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STUDY OF HAEMODYNAMIC CHANGES OF TWO DIFFERENT DOSES OF INTRAVENOUS CLONIDINE PREMEDICATION DURING LAPAROSCOPIC CHOLECYSTECTOMY

Anesthesiology

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ABSTRACT

BACKGROUND: Clonidine is a useful drug for premedication in laparoscopic surgery to attenuate significant hemodynamic stress responses during intubation,insufflation of CO2 &extubation.

AIM: Present study was undertaken to determine its minimum effective&safe dose ,by comparing hemodynamic changes by two different doses of intravenous clonidine as premedicant.

MATERIAL&METHODS: It is a prospective study conducted in OT2 of SMS Hospital.30subjects were taken for each of three groups-(A)control, (B)1mcg/kg &(C)2mcg/kg of clonidine.Heart Rate, SystolicBP, DiastolicBP &Mean Arterial Pressure were recorded at specified timings from premedication till extubation.

RESULTS: Rise in HR,SBP,DBP&MAP was lowest in GroupC than in GroupB whereas significant changes were observed in GroupA. Clonidine in GroupB could not effectively attenuate hemodynamic stress responses during intubation and extubation.

CONCLUSION:Clonidine 2µg/kg intravenous can safely and effectively be recommended as a premedicant for laparoscopic cholecystectomy.

KEYWORDS

Clonidine, Laparoscopic cholecystectomy, Hemodynamic changes

INTRODUCTION

Laparoscopic cholecystectomy has become gold standard surgery for cholelithiasis due to shorter hospital stay, early ambulation, smaller scar& less compromised postoperative respiratory and gastrointestinal functions. However, the procedure is not risk free as it is associated with significant hemodynamic changes due to creation of pneumoperitoneum, potential for systemic absorption of carbon dioxide& reverse Trendelenberg position.[1] Various pharmacological agents like nitroglycerine, beta blockers, and opioids are used to provide hemodynamic stability during pneumoperitoneum,[2]but they have their own disadvantages. Clonidine is a useful premedicant that produces anxiolysis, sedation,hemodynamic stability, reduces analgesic& volatile anesthetic requirement and decreases the doses of barbiturates needed to produce anesthesia in adults.[1]

Laryngoscopy and endotracheal intubation is mandatory in most patients requiring operative intervention under general anaesthesia. Passage of endotracheal tube and emergence is accompanied by certain cardiovascular changes like tachycardia/bradycardia, rise in blood pressure and wide variety of cardiac arrhythmias. Clonidine, an α-2 adrenergic receptor agonist, has shown promising results for attenuation of these hemodynamic responses.[3-7] It is antiemetic &also decreases post-operative shivering& delirium.[8] However, there is wide difference in doses of clonidine used. Present study was undertaken to determine its minimum effective &safe dose ,by comparing hemodynamic changes by two different doses of intravenous clonidine as premedicant.

MATERIALS&METHODS-

This is a Hospital based prospective randomized double-blind controlled clinical study conducted in Operation-Theatre2 (Ot2), S.M.S. Medical College and Attached Group of Hospitals, Jaipur with due permission from Institutional Ethics Committee and Research Review Board(EC No:3435/MC/IEC/2017 dated 07.10.2017). Study subjects were 90patients (30in each group)planned for elective laparoscopic cholecystectomy under GA. Patients in GroupA who will receive 100ml of normal saline(NS), GroupB who will receive 1µg/kg of clonidine in 100ml NS and GroupC who will receive 2µg/kg of clonidine in 100ml NS respectively.

Inclusion Criteria

- Patients who gave written informed consent
- ASA Grade I &II
- Age between 18-60 yrs

Exclusion Criteria

- Known sensitivity to clonidine
- Compromised renal, cardiac and respiratory status
- Patients on antihypertensive medication.
- ASA Grade III &IV

Hemodynamic parameters to be studied–

- Heart Rate(HR)
- Systolic Blood Pressure(SBP)
- Diastolic Blood Pressure(DBP)
- Mean Arterial Pressure(MAP)

During premedication, study drug was injected slowly in 15minutes with glycopyrrolate 0.004mg/kg and tramadol 1.5mg/kg,30minutes prior to surgery. Hemodynamic parameters were recorded just before giving i.v. clonidine (baseline), at 15and 30minutes after premedication, after laryngoscopy & intubation, at insufflation of CO2, 5,10,15,30,45,60 minutes after insufflation, after release of CO_2&at extubation.

Induction:

Patient induced with 2.5%thiopentone sodium(5mg/kg) followed by succinyl choline(2mg/kg) to facilitate tracheal intubation. Patient was intubated with a cuffed, disposable endotracheal tube of appropriate size after direct laryngoscopy.

Maintenance:

Lungs were mechanically ventilated with O_2-N_2O (50%- 50%), sevoflurane(1-2%), and atracurium(0.5mg/kg) bolus followed by 0.1mg/kg intermittently for neuromuscular blockade. Tidal volume &ventilator frequency were adjusted to maintain normocapnia ($EtCO_2$ 40 ± 4 mmHg).

