

Comparison of Intravenous Clonidine and Magnesium Sulfate on Hemodynamic Response during Laparoscopic Surgeries

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Abstract

Background: Both magnesium and clonidine are known to inhibit catecholamine and vasopressin release and attenuate hemodynamic response to pneumoperitoneum. This randomized, double blinded, placebo controlled study was designed to assess which agent attenuates hemodynamic stress response to pneumoperitoneum in a better way. **Materials and Methods:** 60 patients undergoing elective laparoscopic cholecystectomy were randomized into 2 groups of 30 each. Group M patients received 50 mg/kg of magnesium sulfate in normal saline (total volume 50 ml) over 15 minutes and group C patients received 1.5 µg/kg clonidine in 50 ml of normal saline (total volume 50 ml) before pneumoperitoneum. Blood pressure and heart rate were recorded before induction (baseline value), at the end of infusions and every 5 minutes after pneumoperitoneum. **Statistical Analysis:** Chi-Square test was used for categorical data and ANOVA for inter-group comparison. **Results:** Intravenous administration of clonidine 1.5 µg/kg before pneumoperitoneum was as effective as intravenous magnesium sulfate 50 mg/kg before pneumoperitoneum in blunting the haemodynamic stress responses during laparoscopic surgeries and clonidine has lesser sedation than magnesium at extubation.

Keywords: Clonidine; Laparoscopic Surgery; Magnesium Sulfate; Pneumoperitoneum.

Introduction

Pneumoperitoneum during laparoscopy and its consequent hemodynamic changes can be attenuated by pharmacological agents such as nitroglycerine, β blocker, opioids and α_2 agonists to provide hemodynamic stability. Clonidine, a selective α_2 adrenergic receptor agonist has shown promising results for attenuation of hemodynamic response associated with laparoscopic surgery. Magnesium blocks release of catecholamines from both adrenergic nerve terminals and adrenal gland. It also produces vasodilation by acting directly on blood vessels.

This study was designed in a prospective, randomized, double-blinded fashion to compare the efficacy of intravenously administered clonidine

and magnesium sulfate on hemodynamic stress response during laparoscopic surgeries.

Aim of the Study

The aim of this study was to compare the intravenously administered clonidine and magnesium sulfate on hemodynamic responses during laparoscopic surgeries in terms of:

1. Heart rate
2. Systolic blood pressure
3. Diastolic blood pressure
4. Mean arterial pressure
5. Level of sedation on recovery
6. Adverse effects

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Materials and Methods

This study was conducted in a tertiary care hospital after obtaining institutional ethical committee approval and informed consent. 60 ASA physical status I and II subjects within the age group of 20-60 years planned for elective laparoscopic surgeries were enrolled in this study. They were randomly allocated to one of the two groups such as Group C (Clonidine group) and Group M (Magnesium group).

Aim of the Study

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.

Inclusion Criteria

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

Comparison

Exclusion Criteria

1. Patients who refuse to give informed written consent
2. Patients with systemic disorders
3. Patients on calcium channel blockers, beta blockers, methyl dopa, tricyclic antidepressants, benzodiazepines, monamine oxidase inhibitors

Preoperative Preparation

All patients were kept on 6 hours nil per oral. Patients were premedicated with intravenous injection ranitidine 0.25 mg/kg, metoclopramide 0.15mg/kg and intramuscular injection glycopyrrolate 0.02 mg/kg in the preoperative room, 45 minutes before surgery.

In the Operating Room

On arrival in the operation theater, monitors were connected and baseline vital parameters were recorded. Intravenous injection Fentanyl 2 µg/kg was given for analgesia. After pre-oxygenation,

induction agent injection propofol 2mg/kg and succinyl choline chloride 2mg/kg were given intravenously and intubated with appropriate size endotracheal tube. After intubation, Group C Patients received clonidine 1.5 µg/kg (group C) in 50 ml of normal saline over a period of 15 min and Group M Patients received 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), sevoflurane inhalational agent 1% and injection vecuronium bromide 0.08mg/kg as loading dose and 0.02mg/kg as maintenance dose for muscle relaxation. The tidal volume and respiratory rate were adjusted to maintain end tidal carbon dioxide value between 35 and 45 mm Hg. CO₂ pneumoperitoneum was created and intra-abdominal pressure maintained at 14 mm Hg. Trendelenburg position was used for laparoscopic appendectomy and reverse Trendelenburg position was used for laparoscopic cholecystectomy.

