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Original Research Article

Hemodynamic response in laparoscopic cholecystectomy after magnesium sulphate versus clonidine administration

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ABSTRACT

Background: Magnesium and clonidine both inhibit catecholamine and vasopressin release. They also attenuate hemodynamic response to pneumoperitoneum.
Methods: This randomized double-blind study was designed to assess which agent attenuates hemodynamic stress response to pneumoperitoneum better in 70 patients undergoing laparoscopic cholecystectomy.
Results: After the administration of drug, heart rate in group M was mean 84.29 while in group C was mean 79.89. Thus, there was more fall in Heart rate in C group. After intubation, heart rate at 1min, 3 min, 5 min was 101.20, 96.69, 93.94 respectively in group M and in C group was 96.37, 85.83, 86.17 respectively with p values (0.12, 0.001, 0.008). After giving drug, there was fall in blood pressure in both groups but in C group, there was significant fall in systolic blood pressure. There was no significant difference in the mean diastolic BP in both the groups immediately at intubation (76.17±10.74 for group M and 78.86±10.48 for group C with $p>0.05$) as also at 3 min (63.29±8.76 for M group and 65.14±11.705 for clonidine with $p>0.05$) and 5 min (63.03±7.909 for magnesium sulphate and 67.69±13.588 for clonidine with $p>0.05$) following intubation. Thus, the rise in mean diastolic BP was statistically similar in both Group M and Group C. There was no significant difference in the mean for MAP in both the groups immediately at intubation (88.86±12.76 for magnesium sulphate and 91.74±11.59 for clonidine) as also at 3 min (73.17±10.019 for M and 75.80±12.849 for C group. But at 5 min (71.71±9.11 for magnesium sulphate and 77.66±13.715 for clonidine) following intubation with $p<0.05$ which is significant.
Conclusions: Administration of magnesium sulfate or clonidine attenuates hemodynamic response to pneumoperitoneum. Although magnesium sulfate produces hemodynamic stability comparable to clonidine, clonidine blunts the hemodynamic response to pneumoperitoneum more effectively.

Keywords: Clonidine, Laparoscopic cholecystectomy, Magnesium sulfate, Pneumoperitoneum

INTRODUCTION

Laparoscopic cholecystectomy aims to minimize the trauma of the interventional process and also achieves a satisfactory therapeutic result. Tissue trauma is significantly less than conventional open procedures. So, there is reduced post-operative pain, shorter hospital stay, more rapid return to normal activities and less cost. Intra-operative complications can be traumatic injuries with

blind trocar insertion, gas embolism, pneumothorax and surgical emphysema with extraperitoneal insufflation.[1]

Peritoneal gas insufflation is required for exposure, visualization, and manipulation of intra-abdominal contents. CO_2 is gas of choice for insufflation in laparoscopic surgery due to its efficacy and safety during electrocautery and laser surgery. It is excreted by lungs.[2]

General anesthesia with endotracheal intubation and controlled ventilation is the safest and most commonly used technique. During pneumoperitoneum, controlled ventilation demands some adjustments to maintain $PETCO_2$. A 15% to 25% increase in minute ventilation is mostly sufficient for the same.[3]

Pneumoperitoneum and reverse trendelenberg position in laparoscopic cholecystectomy is associated with various changes in cardiovascular and respiratory physiology. Pneumoperitoneum reduces pulmonary compliance, functional residual capacity and total lung capacity. It facilitates development of atelectasis due to elevation of the diaphragm.[3]

Pneumoperitoneum affects homeostasis and leads to changes in cardiovascular and pulmonary physiology and stress response. Cardiovascular changes include increase in mean arterial pressure (MAP) with no significant change in heart rate, decrease in cardiac output and increase in systemic vascular resistance (SVR). These changes are due to hypercarbia-induced release of catecholamines, vasopressin, or both.[4]

Manipulation of the respiratory tract in laryngoscopy and tracheal intubation are associated with hemodynamic and cardiovascular responses consisting of increased circulating catecholamines, heart rate, blood pressure, myocardial oxygen demand, tachycardia and dysrhythmias.[5]

