ORIGINAL ARTICLE

ORAL CLONIDINE FOR ATTENUATION OF HAEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION IN KNOWN HYPERTENSIVE PATIENTS

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Background: Sympathetic response associated with laryngoscopy and endotracheal intubation is recognised as a potential cause for a number of complications especially in hypertensive patients. Various methods have been used to attenuate these haemodynamic responses; however most of the studies are in normotensive patients. The aim of our study was to compare the effect of oral clonidine and I/V fentanyl with oral placebo and I/V fentanyl in attenuating the haemodynamic responses to laryngoscopy and intubation in known hypertensive patients. **Method:** In a double blind randomised controlled trial, 60 hypertensive patients, taking antihypertensive drugs and with systolic blood pressure below 160 mmHg and diastolic blood pressure below 100 mmHg scheduled for elective surgeries, requiring oral endotracheal intubation and age ranging from 40–65 years were included in this study and randomly divided into Group A (clonidine 0.2 mg + fentanyl 2 μg/Kg) and Group B (Placebo + fentanyl 2 μg/Kg). **Results:** Demographic data were comparable in both groups. There were no statistically significant differences between the two groups in the duration of laryngoscopy and intubation. There was statistically significant attenuation in heart rate in both groups (p=0.020). The trends of attenuation of systolic blood pressure, diastolic blood pressure and mean arterial pressure in Group A compared to Group B, were statistically significant (p=0.034, 0.011, 0.011 respectively). **Conclusion:** Clonidine, under the present study design attenuates the haemodynamic response to laryngoscopy and endotracheal intubation in known hypertensive patients.

Keywords: Clonidine, haemodynamic response, laryngoscopy, endotracheal intubation, hypertension

INTRODUCTION

In 1940, Reid and Brace first described haemodynamic response to laryngoscopy and intubation.[1] Reflex changes in the cardiovascular system are most marked after laryngoscopy and intubation and lead to an average increase in blood pressure by 40–50% and 20% increase in heart rate.[2]

This hemodynamic response is much higher in hypertensive patients.[3,4] This response can lead to cardiac dysrhythmias (e.g., ventricular bigeminy), myocardial ischemia, raised intracranial pressure and even intracranial bleed.[5]

Clonidine a 2-imidazoline derivative is a centrally acting alpha 2 receptor agonist. Alpha 2 receptor is coupled via a G-protein to several effecter mechanisms, including inhibition of adenylate cyclase and effects at potassium and calcium channels.[6] Clonidine acts at the medulla (in the nucleus tractus solitarius and nucleus reticularis lateralis region of rostroventro-lateral medulla), reduces sympathetic and increases parasympathetic tone, resulting in decrease in heart rate and blood pressure. It sensitizes brain stem pressor centres to inhibition by baro-reflexes. Clonidine also binds to imidazoline receptors, which mediate antihypertensive effects.

Clonidine is used primarily as anti hypertensive drug but it has got sedative effect as well. Therefore, use of clonidine in hypertensive patients as a premedication has got additive advantage of sedation which is required in preoperative period and also hemodynamic stability during operation.

The aim of this study was to compare the effect of oral clonidine and fentanyl in attenuating the haemodynamic responses to laryngoscopy and intubation in known hypertensive patients.

MATERIAL AND METHODS

After obtaining approval from the Hospital Ethics Committee and patients' informed consent, 60 hypertensive patients, taking antihypertensive drugs and with systolic blood pressure (SBP) below 160 mmHg and diastolic blood pressure (DBP) below 100 mmHg scheduled for elective surgeries, requiring oral endotracheal intubation and ranging from 40–65 years of age were included in this study.

Exclusion criteria were refusal to give consent, anticipated difficult airway, emergency cases, history of allergy to clonidine or midazolam, ASA IV and V, morbidly obese patients, patients with history asthma, laryngoscopy and intubation taking more than 30 seconds or more then single attempt, rapid sequence induction, patients taking tricyclic antidepressants, nasal endotracheal intubation and patients who have not taken their routine antihypertensive drugs before surgery.

Patients were randomised for treatment allocation as Group A and Group B. Group A was given drug combination A (Clonidine 0.2 mg + Fentanyl 2 μg/Kg) and Group B was given drug combination B (Placebo + Fentanyl 2 μg/Kg). Patients in both groups

received the study drugs 90 minutes before surgery, and standard pre-medication Tab. Midazolam 7.5 mg, 60 minutes before surgery.

