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To Study the Effect of Oral Clonidine on Attenuation of Hemodynamic Stress Response of Laryngoscopy and Intubation in Surgeries under General Anaesthesia

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Abstract: Laryngoscopy and endotracheal intubation is associated with hemodynamic changes due to activation of nerves present in the oral cavity and beyond. Most commonly hypertension and tachycardia is seen other cardiac changes are also common like arrhythmias, asystole etc. Various methods are used to attenuate this hemodynamic response. In present study, we have used oral clonidine 90 minutes before the surgery to attenuate this reflex response. This randomized control study was conducted on 60 patients of ASA grade 1 and 2 after taking ethics committee approval. Patients were divided into two groups. In Group 1 (n=30), patients received clonidine orally one and half hours prior to surgery and Group 2 (n=30), patients received Placebo orally one and half hours prior to surgery. Diastolic, systolic and mean blood pressure and heart rate were measured throughout the procedure and recorded for five minutes just after the intubation. Oral clonidine given pre-emptively helps attenuating adverse hemodynamic response occurring due to laryngoscopy ($p<0.05$) in comparison to control group. Oral clonidine given pre-emptively reduces adverse hemodynamic response occurring due to laryngoscopy

Keywords: Clonidine, Hemodynamic response, Laryngoscopy, General Anaesthesia.

INTRODUCTION

Endotacheal intubation demanded greater skill from the anesthesiologist and required deeper planes of anaesthesia for successful intubation. With the introduction of new equipment and neuromuscular blockers in the anaesthetic practice coupled with ever-growing technical knowledge and skills of anesthesiologism, endotracheal intubation has become a safe and common Procedure in modern day Anaesthesia.

Endotracheal intubation is always associated with certain hazards. Few common complications are trauma during laryngoscopy, airway obstruction by kinking or malposition of tube, trauma to vocal cords leading to oedema and postoperative horseness and ulceration are not uncommon. Besides these, there are certain cardiovascular disturbances, which often go unnoticed due to lack of proper monitoring cardiac disturbances may be transient and may not lead to deleterious effects in normal healthy individuals but can lead to serious consequences in patient with cardiovascular diseases.

We are particularly interested in the cardiovascular complication arising during laryngoscopy and transient disturbances in cardiac action are caused by reflex excitation of vagus nerves or sympathetic system during laryngoscopy and intubation [1-3]. The haemodynamic response to laryngoscopy and tracheal intubation namely hypertension, arrythmias and tachycardia are of considerable importance to anesthesiologist [4]. Reflex circulatory responses is more marked when intubation is done under light general of anaesthesia [2].

Later workers took pharmacological method to attenuate the blood pressure and heart rate elevation and response to laryngoscopy and intubation. These included topical anaesthesia of the oropharynx [5], intravenous lignocaine [6, 7], adrenergic blocking drugs, vasodilating drugs etc. The +response can be diminished or modified locally, centrally or peripherally

and attempts have been made to accomplish this using all approaches with varying success. Regional topical anaesthesia used to block afferent impulses.

But most of the method required laryngoscopy itself produces similar response. Intravenous lignocaine and deeper inhalational techniques are used to modify the response at the central nervous system.

Other pharmacological approaches are fentanyl [8]**,** beta blocker [9], Alfentonyl [10]**,** calcium channel Blocker like nifedipine [11], MgSo4 [12]**,** Diltriazem [13]**,** nitrogycerine [14], Buprenorphine [15], Esmolol etc.

These pharmacological approaches are not proved to be entirely satisfactory because reflex action is not completely blocked.

Clonidine, an alpha-2 adrenergic agonist, initially introduced as centrally acting antihypertensive agent has been shown to reduce sympathetic out flow in response to stress. It has been in use for treatment of mild and moderate hypertension. This drug act as the reaction site in the medulla oblongata and pre-synaptically at peripheral nerve terminals to cause a reduction in the activity of sympathetic nervous system.

MATERIALS AND METHODS

The present study was conducted in NSCB Medical College and Hospital, Jabalpur. The study was carried out on 60 adult patients of either sex, in the age group 18-65 years. All the patients were normotensive and devoid of any cardiovascular disturbances, belonging to ASA grade I and II. The patients were picked up from the routine operative list scheduled to undergo various types of operating procedures like general surgical, gyaecological and orthopaedic.