Pneumoperitoneum with carbon dioxide insufflation for laparoscopic surgeries causes abrupt elevations of arterial pressure and systemic vascular resistance with significant decrease in cardiac output, with or without changes in heart rate. Cardiac output decreases after the peritoneal insufflation at IAPs <10mmHg. Increased IAP results in caval compression and increased intrathoracic pressure, increases cardiac filling pressure.[6] Magnesium sulphate blocks the release of catecholamines from the adrenergic nerve terminals and adrenal glands in vitro. It also produces vasodilation by acting directly on blood vessels and also on coronaries.[7] High dose magnesium attenuates vasopressin stimulated vasoconstriction and normalizes sensitivity to vasopressin.[8] Magnesium sulphate also blocks the NMDA receptors in CNS thus producing pain relief.[9]

Clonidine is a well-known drug to attenuate haemodynamic responses to pneumoperitoneum. It has the beneficial effect of blunting hemodynamic responses due to laryngoscopy and tracheal intubation and is also decreases post-operative pain. Clonidine is an alpha-2 adrenergic agonist which has sedative, anxiolytic and analgesic properties. It may therefore be a useful premedication for reducing postoperative pain.[10]

This prospective double-blind study was carried out on 70 adult ASA 1 and 2 patients with an aim to evaluate the IV clonidine and magnesium sulphate in controlling the tachycardia and hypertension associated with laryngoscopy and pneumoperitoneum and in post-operative pain relief in laparoscopic cholecystectomy under general anaesthesia.

Aims and objectives was to compare of I.V. magnesium sulphate with I.V. clonidine in laparoscopic cholecystectomy for attenuation of haemodynamic response to laryngoscopy, intubation and attenuation of haemodynamic response to pneumoperitoneum and in post-operative pain relief.

METHODS

This study was conducted to compare I.V. magnesium sulfate and i.v clonidine in laparoscopic tomycholecyste in view of hemodynamic changes during intubation and pneumoperitoneum and duration of analgesia.

This clinical study was conducted on 70 adult patients from January 2016 to June 2017 in patients of 18-60 years of age belonging to ASA class I, II of either sex posted for laparoscopic cholecystectomy after taking informed consent.

Inclusion criteria

- Patients of 18-60 years of age,
- Case lasting for more than one hour,
- Hypertensive patients not on more than one antihypertensive,
- Patients belonging to ASA class I, II of either sex posted for laparoscopic cholecystectomy,
- Patients with Mallampati grading I, II with single intubation attempt,
- Patient giving valid informed consent.

Exclusion criteria

- Patient giving negative consent,
- Patients <18 yrs and >60 yrs age,
- Known allergies and contraindications to the study drugs,
- Patients who show exaggerated hypertensive response (systolic BP >180mmHg or diastolic BP>110mmHg) requiring antihypertensives during surgery,
- Patients in whom surgery cannot be completed laparoscopically and open surgery done,

- Patients on more than one antihypertensives and on beta blocker,
- Patients who have extreme intraoperative haemodynamic instability,
- Patients with Mallampati grading III and IV.

After approval from ethical committee and written informed consent of patients, this study was conducted at Dr PDMMC and Hospital, Amravati, a tertiary care medical college and hospital. 70 patients, were randomly divided into two groups.

- M group: Magnesium group who received 50mg/kg of magnesium sulfate in normal saline (total volume 50ml) over a period of 15min before intubation
- C group: Clonidine group who received 1.5µg/kg clonidine in normal saline (total volume 50ml) over a period of 15min before intubation.

Patients were premedicated with intravenous ranitidine 0.25mg/kg, ondensetron 0.1mg/kg and intramuscular glycopyrrolate 0.01mg/kg in preoperative room. On arrival in the operation theater, monitors were attached (pulse oxymeter, NIBP, ECG, Etco2) and baseline vital parameters like heart rate, systolic and diastolic blood pressure, and oxygen saturation were recorded.

Patients were divided randomly into two groups before intubation. Half patients received magnesium 50mg/kg in normal saline (group M), or half patients received clonidine 1.5µg/kg (group C) in normal saline over a duration of 15min.

Pentazocine, 10-30mg intravenous was given for analgesia and midazolam 0.05-0.1mg/kg i.v. for sedation. Patients were induced with intravenous propofol 2mg/kg and succinyl choline 1-2mg/kg iv was used to facilitate tracheal intubation. Anesthesia was maintained with oxygen, nitrous oxide mixture (50:50), sevoflurane and atracurium intermittent boluses. During surgery, Ringer's lactate was infused in accordance with maintenance volume requirements and blood loss. CO_2 pneumoperitoneum was created and intra-abdominal pressure maintained at 14mmHg. Intermittent positive pressure ventilation (IPPV) was delivered, with tidal volume and respiratory rate adjusted to maintain end tidal carbon dioxide between 35 and 45mmHg. Blood pressure and heart rate were recorded before intubation (baseline value), after the drug (ATD), after intubation at 1min (1I), 3mins (3I), 5mins (5I) and after pneumoperitoneum at 5min (5P), 10min (10P), 20min (20P), 30min (30P) and 60min (60P) after pneumoperitoneum.

