Original Research Article

Attenuation of haemodynamic response to intubation with oral clonidine and oral atenolol

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Abstract

Objective: The aim of this study is to attenuate the heamodynamic response to laryngoscopy and endotracheal intubation using oral atenolol and oral clonidine, to study the extent of change in haemodynamic response and to observe if there are any untoward effects of such premedication. **Design:** A comparative study of oral atenolol and oral clonidine done to compare the attenuation of cardiovascular response during laryngoscopy and intubation. **Duration:** November 2016 to December 2017. **Setting:** Department of Anesthesia, Bhaskar Medical College, Ranga Reddy, Telangana. **Participants:** 50 adult patients undergoing various elective surgeries of ASA Grade – I, Mallampatti Grade– I were selected and informed consent was taken for all the cases. Patients were of both sexes and age ranging from 18-60 years. **Methods:** This study was done in 2 Groups. Group I consisted of 25 patients where atenolol 0.75 mg per kg body weight was given orally 3 hours before scheduled time of surgery. Group II consisted of 25 patients where clonidine 3-3.5 micrograms per kg body weight was given orally 90 minutes before scheduled time of surgery. The drugs given in premedication were injection glycopyrrolate 0.01 mg per kg body weight, midazolam 0.04 mg per kg body weight and ondansetron 0.08 mg per kg body weight. Induction of anaesthesia was achieved by intravenous thiopentone sodium given in a dose of 5 mg per kg body weight. Tracheal intubation was facilitated with intravenous suxamethonium 1.5 to 2 mg per kg bodyweight. Haemodynamic parameters (blood pressure, Heart rate, mean arterial pressure) were recorded at the specific intervals. **Results:** Patients who received oral atenolol did not show a significant increase in the various haemodynamic parameters. Patients who received oral clonidine showed a higher increase in haemodynamic parameters compared to patients who received oral atenolol. The haemodynamic parameters returned to the basal value at the end of 5 minutes in the atenolol group where as in the clonidine group it took more than 5 minutes to return to the basal value and it has less effect on the heart rate when compared atenolol group. **Conclusion:** Oral atenolol in a dose of 0.75 mg per kg body weight given 3 hours before induction of anaesthesia is more effective in attenuating haemodynamic response to laryngoscopy and endotracheal intubation when compared to oral clonidine.

Key Words: Heamodynamic response, Laryngoscopy, Endotracheal intubation, Oral Atenolol and Oral Clonidine.

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INTRODUCTION

Laryngoscopy and intubation violate the patients' protective reflexes and lead to physiological changes involving various systems of the body. Endotracheal Intubation is one of the most commonly performed procedures. Endotracheal intubation is the translaryngeal placement of endotracheal tube into trachea via mouth or nose. Today endotracheal intubation is an integral part of the Anaesthesiologists contribution to patient care. There is substantial evidence that laryngoscopy and endotracheal intubation in lightly anaesthetised patients is accompanied by considerable increase in heart rate and arterial blood pressure. These changes are usually of short

