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PREMEDICATION WITH IV CLONIDINE V/S IV LABETALOL FOR HEMODYNAMIC STABILITY DURING AIRWAY INSTRUMENTATION IN LAPAROSCOPIC CHOLECYSTECTOMY

Anaesthesiology

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ABSTRACT

Laryngoscopy is an intense noxious stimulus leading to a surge in catecholamine release potentially having deleterious effects in patients with known cardiac or neurological compromise. This study was undertaken with the aim to observe the efficacy of iv clonidine and iv labetalol premedication for attenuation of hemodynamic response during airway instrumentation in patients posted for laparoscopic cholecystectomy. 90 ASA I patients were randomly allocated into one of the 3 groups; Group C(Clonidine 2mcg/kg), Group L(Labetalol 0.25mg/kg), Group P(normal saline). Patients were premedicated by 1 of the study drug 10 minutes prior to induction of anaesthesia. All patients were induced by a standard protocol. The patients were observed for 3 hours in post anaesthetic care unit after extubation or until there were no signs of any drug induced side effects. Post operative recovery was monitored using Modified Aldrete score. The mean values of heart rates, systolic blood pressure, diastolic blood pressure, arterial blood pressure, rate pressure product in group C and group L were lower from the baseline at all times after intubation in contrast to group P which displayed values higher than baseline at all times after intubation. There was a significant difference between group C and L as compared with group P but no significant difference between group C and L. Patients who received clonidine displayed more sedation as compared with patients who received labetalol. There were no drug related complications in any patients.

KEYWORDS

clonidine, labetalol, intubation response, laryngoscopy, airway instrumentation.

INRODUCTION

Airway instrumentation is an integral part of general anaesthesia in laparoscopic surgeries. Laryngoscopy is an intense noxious stimulus leading to autonomic activation through vagal and glossopharyngeal afferents leading to a surge in catecholamine release. This manifests as rise in blood pressure, heart rate, intracranial pressure and intraocular pressure.[1] The transient catecholamine surge can have potentially deleterious effects in patients with known cardiac or neurological compromise. It can lead to perioperative myocardial ischemia, infarction, and raised intracranial pressure, rupture of cerebral and aortic aneurysms.[2,3] This area has been under constant clinical investigation in search of a better technique to prevent this response. This study was undertaken to observe the efficacy of iv clonidine and iv labetalol premedication for attenuation of hemodynamic response during airway instrumentation in patients posted for laparoscopic cholecystectomy. Secondary objective was to evaluate any post operative sedation and any dose related complications of clonidine and labetalol.

MATERIALS AND METHODS

This is a prospective double blind randomized controlled study undertaken after approval from institutional ethics committee. 90 ASA I consenting patients between age 18-65 years posted for elective laparoscopic cholecystectomy were recruited and were randomly allocated into one of the 3 Groups (Group C – Clonidine 2mcg/kg, Group L – Labetalol 0.25mg/kg, Group P – normal saline) by computer generated random number tables. Patients were assessed a day prior to surgery. Detailed systemic examination was performed. Patients name, age, sex, weight, registration number and diagnosis were recorded. Patients were informed about the study procedure, drugs that were used, their effects and side effects. A valid written informed consent was taken a day prior to procedure. Patients were kept NBM as per ASA guidelines. After arrival of patient in the operation theatre, routine monitors (ECG, pulse oximetry, noninvasive arterial pressure, and heart rate) were attached. Patients were pre medicated with any 1 of the 3 study drugs 10 mins before induction and 0.03mg/kg midazolam and 2mcg/kg fentanyl. Anaesthesia was induced with 2 mg/kg Propofol and 0.1 mg/kg vecuronium to facilitate endotracheal intubation. Laryngoscopy and tracheal intubation was performed 3 minutes after vecuronium injection by an experienced anaesthetist. Duration of laryngoscopy >22 seconds or patients requiring second attempt at laryngoscopy were excluded from the study. Anaesthesia was maintained with 1 MAC Isoflurane with fresh gas flow 3L/min (50%O2+50%N2O). Intra operatively HR, NIBP, MAP, ECG, SpO2 and EtCO2 levels were continuously monitored and recorded before iv administration of the study drug, 5 and 10 minutes after administration of the study drug, after induction, immediately after intubation and 1, 3, 5 and 10 minutes after intubation. Patients were observed for complications like hypotension, hypertension, arrhythmias, hypoxemia and bronchospasm and treated as required. Intra operatively patients were given iv Paracetamol 15mg/kg for pain relief. At the end of surgery, neuromuscular blockade was reversed with glycopyrrolate and neostigmine. The patients were transferred to post anaesthetic care unit and were observed for 3 hrs or until there were no signs of any drug induced side effects such as nausea, vomiting, any respiratory inadequacy or hemodynamic instability. Post operative recovery was monitored using Modified Aldrete score.