Neuromuscular block was reversed with i.v. neostigmine 0.05mg/kg and glycopyrrolate 6-8µg/kg and endotracheal tube was removed. The patients were also assessed for pain using 10 point visual analogue scale at 30min, 1, 2, 4 and 6hours after extubation. In the postoperative period, inj. diclofenac sodium 1.5mg/kg I.V. was given as rescue analgesic when VAS≥4. The duration of analgesia was noted.

RESULTS

The baseline hemodynamic parameters were compared between study groups i.e. the baseline (preinduction) parameters in group M and C were heart rate (85.51 Vs 84.68)/min, SBP (126.09 Vs 129.62) mmHg, DBP (76.14 Vs 77.65) mmHg and MAP (94.71 Vs 93.00) mmHg, respectively. The heart rate (HR) measured by measuring pulse rate, systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) values were comparable indicated by “not significant” p value. Thus, the two groups were comparable in hemodynamic parameters before induction of anaesthesia (Figure 1).

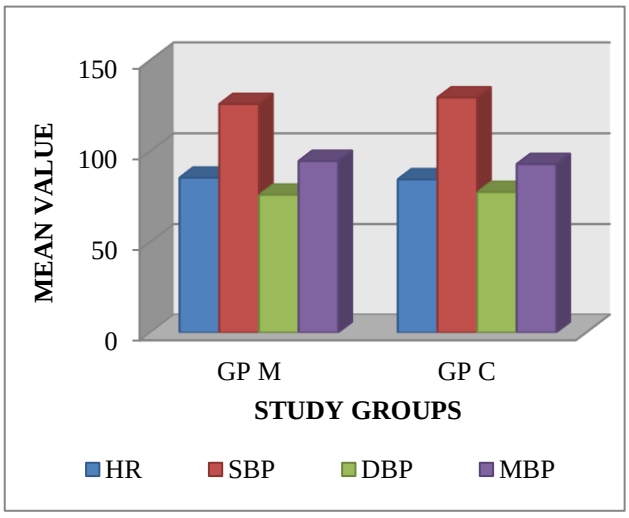

Figure 1: Comparison of baseline hemodynamics.

The basal heart rate in beats per minute was comparable in the both groups and was as follows, group magnesium sulphate (mean 85.51), and group clonidine (mean 84.68) with ‘P’= 0.80.

After the administration of drug, heart rate in group magnesium sulphate (mean 84.29) while that in group clonidine (mean 79.89). Thus, there was more fall in Heart rate in clonidine group as compared to magnesium sulphate group. After intubation, heart rate at 1min, 3 min, 5min was 101.20, 96.69, 93.94 respectively in group magnesium sulphate while that in clonidine group was 96.37, 85.83, 86.17 respectively with p values (0.12, 0.001, 0.008). Thus, p value is highly significant at 3min and 5min after intubation. Thus group clonidine was better than group magnesium sulphate for control in heart rate immediately following intubation (Figure 2).

In the present study, baseline systolic blood pressure was statistically similar in group magnesium sulphate (126.09) and group clonidine (129.62) with (p 0.39) which is non-significant, hence study groups were comparable.

After giving drug, there was fall in blood pressure in both groups but in clonidine group, there was significant fall in systolic blood pressure (Figure 3).

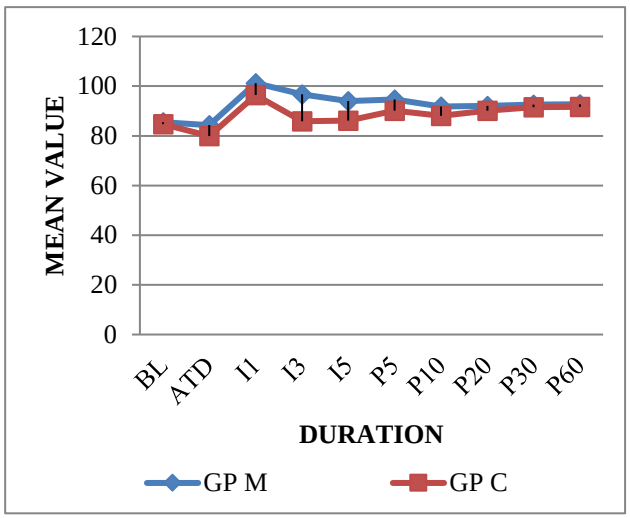

Figure 2: Comparison of HR in study groups.