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duration and well tolerated by patients in absence of cardiovascular diseases or disturbed intracranial pressure homeostasis. The Hypertensive response to laryngoscopy and intubation has been shown to be due to sympathetic discharge caused by stimulation of pharynx and larynx causing increase in the levels of catecholamines, especially noradrenaline and activation of alpha and beta receptors. The reaction is not prevented by routine premedication. The increase in heart rate and blood pressure are transitory, variable and unpredictable. Failure to blunt the response to intubation may have disastrous consequences in patients with hypertension, coronary artery disease, aneurysmal vascular disease, raised ICP and diseased cerebral vasculature. The various, complications observed during endotracheal intubation are arrhythmias, myocardial infarction, intracranial haemorrhage, acute left ventricular failure and pulmonary oedema. In eclamptic patients' convulsions may be precipitated. Almost all types of dysarrhythmias have been reported in addition to sinus tachycardia and sinus bradycardia. The common abnormalities are nodal rhythm, atrial and ventricular extrasystoles and pulsus alternans. Less commonly multifactorial extra systoles, pulses bigeminus and atrial fibrillations have been reported. Heart block, ventricular tachycardia and fibrillation are fortunately rare. Radionuclide studies have shown the stress response of laryngoscopy and endotracheal intubation produce a rapid decline in global left ventricular function within seconds, often exceeding that seen following exercise in patients with symptomatic coronary artery disease. Herniation of intracranial contents and cerebral ischaemia can occur in patients with raised intracranial pressure. Various strategies have been applied to attenuate these responses. These include. : Minimizing the duration of laryngoscopy to less than 15 seconds, use of I.V. or topical lidocaine, deep inhalational anaesthetics, I.V. narcotics,, adrenoceptor blocking agents, vasodilators, calcium channel blockers, intranasal nitroglycerin spray and ointment, ganglion blockers and avoiding laryngoscopy and resorting to blind nasal intubation. Clonidine is chemically 2[(2,6 Dichloropenyl) Imino] Imidazoline Mono hydrochloride. Clonidine is the only clinically available selective alpha-2 agonist with a selectivity ratio of 200:1 for alpha-2: alpha 1 receptors. It is an imidazoline derivative acting on imidazoline receptors I1 and I2 with a higher selectivity for I1 receptors. The imidazoline derivatives cause inhibition or modulation of noradrenaline release by acting on presynaptic imidazoline receptors independent of alpha -2 adrenoreceptor mediators. The recently isolated different Clonidine Displacing Substance (CDS) are the endogenous ligands, each having different selectivity in displacing clonidine form alpha 2 and imidazoline I1 receptors. The wide variety of action of clonidine is because of its action on these receptors and the responses of the target organs are modulated by receptor distribution in these organs, selectivity of clonidine to bind and type of endogenous ligand activated. Atenolol, a synthetic beta1(cardio selective) adrenoreceptor blocking agent chemically described as benzeneacetamide, 4-[2'-hydroxy -3'[(1-methylethyl) amino] propoxy] Atenolol (free base) has a molecular weight of 266.34 it is a relatively polar hydrophilic compound with a water solubility of 26.5mg/mL at 37oC and a log partition coefficient (octanol/water) of 0.23. It is freely soluble in 1N HCl (300 mg/mL at 25oC) and less soluble in chloroform (3 mg/mL at 25oC). Atenolol contains inactive ingredients such as providence, microcrystalline cellulose, corn starch, sodium lauryl sulfate, croscarmellose sodium, colloidal silicon dioxide, sodium stearyl fumarate and magnesium stearate. Atenolol is a beta1 – selective (cardioselective) beta –adrenergic receptor blocking agent without membrane stabilizing or intrinsic sympathomimetic (partial agonist) activities. This preferential effect is not absolute, however, and at higher doses, atenolol inhibits beta2–adrenoreceptors, chiefly located in the bronchial and vascular musculature. The purpose of this study is to attenuate the heamodynamic response to laryngoscopy and endotracheal intubation using oral atenolol and oral clonidine.

MATERIALS AND METHODS

A study of oral atenolol and oral clonidine was done to compare the attenuation of cardiovascular response during laryngoscopy and intubation in 50 adult patients, undergoing surgery under general anaesthesia. Patients of ASA Grade – I and Mallampatti Grade – I, were selected and informed consent was taken for all the cases. The patients were of both sexes age ranging from 18-60 years..Patients undergoing various elective surgical procedures under general anaesthesia were taken for study. This study was taken in 2 groups,

Group I: Consisted of 25 patients, where Oral Atenolol 0.75mg per kg body weight was given 3 hours before scheduled time of surgery.

Group II: Consisted of 25 patients where Oral Clonidine 3-3.5 micrograms per kg body weight was given 90 minutes before scheduled time of surgery. All the patients were assessed clinically preoperatively and investigated to rule out any problems.

Exclusion Criteria

1. History of respiratory problems.
2. History of heart block (atrioventricular conduction block) greater than first degree, congestive heart failure, cardiac arrhythmias,

history of angina, coronary artery diseases, diabetes mellitus, hypertension and other major medical problems.
3. Baseline heart rate < 60/minute.
4. Baseline systolic BP < 100 mm Hg.
5. Treatment with beta blockers or calcium channel blockers.
6. Hepatic or renal problems.
7. Predicted difficult intubation.