The parameters like systolic blood pressure, diastolic blood pressure, mean arterial blood pressure, heart rate and SpO₂ were recorded at the following point of time:

1. Prior to induction (baseline value)
2. At the end of infusion (P0)
3. 5 min after pneumoperitoneum (P5)
4. 10 min after pneumoperitoneum (P10)
5. 20 min after pneumoperitoneum (P20)
6. 30 min after pneumoperitoneum (P30)
7. 40 min after pneumoperitoneum (P40)

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. After extubation, patients were monitored for adverse effects such as nausea, vomiting, shivering and level of sedation which was assessed by Modified Ramsay sedation score.

Modified Ramsay Sedation Score

Score 0 - Paralyzed, unable to evaluate

Score 1 - Awake

Score 2 - Lightly sedated

Score 3 - Moderately sedated, follows simple commands

Score 4 - Deeply sedated, responds to non-painful stimuli

Score 5 - Deeply sedated, responds only to painful stimuli

Score 6 - Deeply sedated, unresponsive to painful stimuli

Observations and Results

The demographic characteristics like age, weight, ASA status of the study population and duration

of the surgery were similar in both the groups, with no statistically significant difference (P > 0.05).

There was no statistically significant difference in the heart rate (Table 1), systolic blood pressure (Table 2), diastolic blood pressure (Table 3), mean arterial blood pressure (Table 4) and oxygen saturation (Table 5) among the groups at any point of time during the study (P > 0.05). But, statistically significant difference observed in the Modified Ramsay sedation scale between the two groups (Table 6). Clonidine was found to have significantly lesser sedation than magnesium at the time of extubation.

Table 1: Comparison of groups based on heart rate

Heart rate (beats per minute)	Group C n=30 (Mean ± Standard deviation)	Group M n=30 (Mean ± Standard deviation)	P Value	Significance
Base line	89.73 ± 10.77	90.57 ± 11.96	0.778	Not significant
0 min	84.07 ± 10.87	85.43 ± 12.63	0.668	Not significant
5 min	86.90 ± 10.78	90.73 ± 12.55	0.234	Not significant
10 min	90.23 ± 10.77	95.90 ± 12.60	0.066	Not significant
20 min	88.03 ± 10.65	93.13 ± 12.54	0.095	Not significant
30 min	90.53 ± 10.94	95.57 ± 12.26	0.099	Not significant
40 min	92.40 ± 11.05	97.07 ± 12.33	0.128	Not significant

Table 2: Comparison of groups based on Mean systolic blood pressure

SBP (mm Hg)	Group C n=30 (Mean ± Standard deviation)	Group M n=30 (Mean ± Standard deviation)	P Value	Significance
Base line	117.40 ± 7.31	119.63 ± 8.24	0.271	Not significant
0 min	112.00 ± 8.46	114.63 ± 8.20	0.226	Not significant
5 min	116.47 ± 9.10	120.17 ± 8.26	0.104	Not significant
10 min	119.67 ± 9.56	124.13 ± 8.42	0.600	Not significant
20 min	116.83 ± 9.78	121.07 ± 8.69	0.820	Not significant
30 min	118.20 ± 9.66	122.60 ± 8.67	0.068	Not significant
40 min	121.17 ± 10.19	125.53 ± 8.78	0.081	Not significant

