International Journal of Science and Research (IJSR)
ISSN: 2319-7064
Index Copernicus Value (2016): 79.57 | Impact Factor (2017): 7.296

Non-Opioidal Management of Perioperative Hemodynamics and Postoperative Pain in Laparoscopy- Role of Magnesium Sulphate and Clonidine

Nimisha S. Shiwalkar[1,2] M.D., D.N.B., Akshay P. Kumar[3], M.D., M.S., M.Ch., Pramod L. Kale[1]M.D., Vishakha S. Khalde[1]D.N.B., Vikas Nair[1]M.D.

[1]Department of Anesthesiology, Joy Hospital, Mumbai, Maharashtra, India

[2]Department of Anesthesiology, University of Texas Health Science Center, TX, USA

[3]Department of Surgery, Rutgers, The State University of New Jersey, PA, USA

***Running title*:** Non opioidal peri-operative anesthesia in laparoscopy

Prior Presentation: Accepted for Presentation on October 16, 2018 at Anesthesiology 2018 meeting, San Franscisco.

Abstract: ***Background*: Laparoscopic cholecystectomy has become one of the most commonly performed abdominal surgery throughout the world. Major hemodynamic perturbations encountered during the creation of pneumoperitoneum for laparoscopy have an impact on peri-operative outcomes. In the present era of opioid crisis, a non-opioidal approach to address the peri-operative management is the need of the day. *Methods*: A prospective randomized double-blinded study was conducted on 90 patients with ASA grade 1 and 2 and undergoing elective laparoscopic cholecystectomy under general anaesthesia. Patients were randomly assigned to receive either MgSO4 (elemental Magnesium 50mg/kg), clonidine 2 micrograms/kg or normal saline (NS) prior to induction and evaluated for hemodynamic responses to pneumoperitoneum; surgical field clarity using Fromme-Boezaart and VAS score and post-operative pain using VAS scores. Data was compared using Oneway ANOVA, Kruskal-Wallis and Chi-Square tests. *Results*: Clonidine was found to be superior to MgSO4 in attenuating the rise in heart rate and blood pressure following pneumoperitoneum. However, the surgical field clarity was similarly superior to control in both MgSO4 and Clonidine groups. Post-operatively, the time to rescue analgesia was more with MgSO4 while the VAS score was less as compared to control. *Conclusion*: Both Magnesium sulphate and Clonidine given prior to the induction of anesthesia in laparoscopic surgery effectively attenuated the hemodynamic response to laryngoscopy and pneumoperitoneum, provided a clear surgical field as well as provided good post-operative analgesia. However, between the two, attenuation of hemodynamic response was better with clonidine whereas, Magnesium sulphate provided a better post-operative analgesia. The surgical field clarity was equal with both the drugs. In the present era of opioid epidemic, it becomes imperative that pain management be revamped and wherever possible be replaced by non-opioidal drugs.***

1. Introduction

Laparoscopic surgery is a technique in which abdominal surgeries are performed through smaller incisions (usually 0.5–1.5 cm) as compared to the larger incisions needed in laparotomy. The advantages of laparoscopic cholecystectomy include reduced post-operative pain, early post-operative recovery, shorter length of stay and lower cost. General anesthesia with endotracheal intubation and controlled ventilation is certainly the safest and the most commonly used technique especially for upper abdominal surgeries like laparoscopic cholecystectomy[1].

Creation of pneumoperitoneum is the major surgical milestone during laparoscopic cholecystectomy. Pneumoperitoneum with carbon-dioxide insufflation for laparoscopic surgeries induces abrupt elevations in mean arterial pressure and systemic vascular resistance with significant decrease in cardiac output, with or without changes in heart rate[2-4]. The rise in sympathetic activity seen during laparoscopic surgeries is associated with a hyperactive hemodynamic system[5,6]. Normal healthy individual can tolerate these hemodynamic changes well; but they are of concern in individuals with high risk conditions like pre-existing essential hypertension, ischemic cardiac diseases, or increased intracranial or intraocular pressure. At the same time the decision to fast tract certain day care laparoscopic surgeries can be impaired. Opiodal agents like fentanyl (intraoperative), oxycodone and hydromorphone (post-operative) are widely used. However, in todays' world of opioid epidemic, health-care providers should resort to non-opioidal options whenever feasible[7,8].