The following investigations were carried out before subjecting the patients for surgery, namely, complete haemogram, urine analysis, blood chemistry, electrocardiogram, and X – ray chest (PA view).

Premedication: No sedation was given on the night before surgery. Pre-medication was limited to glycopyrrolate 0.01 mg per kg bodyweight and midazolam 0.04 mg per kg bodyweight and ondansetron 0.08mg per kg bodyweight was given intravenously.

Venous Cannulation and Monitors: Intravenous cannulation with 18G cannula was inserted and a drip was started with Ringer's lactate solution. Non-invasive blood pressure monitor and pulse oximeter (SaO2) and electrocardiographic leads (limb lead II) were connected to the patient prior to induction of anaesthesia.

Anaesthesia Technique: All the patients were preoxygenated for 3 minutes, with 100% oxygen before induction of anaesthesia. Induction was achieved with injection thiopentone sodium given in a dose of 5 mg per kg bodyweight. Intubation was facilitated by using injection suxamethonium 1.5-2 mg per kg bodyweight. The lungs were ventilated with 100% oxygen for 45-60 seconds. Intubation was carried out by the aid of Macintosh laryngoscope. Oral, cuffed, endotracheal tube of appropriate size was used. Time taken for intubation did not exceed 15 seconds. Anaesthesia was maintained with Vecuronium bromide and intermittent positive pressure ventilation using closed circuit system. Heart rate. E.C.G. changes. Systolic, Diastolic, mean arterial pressures were recorded before induction, after induction, during laryngoscopy and intubation, and 1,3,5, minutes after intubation. Surgery was not allowed to commence till the study was completed. At the end of surgery patients were reversed with injection neostigimine 0.05mg per kg bodyweight and atropine 0.02-0.04 mg per kg bodyweight.

Monitoring

1. Non-Invasive Blood pressure monitoring – Systolic, Diastolic, and Mean arterial pressure.
2. Heart rate.
3. Oxygen Saturation.

OBSERVATIONS AND RESULTS

From the study conducted the following observations regarding Systolic, Diastolic, mean arterial pressures, Heart rate and E.C.G., changes were made at:

1. Pre-induction (Basal value).
2. After induction.
3. During laryngoscopy and Intubation.
4. 1 minute after intubation.
5. 3 minutes after intubation.
6. 5 minutes after intubation.

Table 1: Mean age, weight and sex in atenolol and clonidine groups

	Atenolol	Clonidine
Mean Age	30.5	30.2
Mean Weight	53.5	52.56
Male	8	10
Female	17	15

The clonidine group comprises of 10 males and 15 females and atenolol group comprises 8 males and 17 female patients. The age range for atenolol and clonidine groups is from 18-60 years. The difference in Clonidine and Atenolol groups is not statistically significant with regard to weight, age and sex, (P > 0.05).

Haemodynamic Parameters During Pre-Induction Period

Table 2: Haemodynamic parameters during pre-induction period

Haemodynamic Parameters	Atenolol		Clonidine	
	Mean	S.D	Mean	S.D.
Heart rate	83.32	± 8.56	82.20	± 10.16
Systolic Arterial Pressure	119.76	± 11.13	120.48	± 10.55
Diastolic Arterial Pressure	76.76	± 8.15	74.88	± 6.64
Mean Arterial pressure	91.09	± 8.39	90.08	± 6.94
Electro Cardio Graphic changes	WNL	WNL	WNL	WNL

The above table shows the haemodynamic parameters in atenolol and clonidine groups recorded during the pre-induction time indicate that the difference is not statistically significant (P>0.05).

Haemodynamic Parameters After Induction

Table 3: Haemodynamic parameters after induction

Haemodynamic Parameters	Atenolol		Clonidine	
	Mean	S.D	Mean	S.D.
Heart rate	84.72	± 8.10	83.56	± 9.96
Systolic Arterial Pressure	119.24	± 12.24	121.04	± 11.37
Diastolic Arterial Pressure	74.16	± 7.83	74.68	± 7.11
Mean Arterial pressure	89.19	± 7.43	90.13	± 7.81
Electro Cardio Graphic changes	WNL	WNL	WNL	WNL

The above table shows haemodynamic parameters of both atenolol and clonidine groups following the induction. In both the groups there is a slight increase in the heart rate. There is a slight fall in atenolol group and a slight

increase in clonidine group in systolic arterial pressure, a fall in diastolic arterial pressure in both groups. There is a slight fall in atenolol group and a slight increase in clonidine group in Mean arterial pressure. These changes are not statistically significant (P>0.50).