Table 3: Comparison of groups based on diastolic blood pressure

DBP	Group C n=30 (Mean ± Standard deviation)	Group M n=30 (Mean ± Standard deviation)	P Value	Significance
Base line	81.10 ± 5.96	80.07 ± 6.71	0.531	Not significant
0 min	76.23 ± 5.63	73.47 ± 6.70	0.089	Not significant
5 min	79.63 ± 5.64	77.33 ± 6.65	0.154	Not significant
10 min	81.63 ± 5.85	80.27 ± 6.49	0.395	Not significant
20 min	83.70 ± 6.05	83.13 ± 6.45	0.727	Not significant
30 min	81.73 ± 6.11	79.97 ± 6.62	0.287	Not significant
40 min	83.17 ± 6.10	82.40 ± 6.65	0.644	Not significant

Table 4: Comparison of groups based on Mean arterial pressure

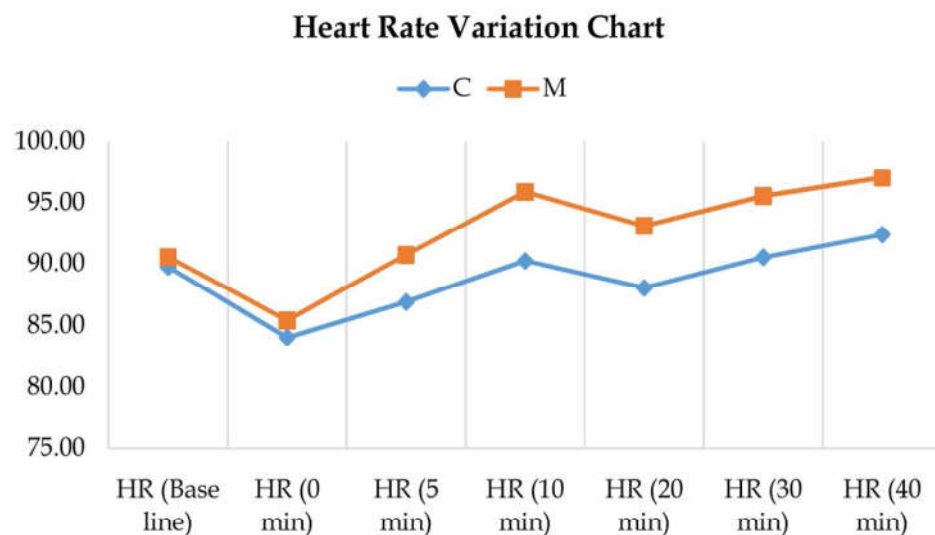
MAP	Group C n=30 (Mean ± Standard deviation)	Group M n=30 (Mean ± Standard deviation)	P Value	Significance
Base line	93.20 ± 4.64	93.26 ± 5.81	0.968	Not Significant
0 min	88.16 ± 5.00	87.19 ± 5.12	0.462	Not Significant
5 min	91.91 ± 5.16	91.61 ± 4.86	0.817	Not Significant
10 min	94.31 ± 5.51	94.89 ± 4.86	0.668	Not Significant
20 min	94.74 ± 5.63	95.78 ± 4.71	0.444	Not Significant
30 min	93.89 ± 5.68	94.18 ± 4.82	0.833	Not Significant
40 min	95.60 ± 5.73	96.78 ± 4.96	0.398	Not Significant

Table 5: Comparison of groups based on oxygen saturation

SPO ₂	Group C n=30	Group M n=30	P Value
Base line	98.6 ± 1.192	98.43 ± 1.104	0.576
0 min	99 ± 0	99 ± 0	-
5 min	99.07 ± 0.785	99.27 ± 0.74	0.314
10 min	99.1 ± 0.885	98.87 ± 0.73	0.270
20 min	99.2 ± 0.805	98.97 ± 0.85	0.280
30 min	99.1 ± 0.845	98.93 ± 0.868	0.454
40 min	99.1 ± 0.803	99.3 ± 0.702	0.309