Clonidine is a centrally acting alpha-2 agonist with a potential to attenuate hemodynamic responses to sympathetic stimulation along with post-operative analgesic properties [9]. Another drug, Magnesium sulphate blocks the release of catecholamines from the adrenergic nerve terminals and adrenal glands in vitro. In addition, magnesium produces vasodilatation by actingdirectly on blood vessels and in high doses attenuates vasopressin stimulated vasoconstriction[10].Magnesium sulphate is also seen to block the NMDA receptors in the CNS & thereby produce pain relief[11]. Though these two drugs have shown positive effects during laparoscopic surgeries separately, very few studies have challenged their individual advantages to determine which is a better drug. We therefore aimed at comparing the effects of Magnesium sulphate and clonidine

in attenuating the hemodynamic responses to pneumoperitoneum, the quality of surgical field & in post-operative pain relief in patients undergoing laparoscopic cholecystectomy. We intend to find whether these drugs alone or in combination can prove beneficial in laparoscopic surgical practice.

2. Materials and Method

Study design

After obtaining approval from the institutional review board (IRB), we investigated 90 patients between age 18 to 60-year-old, ASA Class I and II undergoing elective laparoscopic cholecystectomy under general anesthesia. Patients with uncontrolled hypertension, diabetes mellitus, severe cardiac, hepatic, respiratory or renal disease, history of allergy to any of the study drugs, pregnancy or breast-feeding females, history of opioid or alcohol intake in last 24 hours, patients receiving Alpha 2 agonists and Beta Blocker and other medical, psychiatric, or behavioral limitations that could interfere with study methodology were excluded. Surgeries which could not be completed laparoscopically and required open cholecystectomy were excluded from the study too.

Patients were randomly divided into three groups: Magnesium sulphate (elemental Magnesium 50mg/kg), clonidine (2ug/kg) or Normal saline by computer-generated randomization table. The details of randomization remained with the operating room pharmacist who issued the drug in identical looking bags of 100ml Normal Saline (NS). After thorough preoperative checkup, procedure was explained to each patient & written consent taken. The evaluators remained blinded to the drug and received the drug from the operating room pharmacy. All patients were shifted to recovery and under continuous monitoring of heart rate, rhythm and blood pressure, received the drug, with the detailed randomization code staying with the operating room pharmacy.

After premedication with intravenous Midazolam 0.03mg/kg., patients were induced with Inj. Lidocaine 1mg/kg and Inj. Propofol 2mg/kg, in incremental doses until loss of consciousness. Endotracheal intubation was facilitated by Inj. Rocuronium Bromide 0.7mg/ kg. Thereafter, anesthesia was maintained with Isoflurane 1-1.5% in combination with 50% air in oxygen, on controlled mechanical ventilation in a closed circuit. No dose of Fentanyl or any other opioid was given throughout the surgery. Ventilation of the lungs was adjusted to maintain an end-tidal CO2 of 30 +/-5 mmHg. Bispectral index (BIS) was maintained between 40-60 to prevent any hemodynamic changes arising due to awareness. Muscle relaxation was maintained using intermittent Rocuronium dosages of 0.15mg/kg as per the recordings by peripheral nerve stimulator. Patients were given head-up tilt of 15 degrees and pneumoperitoneum was created by the surgeons by insufflating carbon dioxide at a pressure of <14 mmHg. Hemodynamic parameters monitored were Heart rate(HR), Electrocardiogram(ECG), Systolic Blood Pressure(SBP), Diastolic Blood Pressure(DBP), Mean Arterial Pressure(MAP), End tidal carbon-dioxide(etCO2), Peripheral Oxygen saturation(SPO2) & Intraabdominal pressures (IAP). These were measured at baseline; prior to injection of drugs; after the injection of drugs; after induction; and at every 5minutes interval after creating pneumoperitoneum. Isoflurane inhalation was stopped after desufflation. After completion of surgery, residual neuromuscular blockade was reversed with Inj. Glycopyrrolate 0.008 mg/kg and Inj. Neostigmine 0.05mg/kg.

