Original Research Paper

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TO EVALUATE THE EFFICACY OF A LOW DOSE OF KETAMINE IN ATTENUATING HAEMODYNAMIC STRESS RESPONSE INDUCED BY PNEUMOPERITONEUM IN LAPROSCOPIC CHOLECYSTECTOMY UNDER GENERAL ANAESTHESIA-A PROSPECTIVE STUDY

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ABSTRACT

Background: Pneumoperitoneum affects homeostasis and leads to alterations in cardiovascular and pulmonary stress response during laproscopy. Various pharmacologic interventions have been tried to attenuate the response. N-methyl d-aspartate (NMDA) receptor antagonists like MgSO4 have received great attention. We conducted this study using low dose of ketamine in attenuating pressor response.

Method: Patients who underwent laparoscopic cholecystectomy divided in group K (ketamine0.5 mg/kg)and group N(Normal saline). After induction of general anaesthesia but ten minutes before creation of pneumoperitoneum, the (group K) received ketamine 0.5 mg/kg diluted in normal saline intravenously where as group N received same amount of Normal saline. Haemodynamic parameters recorded and results observed.

Results: Heart Rate,Systolic Blood Pressure, Diastolic Blood Pressure, Mean Arterial Pressure were significantly attenuated in group K($p<0.05$) as compared to group N

Conclusion: ketamine attenuates hemodynamic response in pneumoperitonium in laparoscopic cholecystectomy without changes in ETCO2.

KEYWORDS : Laparoscopic Cholecystectomy, NMDR Antagonist, Ketamine, pneumoperitonium

INTRODUCTION

Laparoscopic surgical procedures aim to achieve a satisfactory therapeutic result while minimizing the traumatic and metabolic stress of the intervention. Tissue trauma is significantly less than conventional open procedures, thus results in less postoperative pain. Other advantages include smaller incisional sites, lower risks of wound complications, shorter hospital stay, more rapid return to normal activities, and cost saving [1]. Pneumoperitoneum required for the smooth conduct of laparoscopy, affects homeostasis and leads to alterations in cardiovascular, pulmonary physiology and stress response. Cardiovascular changes include increase in mean arterial pressure (MAP) with no significant change in heart rate [2], decrease in cardiac output and increase in systemic vascular resistance. Various surgical methods like change in nature of insufflating gas [3], use of low intra-abdominal pressure [4,5] use of abdominal wall lift methods [6], have been tried to decrease the hemodynamic alterations seen with pneumoperitoneum, but all with practical limitations. Various anaesthetic interventions like use of epidural, segmental spinal [7], combined epidural and general anesthesia [8], use of various pharmacologic interventions like nitroglycerine [9], esmolol [10], have been used with varying success and practical limitations. N-methyl d-aspartate (NMDA) receptor antagonists have received greatest attention because NMDA receptors have a role in central sensitization and neural modulation.[11]

There is evidence that a single dose of perioperatively administered ketamine can reduce postoperative analgesic requirement, [12,13,14, 15,16] It is thus plausible that a low dose of preemptive ketamine, which could be insufficient for a major surgery may be adequate for minimally invasive surgery such as laparoscopic cholecystectomy, which causes less tissue trauma.[15] Conceivably, a smaller dose may have the benefit of minimal hemodynamic effects without additional psychotomimetic adverse effects.[15] The lower dose of 0.5 mg/kg being devoid of any adverse effects and hemodynamic changes is an optimal dose for preemptive analgesia in patients undergoing laparoscopic cholecystectomy (17).

Materials and Methods

After obtaining approval from hospital Ethical Committee, details of the procedure was explained to the patients and a written informed consent was taken. 20 ASA I or II patients undergoing laparoscopic cholecystectomy were enrolled into the study. Exclusion criteria were; Patient refusal with poor cardiovascular and respiratory reserve, Patients with ASA III or more, Patients with known allergy ,sensitivity to study drug , Patients with anticipated difficult airway (Mallampati grade 3 & 4), Patients with any contraindication to laproscopic procedures. Patients were randomly divided into two groups. After general anesthesia patient received one of these solutions as a bolus intravenously 10 minutes before pneumoperitoneum was created. In Group K Inj. Ketamine 0.5 mg/kg intravenously diluted in 10 ml syringe given where as Group N received Inj Normal saline in 10ml syringe.

