Indian Journal of Basic & Applied Medical Research; September 2012: Vol.-1, Issue-4, P. 313-323

"Attenuation of cardiovascular responses to laryngoscopy and endotracheal intubation: comparative evaluation of clonidine and lignocaine."

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Abstract:

Introduction: Aim of present study was to evaluate the effectiveness of oral clonidine and lignocaine to attenuate the haemodynamic response; and also to compare these two drugs.

Material and methods: The study evaluated ninety patients of age fifteen to sixty five years, of either sex and ASA grade I and II. These patients were scheduled to undergo elective surgical procedures of 1 to 2 hour duration requiring general anaesthesia and endotracheal intubation. The patients were assigned into either of three groups as – Lignocaine(I) group (1.5 mg/kg., clonidine(III) group (0.2mg orally) and control (I)group (patients not receiving any of the above drugs). The haemodynamic parameters were recorded preoperatively, during and after laryngoscopy and endotracheal intubation.

Observationbs and results : It was observed that, in control group, there was rise in the pulse rate, systolic and diastolic blood pressure at laryngoscopy and intubation, at 1 min. till 10 min. post-intubation. This rise in haemodynamic parameters was statistically significant as compared with the baseline preoperative parameters ($p>0.0001$). In lignocaine and clonidine group , there was small rise in the pulse rate at 1 min. after laryngoscopy and intubation; but this difference was statistically not significant as compared with the baseline values ($p>0.05$).

Conclusion: Clonidine is a better drug for attenuation of cardiovascular responses.

Key words: pressor response, Clonidine, lignocaine

Introduction: Laryngoscopy and endotracheal intubation marked a new era in the history of anaesthesia and has led to provision of safer anaesthesia due to better control of airway and ventilation. Since its introduction, this technique has been shown to be associated with reflex sympathetic stimulation in the form of tachycardia and hypertension, which is known as pressor response to laryngoscopy and intubation.

Hence, various methods/drugs have been tried to reduce this response, like topical anaesthesia with lignocaine,[5,17] deep general anaesthesia[6], narcotics (like fentanyl[2], alfentanil[2]), β blockers(propranalol,[11]esmolol[19])calcium channel blockers (propranalol,[11]esmolol[19])calcium channel blockers (Verapamil[14],Diltiazem[13]) and peripheral vasodilators like sodium nitropruside[17], nitroglycerine[8,12].

This study was undertaken to evaluate the effectiveness of oral clonidine to attenuate the haemodynamic response associated with powerful stimulus like laryngoscopy and endotracheal intubation and its effects were compared with intravenous lignocaine and the control group .

Study Design:

After obtaining approval from the institutional ethics committee, a randomized controlled study was formulated. We evaluated 90 patients between fifteen to sixty five years, of either sex and ASA grade I and II.

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The following patients were excluded- Hypertension, ischaemic heart disease, Diabetes, pregnant and nursing women Written informed consent was obtained in eachpatient. The patients were randomly assigned into three groups of thirty patients.

Lignocaine group (Group II): patients receiving 1.5 mg/kg of preservative free 2% lignocaine intravenously 90 seconds before laryngoscopy.

Clonidine group (Group III): patients receiving clonidine 0.2mg orally 90 min. prior to induction of anaesthesia

Control group(Group I): - patients not receiving any of the above drugs.

All the patients underwent the same anaesthetic plan as below. Preoperatively, patients were kept fasting for 6 hours. Inj. glycopyrrolate 5mcg/kg was given intra-muscularly 30 min. prior to induction. Monitoring included ECG, pulse-oxymetry and non invasive blood pressure. Before induction Inj. Ondansatron 4 mg and Inj. Midazolam 0.03 mg/kg intravenously were given as premedication.

All the patients were pre-oxygenated with 100% oxygen for 3 min. using Bain's circuit with a close fitting facemask. Anaesthesia was induced in all the patients with Inj. Pentothal sodium (2.5%) in the dose of 5-7mg/kg. This was followed by the study drug in group II i.e. 2% lignocaine (preservative free) diluted in 10ml of normal saline given over 10 seconds. Then succinylcholine 2mg/kg intravenously was given to facilitate endotracheal intubation.

