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Original Research Paper

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ROLE OF CLONIDINE AND ATENOLOL IN ATTENUATION OF HAEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION

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ABSTRACT

Introduction: Laryngoscopy and endotracheal intubation are potent stimuli that can induce increased sympathetic activity leading to tachycardia, hypertension and dysrhythmias. Various techniques and drugs have been tried to attenuate this circulatory response.

Material and Method: 120 ASA Grade I and II patients of either sex ,aged between 25- 60 years, weight ranging from 50-60 kg undergoing elective surgical procedures under general anaesthesia were divided in 2 groups through random allocation.

Group allocation and study design:

GroupA: Received oral clonidine 150 mcg 60 minutes before induction.

Group B: Received oral atenolol 25 mg 2.5 hours before induction .

Haemodynamic parameters were recorded at preinduction, postinduction, during laryngoscopy and 1,3,5 and 15 minutes after laryngoscopy.

Results: Heart rate decreased after giving tablet clonidine and tablet atenolol in both the groups. Increase in heart rate at T1 in clonidine group A took more than 10 minutes to return to baseline, However, heart rate remained below the baseline in atenolol group except at 1 min when transient rise was seen in the atenolol group.Haemodynamic parameters are fairly attenuated by atenolol as compared to clonidine.

KEYWORDS :

INTRODUCTION

Laryngoscopy and endotracheal intubation are potent stimuli that can induce increased sympathetic activity leading to tachycardia, hypertension and dysrhythmias. When laryngoscopy and intubation is carried out, there is mechanical irritation of stretch receptors situated in the respiratory tract leading to reflex haemodynamic responses through a sympathetic reflex.[1,2,3,4]

Laurtio CE et al (1993), observed that oral clonidine blunts the haemodynamic response to brief but not prolonged laryngoscopy. Oral clonidine provides haemodynamic protection to patients undergoing a 15 seconds laryngoscopy.[5]

Boussofara M et al (2001), compared the effects of clonidine and hydroxyzine on haemodynamic and catecholamine response to suspension microlaryngoscopy.[6]

Atenolol is a beta-selective (cardio selective) adrenoceptor blocking drug without partial agonist or membrane stabilizing activity.

Gupta D et al observed severe cardiovascular response in the form of tachycardia and hypertension following nasal speculum insertion during sublabialrhinoseptal trans-sphenoid approach for resection of small pituitary tumours. They suggested that oral clonidine and oral atenolol is an equally effective and safe method of attenuating haemodynamic response caused by nasal speculum insertion during trans- sphenoid pituitary resection.[7]

MATERIAL AND METHODS

This prospective,randomized, comparative study was conducted in the department of Anaesthesiology, Maharaja Agrasen Medical College, Agroha. After obtaining approval from Hospital Ethical Committee, 120 ASA Grade I and II patients of either sex ,aged between 25- 60 years, weight ranging from 50-60 kg undergoing elective surgical procedure under general anaesthesia were enrolled for the study with informed and written consent obtained from each patient. Study population was divided in 2 groups through random allocation.

EXCLUSION CRITERIA

Patients having

- Respiratory, hepatic and renal disease
- History of heart block
- Congestive heart failure
- History of angina,coronary artery disease, baseline heart rate lessthan 50 beats /min
- Treatment with beta blockers and calcium channel blockers, or anyother drug causing haemodynamic instability
- Laryngoscopy time more than 30 seconds

Group allocation and study design

Group A: Received oral clonidine 150 mcg 60 minutes before induction.

Group B: Received oral atenolol 25 mg 2.5 hours before induction.

ANAESTHESIA TECHNIQUE

Non invasive blood pressure monitor, pulse oximeter and electrocardiographic leads were connected to the patient before the induction of anaesthesia and basal readings were recorded. Standard monitoring comprising of ECG, Pulse oximetry,Non invasive blood pressure monitoring was done. After preoxygenating with 100% 0_2 for 3 minutes with oxygen flow rate 6 L min^{-1} on circle breathing system, patient werepremedicated with injection Glycopyrollate 0.2 mg, inj. midazolam 0.03 $mgkg^{-1}$and inj. Fentanyl 1.5 $\mu gmkg^{-1}$.I.V. Induction done with propofol $2mgkg^{-1}$, muscle relaxation was achieved with injection vecuronium 0.1 $mgkg^{-1}$ i.v. The patient is then ventilated with oxygen and nitrous oxide (50: 50) and 1% of isoflurane, followed 3 minutes later by laryngoscopy and endotracheal intubation by oral cuffed endotracheal tube, of duration less than 40 seconds.