Any untoward side effects like bradycardia (HR<60 or if reduced by 20% than baseline, whichever was less) lasting >1 minute was noted and treated with injection Atropine 0.6mg IV bolus, hypotension (MAP reduced by 20% of the baseline MAP) for duration of >1 min was treated with titration of Isoflurane inhalation and if persisted, treated with injection Mephentermine sulphate 3mg IV bolus, exaggerated hypertension SBP>180mmHg, DBP>110mmHg was treated with an infusion of Injection Nitroglycerine 10mg in 100ccNS or Injection Metoprolol 1mg bolus.

The intra-operative surgical field was graded using the Frommme-Boezaart scale which was originally framed by Fromme et al. and later modified by Boezaart et al. wherein the surgeons scored the surgical field depending on intra-operative oozing and difficulty in controlling the bleeders every 15 minutes during the surgery [12-14]. The scores ranged from 0 to 5, where 0 = no bleeding (cadaveric condition), followed by 1=slight bleeding going up to 5 = severe bleeding faster than can be removed by suctioning. To support the readings of Fromme-Boezaart score, VAS score by surgeons was also added to grade the surgical field conditions after completion of the surgery, where 0 = best possible surgical conditions with minimal bleeding and 10 = worst surgical conditions with severe bleeding[12].

The awakening time was recoded as time taken from discontinuing of the Isoflurane inhalation to the obeying of verbal commands by the patient. Again, orientation time was recorded as time taken from discontinuing the Isoflurane inhalation to orientation of time, place and person. Postoperative pain was assessed by Visual Analogue Score (VAS) on a scale of 0-10 with 0 indicating no pain while maximum pain is indicated by a score of 10. Time to rescue analgesia was also used to measure the postoperative pain in these patients wherein analgesic diclofenac sodium 1.5mg/kg and/or tramadol 2mg/kg was given on demand to the patient.

Statistical Analysis

A power analysis was performed before the study began. The analysis suggested that 30 patients in each group would be adequate for statistical significance in this study. Data collected was entered in Excel sheet and data analysis was done with the help of SPSS Software ver 25.0 and Sigmaplot Ver 13. Quantitative data presented with the help of Mean, SD, Median and IQR, comparison among study group was done with the help of One-way ANOVA or Kruskal Wallis test as per the results of Normality test. Qualitative data was presented with the help of Frequency and Percentage table, whereas comparison among study group was done with the help of Chi-Square test. A probability value less than 0.05 is taken as significant.

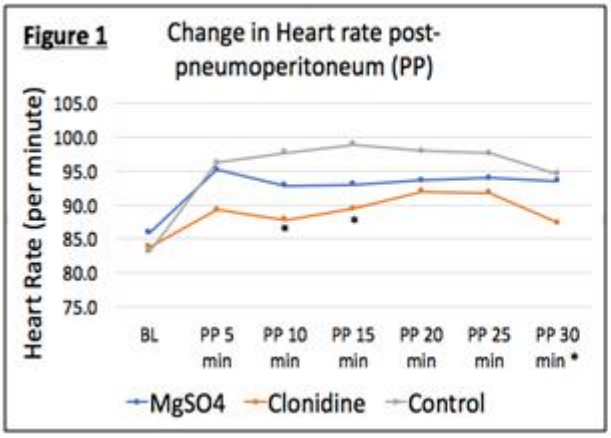
3. Results

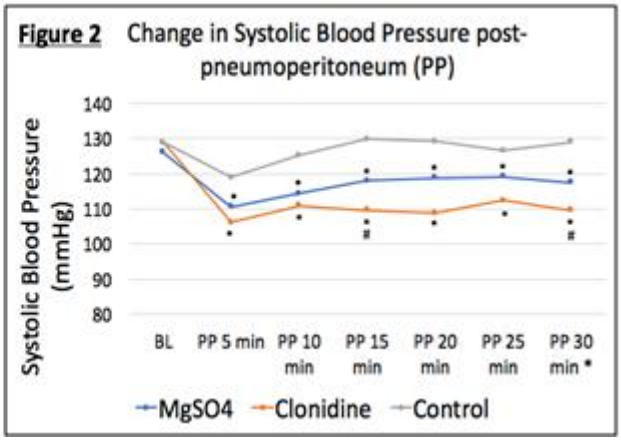
The three study groups A (MgSO4), B (Clonidine) and C (Normal Saline-Control) were comparable in terms of age, sex and weight; baseline hemodynamic parameters including heart rate, systolic BP, diastolic BP and Mean BP (Table 1).