Patients were ventilated with 100% oxygen and upon full relaxation, laryngoscopy and endotracheal intubation with proper sized cuffed endotracheal tube were carried out under vision using Macintosh laryngoscope blade by the same person each time. All intubations which were smooth gentle and within thirty seconds were selected. After intubation, anaesthesia was maintained with 50% oxygen, 50% N_2O, and isoflurane. Pulse and blood pressure were monitored for 10 minutes as cardiovascular effect of laryngoscopy is known to last for ten minutes. Muscle relaxation was maintained with vecuronium and analgesia was supplemented with pentazocin (0.4mg/kg). Clonidine group was evaluated for complications like bradycardia, hypotension, if any.

DATA COLLECTION- The pulse rate, the systolic and diastolic blood pressure were recorded preoperatively as baseline value. These parameters were recorded immediately before induction of anaesthesia, at laryngoscopy and endotracheal intubation (0 min.) and every minute till ten minutes after intubation The monitoring continued throughout the intraoperative period and post-operatively also.

Observations and results:

The patients were randomly divided into three groups as- Control group (Group I), Lignocaine group (Group II) and Clonidine group (Group III). The data was analyzed by applying Chi – square test ($p > 0.05$). and 'Z test' for comparison between the groups and paired 't' test for comparison within the group.

Table 1: Comparison of Mean Age and Weight in study groups

Parameters	**Gr. I**	**Gr.II**	**Gr. III**
	Mean ± S.D. (n=25)	Mean ± S.D. (n=25)	Mean ± S.D. (n=25)
Age (Yrs)	36.87 ± 13.12	33.5 ± 10.6	36.6 ± 12.36
Weight (Kg)	54.4 ± 6	51.5 ± 7.79	52.1 ± 3.96

In above three groups, age and weight distribution was comparable (Table 1). Both the sexes were equally represented in all three groups .

Table 2: Age wise distribution of cases in study groups

Age (Yrs)	**Gr. I**		**Gr. II**		**Gr. III**		**Total**	
	No.	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**
15 – 25	5	5.56	6	6.67	7	7.78	18	20
25 – 35	9	10	9	10	8	8.89	26	28.89
35 – 45	7	7.78	11	12.22	5	5.56	23	25.56
45 – 55	6	6.67	4	4.44	8	8.89	18	20
55 – 65	3	3.33	0	0	2	2.22	5	5.55
Total	30	33.33	30	33.33	30	33.33	90	100

By applying Chi-square test, ($P>0.05$)

Age wise distribution was similar in the above three groups.

Table 3: Sex wise distribution of Cases in study groups

Sex	Gr. I		Gr. II		Gr. III		Total	
	No.	%	No.	%	No.	%	No.	%
Male	14	15.55	15	16.67	13	14.44	42	46.67
Female	16	17.78	15	16.66	17	18.89	48	53.33
Total	30	33.33	30	33.33	30	33.33	90	100

$\chi^2 = 3.14$, $P>0.05$ (Chi-square test)

Sex distribution was comparable in all the three groups.

Table 4: Comparison of Mean Pulse Rate (beats/min) in study groups

Parameters		Gr. I	Gr. II	Gr. III
		Mean ± S.D. (n=30)	Mean ± S.D. (n=30)	Mean ± S.D. (n=30)
Baseline		80.03 ± 9.47	82.13 ± 6.42	82.33 ± 8.66
Before induction		81.63 ± 6.75 a	81.47 ± 7.49 a	76.23 ± 8.59 *
At laryngoscopy		99.4 ± 11.9 *	82.93 ± 7.69 a	81.67 ± 7.52 a
After laryngoscopy and intubation	1min	111.3 ± 11.3 *	85.93 ± 7.39 a	85.8 ± 8.01 a
	2min	103.7 ± 6.7 *	84.83 ± 6.40 a	78.73 ± 7.86 #
	3min	93.5 ± 7.78 *	83.3 ± 7.03 a	78.33 ± 8.32 #
	5min	89.33 ± 9.55 *	81.26 ± 6.86 a	76.46 ± 8.54 *
	10min	86.1 ± 9.34 *	80.73 ± 6.59 a	76.33 ± 7.72 *