On the night prior to surgery all patients received tab Pantoprozole 40 mg and Tab Alprazolam 0.5 mg orally as premedication and patients were kept nil by mouth 8 hrs prior to surgery. On arrival in the operating room, after confirming the identity of the patient, the consent was checked; the preoperative assessment was reviewed and up dated. The nil by mouth status of the patient was confirmed. Anesthesia machine, monitors and resuscitation equipments were checked. ECG, NIBP and pulse oximeter were applied and baseline readings of parameters like HR(HEART RATE), SBP(Systolic Blood Pressure), DBP(Diastolic Blood Pressure), MAP(Mean Arterial Pressure) and SpO2 were noted. Capnometer (ETCO2) was attached after intubation.

All the patients were pre-loaded with Ringer lactate 10 ml/kg intravenously

All patients received premedication injection midazolam 0.02 mg/kg, and injection Glycopyrolate 4 µg/kg and inj ondansetron 0.08mg/kg, body weight intravenous. Patients were pre-oxygenated with 100% Oxygen for 5 minutes before induction. Induction of anaesthesia was done with Inj.Thiopentone 5-7mg /kg intravenously followed by Inj. Suxamethonium 1.5-2mg/kg intravenously, to facilitate endotracheal intubation. Bilateral air entry was confirmed by auscultation, ETCO2

reading noted and the endotracheal tube was firmly secured using adhesive tape, ventilation was controlled at a tidal volume of 6-8 ml/kg and a respiratory rate of 12 breaths/min. study drug given intravenously 10 minutes before creating pneumoperitonium. Anaesthesia was maintained with 40% oxygen in 60% nitrous oxide, and isoflurane through out the study period. Muscle relaxation was maintained with Injection Atracurium 0.5 mg/kg (loading dose) followed by 0.1 mg/kg (maintainece dose). Study drug was given 10 minutes before creation of pneumoperitonum.

All the patients included in study were divided in two groups (10 patients each) namely Group K (ketamine group) and group N (control group) .

Group K were injected Inj. Ketamine 0.5 mg/kg intravenously diluted in 10 ml syringe .Where as Group N were injected Inj Normal saline in 10ml syringe.

During surgery ringer lactate was infused in accordance with deficit, maintenance and blood loss. CO2 pneumoperitoneum was created and intra-abdominal pressure maintained between 12-14 mm Hg. Patients were ventilated mechanically. Tidal volume and respiratory rate were adjusted to maintain end-tidal CO2 between 35-45mm Hg. Monitoring of HR, SBP, DBP, MBP, SPO_2, $ETCO_2$ and TOF was done on a multichannel monitor and TOF monitor. All patients were given injection ondanseteron 4mg, injection diclofenac sodium 75mg intravenous towards the end of surgery.

Reversal and Extubation

After completion of surgery and achieving complete haemostasis and placement of dressing at the site of surgery, residual neuromuscular blockade was reversed with a combination of Injection Neostigmine 0.05 mg/kg and Injection Glycopyrrolate 8 µg/kg. The patients were extubated once TOF was between 90 % and 100%. Extubation time was noted. All patients were monitored for 30 minutes in recovery room following extubation.

Monitoring and recording of parameters was done at following intervals and analyzed for study.

Pre induction, 5,10 min after drug administration 1,5,10,15,20,30, 45, 60,75 minutes after inflation of pneumoperitonium and after extubation.

The mean age of patients was 46.86 yrs in Group K and 43.33 yrs in Group N.

The distribution of patients was comparable in both the groups with respect to the age of the patients. Here, we found no statistical significance in the distribution of patients with respect to weight.

Comparing Mean Arterial Blood pressure and pulse

After 30 minutes of tourniquet inflation difference in Mean blood pressure between group K (96.7± 5.64) and Group N (103± 1.22) and pulse between group K (81± 4.616) and Group N (86± 0.83) was statistically significant (P 0.001)

After 45 minutes of tourniquet inflation difference in Mean blood pressure between group K (98.3± 6.52) and Group N (108.22± 1.22) and pulse between group K (80.33± 4.56) and Group N (84.5± 0.83) was statistically significant (P 0.001)

After 60 minutes of tourniquet inflation difference in Mean blood pressure between group K (97.9±5.45) and Group N (107.5± 0.84) and pulse between group K (82.67± 5.1) and Group N (84.5±1.83) was statistically significant (P 0.001)

The statistically significant difference in Mean blood pressure and pulse were seen at time intervals from pre induction to 30,45, 60 minutes after creation of pneumoperitonum as shown in figures 1 & 2.