The patients who required administration of general anaesthesia for the particular surgery were included in the study. Any patients who gave history of receiving antihypertensive, antiarrythmic and steroids were excluded from the study. Patients with systolic BP of 140 mmHg or less and diastolic BP of 90 mmHg or less were considered as normotensive and only such patients were included in the study. Patients with any abnormally in the ECG were not included in the study.

All the patients were examined the day prior to the surgery. Informed consent was obtained and the patients were briefed about the drug regime and the method of administration so that full cooperation of the patients was achieved. Thorough, general physical and systemic examinations was carried out to rule out any systemic disorders. All routine and special investigations of blood and urine were carried out. Chest skiagrams, electrocardiogram, ultrasonography etc. were done as per indication.

On the morning of operation, the patients were shifted to the operation theatre. Systolic blood pressure, diastolic blood pressure, and heart rate were recorded.

Patients were divided into 2 groups of 30 patients each. Depending upon the drugs employed to attenuate the cardiovascular responses during laryngoscopy and intubation, patients were randomly allotted to either group. The groups were designated as I and II.

Group I (n=30) the patients of this group received only normal saline and served as control group.

Group II (n=30) the patients of this group received oral clonidine 3 □ /kg 90 minute before induction.

ANAESTHESIA TECHNIQUE

In all the groups, the pre-medication with parasympatholytics were avoided as they could cause tachycardia which would invalidate the results. No other pre-medicant such as sedative or narcotic was given to any patient.

All the patients were preoxygenated with 100% oxygen for three minutes. Technique of anaesthesia was standardized for all the patients in the study. This consisted of induction with I.V. thiopentone sodium (2.5) 5mg/kg BW followed by I.V. succinylcholine 1.5 mg/kg BW to facilitate endotracheal intubation.

Gentle ventilation with 100% oxygen was done till cessation of fasciculation thereafter gentle laryngoscopy was performed and endotracheal intuition was done with cuffed endotracheal tube of adequate size. The cuff was immediately inflated. The endotracheal tube was then connected to the Boyles machine through Bain's circuit. Nitrous oxide: oxygen (60:40), halothane and non deplarising muscle relaxant was used for maintenance of anaesthesia. No kind of stimulation like urinary Catheterization, Ryle tube insertion cleaning draping, insertion, of additional IV line, IM injections will be allowed during the study period.

To study the effect of clonidine on cardiovascular changes during laryngoscopy and intubation, pulse rate and blood pressure were recorded at fixed time intervals. The observation were made as under:

- Just before induction
- Just before laryngoscopy
- Immediately after intubation
- One minute after intubation
- Two minutes after intubation
- Four minutes after intubation
- Five minutes after intubation

The parameter like SBP, DBP, and PR were recorded every minute after ET till up to 5 min. Patients were continuously monitored for arterial oxygen saturation. Any period of desaturation, gross fluctuation of blood pressure on either side and any abnormality in the pulse rhythm was noted and recorded.

All the relevant data was recorded in proforma prepared for the study and results thus obtained were subjected to statistical analysis by paired t-test and Z test where ever applicable and degree of significance was obtained.

RESULTS

Data obtained from the patients involved in the study were analyzed. The mean age, weight, sex, duration of anaesthesia and surgery were comparable in two groups as shown in table-1.

Preoperative heart rate, systolic, diastolic and mean blood pressures were comparable in both the groups.

Table-1: Showing demographic variables of two groups

Demographic data	Group 1	Group 2
Age	37.06±10.63	37.90±10.20
Weight (Kg)	58.36±12.15	57.60±9.56
Sex (Female)	76.7%	86.7%
Duration Of Anaesthesia (Min)	97.16±17.05	98.00±20.82