a : Not Significant, #: Significant, *: Highly significant

Table 4a: Comparison of Mean Pulse Rate (beats/min) in II and III groups

Parameters		**Gr. II**	**Gr. III**	**Z-Value**	**P-Value**
		Mean ± S.D. (n=30)	**Mean ± S.D. (n=30)**		
Baseline		82.13 ± 6.42	82.33 ± 8.66	0.90	>0.05 a
Before induction		81.47 ± 7.49	76.23 ± 8.59	2.52	<0.05 #
At laryngoscopy		82.93 ± 7.69	81.67 ± 7.52	0.64	>0.05 a
After laryngoscopy and intubation	1min	85.93 ± 7.39	85.86 ± 8.05	0.03	>0.05 a
	2min	84.83 ± 6.40	78.73 ± 7.86	3.29	<0.001 *
	3min	83.3 ± 7.03	78.33 ± 8.32	2.49	<0.05 #
	5min	81.26 ± 6.86	76.46 ± 8.54	2.39	<0.05 #
	10min	80.73 ± 6.59	76.33 ± 7.72	2.37	<0.05 #

a: Not significant, #: Significant *: Highly significant

Changes in Pulse Rate: In control group, the pulse rate rose significantly above baseline by 31.27 (39.07%) at 1 min. and remained above baseline till 10 min. post intubation. This increase in pulse rate from baseline was statistically highly significant. ($P < 0.0001$)

The patients in clonidine group demonstrated fall in pulse rate, following administration of oral clonidine to a mean preoperative value of 76.23 ± 8.59 (fall by 7.7 beats/min). This fall in the pulse rate was statistically significant ($p<0.0001$).

When clonidine group and lignocaine group were compared, (Table 4a) there was no significant difference in the pulse rate during laryngoscopy and intubation, at 1 min post intubation. ($P > 0.05$)

In the clonidine group, the rise in mean pulse rate after intubation returned to baseline value at 2 min. where as in lignocaine group the rise persisted till 5 min. post- intubation.

Table 5: Comparison of Mean Systolic Blood Pressure (SBP) (mmHg) in study groups

Parameters		**Gr. I**	**Gr. II**	**Gr. III**
		Mean ± S.D. (n=30)	**Mean ± S.D. (n=30)**	**Mean ± S.D. (n=30)**
Baseline		122.6 ± 8.43	121.8 ± 6.08	123.7 ± 11.01
Before induction		124.3 ± 10.32 a	120.8 ± 5.86 a	114.5 ± 7.31 *
At laryngoscopy		138.93 ± 14.30 *	123.6 ± 6.27 a	114.67 ± 7.26 *
After laryngoscopy And intubation	1min	151.33 ± 8.47 *	123.9 ± 5.11a	122.8 ± 5.55 a
	2min	144.6 ± 8.24 *	123.7 ± 3.95 a	122.3 ± 6.61 a
	3min	129.53 ± 8.22 *	123.5 ± 5.33 a	121.07 ± 6.23 a
	5min	126.2 ± 7.95 #	123.05 ± 7.58 a	117.4 ± 6.85 *
	10min	124 ± 7.43 a	121.1 ± 6.25 a	116.3 ± 7.07 *

Table 5a: Comparison of Mean Systolic Blood Pressure (SBP) (mm Hg) in II and III group

Parameters		**Gr. II**	**Gr. III**	**Z-Value**	**P-Value**
		Mean ± S.D. (n=30)	**Mean ± S.D. (n=30)**		
Baseline		121.8 ± 6.08	123.7 ± 11.01	0.81	>0.05 a
Before induction		120.8 ± 5.86	114.5 ± 7.31	3.66	<0.0001 *
At laryngoscopy		123.6 ± 6.27	114.67 ± 7.26	5.09	<0.0001 *
After laryngoscopy and intubation	1min	123.9 ± 5.11	122.8 ± 5.55	0.82	>0.05 a
	2min	123.7 ± 3.95	122.3 ± 6.61	0.14	>0.05 a
	3min	123.5 ± 5.33	121.07 ± 6.23	1.73	>0.05 a
	5min	123.05 ± 7.58	117.4 ± 6.85	3.29	<0.0001 *
	10min	121.1 ± 6.25	116.3 ± 7.07	2.75	<0.01 *

Changes in mean systolic blood pressure (SBP)

In control group, the mean systolic blood pressure rose significantly above the baseline value during laryngoscopy and remained above baseline till 10 min. post intubation (P< 0.0001). In clonidine groupbefore induction SBP was 114.5 ± 7.31 mmHg.; a fall by 9.2 mmHg. This fall in the SBP was statistically significant.