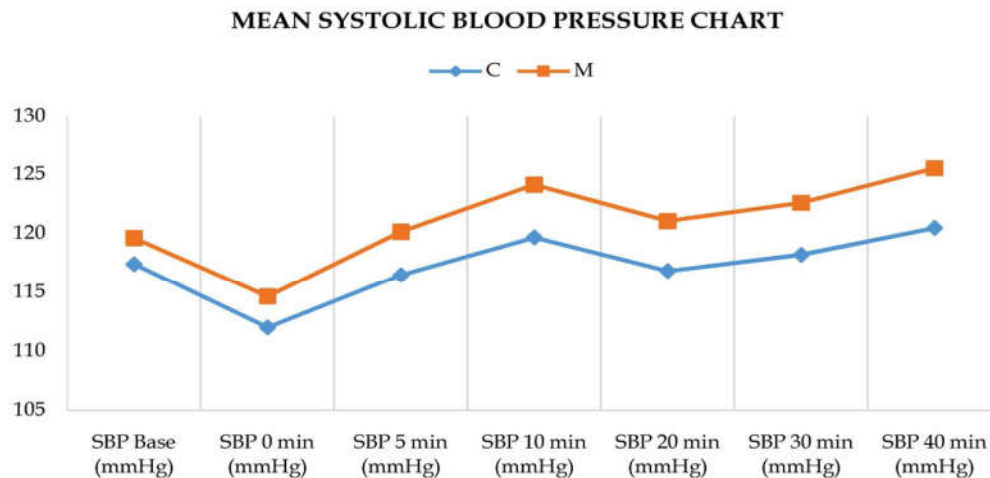
Table 6: Modified Ramsay sedation score

Study Group	N	Score Range	Mean ± Standard Deviation	P Value	Significance
C	30	3-4	3.10 ± 0.31	0.003	Significant
M	30	3-4	3.43 ± 0.50		



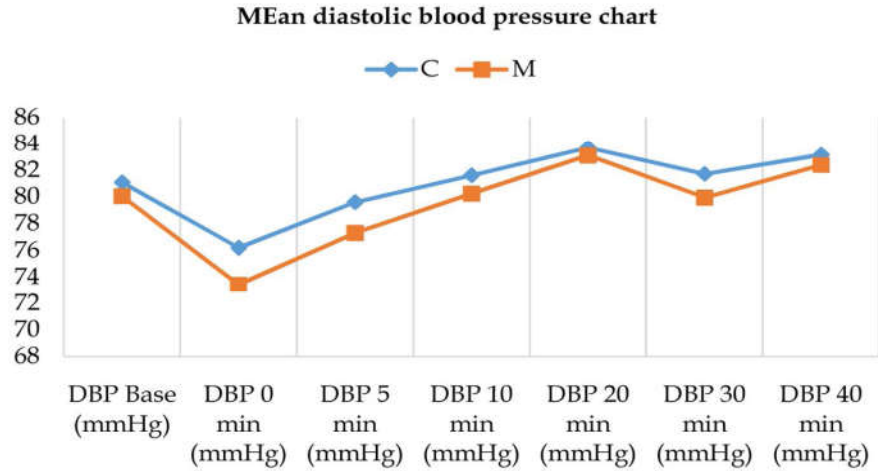
HR-Hear rate, C-Clonidine group, M-Magnesium sulfate group