Haemodynamic Parameters During Laryngoscopy and Intubation

Table 4: Haemodynamic parameters during laryngoscopy and intubation

Laryngoscopy and intubation	Atenolol		Clonidine	
	Mean	S.D	Mean	S.D.
Heart rate	87.36	± 11.81	97.60	± 14.01
Systolic Arterial Pressure	120.36	± 15.90	133.96	± 14.36
Diastolic Arterial Pressure	73.72	± 9.64	80.96	± 11.15
Mean Arterial pressure	89.27	± 10.83	98.63	± 11.72
Electro Cardio Graphic changes	WNL	WNL	WNL	WNL

The above table shows the values of haemodynamic parameters at laryngoscopy and intubation. There was an increase in all the parameters in both atenolol and clonidine groups. The increase is statistically significant in clonidine group (P< 0.05).

Haemodynamic Parameters 1 Minute After Intubation

Table 5: Haemodynamic parameters 1 minute after intubation

1 Minute after intubation	Atenolol		Clonidine	
	Mean	S.D	Mean	S.D.
Heart rate	84.88	± 11.81	97.40	± 16.33
Systolic Arterial Pressure	117.28	± 16.69	130.56	± 14.32
Diastolic Arterial Pressure	74.24	± 10.20	80.48	± 11.39
Mean Arterial pressure	89.59	± 11.59	97.17	± 11.99
Electro Cardio Graphic	WNL	WNL	WNL	WNL

In both the groups there was an increase in the heart rate, but there was a decrease in atenolol group and increase in clonidine group in systolic, diastolic and mean pressure, compared to basal value (pre-induction value). However, the increase was statistically significant in clonidine group (P < 0.05).

Haemodynamic Parameters 3 Minutes After Intubation

Table 6: Haemodynamic parameters 3 minutes after Intubation

3 Minutes after intubation	Atenolol		Clonidine	
	Mean	S.D	Mean	S.D.
Heart rate	83.72	± 12.51	96.52	± 16.64
Systolic Arterial Pressure	114.40	± 15.15	127.72	± 13.59
Diastolic Arterial Pressure	72.64	± 10.26	79.84	± 9.88
Mean Arterial pressure	86.56	± 11.31	95.80	± 10.73
Electro Cardio Graphic changes	WNL	WNL	WNL	WNL

In both the groups there was an increase in the heart rate,but there was a decrease in atenolol group and increase in clonidine group in systolic,diastolic and mean arterial pressure, compared to basal value (pre induction value). However the increase is statistically significant in clonidine group (P < 0.05).

Haemodynamic Parameters 5 Minutes after Intubation

Table 7: Haemodynamic Parameters 5 Minutes After Intubation

5 Minutes after intubation	Atenolol		Clonidine	
	Mean	S.D	Mean	S.D.
Heart rate	83.36	± 11.94	95.68	± 16.72
Systolic Arterial Pressure	114.96	± 14.08	126.32	± 12.42
Diastolic Arterial Pressure	74.16	± 9.66	78.96	± 9.28
Mean Arterial pressure	87.76	± 10.32	94.75	± 9.70
Electro Cardio Graphic changes	WNL	WNL	WNL	WNL

In atenolol group heart rate, systolic, diastolic, mean arterial pressure is almost equal to the basal value (Pre-induction value), but in the clonidine group there is still increase in all the parameters. However, the increase was statistically significant in clonidine group (P < 0.05).