Table 6: Comparison of Mean Diastolic Blood Pressure (DBP) (mm Hg) in study groups

Parameters		**Gr. I**	**Gr. II**	**Gr. III**
		Mean ± S.D. (n=30)	**Mean ± S.D. (n=30)**	**Mean ± S.D. (n=30)**
Baseline		78.4 ± 6.95	76.93 ± 6.19	79.67 ± 5.20
Before induction		80.10 ± 5.94 a	78.2 ± 5.97 a	74.10 ± 5.38 *
At laryngoscopy		91.4 ± 8.39 *	79 ± 6.12 a	75.73 ± 4.69 *
After laryngoscopy and intubation	1min	100 ± 6.71 *	79.6 ± 7.58 a	78.93 ± 6.34 a
	2min	96.2 ± 6.39 *	78.2 ± 6.13 a	78.13 ± 5.4 a
	3min	84.53 ± 9.44 *	78.03 ± 6.82 a	76.53 ± 6.97 *
	5min	82.67 ± 7.09 *	78 ± 7.52 a	73.33 ± 5.74 *
	10min	80.27 ± 6.38 *	77.23 ± 8.69 a	72.73 ± 5.62 *

Table 6a : Comparison of Mean Diastolic Blood Pressure (DBP) (mm Hg) in II and III groups

Parameters		Gr. II	Gr. III	Z-Value	P-Value
		Mean ± S.D. (n=30)	Mean ± S.D. (n=30)		
Baseline		76.93 ± 6.19	79.67 ± 5.20	1.85	>0.05 a
Before induction		78.2 ± 5.97	74.10 ± 5.38	2.77	<0.01 *
At laryngoscopy		79 ± 6.12	75.73 ± 4.69	2.32	<0.05 #
After laryngoscopy	1min	79.6 ± 7.58	78.93 ± 6.34	0.37	>0.05 a
	2min	78.2 ± 6.13	78.13 ± 5.4	0.05	>0.05 a
	3min	78.03 ± 6.82	76.53 ± 6.97	1.35	>0.05 a
	5min	78 ± 7.52	73.33 ± 5.74	3.24	<0.0001 *
	10min	77.23 ± 8.69	72.73 ± 5.62	2.38	<0.05 #

Changes in Mean Diastolic Blood Pressure (DBP):

In Control group, the mean baseline DBP was 78.4 ± 6.95 mmHg. Pressure response associated with laryngoscopy and intubation caused mean DBP to rise to a value of 100 ± 6.71 %, an increase of 21.6 (27.55%) at 1 min. post intubation. The rise in mean DBP after intubation was highly significant (P<0.0001) as compared to baseline and remained above baseline thereafter till 10 min. after intubation.

In Clonidine group, the mean diastolic blood pressure was 79.67 ± 5.20 mmHg. After administration of oral clonidine, it showed, a change to preinduction value of 74.10 ± 5.38 mmHg a decrease by 5.57 mmHg. After laryngoscopy and intubation mean DBP rose to maximum of 78.93 ± 5.24 mmHg at 1 min., decrease above baseline by 0.74. The difference in the DBP value as compared to baseline was not statistically significant. (p >0.05).

When clonidineand lignocaine groups were compared, the difference in the values of DBP was not significant statistically (P>0.05) till 3 min. post intubation. Also the mean DBP in clonidine group returned to baseline at 2 min. post intubation, where as in lignocaine group, it returned to baseline at 10 min. post intubation.

DISCUSSION:

The patients in clonidine group demonstrated fall in pulse rate following administration of oral clonidine to a mean preoperative value.The rise in mean pulse rate after intubation returned to baseline value at 2 min. where as in control group the rise persisted till 10 min. post intubation. This effect could be due to centrally mediated α_2 adrenergic action of clonidine. K. Filos et al (1993)[10] Studied effects of premedication with oral clonidine in doses of 150mcg. and 300mcg. for sedation, intraocular pressure and hemodynamic profile in elderly ophthalmic patients (mean age 73.7 ± 5.5) undergoing cataract surgery. They observed that heart rate decreased by 8.2% after 150 mcg. clonidine and decreased by 18.5% after 300 mcg. clonidine. Bradycardia was noticed in 2 patients (10%) with low dose where as 10 patients (50%) in high dose group.