Laryngoscopy was done using Macintosh laryngoscopic blade. Cuff inflated and correct placement of endotracheal tube was confirmed by capnography using manual positive pressure ventilation. After study anaesthesia was maintained as per requirement of the surgical procedure which was maintained using 1 MAC of isoflurane in oxygen (50 %) and nitrous oxide (50%). Patient was mechanically ventilated with tidal volume 7 ml kg^{-1} and respiratory rate 14 $minute^{-1}$. Concomitantly blood pressure (Systolic,Diastolic and Mean blood pressure) via non invasive blood pressure monitoring and heart rate through continuous ecg monitoring was recorded by single observer at preinduction, postinduction, during laryngoscopy and

1,3, 5 and 15 minutes after laryngoscopy and intubation in both groups.

OBSERVATION AND RESULTS

Table -1 Comparison of Mean age, Weight, Laryngoscopy time

	GROUP	N	Mean	Std. Deviation
Age	GROUP A	60	39	11.916
	GROUP B	60	40.2	7.688
Weight	GROUP A	60	58.03	4.364
	GROUP B	60	56.7	7.188
Time (sec.)	GROUP A	60	14	1.098
	GROUP B	60	15.2	1.864

Above table shows age, weight, laryngoscopy time distribution in Group A and Group B. The difference between clonidine and atenolol is not statistically significant with regard to age, weight and laryngoscopy time distribution.

Table -2 Changes in Heart rate in two groups at various time intervals

	GROUP	N	Mean	Std. Deviation	P VALUE
HEART RATE B1	GROUP A	60	83.78	8.148	0.387
	GROUP B	60	84.66	11.712	
HEART RATE B2	GROUP A	60	83.12	9.412	0.2419
	GROUP B	60	80.46	13.161	
HEART RATE T0	GROUP A	60	91.27	9.251	<0.001
	GROUP B	60	81.2	14.128	
HEART RATE T1	GROUP A	60	96.07	8.423	<0.001
	GROUP B	60	82.97	13.471	
HEART RATE T3	GROUP A	60	87.26	7.498	<0.001
	GROUP B	60	78.66	11.982	
HEART RATE T5	GROUP A	60	84.01	7.312	<0.001
	GROUP B	60	75.56	11.215	
HEART RATE T15	GROUP A	60	82.03	7.913	<0.001
	GROUP B	60	75.67	10.49	

Both the groups were statistically comparable with respect to baseline heart rate (B1) and postinduction heart rate (B2). But heart rate at intubation (T0), 1 min (T0), 3min (T3), 5 min (T5) and 15 min (T15) after intubation were significantly higher in group A (p <0.001)

Table -3 Changes in Mean blood pressure at various time intervals in two groups

	GROUP	N	Mean	Std. Deviation	P VALUE
SBP B1	GROUP A	60	92.76	6.201	0.243
	GROUP B	60	94.74	8.141	
SBP B2	GROUP A	60	91.62	6.921	0.168
	GROUP B	60	89.1	8.708	
SBP T0	GROUP A	60	87.36	7.581	0.139
	GROUP B	60	82.92	9.279	
SBP T1	GROUP A	60	98.78	6.189	<0.001
	GROUP B	60	91.8	8.758	
SBP T3	GROUP A	60	91.52	7.359	<0.001
	GROUP B	60	83.76	9.418	
SBP T5	GROUP A	60	84.72	6.89	<0.001
	GROUP B	60	79.08	9.376	
SBP T15	GROUP A	60	90.76	8.041	<0.001

Till intubation , MAP was statistically comparable in both the groups. But after intubation there was statistically significant (p <0.001) rise in Group A as compared to Group B.

Table -4 Comparison of Baseline Mean blood pressure with Mean Blood Pressure at various time intervals in Group A.

	N	Mean	Std. Deviation	Paired Differences		P Value
				Mean Difference	Std. Deviation	
MBP B1	60	92.76	6.127	1.14	4.828	0.003
MBP B2	60	91.62	6.928			
MBP B1	60	91.78	6.227	4.08	6.82	<0.001
MBP T0	60	95.86	7.605			
MBP B1	60	92.82	6.237	6.94	5.436	<0.001
MBP T1	60	99.76	6.349			
MBP B1	60	92.68	6.229	2.06	6.12	0.016
MBP T3	60	90.62	7.851			
MBP B1	60	92.66	6.247	9.7	6.624	<0.001
MBP T5	60	83.96	6.98			
MBP B1	60	93.12	6.237	3.40	7.628	0.008
MBP T15	60	89.72	8.008			

MAP increment was highly significant in group A (p<0.001) as compared to baseline after intubation. Following intubation at 5 min MAP showed highly significant fall (p <0.001)

Table -5 Comparison of Baseline Mean arterial pressure (MAP-B1) with Mean arterial Pressure at various intervals in Group B.

