insignificant (table 1).

Table 1: Comparison of variables in between groups

Variables	Group- C (N=25)	Group-M (N=25)	P-value
Age (yrs)	39.25±10.13	42.78±10.76	>0.05
Body weight (Kg)	59.23±11.27	60.89±12.28	>0.05
Duration of surgery (Min.)	53.15±5.62	52.78±4.56	>0.05

Hemodynamic changes such as Systolic blood pressure, Diastolic blood pressure, mean arterial Blood pressure, heart rate and SPO2 was statistical nonsignificant in different time interval in figure 1 to figure 5 in our study.





Statistically significant difference observed in the Modified Ramsay sedation scale between the two groups. Clonidine found to have significantly lesser sedation than magnesium at the time of extubation (table 2).

Table 2: Comparison of Modified Ramsay Sedation score in between groups

Modified Ramsay Sedation score	Group- C (N=25)	Group-M (N=25)	P-value
Mean \pm SD	3.12 \pm 0.28	3.38 \pm 0.42	<0.05**

DISCUSSION

Laparoscopic surgeries are being performed more and more frequently now a days for various elective procedures. Though Open procedures are being done, laparoscopy is preferred by both the patients and surgeon for its advantages. So, there is a need for the better control of hemodynamics intraoperatively in the types of surgeries.

Various pharmacological agents have been studied in the recent past for attenuating the hemodynamic responses to the laparoscopy. Most of the studies have compared the effect of intravenous clonidine or magnesium with that of the control. Very few studies are available that compare intravenous clonidine with magnesium for attenuation of the hemodynamic responses to laparoscopy.

The demographic characteristics like age, weight, ASA status of the study population and duration of the surgery were similar in both the two groups, with no statistically significant difference.

In Group C we have used clonidine 1.5 μ g/kg in 50ml normal saline and in Group M magnesium sulfate 50mg/kg in 50ml of normal saline was used. The test drug solution were infused over a period of 15 minutes before pneumoperitoneum.

In the study by Nand Kishore Kalra et al⁵ compared the attenuation of hemodynamic response during laparoscopic cholecystectomy due to pneumoperitoneum was infused with intravenous clonidine 1 μ g/kg, clonidine 1.5 μ g/kg, magnesium 50mg/kg and placebo and found that both clonidine doses and magnesium had significant attenuation on hemodynamic stress response when compared with placebo. The test drugs solution was infused after intubation for 15 minutes. Clonidine 1.5 μ g/kg showed statistically significant difference with magnesium 50mg/kg with no incidence of adverse events like bradycardia and hypotension.

Similarly, Altan and Turgut et al⁴ used clonidine 3 μ g/kg intravenously over a period of 15 minutes before induction and then 2 μ g/kg/min by continuous infusion intraoperatively. They observed significant incidences of bradycardia and hypotension in their study. Ray et al⁶ used 3 μ g/kg of clonidine intravenously over a period of 15 min before induction and then 1 μ g/kg/min by continuous infusion during surgery and observed significant incidences of bradycardia and hypotension in their study. Therefore, we reduced the dose of clonidine, given before pneumoperitoneum, to 1.5 μ g/kg. Even though we reduced the dose of clonidine and avoided the intraoperative infusion, we observed 7% incidence of bradycardia in clonidine group patients.

Jee et al⁷ administered magnesium sulfate 50 mg/kg over 2-3 minutes, before pneumoperitoneum in patients undergoing laparoscopic cholecystectomy and observed that it effectively attenuated the hemodynamic stress response due to pneumoperitoneum without any episode of severe hypotension or bradycardia. We used same dose of magnesium sulfate in our study to compare it with clonidine. The magnesium dose selected by us resulted in a steady and smooth reduction of mean arterial pressure and heart rate, with no episodes of hypotension and bradycardia.

Similarly, Paul S et al⁸ studied the effects of magnesium in hemodynamic response to laparoscopic surgery and concluded that the mean arterial pressure and heart rate were significantly less throughout the period of pneumoperitoneum in patients who received magnesium 30mg/kg when compared with placebo. Telci L et al⁹ also concluded that the

administration of magnesium led to a significant reduction in the requirements of anaesthetic drugs during total intravenous anaesthesia with propofol, remifentanyl and vecuronium with better control of hemodynamics.

Hemodynamic changes such as Systolic blood pressure, Diastolic blood pressure, mean arterial Blood pressure, heart rate and SPO₂ was statistical nonsignificant in different time interval in our study. A Altan et al⁴ observed hemodynamic changes was statistical non-significant.

All the studies done to compare the effect of clonidine and magnesium to blunt the stress response to pneumoperitoneum were done in laparoscopic cholecystectomy. But in our study both laparoscopic appendectomy and laparoscopic cholecystectomy were included. In laparoscopic cholecystectomy the positioning is the head up tilt, whereas in laparoscopic appendectomy trendelenburg position was used, which is in contrast each other.

The effect of positioning on the hemodynamics during laparoscopy and its influence on the result of studies is not addressed in various studies.

Both clonidine and magnesium produces sedation. In our study, we compared the sedative effect of clonidine and magnesium by using the modified Ramsay sedation scale at the time of extubation. This difference in sedative effect could be explained by the prolonged sedative effect of magnesium than clonidine. The p value is <0.003 and found to be statistically significant.

Nand K et al⁵ also concluded that patients receiving magnesium for attenuation of hemodynamic stress response showed that time to respond to verbal command like eye opening was not statistically significant between the clonidine group and magnesium group. This is in contrast with our study.

Javaherfroosh F et al¹⁰ conducted a study to observe the effects of clonidine to reduce the post-operative nausea and vomiting in laparoscopic gynecological surgery. They found that the Ramsay sedation score is <3 (P<0.05) in 31/43 (72%) patients and >3 (P<0.05) in 12/43 (28%) patients and found to be statistically significant. This is similar to our study result.

Eduardo Tocchetto Lemes et al¹¹ conducted a study to observe effects of preoperative intravenous clonidine in the surgical treatment of cataract. They observed that the patients who received clonidine showed small increase in the degree of sedation at 30 minutes after the surgery when compared with placebo group. This is similar to our study result.

Abass Sedighinejad et al¹² conducted a study to compare magnesium Sulfate and sufentanil for Patient-Controlled Analgesia in Orthopedic Surgery. They concluded that the magnesium group showed no significant difference in sedation score with sufentanil. However, in our study there is significant difference between the clonidine and magnesium sulfate.

A greater fall in the systolic blood pressure, diastolic blood pressure and mean arterial pressure in clonidine group over magnesium group was observed in laparoscopic cholecystectomy only, whereas in our study majority of cases were laparoscopic appendectomy cases, in which trendelenburg position was used. The enhanced effect of clonidine over magnesium in attenuation the systolic blood pressure, diastolic blood pressure and mean arterial pressure to pneumoperitoneum is probably offset by the head down tilt or trendelenburg position used in laparoscopic appendectomy. So, our study shows that clonidine and magnesium are equally effective in attenuating the stress response to pneumoperitoneum.

CONCLUSION

We concluded that intravenous administration of clonidine 1.5µg/kg before pneumoperitoneum is as effective as intravenous magnesium sulfate 50mg/kg before pneumoperitoneum in blunting the haemodynamic stress responses during laparoscopic surgeries and clonidine has lesser sedation than magnesium at extubation.

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