The results of our study are comparable to Filos et al with respect to reduction in mean pulse rate after premedication with 150 mg oral clonidine. However we did not notice bradycardia throughout the study even at slightly higher dose (200 mcg). This could be because of younger age and healthy status of the patients included in our study. Ghignone et al (1987)[7] studied the effect of clonidine (5mcg./kg orally) on peri-operative haemodynamics and isoflurane requirement and compared with diazepam (0.15 mg/kg 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 different study design, higher clonidine dose and co-administration of drugs like lignocaine and fentanyl. Raval et al (2002)[15] studied attenuation with 200 mcg.clonidine orally and found mean pulse rate fall by 10.8%. Laryngoscopy and intubation lead to increase in mean pulse rate above baseline value by 5.89%.The results of this study correlate well with our study.

Change in mean Systolic blood pressure (SBP) and mean Diastolic blood pressure (DBP): We observed that lignocaine causes significant attenuation of hemodynamic response to laryngoscopy and intubation. Our findings were comparable to the findings of Abou-Modi, Keszer and Yacoub (1977)[1] who had used intravenous lignocaine in 1.5 mg/kg and 0.7mg/kg doses. They had found that intravenous lignocaine in 1.5 mg/kg dose provided complete protection against arrhythmias, but only a borderline protection against increase in blood pressure and heart rate, while the dose 0.7mg/kg was inadequate in providing protection against arrythmias, only preventing blood pressure elevation. Abou-Modiet al[1] have described the possible mechanisms of action of lignocaine as- direct myocardial depressant effect, peripheral vasodilating effect and effect of synaptic transmission. Robert Stoelting (1977)[17]found that lignocaine in 1.5 mg/kg intravenously can attenuate the pressor response effectively.

D. G. Clayton et al (1983) [4] studied effects of pretreatment with intravenous lignocaine 1.5 mg/kg given 1 min. prior to induction of anaesthesia. It was shown to reduce significantly, the incidence of dysrrhythmias during dental anaesthesia and also to reduce the rise in blood pressor associated with endotracheal intubation. The results obtained by us with intravenous lignocaine in the dose of 1.5 mg/kg correlate quite well with most of the above workers. Thus, we observed that lignocaine causes significant attenuation of hemodynamic response to laryngoscopy and intubation.

K. Filos et al (1993)[10] observed a significant fall in SBP 90 min. after administration of oral clonidine (150 mg). They noticed hypotension (MAP <70 mmHg) in only 5% patients in low dose group as compared to 40% patients in high dose group probably because of the older age group included in the study. We observed a similar fall in mean SBP after

premedication; but significant hypotension (SBP <25% of baseline) was not observed in any of the patient from our study. This could be because of younger age and healthy status of the patients included in our study. Ghignone et al (1987)[7] in their study found reduction in mean SBP due to oral clonidine premedication (5 mcg/kg) by 18.07%. After intubation the mean SBP and DBP never rose beyond the baseline value producing statistically significant attenuation of rise in SBP due to laryngoscopy and intubation. The results obtained by Ghignone et al differ from our study due to different study design, including patients with controlled hypertension and co-administration of drugs like lignocaine and fentanyl.

Raval et al (2002) [15] observed reduction in SBPand DBP following premedication with oral clonidine 0.2 mg by 7.63%. In post intubation period SBP and DBP remained below baseline value producing significant attenuation of rise in SBP due to laryngoscopy and intubation. The result obtained by Raval et al is similar to our study result. We concluded that clonidine in low dose of 0.2 mg per orally maintains hemodynamic stability and attenuates pressor response to laryngoscopy and intubation without causing undue hypotension.

None of the patients had significant hypotension (i.e. 25% fall from baseline value). None of the patients had significant bradycardia (HR <60 beat/min). The side effects of clonidine such as dermatological rash, pruritis, angioneurotic edema, seen with high dose of clonidine were not observed.

CONCLUSIONS:

Among these two drugs, clonidine is a better drug for attenuation of cardiovascular responses to laryngoscopy and endotracheal intubation as compared to lignocaine.

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