Fig. 1: Graph showing the Heart rate variation

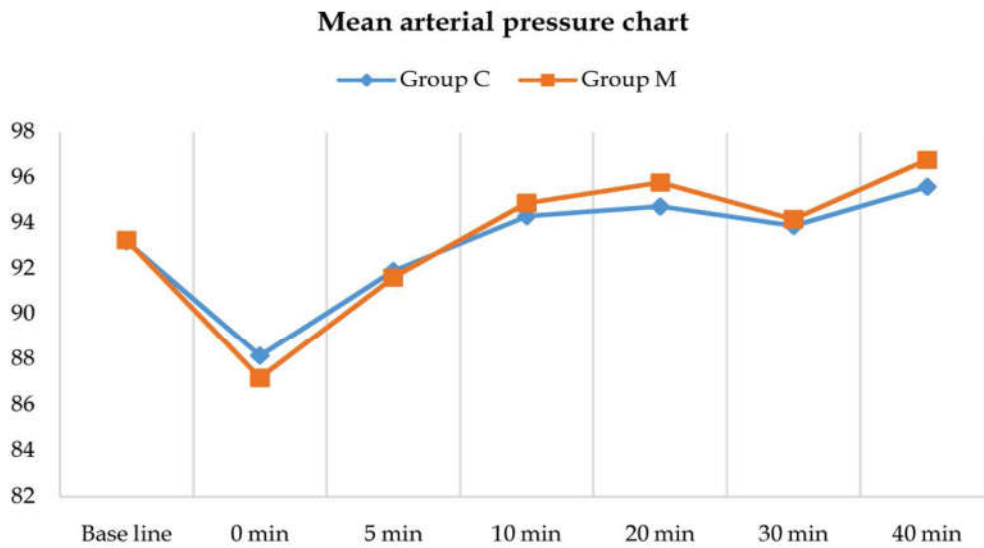


SBP-Systolic blood pressure, C-Clonidine group, M-Magnesium sulfate group

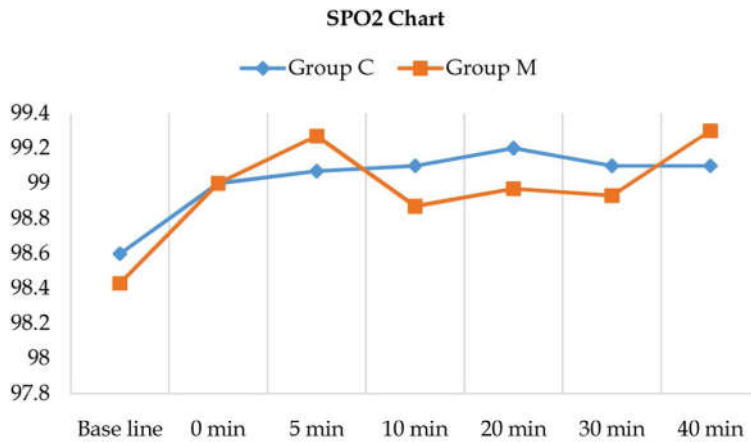
Fig. 2: Graph showing the mean systolic blood pressure variation



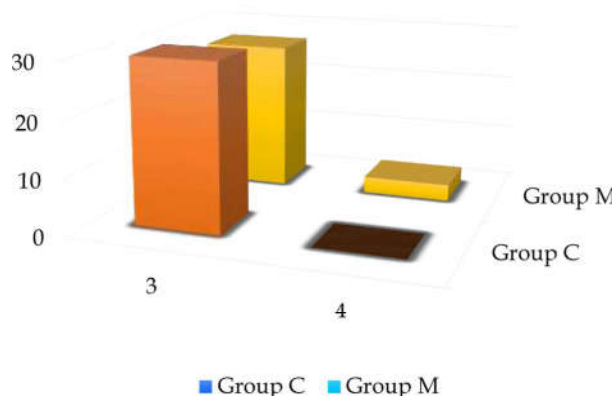
DBP-Diastolic blood pressure, C-Clonidine group, M-Magnesium sulfate group
 Fig. 3: Graph showing mean diastolic blood pressure



C-Clonidine group, M-Magnesium sulfate group
 Fig. 4: Graph showing the mean arterial pressure



C-Clonidine group, M-Magnesium sulfate group
 Fig. 5: Graph showing the oxygen saturation