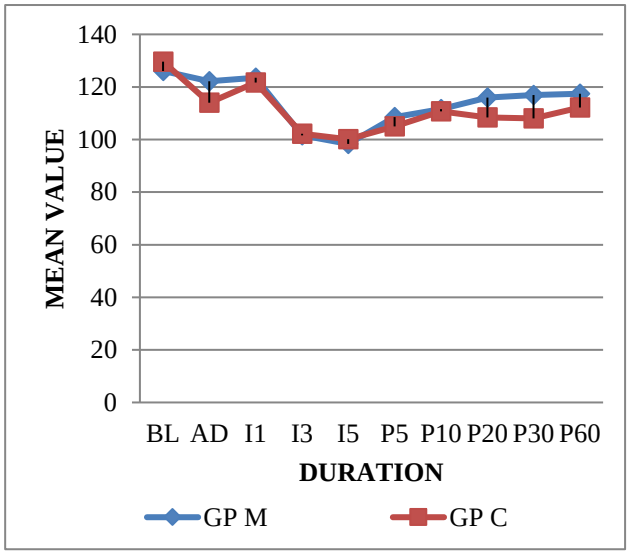

Figure 3: Comparison of SBP in study groups.

In the present study, baseline diastolic blood pressure was statistically similar in group magnesium sulphate (76.14) and group clonidine (77.65) with p>0.05, hence both groups were comparable.

When comparing group magnesium sulphate with the group clonidine there was no significant difference in the mean diastolic BP in both the groups immediately at intubation (76.17±10.74 for magnesium sulphate and 78.86±10.48 for clonidine with p>0.05) as also at 3 min (63.29+8.76 for magnesium sulphate and 65.14±11.705 for clonidine with p>0.05) and 5min (63.03±7.909 for magnesium sulphate and 67.69±13.588 for clonidine with p>0.05) following intubation. Thus, the rise in mean diastolic BP was statistically similar in both group magnesium sulphate and group clonidine.

Among the two, group magnesium sulphate and group clonidine both were effective in controlling the rise in diastolic BP immediately, 3min and 5min after intubation but group magnesium sulphate was comparatively better than group clonidine in attenuating the rise in diastolic BP after intubation (Figure 4).

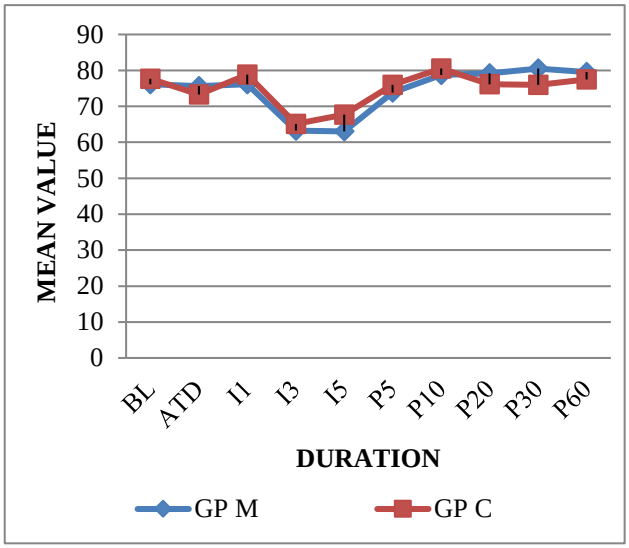

Figure 4: Comparison of DBP in study groups.

In the present study, baseline mean arterial pressure was comparable in group magnesium sulphate (94.71±15.86) and group clonidine (93.00±9.195) with p>0.919.