Standard monitoring, consisting of inspired oxygen concentration, ECG, pulse oximetry, capnography and non-invasive blood pressure/invasive blood pressure. Intra-operatively, the inspired and end-tidal concentrations of carbon dioxide, oxygen, and inhalational anaesthetics concentration were monitored. General anaesthesia with oral endotracheal intubation and controlled mechanical ventilation were given to all patients. Anaesthetists were blinded to the drugs administered. Baseline vitals (blood pressure, heart rate and oxygen saturation) were recorded. Patients were pre-oxygenated for 3 minutes with oxygen flow rate of 6 L/min on circle breathing system.

Anaesthesia was induced in all patients with Fentanyl I/V 2 µg/Kg, thiopentone I/V 5 mg/Kg and atracurium I/V 0.5 mg/Kg to facilitate the tracheal intubation and controlled ventilation. Laryngoscopy and intubation were done by the primary anaesthetist, and PVC endotracheal tube, size 7.5 mm for females and 8.5 mm for males were used.

Blood pressures were recorded before start of induction, then before intubation, immediately after intubation and every minute for 5 minutes. Twenty-five percent increase or decrease in blood pressure and heart rate were taken as significant. Management of variations in blood pressure and heart rate were left to the discretion of the primary anaesthetist.

Data were analysed using SPSS-10. Repeated measures ANOVA were used to analyse haemodynamic responses, i.e., heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure (MAP). The Chi-squared test was used for categorical data, and $p<0.05$ was considered significant. Continuous response variables like age, weight, height, BMI, duration of laryngoscopy, heart rate, SBP, DBP and mean arterial pressure were presented by Mean±SD. Student's *t*-test was applied to compare age, weight, height, BMI and duration of laryngoscopy.

RESULTS

Three cases dropped out from the study, two from Group A and one from Group B. Mean age of the patients was 53.30±6.88 (range: 40–65) years. Mean age of patients in Group A was slightly higher than Group B, but the difference was statistically insignificant. The same pattern of insignificant differences was found between weight and height. Duration of laryngoscopy was 17.31±5.23 seconds in Group A and 17.90±5.18 seconds in Group B. The difference of duration of laryngoscopy was statistically insignificant between the groups (p=0.670) (Table-1).

Baseline heart rate was 69.8±13.3 per minute and in Group A and 79.4±19.6 per minute in Group B, (p=0.032). The same pattern of significance was followed till 2 minutes after intubation. After 3 minutes, there was no statistically significant difference between the two groups (Table-2). The trend of attenuation in HR in both groups was statistically significant (F=5.71, p=0.020).

There was no significant difference in the mean baseline SBP of the patients in both groups. A continuous fall in SBP till 5 minutes after intubation with the exception of SBP immediately after intubation was observed in both groups. The difference of mean SBP between groups was not significant (p=0.222). However, trend of attenuation in SBP was statistically significant in Group A (F=4.703, p=0.034).

The mean baseline DBP in Group A was 77.6±11.0 mmHg and in Group B it was 87.2±8.4 mmHg. After continuous attenuation these readings were 60.50±11.86 mmHg and 64.69±14.05 mmHg respectively and this difference between the groups was not significant (p=0.230). The trend of DBP was different from that of SBP as in spite of significantly consistent attenuation in DBP compared with baseline data except immediately after intubation in both groups, the difference of means between the groups was statistically significant. Trend of attenuation in DBP was statistically significant in Group A (F=7.004, p=0.011).

The mean baseline MAP in Group A was 93.8±11.9 mmHg and that of Group B was 104.2±10.4 mmHg. This difference between the two groups was statistically significant (p=0.001). Almost same figures were observed immediately after intubation but significant decline (p=0.001) in MAP was observed after 2, 3, 4 and 5 minutes of intubation. The difference between the groups was significant (p=0.011) except the mean MAP taken at 5 minutes after intubation (p=0.201). Trend of attenuation in MAP was statistically significant in Group A (F=6.84, p=0.011).

Twelve patients (42.9%) of Group A were on beta blockers, 9 (32.1%) on non-beta blocker, and 7 (25%) patients were on both beta blockers and non-beta blockers. In Group B, 11 (37.8%) patients were on beta blockers, 14 (48.3%) on non-beta blockers, and 4 (13.8%) patients were on both beta blockers and non-beta blockers. There were no significant difference between the two groups (χ^2=1.93, p=0.381).