Pneumoperitoneum was created by insufflation of CO_2 and operation table was tilted to about 15° reverse trendelenberg position. Intra-abdominal pressure was not allowed to exceed 15 mmHg.

Any change in hemodynamic variables more than 20% on either side of baseline was considered significant. Any increase in MAP up to 20% from baseline was treated by increasing the concentration of sevoflurane to a maximum of 2%.

RESULTS

All 90 patients completed the study. P values<0.05 were considered as significant(S) and P value>0.05 as statistically Non-Significant(NS).

Various demographic parameters were comparable among the 3 groups[Table1].

TABLE 1. DEMOGRAPHIC PARAMETERS (MEAN+/- SD)

Parameters	Group A	Group B	Group C	P Value
Age (years)	39.83+/-4.09	39.83+/-4.09	39.77+/-4.08	0.99 NS
Weight(kg)	54.97+/-7.26	57.57+/-7.82	53.53+/-8.32	0.134 NS
Sex(m:f)	5:25	4:26	5:25	0.92 NS
ASA physical status(I:II)	27:3	22:8	27:3	0.12 NS
Duration Of Surgery	96.03+/-10.47	96.67+/-8.42	95.03+/-8.45	0.78 NS

Hemodynamic parameters recorded at specified timings are shown in figures[Figure1-4].

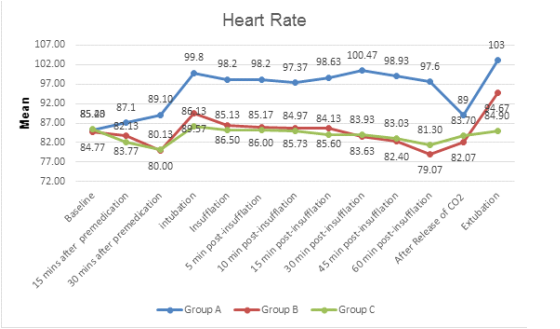


FIGURE 1. Heart Rate (beats /min) at different time intervals among the study groups

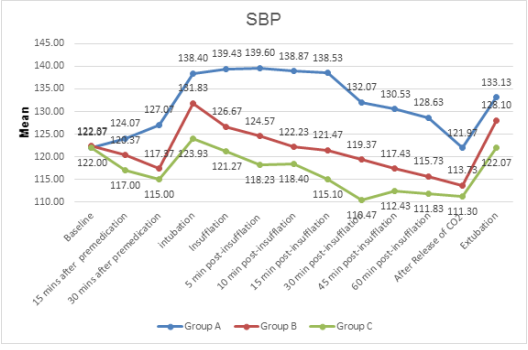


FIGURE 2.Systolic Blood pressure (mmHg) at different time intervals among the study groups

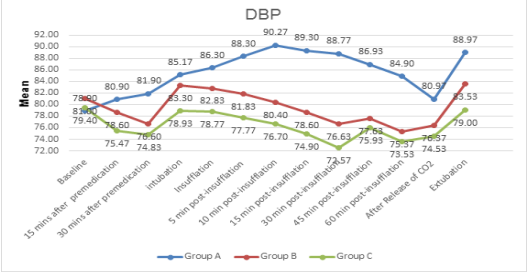


FIGURE 3.Diastolic Blood pressure (mmHg) at different time intervals among the study groups

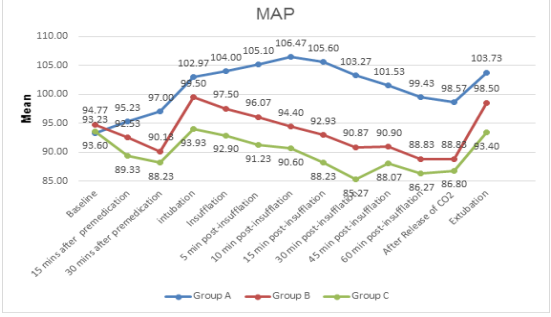


FIGURE 4.Mean Arterial Pressure (mmHg) at different time intervals among the study group There was no statistically significant difference in hemodynamic parameters(HR,SBP,DBP & MAP) between the three groups preoperatively(P value >0.05).The increase in these parameters was significantly higher at intubation &insufflation in groupA, which remained high till extubation as compared to groups B & C. Also, the rise was lowest in GroupC (Clonidine 2mcg/kg) than in GroupB (Clonidine 1mcg/kg) (A>B>C). However, Clonidine in groupB could not effectively attenuate hemodynamic stress responses during intubation and extubation. Hemodynamic variables at intubation, insufflation& extubation remained comparable to baseline in groupC.