Table 1: Demographic data, Baseline hemodynamic parameters, intra-operative EtCO2, awakening time and orientation time.

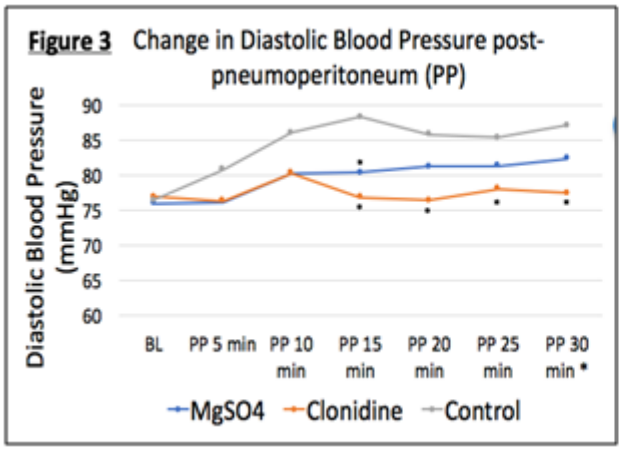
	MgSO4	Clonidine	Control
Age (years)	43	46.47	43
Weight (kilograms)	64	63.3	67.73
Male: Female	0.66	0.5	0.50
Heart rate (per minute)	85.9	83.8	83.10
Systolic BP (mm of Hg)	126.1	128.97	126.87
Diastolic BP (mm of Hg)	76.03	76.93	74.47
Mean BP (mm of Hg)	93.37	92.43	93.9
Intra-operative EtCO2 (mm of Hg)	30.35	30.77	30.51
Duration of Surgery (minutes)	64.67	60.22	63.24
Awakening time (minutes)	9.45	8.89	8.67
Orientation time (minutes)	14.47	13.98	14.10

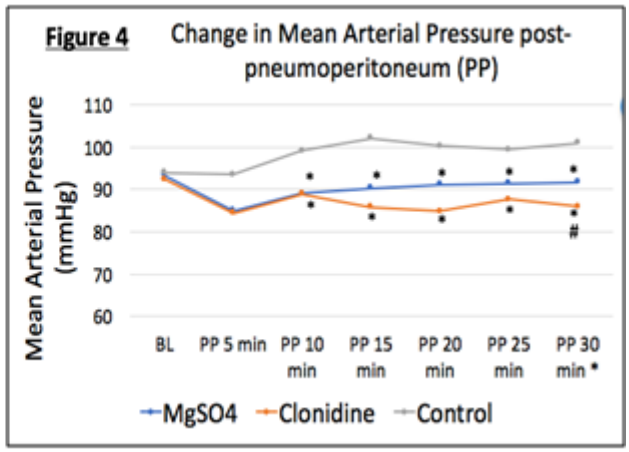
When Clonidine was compared to Control, the mean heart rate at 10min ($p<0.001$) and 15min ($p<0.01$) post pneumoperitoneum were significantly lower (Figure 1). There was no significant difference in the heart rate between the three groups at any other time points (Figure 1).