Among 29 patients in the Group B, 9 (31%) were diabetics while 20 (69) had no associated disease. Among the 28 patients in the Group A, 4 (14.3%) were diabetics while 24 (85.7%) had no associated disease.

Eight out of 28 patients (28.57%) in the Group A developed clinically significant (25% change from the baseline) decrease in heart rate and blood pressure, of which 4 responded to crystalloid bolus (500 ml of Ringer's lactate or normal saline) and others required crystalloids plus vasopressors including ephedrine and phenylephrine depending upon the heart rate. Eight patients out of 29 (27.58%) in Group B also sustained clinically significant decrease in blood pressure/heart rate, 5 responded to crystalloid bolus and 3 required crystalloids plus

vasopressors including ephedrine and phenylephrine depending upon the heart rate. One patient in each group developed clinically significant increase in blood pressure and heart rate after laryngoscopy and intubation; metoprolol 1 mg I/V boluses were used to treat this response. All patients were followed postoperatively and no cardiovascular and neurological sequels were observed.

Table-1: Demographic and procedural features of the groups

Variables	Group A (n=28)	Group B (n=29)
Age (Year)	53.63±7.41	52.97±6.42
Weight (Kg)	70.9±8.66	69.9±12.4
Height (Cm)	156.3±10.3	156.2±8.1
BMI (Kg/m^2)	28.71±2.72	28.50±3.56
Duration of laryngoscopy (min)	17.31±5.23	17.90±5.18

Table-2: Haemodynamic attenuation in the groups

Response	Drug Combination	Baseline	Before Intubation	After Intubation	After 2 min	After 3 min	After 4 min	After 5 min
Heart Rate	A	69.9±13.3*	66.9±13.1*	73.8±13.8*	69.9±12.0*	66.9±11.1	63.5±11.1	62.6±11.6
	B	79.4±19.6	75.8±16.9	86.8±15.6	78.4±14.9	73.0±15.7	70.5±15.4	68.6±14.7
Systolic BP	A	125.9±16.1*	102.9±23.2	121.6±28.8*	113.5±21.0	102.3±14.7*	99.8±16.1	98.0±16.0
	B	137.4±15.9	111.1±28.0	136.2±24.8	124.9±26.7	114.9±23.6	107.5±21.0	102.5±19.7
Diastolic BP	A	77.6±11.0*	63.4±16.6	78.7±20.2	70.2±14.5	65.3±14.0*	58.8±13.4*	60.5±11.9
	B	87.2±8.4	70.4±15.2	87.9±17.6	81.9±18.4	73.3±15.5	69.6±14.1	64.7±14.1
Mean arterial pressure	A	93.8±11.9*	76.7±18.4	93.0±22.1*	84.5±15.9*	77.5±13.9*	71.9±13.8*	73.0±12.9
	B	104.2±10.4	84.0±18.9	104.1±18.7	96.3±20.0	87.2±17.6	82.4±16.1	77.9±15.8

*$p \leq 0.05$

DISCUSSION

Our results showed that clonidine attenuated the haemodynamic responses to laryngoscopy and intubation in known hypertensive patients. Heart rate was significantly lower in both groups probably because of fentanyl. The cardiovascular responses to laryngoscopy and tracheal intubation are well known,[7,8] and linked with increases in catecholamine blood levels[9]. Shribman *et al*[8] found that laryngoscopy alone or followed by tracheal intubation increases arterial pressure and catecholamine levels while intubation significantly increases HR.

To attenuate this haemodynamic response to laryngoscopy and endotracheal intubation different methods have been used to varying success including opioids, beta adrenergic blockers, nitroprusside or nitroglycerine, calcium channel blockers, intravenous xylocaine, topical airway anaesthesia, and MAC bar (inhalational anaesthetics).[3,10–12] Clonidine as a premedicant to attenuate the haemodynamic response to laryngoscopy and intubation has been studied in normotensive patients. Raval *et al*[13] in normotensive patients showed that clonidine produces marked sedation and better anxiolysis as compared to placebo but less sedation and same level of anxiolysis as compared to diazepam. Respiratory rate was not changed in either group. Extra advantage with clonidine over diazepam and placebo is its attenuating haemodynamic responses during laryngoscopy and endotracheal intubation, and also by its anti-sialagogue effect.[13]

CONCLUSION

Preoperatively administered oral clonidine attenuates the haemodynamic responses to laryngoscopy and intubation in known hypertensive patients.

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