DISCUSSION-

Large number of laparoscopic surgeries are performed each year.[9] Laparoscopic cholecystectomy is the treatment of choice for cholelithiasis.[10] The anesthetic technique for upper abdominal laparoscopic surgery is generally limited to general anesthesia with neuromuscular blockade, tracheal intubation, and mechanical ventilation. Pneumoperitoneum during laparoscopic surgery leads to significant hemodynamic changes such as an increase in MAP and systemic vascular resistance (SVR) and a decrease in cardiac output. The decline in cardiac output and venous return can be attenuated by volume infusion before pneumoperitoneum. However, an increase in MAP and SVR requires therapeutic intervention.[1]

Various techniques and pharmacological agents have used to counteract these detrimental effects of pneumoperitoneum. Clonidine (an alpha2 adrenergic receptor agonist) inhibits catecholamine and vasopressin-mediated increase in SVR caused by pneumoperitoneum.[11] Clonidine is a useful premedicant that produces anxiolysis, sedation & hemodynamic stability and reduces analgesic & volatile anesthetic requirement& decreases the doses of barbiturates needed to produce anesthesia in adults. Attenuation of sympathoadrenal response to laryngoscopy and intubation is also observed. It is antiemetic &also decreases post-operative shivering, decreases post-operative delirium& causes inhibition of opioid induced muscle rigidity.[1] Clonidine has anti–hypertensive properties and augments the effects of anesthesia. Thus, it is potentially an ideal agent to contain the stress response to pneumoperitoneum.[10]

We conducted a double blind prospective randomized controlled study in 90healthy (ASA I and II) adult patients to study the hemodynamic changes of two different doses of intravenous clonidine premedication during laparoscopic cholecystectomy.

Demographic profile and preoperative vital parameters(baseline) were compared between the three groups of patients and no significant difference was found. These findings correlated with study done by P.K.Omar et al[12] and D.C.Tripathi et al[1].

Our study correlated with study done by DC Tripathi et al, in terms of hemodynamic variables too. In their study, in groupI (100ml NS), there was a significant increase in hemodynamic variables during intubation, pneumoperitoneum and extubation (P<0.001).Clonidine given 1µg/kg intravenous in 100ml NS (groupII) attenuated hemodynamic stress response to pneumoperitoneum (P<0.05), but not that associated with intubation and extubation. Clonidine 2µg/kg intravenous in 100ml NS (groupIII) prevented hemodynamic stress response to pneumoperitoneum and that associated with intubation& extubation too(P<0.05).[1]

P.K.Omar et al (2013) compared the two groups to receive either nitroglycerine infusion (Group I) or i.v. clonidine 2mcg/kg (Group II), before induction of anaesthesia. Significant rise in heart rate was observed following pneumoperitoneum in Group I as compared to Group II (99.23±14.02 Vs 81.26±8.40 bpm). This correlated with our study since in group C (i.v. clonidine 2mcg/kg) ,HR was 83.13+/-7.85 (vs 95.93±15.09 beats per minute in control group). They concluded that clonidine (2mcg/kg) premedication provides better perioperative haemodynamic stability, hence it can be recommended as a routine premedication for laparoscopic cholecystectomy.[12]

PM Bhalerao et al concluded that premedication with intravenous clonidine(1mcg/kg), is relatively safe as well as an effective method that provides stable haemodynamics and protection against stress response induced by pneumoperitoneum in patients undergoing laparoscopic cholecystectomy.[13]

Jean L. Joris et al studied hemodynamic changes induced by laparoscopy and their endocrine correlates& effect of intravenous

Clonidine in 20healthy patients scheduled for elective laparoscopic cholecystectomy. They found that Clonidine administered prior to pneumoperitoneum reduces catecholamine release and attenuates hemodynamic changes during laparoscopy.[7]

Rita Singh et al compared group1 of oral clonidine(150mcg) and group2(placebo) with respect to haemodynamic parameters i.e. pulse rate, SBP,MAP &DBP. They were significantly lower and stable in the clonidine group as compared to placebo group.[10]

Toshu Yotsui studied effects of oral administration of Clonidine on sympathetic and endocrinological responses in 20 patients undergoing elective laparoscopic cholecystectomy and found that systolic and diastolic blood pressures were lower in Clonidine group than in control group immediately after endotracheal intubation &extubation. Patients in Clonidine group showed lower plasma concentrations of noradrenaline 2hours after beginning of the surgery than patients in the control group. He concluded that Clonidine premedication prevents sympathetic hyperactivity in patients undergoing laparoscopic cholecystectomy.[14]

Manjaree Mishra MD et al concluded as clonidine to be more effective than nitroglycerin at preventing changes in hemodynamic parameters and intraocular pressure induced by carbon dioxide insufflation during laparoscopic cholecystectomy.[15]

CONCLUSION-

We concluded that to limit hemodynamic stress responses during intubation, pneumoperitoneum and extubation in laparoscopic cholecystectomy procedures, **2µg/kg intravenous Clonidine infusion** can safely &effectively be recommended as a premedicant 30minutes prior to the surgery.

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