	N	Mean	Std. Deviation	Paired Differences		P Value
				Mean Difference	Std. Deviation	
MBP B1	60	94.46	8.214	6.04	4.278	<0.001
MBP B2	60	88.42	8.759			
MBP B1	60	93.52	8.241	10.96	7.148	<0.001
MBP T0	60	82.56	9.273			
MBP B1	60	92.42	8.249	0.60	6.762	0.014
MBP T1	60	91.82	8.769			
MBP B1	60	94.36	8.247	10.46	7.281	<0.001
MBP T3	60	83.72	9.401			
MBP B1	60	94.26	8.247	15.14	8.251	<0.001
MBP T5	60	79.12	9.481			
MBP B1	60	94.48	8.279	16.92	7.672	<0.001
MBP T15	60	77.56	9.237			

There was highly significant (p<0.001) fall in MAP in comparison to baseline and remained so except at 1 min after intubation (p= 0.014)

DISCUSSION

The present study is aimed at comparing the role of oral clonidine and oral atenolol in attenuation of haemodynamic response to laryngoscopy and intubation.These haemodynamic responses are somato-visceral reflexes due to sympathetic stimulation. The haemodynamic changes brought about by laryngoscopy and intubation was first described by Reid and Brace.[1] The haemodynamic response is initiated within seconds of direct laryngoscopy and further increases with passage of endotracheal tube. These changes are usually short lived and well tolerated by normal patients.The sympathoadrenal activation associated with laryngoscopy and tracheal intubation is detrimental in individuals who have low myocardial reserve due to coronary artery disease, hypertension, cardiomyopathy and raised intracranial tension.Several strategies have been evolved to blunt this undesirable response to laryngoscopy and endotracheal intubation.[1-3,8]Clonidine is absorbed almost completely after oral administration. The peak blood pressure reducing effect occurs approximately 90 minutes after oral administration and peak plasma concentrations are observed between 1 and 3 hour. Atenolol competitively inhibits the binding of catecholamines to beta adrenergic receptors on heart and blood vessels and thus reduce heart rate,blood pressure, cardiac output and myocardial contractility.

Time taken for laryngoscopy and intubation was comparable in both the groups, mean laryngoscopy time in group A is 12 sec and in group B is 11.6 sec (p> 0.05). It is known that response to laryngoscopy is dependant on duration of laryngoscopy, peaking at 45 seconds. Hence those patients requiring more than one attempt and more than 40 sec for laryngoscopy were excluded from the study. In our study, baseline haemodynamic parameters heart rate (HR), systolic blood comparable in both the groups (p>0.05).

In our study heart rate decreased after giving oral clonidine(Group A) and oral atenolol (Group B).Following intubation there was significant increase in H.R in clonidine group at 1 min.In group A at 1 minute, immediately after laryngoscopy and intubation, the rise of heart rate was maximum ; it increased from 83.78±8.14 (B1) to 96.07±8.4 (T1) with p value <0.001 which is highly significant (Table 2). The plasma catecholamine concentration increased to maximumat 1 minute after the laryngoscopy. The decrease in pulse rate after clonidine administration was due to reduction in sympathetic outflow,simultaneous increase of the parasympathetic tone of central origin and the influence of clonidine on the neurons which receive the baroreceptor afferents.

At 5 minutes, there was a rise from preinduction values of heart rate in clonidine group but the values showed decline from those at 1 minute.The results of our study are comparable to Filos et al.[9] with respect to reduction in mean heart rate after premedication with 150 µgm of oral clonidine. Ghignoneet al.[10] (1986) studied the effect of clonidine (5 $\mu gmkg^{-1}$ orally) on perioperative haemodynamics and isoflurane requirement and compared with diazepam (0.15 mg kg^{-1} orally). They found heart rate to be consistently lower in clonidine group, throughout the operative period and never rose above the baseline in peri-intubation period. The results obtained by Ghignone et al. showed much better attenuation as compared to our study because of higher dose and coadministrationof drugs like lignocaine and fentanyl. Raval et al.[11](2002) studied attenuation with 200 µgm clonidine orally and found mean rate by 5.89%. The results of this study correlate well with our study. So more degree of haemodynamic attenuation was observed with atenolol in our study.Our results are comparable with Koti et al.[12] which reveals that the haemodynamicparameters returned to baseline at the end of 5 minutes in the atenolol group as compared to clonidine which took more time to return to baseline.