Mean and Standard Deviation in Atenolol and Clonidine Groups for Heart Rate Changes

Table 8: Mean and standard deviation in atenolol and clonidine groups for heart rate changes

	Atenolol		Clonidine	
	Mean	S.D	Mean	S.D.
Pre-induction	83.32	± 8.56	82.20	± 10.16
After induction	84.72	± 8.10	83.56	± 9.96
Laryngoscopy and intubation	87.36	± 11.81	97.60	± 14.01
1 minute after intubation	84.88	± 11.81	97.40	± 16.33
3 minutes after intubation	83.72	± 12.51	96.52	± 16.64
5 minutes after intubation	83.36	± 11.94	95.68	± 16.72

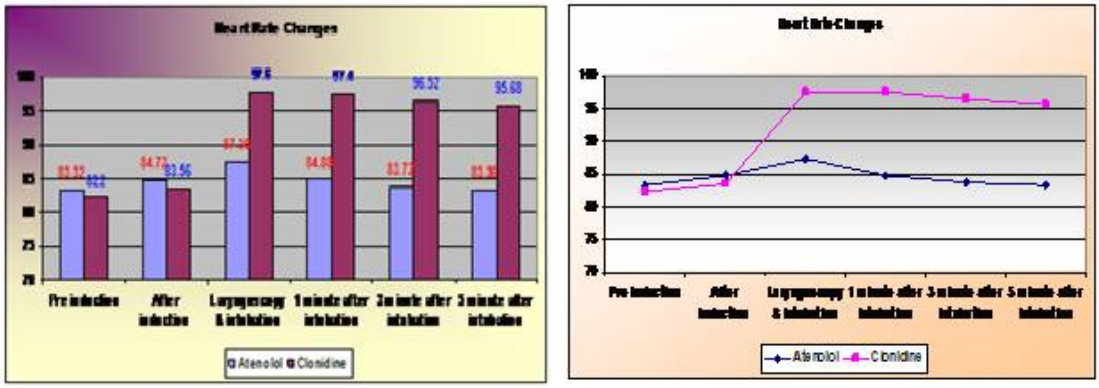

Figure 1: Mean and Standard Deviation In atenolol and clonidine groups for heart rate changes

Mean and standard deviation in atenolol and clonidine groups for mean arterial pressure changes

Table 9: Mean and standard deviation in atenolol and clonidine groups for mean arterial pressure changes

	Atenolol		Clonidine	
	Mean	S.D	Mean	S.D.
Pre-induction	91.09	± 8.39	90.08	± 6.94
After induction	89.19	± 17.43	90.13	± 7.81
Laryngoscopy and intubation	89.27	± 10.83	98.63	± 11.72
1 minute after intubation	88.59	± 11.59	97.17	± 11.99
3 minutes after intubation	86.56	± 11.31	95.80	± 10.73
5 minutes after intubation	87.76	± 10.32	94.75	± 9.70

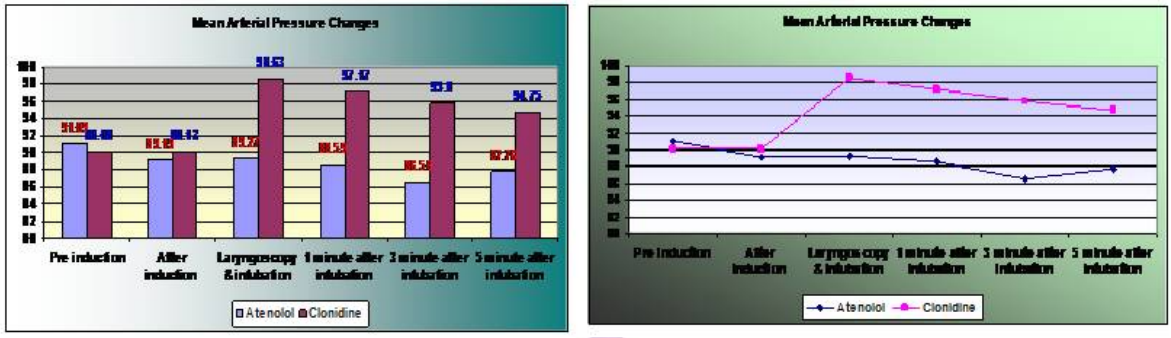

Figure 2: Mean and Standard deviation in atenolol and clonidine groups for mean arterial pressure changes