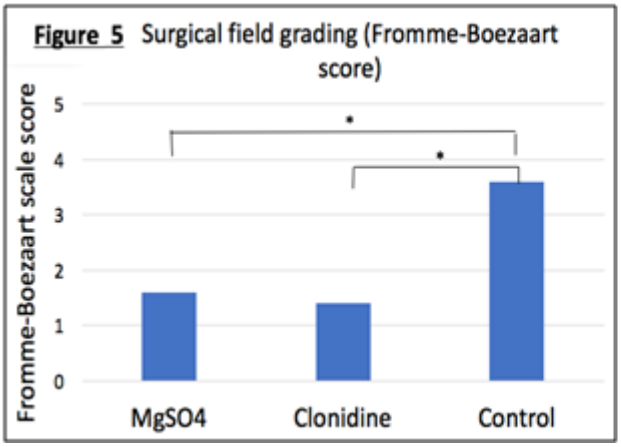


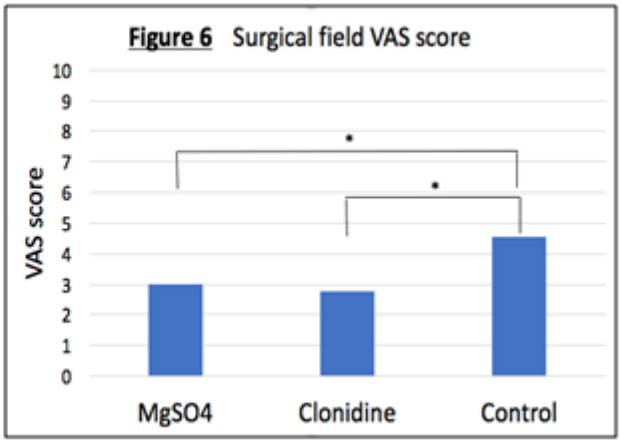


The rise in systolic BP was significantly lesser in Clonidine and MgSO4 groups as compared to control up to 30 minutes post-pneumoperitoneum (Figure 2). In addition, the systolic blood pressure readings were significantly lesser in Clonidine than MgSO4 at 15min($p=0.042$) and 30min($p=0.03$) post-pneumoperitoneum (Figure 2). Clonidine could attenuate the rise in diastolic BP from 15 minutes to 30 minutes post pneumoperitoneum ($p<0.05$) when compared separately to control (Figure 3). MgSO4 could control the rise in diastolic BP only at 15 minutes post-pneumoperitoneum (Figure 3). MgSO4 and Clonidine both were equally better than Control in attenuating the rise in MAP($p<0.01$) from 10min up to 30min post pneumoperitoneum($p<0.001$). At 30min post pneumoperitoneum, Clonidine was found even more superior to MgSO4 ($p=0.031$) in controlling the rise in MAP (Figure 4).



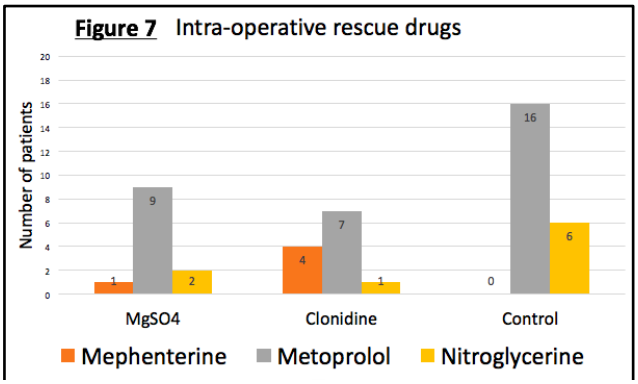


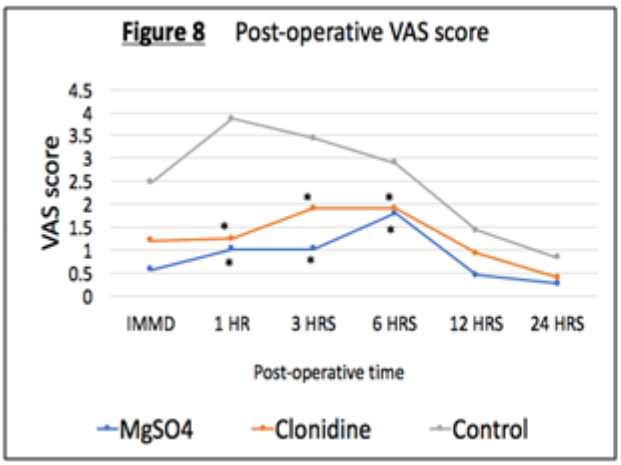


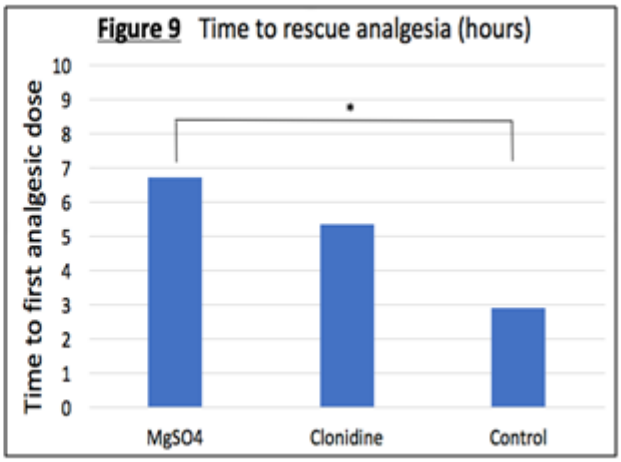


Surgical field Boezaart scores (Figure 5) were significantly lower in Group MgSO4 and Clonidine than in Group Control. However, there was no significant difference when MgSO4 was compared to Clonidine. Similarly, Surgical field VAS scores (Figure 6) were significantly lower in Group MgSO4 and Clonidine than in Group Control. However, there was no significant difference when MgSO4 was compared to Clonidine.