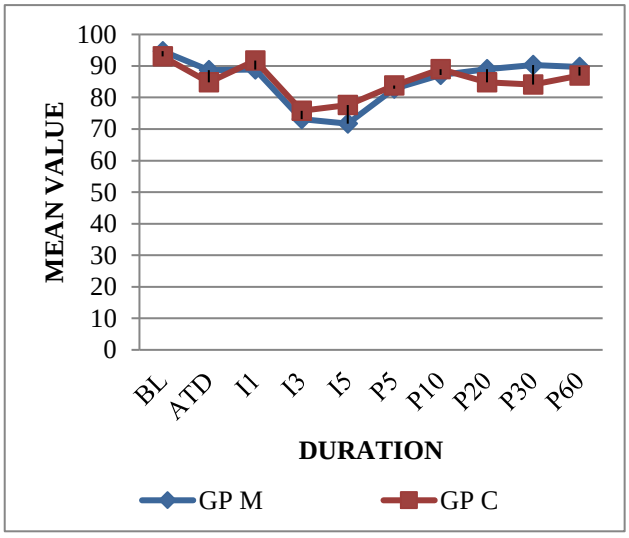

Figure 5: Comparison of MBP in study groups.

When comparing group magnesium sulphate with the group clonidine there was no significant difference in the mean for MAP in both the groups immediately at intubation (88.86±12.76 for magnesium sulphate and 91.74±11.59 for clonidine) as also at 3min (73.17±10.019 for magnesium sulphate and 75.80±12.849 for clonidine). But at 5min (71.71±9.11 for magnesium sulphate and 77.66±13.715 for clonidine) following intubation with

p<0.05 which is significant. On the whole, both groups magnesium sulphate and clonidine attenuate rise in mean arterial pressure after intubation but group magnesium sulphate has better control (Figure 5).

Group M was better in maintaining analgesia as compared to group C (Figure 6).

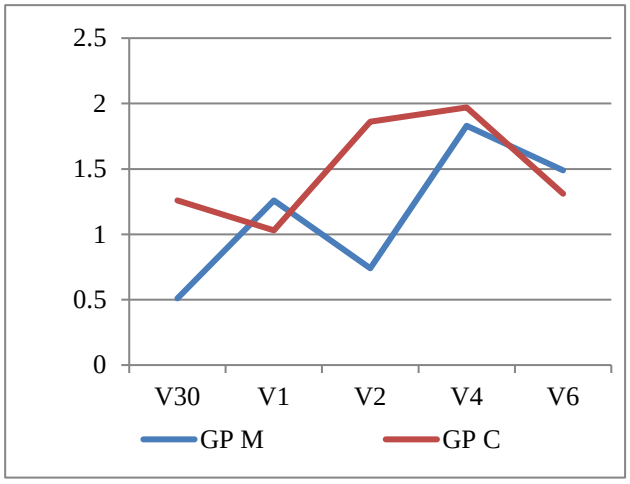

Figure 6: Post operative analgesia.

DISCUSSION

The laparoscopic approach in gall bladder surgery has the advantage of lesser affection of respiratory mechanics as it avoids the need for subcostal incision. This approach for surgery gives a cosmetically better scar, lesser abdominal wound infection and lesser risk of incisional hernias (especially in morbidly obese patients).

The basal heart rate in beats per minute was comparable in the both groups. It was in group magnesium sulphate as (mean 85.51), and group clonidine as (mean 84.68) with 'P'= 0.80 (Figure 2).

Similar to our study, Batra YK et al found that after the administration of drug, heart rate in group magnesium sulphate was mean (84.29) while that in group clonidine was (mean 79.89). Thus, there was more fall in heart rate in clonidine group as compared to magnesium sulphate group. After intubation, heart rate at 1min, 3min, 5min was 101.20, 96.69, 93.94 respectively in group magnesium sulphate while that in clonidine group was 96.37, 85.83, 86.17 respectively with p values (0.12, 0.001, 0.008). Thus, p value is highly significant at 3min and 5 min after intubation. Thus, group clonidine was better than group magnesium sulphate for control in heart rate immediately following intubation (Table 2).

Batra YK et al, in double-blind randomized study found that oral clonidine 5micrograms/kg 90min before induction of anaesthesia is associated with less rise in heart rate and blood pressure than that is associated with laryngoscopy and intubation during a routine induction sequence though dose of clonidine used by us was lesser, yet the results were similar.[11]

When comparing group magnesium sulphate with the group clonidine there was no significant difference in the mean systolic BP in both the groups immediately at intubation (mean 123.46) for magnesium sulphate and (mean 121.71) for clonidine. Also, at 3min (101.60±12.69 for magnesium sulphate and 102.20±15.90 for clonidine) and 5min (98.34+9.867 for magnesium sulphate and 100.09±14.89 for clonidine) following intubation. Thus, the rise in mean systolic BP was statistically similar in both group magnesium sulphate and group clonidine. On the whole, both group magnesium sulphate and group clonidine were equally superior in attenuating the rise in systolic BP (Figure 3).