DISCUSSION

Attenuation of haemodynamic response to laryngoscopy and endotracheal intubation is of great importance in prevention of perioperative morbidity and mortality. Reflex changes in the cardiovascular system after laryngoscopy and intubation are the most marked. They manifest themselves in the form of tachycardia, hypertension cardiac arrhythmias, ectopics being the most common. REID and BRACE (1940) reported following laryngoscopy and endotracheal intubation cardiac and haemodynamic disturbances with traditionally used anaesthetic techniques. Reflex cardiovascular effects of laryngoscopy and intubation in anaesthetised patients have been described previously and include a pressor response (tachycardia and increase in systemic arterial pressure (King *et al*, 1951). Hypertension and tachycardia are the common responses in normotensive patients (Prys Roberts *et al*, 1971, Fox *et al* 1977). Although direct recording of sympathetic nervous activity is difficult, measurements of plasma concentration of catecholamine have consistently demonstrated increased nor-adrenaline, following laryngoscopy and sympathetically mediated response (Russel *et al* 1984). There are many studies which demonstrate increased sympathetic response to laryngoscopy and endotracheal intubation. In our study also, we have confirmed the haemodynamic response to laryngoscopy and intubation. Various methods to attenuate the sympathetic response to laryngoscopy have been studied such as topical anaesthesia of the pharynx along with superior laryngeal nerve block, lidocaine spray, intravenous lidocaine, deeper planes of inhalational anaesthesia, betablockers, alpha blockers, sodium

nitroprusside, nifidipine, increased dose of thiopentone, nitroglycerine, (intranasal, ointment, intravenous,) narcotics such as buprenorphine, fentanyl, al-fentanyl. In the present study oral atenolol and oral clonidine have been used to compare the effect of attenuation of haemodynamic response to laryngoscopy and endotracheal intubation. This study was done in 2 groups. Group I and Group II. Each group consisted of 25 healthy ASA Grade-I and Mallampatti Grade–I patients comparable in age, sex and weight, undergoing for various elective surgeries were selected and informed consent was taken. Group-I received oral atenolol 0.75 mg per kg body weight 3 hours before scheduled time of surgery. Group-II received oral clonidine 3-3.5 micrograms per kg body weight 90 minutes before scheduled time of surgery. The rise of haemodynamic parameters from pre-induction was both clinically and statistically significant in clonidine group when compared to atenolol group. The findings of clonidine group are in accordance with the study by DERBYSHIRE *et al* (1983). In the present study atenolol showed a better response in attenuating haemodynamic parameters (Heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure) during laryngoscopy and intubation when compared to clonidine group both clinically and statistically. ($P< 0.05$) Observations at 1 minute after intubation showed that the various, haemodynamic parameters in clonidine group were higher than the atenolol group. The findings of clonidine group are in agreement with the study by SMITH and DERBYSHIRE *et al* and SHIRBMAN, SMITH *et al.* Observations at 3 minutes after intubation showed that the haemodynamic parameters in clonidine group were still higher than atenolol group. The clonidine group findings are in accordance with the study by SHIRBMAN and SMITH which shows that plasma catecholamine concentration comes down by 3-5 minutes after laryngoscopy. Observations at 5 minutes after laryngoscopy revealed that the heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure in atenolol group returned to the basal value. Clonidine group values showed an increase and the increase was clinically and statistically significant ($P<0.05$). Both oral atenolol and oral clonidine attenuate haemodynamic response associated with laryngoscopy and intubation. Comparing the clonidine group to atenolol group a significant ($p<0.05$) fall in heart rate and a significant ($P<0.05$) decrease in mean arterial pressure was observed in atenolol group. Hence oral atenolol has been found to be better than oral clonidine with regard to the blunting of haemodynamic response during laryngoscopy and intubation.

CONCLUSIONS

Oral atenolol attenuates the increase in heart rate to laryngoscopy and intubation more effectively than oral clonidine. Oral atenolol blunts the increase in systolic, diastolic and mean arterial pressure effectively and the values returned to the basal value within 5 minutes of intubation when compared to oral clonidine. No side effects were noted in atenolol and clonidine groups in our study. Oral atenolol in a dose of 0.75 mg per kg body weight given 3 hours before induction of anaesthesia is more effective in attenuating haemodynamic response to laryngoscopy and endotracheal intubation when compared to oral clonidine.

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