Table-2: Showing pulse rate at various time interval in study groups

GROUP		PR_POP	PR_BI	PR_BL	PR_AI	PR1	PR2	PR3	PR4	PR5
I	Mean	86.9	91.2	99.4	112.6	113.3	110.1	106.6	104.9	101.7
	SD	±10.2	±9.4	±10.5	±10.9	±7.4	±7.2	±8.0	±9.0	±8.4
	N	30	30	30	30	30	30	30	30	30
t value			1.709	4.698	9.424	11.480	10.193	8.354	7.282	6.146
p			P>0.05	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001
II	Mean	81.1	79.6	86.7	93.9	92.7	92.1	90.3	89.2	88.1
	SD	±8.1	±7.7	±8.2	±9.3	±9.3	±8.9	±8.9	±8.6	±8.2
	N	30	30	30	30	30	30	30	30	30
T value			0.716	2.680	5.673	5.153	5.038	4.214	3.762	3.324
p			P>0.05	0.01	0.0001	0.0001	0.0001	0.0001	0.001	0.001

Table-3: Showing systolic arterial pressure at various time interval in study groups

GROUP		SAP_POP	SAP_BI	SAP_BL	SAP_AI	SAP1	SAP2	SAP3	SAP4	SAP5
1	Mean	125.3	125.7	126.5	163.7	154.3	143.0	137.7	133.5	128.1
	SD	±8.7	±11.3	±12.7	±16.1	±14.4	±12.2	±12.1	±10.5	±9.9
	N	30	30	30	30	30	30	30	30	30
			0.153	0.427	11.498	9.387	6.453	4.546	3.289	1.135
			P>0.05	P>0.05	0.0001	0.0001	0.0001	0.0001	0.001	9999
2	Mean	122.6	121.0	117.1	134.3	131.7	128.9	125.8	122.5	119.1
	SD	±10.4	±11.7	±12.3	±14.4	±14.0	±13.6	±13.2	±11.3	±10.3
	N	30	30	30	30	30	30	30	30	30
			0.560	1.879	3.619	2.865	2.021	1.041	0.048	1.299
			P>0.05	P>0.05	0.001	0.005	0.05	P>0.05	P>0.05	P>0.05

Table-4: Showing diastolic arterial pressure at various time interval in study groups

GROUP		DAP_POP	DAP_BI	DAP_BL	DAP_AI	DAP1	DAP2	DAP3	DAP4	DAP5
1	Mean	81.9	82.1	83.5	104.9	97.2	92.3	88.3	85.6	82.9
	SD	±5.6	±6.1	±7.0	±7.3	±6.8	±6.3	±5.9	±5.6	±5.5
	N	30	30	30	30	30	30	30	30	30
			0.176	0.975	13.675	9.547	6.795	4.344	2.594	0.702
			P>0.05	P>0.05	0.0001	0.0001	0.0001	0.0001	0.01	P>0.05
2	Mean	77.9	77.7	75.7	87.0	85.0	82.8	81.3	79.5	77.8
	SD	±6.0	±5.9	±6.2	±7.0	±6.5	±6.6	±6.4	±6.1	±6.0
	N	30	30	30	30	30	30	30	30	30
			0.130	1.401	5.368	4.379	2.995	2.127	0.980	0.086
			P>0.05	P>0.05	0.0001	0.0001	0.005	0.05	P>0.05	P>0.05

DISCUSSION

The present study entitled "To Study The Effect of Oral Clonidine on Attenuation of Hemodynamic Stress Response of Laryngoscopy And Intubation In Surgeries Under General Anaesthesia" was conducted on 60 patients of ASA grade I and II of either sex of age group 18 - 50 years scheduled for surgeries under general anesthesia who were randomly divided into two groups according to the drugs received as shown below:

Group I (n=30) the patients of this group received only normal saline and served as control group.

Group II (n=30) the patients of this group received oral clonidine 3 □ /kg 90 minute before induction.

Endotracheal intubation is always associated with certain hazards. Few common complications are trauma during laryngoscopy, airway obstruction by kinking or malposition of tube, trauma to vocal cords leading to oedema and postoperative horseness and ulceration are not uncommon. Besides these, there are certain cardiovascular disturbances, which often go unnoticed due to lack of proper monitoring cardiac disturbances may be transient and may not lead to deleterious effects in normal healthy individuals but can lead to serious consequences in patient with cardiovascular diseases.

Later workers took pharmacological method to attenuate the blood pressure and heart rate elevation and response to laryngoscopy and intubation. These included topical anaesthesia of the oropharynx, intravenous lignocaine, adrenergic blocking drugs, vasodilating drugs etc. The response can be diminished or modified locally, centrally or peripherally and attempts have been made to accomplish this using all approaches with varying success. Regional topical anaesthesia used to block afferent impulses.