RESULTS-

Data were statistically described in terms of mean (±SD), frequencies (number of cases) and percentages when appropriate. Data were tested first for normal distribution by Kolmogorov– Smirnov test. Comparison of quantitative variables between the 3 groups was done using ANOVA test with post-hoc Tukey's test for independent samples if normally distributed. Kruskal Wallis test was used for non-normally distributed quantitative data. For comparing categorical data, Chi square test was performed. Exact test was used instead when the expected frequency is less than 5. All statistical calculations were done using computer programs Microsoft Excel 2007 (Microsoft Corporation, NY, USA) and SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 21.

The peak values of mean heart rates, systolic, diastolic and mean arterial blood pressure and rate pressure product were observed at 1 minute post intubation. There was a gradual fall in all the parameters in all the 3 groups 1 minute after intubation and were lower from baseline in group C and group L at all times after intubation. This was in contrast to group P which displayed all parameter values higher than baseline at all times after intubation. The difference in the mean values in group C and L as compared with group P was statistically significant at all times after intubation.

Heart rate in all 3 groups increased gradually after intubation to a maximum observed at 1 minute and then gradually decreased up to 10 minutes after intubation. The heart rate in group P remained higher than the baseline values at all times after intubation. The heart rates in group C, group L showed a decrease of 11.6% and 11.9% respectively and group P showed a rise of 5.51% from the baseline at 10 minutes post intubation. There was no significant difference observed between group C and group L. (TABLE 1.1)

There was a significant decrease in systolic, diastolic and mean blood

pressures in group C and L after intubation as compared with group P. Peak values were observed at 1 minute post intubation. No significant difference was observed between group C and L. At 1 minute after intubation, there was 4% decrease in mean arterial pressure in group C, 2.4% decrease in group L and 4.5% increase in group P. The MAP at 10 minutes in group C and group L was 10.23% and 10.67% lower from baseline respectively and in group P 0.5% higher from baseline. (TABLE 1.2)

Mean Aldrete score at all times in group L and group P was 10. In group C, mean Aldrete score at 2, 2.5 and 3 hours was 10. At 0.5, 1, 1.5 hours mean Aldrete score was 9.57, 9.60 and 9.77 respectively in group C. This was observed to be statistically significant with p value <0.01. The difference was observed in the consciousness component of the score. (TABLE 1.3)

There were no drug related side effects or complications observed in any patient.

DISCUSSION-

Airway instrumentation by direct laryngoscopy and endotracheal intubation is the most common method of securing airway during laparoscopic surgeries. This is associated with various hemodynamic changes and can have detrimental effects on various organ systems.[2,4] A typical pressure response can include a 40-50% increase in blood pressure, a 20%increase in heart rate and an elevation of both epinephrine and norepinephrine levels.[5] The effect of stress response usually begins within 30 seconds and lasts for 5-10 minutes after intubation.[6] This can be detrimental in patients with cardiac or cerebrovascular comorbidities. Thus there is a need to suppress this response to improve the perioperative outcome of the patient.[7] In 1940, Reid et al. first found that the stimulation of the upper respiratory tract provoked an increase in the vagal activity.[8] In contrast to this study, Burstein et al, in 1950, observed that stimulation of upper respiratory tract leads to an increase in the sympathetic activity.[9] This was further confirmed by a study done by Prys-Roberts.[10] Since then this area has been under constant research to blunt the hemodynamic response to airway instrumentation with various pharmacological agents like use of anaesthetics[11,12], intravenous lidocaine[13,14], Opioids[3,15,16], vasodilators – SNP(Sodium nitroprusside)[17], Nitroglycerin[18–20], Calcium channel blockers[21,22] and β –blockers[4,23]. But the search for an ideal drug for this purpose continues to be the area of interest of many research clinicians.