Contrast to our study, Kalra NK et al found that systolic blood pressure was significantly higher in control group as compared to all other groups during pneumoperitoneum. On comparing patients in group M and group C1, no significant difference in systolic BP was found at any time interval. Patients in group C2 showed best control of systolic BP. As compared to group M and group C1, BP was significantly lower at 10, 30 and 40min post pneumoperitoneum. No significant episodes of hypotension were found in any of the groups. Extubation time and time to response to verbal command like eye opening was significantly longer in group M as compared to other groups.[12]

Contrast to our study, Ramesh VJ et al found that there was significant (p>0.01) attenuation of hemodynamic intubation response with clonidine. The recovery with clonidine was not delayed (p<0.01). Clinically significant hypotension and bradycardia were not observed in any of the patients. In our study, clonidine similarly attenuated the intubation response with no significant hypotension or bradycardia.[13]

In the present study, baseline diastolic blood pressure was statistically similar in group magnesium sulphate (76.14) and group clonidine (77.65) with p>0.05, hence both groups were comparable.

When comparing group magnesium sulphate with the group clonidine there was no significant difference in the mean diastolic BP in both the groups immediately at intubation (76.17±10.74 for magnesium sulphate and 78.86±10.48 for clonidine with p>0.05) as also at 3min (63.29±8.76 for magnesium sulphate and 65.14±11.705 for clonidine with p>0.05) and 5min (63.03±7.909 for magnesium sulphate and 67.69±13.588 for clonidine with p>0.05) following intubation. Thus, the rise in mean diastolic BP was statistically similar in both group magnesium sulphate and group clonidine (Figure 4).

In the present study, both groups were effective in controlling the rise in diastolic BP immediately, 3min and 5min after intubation but group magnesium sulphate was

comparatively better than group clonidine in attenuating the rise in diastolic BP after intubation (Figure 5).

Kamble SP et al, found that systolic blood pressure, diastolic blood pressure (DBP), mean arterial pressure (MAP), and heart rate (HR) were all significantly higher in the normal saline group compared to magnesium and clonidine. On comparing patients in group M and group C, DBP, MAP, and HR were significantly lower in the magnesium group. Mean extubation time and time to response to verbal commands were significantly longer in the magnesium group.[14]

In the present study, baseline mean arterial pressure was comparable in group magnesium sulphate (94.71±15.86) and group clonidine (93.00±9.195) with p>0.919.

When comparing group magnesium sulphate with the group clonidine there was no significant difference in the mean for MAP in both the groups immediately at intubation (88.86±12.76 for magnesium sulphate and 91.74±11.59 for clonidine) as also at 3min (73.17±10.019 for magnesium sulphate and 75.80+12.849 for clonidine). But at 5 min (71.71±9.11 for magnesium sulphate and 77.66±13.715 for clonidine) following intubation with p<0.05 which is significant. On the whole, both groups magnesium sulphate and clonidine attenuate rise in mean arterial pressure after intubation but group magnesium sulphate has better control (Figure 6).

Similar to our study, Zhang Y et al found that, clonidine intervention was found to significantly reduce the MAP at pneumoperitoneum [standard mean difference=-2.58; 95% confidence interval (CI),-4.63 to -0.53; P=0.01), HR at pneumoperitoneum (standard mean difference=-3.67; 95% CI, -6.57 to -0.76; P=0.01), MAP at intubation (standard mean difference=-2.40; 95% CI, -4.75 to -0.06; P=0.04), HR at intubation (standard mean difference=-3.39; 95% CI, -5.75 to -1.02; P=0.005), propofol requirement (standard mean difference=-2.25; 95% CI, -4.01 to -0.48; P=0.01), as well as postoperative nausea and vomiting (risk ratio, 0.35; 95% CI, 0.19-0.63; P=0.0005).[15]

CONCLUSION

Both IV Magnesium sulphate 50mg/kg and IV Clonidine 1.5mcg/kg given prior to the induction of anaesthesia in laparoscopic cholecystectomy effectively attenuated the haemodynamic response to laryngoscopy and pneumoperitoneum as well as provided post-operative analgesia. However, between the two, IV Clonidine 1.5mcg/kg attenuated the haemodynamic response to laryngoscopy and pneumoperitoneum better than IV Magnesium sulphate 50mg/kg whereas, IV Magnesium sulphate 50mg/kg can provided a better post-operative analgesia than IV Clonidine 1.5mcg/kg.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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