Study done by Islam A et al.[13]observed clonidine is superior in controlling heart rate as a premedicant is in contrast to our study results. Difference in the results could be due to difference in atenolol dose and time of administration as oral atenolol in above study was given 1 hour prior to induction and in our study it was given 2.5 hours before surgery. Peak effect of oral atenolol take 2-3 hours.

Baseline systolic blood pressure, diastolic blood pressure and mean arterial pressure were similar in both the groups. Fall of SBP, DBP, MAP was seen in both the groups, but this fall was significantly more in atenolol group,($p<0.001$). MAP in group A decreased from baseline 92.76±6.12 to 91.62±6.9 and in group B it decreased from baseline, fall being more significant in atenolol group. With atenolol our results are similar to Koti et al.[12]in which haemodynamic parameters returned to baseline in 5 minutes in atenolol group whereas in clonidine group it took long to reach baseline. Our results show that single oral dose of beta-blocker given 2.5 hours before induction of anaesthesia will attenuate the pressor and heart rate response to tracheal intubation. The advantage of single oral dose of the beta blocking drug include simplicity of administration and safety of patient.

SUMMARY

Heart rate decreased after giving tablet clonidine and tablet atenolol in both the groups. The increase in heart rate is observed during laryngoscopy (T0) which further increases at T1(1 min after intubation) in clonidine group A and it took more than 10 minutes to return to baseline. However, heart rate remained below the baseline in atenolol group except at 1 min when transient rise was seen in the atenolol group.

REFERENCES

1. Reid LC, Brace DE. Irritation of the respiratory tract and its reflex effect upon the heart.SurgGynec and Obst. 1940;70:157-62.
2. King BD,Harris LC,Griefenstein FE,Elder JD,Dripps RD. Reflex circulatory responses to direct laryngoscopy and tracheal intubation performedduring general anaesthesia. Anesthesiology 1951;12:556-66.
3. King BD, Elder JD, Proctor DF, Dripps RD. Reflex circulatory responses to tracheal intubation performed under topical anaesthesia. Anesthesiology 1954;15:231-8.
4. Forbes AM, Daily FG. Acute hypertension during induction of anaesthesia and endotracheal intubation in normotensive man. Br J Anaesth 1970;42:618-24
5. Laurito CE, Baughman VL, Becker GL, Cunnigham F, Pygon BH, Citron GM. Oral clonidine blunts the haemodynamic response to brief but not prolonged laryngoscopy. J ClinAnesth 1993;5:54-7.
6. Boussofara M, Bracco D, Ravussin P. Comparison of effects of clonidine and hydroxyzine on haemodynamic and catecholamine reactions to microlaryngoscopy. Eur J Anaesthesiol 2001;18:75-8.
7. Gupta D, Srivastava S, Dubey RK, Prakash PS, Singh PK,Singh U. Comparative evaluation of atenolol and clonidine premedication on cardiovascular response to nasal speculum insertion during trans-sphenoid surgery for resection of pituitary adenoma: A prospective,randomized, double blind, controlled study. Ind J Anaesth 2011;55:135-40.
8. Russel WJ, Morris RJ, Frewin DB, Drew SE. Changes in plasma catecholamine concentrations during endotracheal intubation. Br J Anaesth1981;53:837-9
9. Filos KS, Patroni Q, Goudas LC, Bosas O, Kassaras A, Gartaganis S. A dose response study of orally administered clonidine as premedication in the elderly: Evaluating Haemodynamic Safety. AnesthAnalg 1993;77:1185-92.
10. Raval D, Mehta M. Oral clonidine premedication for attenuation of haemodynamic response to laryngoscopy and intubation. Ind J Anaesth 2002;46:124-9.
11. Yu HP, Hues SS, Yuen HW, Tang YH, Chan KH. Oral clonidine premedication preserves heart rate variability for patients undergoing laproscopic cholecystectomy. Acta Anesthesiology Scand. 2003;47:185-90.
12. Koti VR, Chevuri SB, Pulla S, VarunchanderG. Attenuation of haemodynamic response to intubation with oral clonidine and oral atenolol. Ind J ClinAnaesth 2016;3:251-6.
13. Islam A, Houssain M, Akhtaruzzaman AKM, Khatun UHS. A Comparative study on the role of oral clonidine in laproscopiccholecystectomy surgery. JBSA. 2008;21:12-20.