Clonidine is a selective alpha-2 adrenergic agonist. The cardiovascular effects of clonidine are fall in heart rate and blood pressure. As a premedication, it decreases sympathetic outflow and reduces perioperative stress response[24]. Favorable effects of anaesthetic importance are sedation, analgesia, sympatholysis, vasoconstriction and antishivering[25].

Labetalol is an adrenergic blocker with selective alpha 1 and non-selective beta actions. It causes decrease in the peripheral vascular resistance without reflex tachycardia and significant changes in the cardiac output[26].

In this study, iv clonidine 2 mcg/kg and iv labetalol 0.25 mg/kg were evaluated for their action to suppress the pressure response to laryngoscopy and tracheal intubation.

In 1997, Zalunrdo et al compared intravenous and oral clonidine for attenuating the pressor response and observed iv clonidine superior to oral clonidine[27].

Chung et al observed the effect of labetalol in a dose of 0.4mg/kg on hemodynamics in response to laryngoscopy and intubation[23]. They did not observe significant difference in MAP between 2 groups after laryngoscopy and intubation but a statistically significant difference was noted in heart rate response to laryngoscopy. They concluded that labetalol attenuated heart rate response but not blood pressure to laryngoscopy.

Sakshi Arora et al studied iv clonidine in a dose of 1 mcg/kg and 2mcg/kg with iv fentanyl 2mcg/kg and concluded that clonidine 1mcg/kg with fentanyl 2 mcg/kg can be safely used to attenuate hemodynamic response to laryngoscopy and intubation[28].

Sameena Kousar, et al compared Fentanyl and Clonidine for Attenuation of the haemodynamic response to laryngoscopy and endotracheal intubation[29]. They recommended intravenous 2mcg/kg clonidine to be given 5 minutes prior to laryngoscopy to decrease the pressor response to airway instrumentation without many side effects.

Meftahuzzaman SM et al compared iv labetalol and iv fentanyl to blunt the hemodynamic response to laryngoscopy and tracheal intubation[30]. They observed that labetalol 0.25mg/kg and fentanyl 2 mcg/kg attenuated hemodynamic response to intubation as compared with control group. They concluded labetalol to be a better drug than fentanyl to attenuate hemodynamic response.

In our study, there was an increase in hemodynamic parameters after intubation. The peak values of all hemodynamic parameters were observed at 1 minute post intubation, after which these parameters gradually decreased. The mean values of all parameters were lower from the baseline in group C and L as compared with group P which remained higher than the baseline at all times. However, there was no statistically significant difference between group C and group L. Patients receiving clonidine had decreased modified Aldrete score as compared with patients receiving labetalol or placebo. This was attributed to sedative properties of clonidine. No other complications were noted in the patients. Patients were observed in the post anaesthesia care unit for 3 hours or until no drug related side effects were observed.

CONCLUSION-

We conclude that clonidine and labetalol premedication attenuated hemodynamic response to intubation which was statistically significant as compared with placebo. There was no significant difference between clonidine and labetalol in attenuating hemodynamic response to intubation. Patients who received clonidine displayed more sedation as compared with patients who received labetalol. There were no drug related complications in any patients.

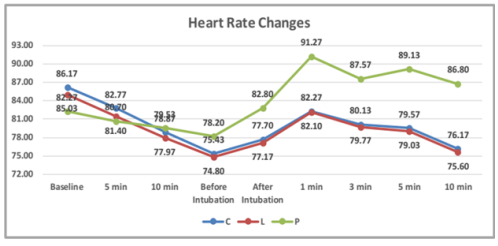

TABLE 1.1

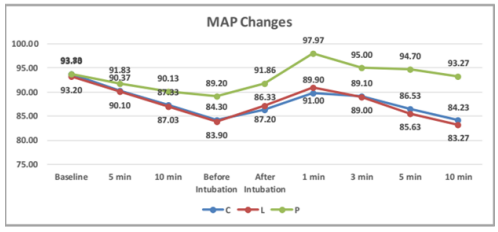

TABLE 1.2

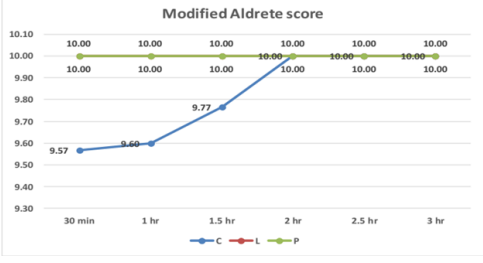

TABLE 1.3

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