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Clonidine, an alpha-2 adrenergic agonist, initially introduced as centrally acting antihypertensive agent has been shown to reduce sympathetic out flow in response to stress. It has been in use for treatment of mild and moderate hypertension. This drug act as the reaction site in the medulla oblongata and pre-synaptically at peripheral nerve terminals to cause a reduction in the activity of sympathetic nervous system.

All the demographic data like age, sex, weight of the patients, duration and type of the surgery were comparable in both the groups i.e. statistically insignificant (p>0.0.5) as shown in table-1.

Pulse rate was significantly lower and maintained in clonidine group as compared to the control group as shown in table-2 and results were statistically significant (p<0.05).

Blood BC and Flacke WE [16] studied the reduction in Halothane Anaesthetic requirement by clonidine, an alpha-adrenergic agonist and shown that clonidine causes marked increase in halothane anaesthetic requirement in the dogs. The effect is medicated through an alpha-adrenergic mechanism.

Batra *et al.*, [17], conducted a double blind randomized trial to study the effect of clonidine on pluse rate and blood pressure response to laryngoscopy and tracheal intubation. The increase was significantly lower in the clonidine treated group immediately after intubation (P< 0.001). The authors concluded that the rise in heart rate blood pressure associated with laryngoscopy and intubation during a routine induction sequence can be altered by the use of oral clonidine.

Wright *et al.*, [18], evaluated the efficacy of oral clonidine in a dose of 0:3mg as a routine premedicant compared with placebo. In the clonidine treated patients, heart rate was reduced than the control group and then persisted through induction and maintenance of anaesthesia.

Nishikawa *et al*., [19], evaluated the effects of oral clonidine premedication on the haemodynamic changes associated with laryngoscopy and tracheal intubation. There was also a significant difference between the two groups in the incidence of systolic blood pressure increase above 180mmHg following laryngoscopy and tracheal intubation (0% versus 26%, p<0.05). However, no significant difference was noticed between the two groups in heart rate response to larygoscopy and tracheal intubation. The authors concluded that oral clonidine 5 mcg.kg.-1 as a preanaesthetic medication could attenuate the presser responses associated with laryngoscopy and tracheal intubation.

Systolic and diastolic arterial blood pressures were significantly lower and maintained in clonidine group as compared to the control group as shown in table-3 and 4 and results were statistically significant ($p<0.05$).

Carbine UA *et al.*, [20] studied the effect of clonidine on the pressor and heart rate response to endotracheal intubation. 30 patients were pretreated with either clonidine 1.25 g/Kg or clonidine 0.625 g/Kg or an equivalent volume of normal saline, given IV 15 mins before induction of aneathesia. The attenuation of the pressor response to intubation of both clonidine groups was statistically significant compared to the saline group.

Dorothee M. Gaumann *et al.*, [21] This study was conducted to examine the haemodynamic and endocrine effects of clonidine, given as sole preanaesthetic medication, in neurosurgical patients. Though statistically significant, the observed inhibitory haemodynamic and endocrine effects of clonidine seem to be of minor clinical importance.

Leslie *et al.*, [22], conducted a randomized double blind control trial to investigate the influences of intravenous clonidine on thiopentone dose requirements, when used for induction of anaesthesia and associated haemodynamic effects. Significant decreases in thiopentone doses were observed in group receiving clonidine compared with control group.

Carbine UA, Allen *et al.*, [23] studied the effects of IV clonidine, fentanyl and saline for both their effect on the cardiovascular response to intubation and early postoperative pain. The increase in heart rate with intubation was significantly lower in the fentanyl and clonidine groups compared to the control group ($P < 0.05$) and these changes persisted for 90 seconds after intubation.

CONCLUSION

This study was carried out to study the effect of pre-emptive doses of oral clonidine on attenuation of hemodynamic stress response of laryngoscopy and intubation in surgeries under general anaesthesia. We found that oral clonidine, when given pre-emptively 1.5 hours before surgery reduces hemodynamic changes like hyprtension and tachycardia associated with laryngoscopy and intubation.

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