In our study (Figure 7), none of the groups required atropine. 1 patient in MgSO4 group and 4 patients in Clonidine group and none in control group required IV mephenterine. 16 patients in control group, 9 in MgSO4 group and 7 in Clonidine group required IV Metoprolol. The number of patients requiring metoprolol was significantly lower in clonidine group compared to control group. 6 patients in control group, 2 in MgSO4 group and 1 in Clonidine group required IV Nitroglycerine. Similar to Metoprolol, the number of patients requiring Nitroglycerine was significantly lower in Clonidine group compared to control.







MgSO4 group showed lower VAS scores for pain compared to Clonidine and Control group immediately after the surgery ($p<0.05$). However, both MgSO4 and Clonidine were equally effective in relieving the pain after 1hr post-operatively (Figure 8). In addition, the time required to the first dose of rescue analgesic was significantly more in MgSO4 group($p<0.05$) as compared to Control. No significant difference was seen between Clonidine or Control group (Figure 9).

4. Discussion

With the growing awareness supporting the advantage of day care surgeries and fast-track anesthesia techniques, laparoscopic surgeries have become an essential practice in every operating room. Obviously, there remains an emphasis on patient safety as well as patient satisfaction in these types of surgeries.

Pneumoperitoneum with carbon dioxide insufflation has been associated with an exaggerated stress response culminating in increased sympathetic drive and thereby rise in heart rate, blood pressure etc seen during laparoscopic surgeries. While one of the reasons causing a rise in blood pressure and heart rate can be the CO2 absorption[15], this was avoided in our study by maintaining the EtCO2 at 30 ± 5 mmHg (Table 1). Peritoneal stretching is believed to result in noxious stimuli[16]. This along with the phrenic nerve stimulation during pneumoperitoneum may induce an increased sympathetic response via the hypothalamo-pituitary-adrenal axis, in turn causing a rise in heart rate and blood pressure[5,16,17].

Many drugs have been previously tried to ensure better hemodynamics and operating conditions during laparoscopic surgeries by attenuating this sympathetic response, of which MgSO4 and clonidine have also been an important part. For example, Shivinder Singh and Kapil Arora et al.[9] observed that administration of oral clonidine 150µg as a simple and cost-effective form of premedication in patients undergoing laparoscopic cholecystectomy results in improved perioperative hemodynamic stability and reduction in anesthetic requirements. Similarly, Deepshikha C Tripathi, et al.[18], concluded that clonidine 2 mcg/kg intravenous prevented hemodynamic stress response to pneumoperitoneum and that associated with intubation and extubation in laparoscopic cholecystectomies.Here we compared the benefit of using these two different groups of drugs by evaluating their role in intraoperative hemodynamic stability and postoperative pain relief in patients undergoing laparoscopic cholecystectomy.