Modified Ramsay sedation score chart

C-Clonidine group, M-Magnesium sulfate group

Fig. 6: Graph showing the Modified Ramsay sedation score

Discussion

Various pharmacological agents have been studied in the recent past for attenuating the hemodynamic responses during laparoscopy. Only very few studies are available that compare intravenous clonidine with magnesium sulfate for attenuation of hemodynamic responses to laparoscopy. Altan and Turgut et al. [2], and Ray et al. [10], used clonidine 3 µg/kg intravenously over a period of 15 minutes before induction and then 2 µg/kg/min by continuous infusion intraoperatively. They observed significant incidences of bradycardia and hypotension. Based on these observations, we reduced the dose of clonidine to 1.5 µg/kg to avoid bradycardia and hypotension. Jeet et al. [11], administered magnesium sulfate 50 mg/kg over 2-3 minutes, before pneumoperitoneum and observed that it effectively attenuated the hemodynamic stress response without any adverse effects. So, we selected the dose of magnesium sulfate as 50 mg/kg in our study. In our study, there was no statistically significant difference in heart rate, systolic blood pressure, diastolic blood pressure and mean arterial blood pressure were observed between the two groups at any intervals.

A Altan et al. [2], and Ray et al. [10], observed that there was no statistically significant difference in heart rate, systolic blood pressure, diastolic blood pressure and mean arterial blood pressure between the groups similar to our study. But, R. Uma et al. [7], observed a statistically significant decrease in heart rate in clonidine group when compared to placebo in their study. Mishra M et al. [9], and Sahajananda H et al. [8], also observed similar results like R. Uma et al. [7].

Nand Kishore Kalra et al. [6], study shows that the systolic blood pressure is statistically significant between the clonidine 1.5 µg/kg and magnesium groups, this is in contrast to our study. Deepshikha C Tripathi et al. [17], compared clonidine and placebo and Jeet et al. [11], compared magnesium sulfate and placebo, both of the study shows significant difference in the systolic blood pressure.

Nand Kishore Kalra et al. [6], Deepshikha C Tripathi et al. [17], and Jeet et al., observed statistically significant reduction in diastolic blood pressure in between the groups in clonidine group patients. This is in contrast to our study result.

A Altan et al. [4], observed that there was no statistically significant difference in mean arterial blood pressure between the clonidine & magnesium group patients. This is similar to our study. Manjeree Mishra et al. [7], observed a statistically significant difference in mean arterial pressure between the groups, at all intervals of time following pneumoperitoneum ($P < 0.01$). R. Uma et al. [7], and Suhritapaul et al., also observed similar results in their study. This is in contrast to our study results.

In our study, we included both laparoscopic appendectomy and laparoscopic cholecystectomy. Laparoscopic cholecystectomy requires the head up tilt position (reverse Trendelenburg), whereas laparoscopic appendectomy requires the head down tilt position (Trendelenburg). The effect of positioning on the hemodynamics during laparoscopy and its influence on the result of studies was not addressed in most of the studies. In our study, there was no statistically significant variations in mean arterial blood pressure observed between the two groups at any intervals.

Nand Kishore Kalra et al. [6], study took only laparoscopic cholecystectomies, where the head up position is used. In our study majority of cases were laparoscopic appendectomy in both the groups. 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, where as 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 of the haemodynamic stress response to pneumoperitoneum is probably offset by the head down tilt or Trendelenburg position. In laparoscopic appendectomy, Trendelenburg position causes pooling of blood into the upper torso and head from the lower limbs. Thus, our study result shows that clonidine and magnesium sulfate are equally

effective in attenuating the stress response to pneumoperitoneum.

We observed the modified sedation score as, 27 patients out of 30 in the clonidine group had a score of 3 (90%) and 3 patients had a score of 4 (10%). But in the magnesium group out of 30 patients, 18 patients had a score of 3 (60%) and rest of the 12 patients had the score of 4 (40%). This difference in sedation could be explained by the prolonged sedative effect of magnesium than clonidine. The p value is 0.003 and it is statistically highly significant. Nand K et al [6] 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.

In our study, in the clonidine group we observed episodes of bradycardia in 2 out of 30 patients (7%). In the magnesium group, no patients had any adverse effects. Altan and Turgut et al. [2], and Ray et al. [10], observed significant incidences of bradycardia and hypotension in clonidine group patients, in their study. This is in concordance with our study.

Conclusion

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 during extubation.

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