Table – 1 Baseline Comparison of the study groups according to age

Groups	Group K	Group N	P value
Age in years (mean ± SD)	46.866 ± 9.576	43.33 ± 7.470	0.1138 (non-significant)

Table – 2 Baseline Comparison of the study groups according to weight

Groups	Group K	Group	P value
Weight in kg (mean ± SD)	53.3 ± 4.524	53.7 ± 5.923	0.844 (non-significant)

Figure 1: Mean pulse rate (/min) at different time intervals in the study group

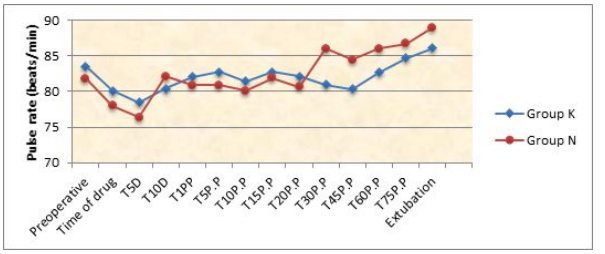
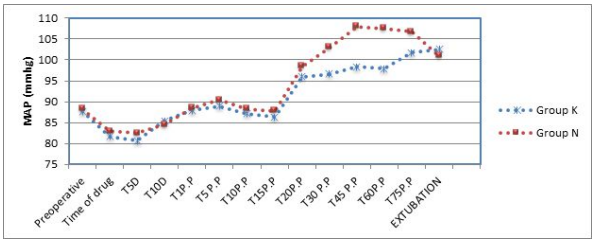


Figure – 2 Comparison of MBP (mmHg) in study and control groups at different time intervals



Discussion

This placebo controlled, double blind study was designed to assess the effects of ketamine on attenuation of hemodynamic stress responses during laparoscopic cholecystectomy. Diamant et al. [18] reported 35% decrease in cardiac output in dog with a raised intra-abdominal pressure of 40mmHg. Ishizaki et al. [19] Tried to evaluate the safe intra-abdominal pressure during laparoscopic surgery. They observed significant fall in cardiac output at 16 mm Hg of intra-abdominal pressure and hemodynamic alterations. So we kept intra-abdominal in our study between 12-14 mm Hg and decided to use ketamine to attenuate hemodynamic changes during laparoscopic surgeries. Study by Joris JL et al. [20] concluded that vasopressin and catecholamines probably mediate the increase in systemic vascular resistance observed during pneumoperitoneum. NMDR antagonist are effective in blocking the release of catecholamines from both adrenergic nerve terminals and the adrenal gland. Besides, magnesium produces vasodilatation by acting directly on blood vessels. Because of the ability of magnesium sulphate an NMDR antagonist to attenuate adverse hemodynamic response, we have administered 0.5 mg/kg ketamine 10 minutes before pneumoperitonum. The purpose of this study was to study the effect of ketamine, which is a potent NMDR Antagonist, in attenuating the hemodynamic stress response to the effects of pneumoperitoneum, which is the key element in laparoscopic surgeries. This attenuation of the effects is apparently related to the reduction in the release of catecholamine, vasopressin or both. NMDA receptors play a significant role in central sensitization in spinal cord. In previous studies conducted by D. Jee and D. Lee et al, they observed that magnesium sulphate an NMDR antagonist effectively prevented sympathoadrenal hemodynamic stress responses during pneumoperitoneum. In similar scenario Ketamine being an NMDR antagonist was able to attenuate sympathoadrenal stress response following Pneumoperitonium in our study.

CONCLUSION

- In our study, significant increase was observed in heart rate, blood pressure and mean blood pressure in the placebo group compared to study group. Small dose of ketamine given before creating pneumoperitoneum, attenuates the hemodynamic stress responses caused by pneumoperitoneum, by changing neurohumoral responses during laparoscopic cholecystectomies.
- There was no incidence of bradycardia or sudden hypotension in both groups.

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Conflict of Interest: None

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