Earlier study by Kamble et al[19]. concluded that 50mg/kg MgSO4 attenuated the hemodynamic response better than 1ug/kg Clonidine. We observed that a higher dose of Clonidine 2ug/kg was statistically better than MgSO4 in attenuating the hemodynamic response to pneumoperitoneum during Laparoscopic surgery though both were better than the control group. This was observed both with respect to heart rate as well as systolic, diastolic and mean blood pressure. We chose this dose considering that a dose of 3ug/kg Clonidine resulted in significant bradycardia and hypotension[20]. Our findings were similar to Kalra NK et al.[21] who observed that intravenous clonidine 1.5mg/kg has a better control over the hemodynamics during laparoscopic cholecystectomy compared to MgSO4 50mg/kg. Creation of pneumoperitoneum is said to result in increased sympathetic response that is responsible for the hemodynamic stability resulting in increased heart rate and blood pressure[5,6]. Clonidine being a centrally acting alpha2 agonist, blocks the central sympathetic system [9] while MgSO4 lowers blood pressure through vasodilation[10]. This could be the major reason for a superior action of Clonidine over MgSO4 in pneumoperitoneum induced rise in heart rate and blood pressure. A better control of hemodynamic parameters like heart rate and blood pressure within a normal range is helpful in controlling bleeding and in turn a good surgical exposure and lesser blood loss. These characteristics are important when fast tracking patients during day care surgeries. We supported the advantage of using either MgSO4 or Clonidine in Laparoscopic cholecystectomy by demonstrating a better Surgical field score when compared with the control group. However, the surgeons did not notice any difference between the two drugs. However, significantly less number of patients in Clonidine group required Metoprolol and NTG for a similar surgical field score. However, larger studies may be required to arrive at a conclusion on the use of hypotensive drugs in this setting. The attenuation of sympathetic rise in heart rate and blood pressure resulting in better control of bleeders may have been responsible for the superior surgical field scored by the surgeons in case of MgSO4 and Clonidine over control drug.

We also aimed to evaluate the postoperative advantage of using these drugs by evaluating the postoperative pain score in these patients. While the analgesic advantage of Clonidine[9] and MgSO4[22] have been observed in separate studies previously, here we compared the two drugs. The study by Shashi Kiran et al.[22]found that a single 50mg/kg dose of preoperative magnesium sulphate infusion decreases postoperative pain and requirement of rescue analgesia while another study by Singh et al.[9] observed that administration of oral clonidine 150µg before laparoscopic cholecystectomy also reduced the post-operative analgesic.We observed that Magnesium sulphate was more effective in controlling the immediate post-operative pain better than clonidine or control inferred by a relatively longer time taken for the first dose of rescue analgesic; but thereafter both magnesium sulphate and clonidine showed equal analgesic potency from 1 hour post-operatively inferred by the VAS score comparison in these groups. MgSO4 being a NMDA receptor antagonist has a potential to prevent and reduce pain [11].

In summary, though earlier studies working on similar subject give relevant information on use of Clonidine and Magnesium sulphate in peri-operative management, our study measures and further compares the effect of these two important drugs during different stages of laparoscopic surgery. Considering that clonidine 2mg/kg has a better control of hemodynamics but MgSO4 has a similar surgeon satisfaction along with better post-operative analgesic effect, we propose a combination of these drugs in laparoscopic surgeries to get the maximum benefit while avoiding the side-effects of each. In the present era of multimodal analgesia, such an option of management would be safe, cost-effective and regulate post-operative opioid prescription and abuse.

Funding: Support was provided solely from institutional and departmental sources

Conflicts of Interest: The authors declare no competing interests.

References

[1] Ronald Miller LE, Lee Fleisher, Jeanine Wiener-Kronish, Neal Cohen, William Young. Miller's Anesthesia. 8 ed. Philadelphia: Elsevier/Saunders; 2014.
[2] Gurulingappa, Aleem MA, Awati MN, Adarsh S. Attenuation of Cardiovascular Responses to Direct Laryngoscopy and Intubation-A Comparative Study Between iv Bolus Fentanyl, Lignocaine and

Placebo(NS). *Journal of clinical and diagnostic research : JCDR* 2012; **6**(10): 1749-52.
[3] Khare A, Sharma SP, Deganwa ML, Sharma M, Gill N. Effects of Dexmedetomidine on Intraoperative Hemodynamics and Propofol Requirement in Patients Undergoing Laparoscopic Cholecystectomy. *Anesthesia, essays and researches* 2017; **11**(4): 1040-5.
[4] Wahba RW, Beique F, Kleiman SJ. Cardiopulmonary function and laparoscopic cholecystectomy. *Canadian journal of anaesthesia = Journal canadien d'anesthesie* 1995; **42**(1): 51-63.
[5] Donald RA, Perry EG, Wittert GA, et al. The plasma ACTH, AVP, CRH and catecholamine responses to conventional and laparoscopic cholecystectomy. *Clinical endocrinology* 1993; **38**(6): 609-15.
[6] Feig BW, Berger DH, Dougherty TB, et al. Pharmacologic intervention can reestablish baseline hemodynamic parameters during laparoscopy. *Surgery* 1994; **116**(4): 733-9; discussion 9-41.
[7] Hah JM, Bateman BT, Ratliff J, Curtin C, Sun E. Chronic Opioid Use After Surgery: Implications for Perioperative Management in the Face of the Opioid Epidemic. *Anesthesia and analgesia* 2017; **125**(5): 1733-40.
[8] Soffin EM, Waldman SA, Stack RJ, Liguori GA. An Evidence-Based Approach to the Prescription Opioid Epidemic in Orthopedic Surgery. *Anesthesia and analgesia* 2017; **125**(5): 1704-13.
[9] Singh S, Arora K. Effect of oral clonidine premedication on perioperative haemodynamic response and postoperative analgesic requirement for patients undergoing laparoscopic cholecystectomy. *Indian journal of anaesthesia* 2011; **55**(1): 26-30.
[10] Herroeder MDS, Schönherr MDDESAME, De Hert MDPDSG, Hollmann MDPDDEAAMW. Magnesium—Essentials for Anesthesiologists. *Anesthesiology* 2011; **114**(4): 971-93.
[11] Mentes O, Harlak A, Yigit T, et al. Effect of intraoperative magnesium sulphate infusion on pain relief after laparoscopic cholecystectomy. *Acta anaesthesiologica Scandinavica* 2008; **52**(10): 1353-9.
[12] Eberhart LH, Folz BJ, Wulf H, Geldner G. Intravenous anesthesia provides optimal surgical conditions during microscopic and endoscopic sinus surgery. *The Laryngoscope* 2003; **113**(8): 1369-73.
[13] Boezaart AP, van der Merwe J, Coetzee A. Comparison of sodium nitroprusside- and esmolol-induced controlled hypotension for functional endoscopic sinus surgery. *Canadian journal of anaesthesia = Journal canadien d'anesthesie* 1995; **42**(5 Pt 1): 373-6.
[14] Fromme GA, MacKenzie RA, Gould AB, Jr., Lund BA, Offord KP. Controlled hypotension for orthognathic surgery. *Anesthesia and analgesia* 1986; **65**(6): 683-6.
[15] Wolf JS, Jr., Clayman RV, Monk TG, McClennan BL, McDougall EM. Carbon dioxide absorption during laparoscopic pelvic operation. *Journal of the American College of Surgeons* 1995; **180**(5): 555-60.
[16] Aono H, Takeda A, Tarver SD, Goto H. Stress responses in three different anesthetic techniques for carbon dioxide laparoscopic cholecystectomy. *Journal of clinical anesthesia* 1998; **10**(7): 546-50.
[17] Segawa H, Mori K, Kasai K, Fukata J, Nakao K. The role of the phrenic nerves in stress response in upper abdominal surgery. *Anesthesia and analgesia* 1996; **82**(6): 1215-24.
[18] Tripathi DC, Shah KS, Dubey SR, Doshi SM, Raval PV. Hemodynamic stress response during laparoscopic cholecystectomy: Effect of two different doses of intravenous clonidine premedication. *J Anaesthesiol Clin Pharmacol* 2011; **27**(4): 475-80.
[19] Kamble SP, Bevinaguddaiah Y, Nagaraja DC, Pujar VS, Anandaswamy TC. Effect of Magnesium Sulfate and Clonidine in Attenuating Hemodynamic Response to Pneumoperitoneum in Laparoscopic Cholecystectomy. *Anesthesia, essays and researches* 2017; **11**(1): 67-71.
[20] Altan A, Turgut N, Yildiz F, Turkmen A, Ustun H. Effects of magnesium sulphate and clonidine on propofol consumption, haemodynamics and postoperative recovery. *British journal of anaesthesia* 2005; **94**(4): 438-41.
[21] Kalra NK, Verma A, Agarwal A, Pandey H. Comparative study of intravenously administered clonidine and magnesium sulfate on hemodynamic responses during laparoscopic cholecystectomy. *J Anaesthesiol Clin Pharmacol* 2011; **27**(3): 344-8.
[22] Kiran S, Gupta R, Verma D. Evaluation of a single-dose of intravenous magnesium sulphate for prevention of postoperative pain after inguinal surgery. *Indian journal of anaesthesia* 2011; **55**(1): 31-5.