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An observational study of oral clonidine as a pre-medicant for attenuation of hemodynamic responses to laryngoscopy and intubation

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***Abstract*---**Introduction: Endo-tracheal intubation causes noxious stimulation to hemodynamics. In search for an ideal agent to attenuate this response, many drugs have been used. Clonidine is an α_2-agonist and have been used as a premedicant to attenuate hemodynamic response. Aim: To observe the attenuating effect of oral clonidine on hemodynamic response to laryngoscopy and tracheal intubation. Setting and Design: This was an observational comparative study. Material and Method: 44 patients of either sex,

aged of 18- 65 years,ASA I and II undergoing for elective surgery under general anesthesia were enrolled. They were randomly allocated to receive oral clonidine (100 mcg) or placebo (vitamin B complex) as premedication 60- 90 min before induction. Heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure were recorded before, immediately after and then 1, 3 min and thereafter every 5 min after intubation until 30 min. Result:A statistically significant difference was observed in heart rate, systolic blood pressures and means arterial pressure and was significantly higher in Placebo group following intubation. Conclusion:Oral clonidine 100mcg in preanesthetic period, provide more haemodynamic stability and attenuate the stress response to laryngoscopy and intubation.

***Keywords*---**general anaesthesia, airway, vital parameters**.**

Introduction

Airway management is a fundamental and crucial aspect of anesthesia practice.Induction of general anesthesia, direct laryngoscopy and endotracheal intubation causes cardiovascular changes and autonomic reflex activity [1]. Airway instrumentation causes stimulation of nerves that carry afferent impulses to the vasomotor center and activates the sympatho-adrenal system and release catecholamine resulting in increase in the heart rate and blood pressure [2].

Common methods to reduce stress response to laryngoscopy are, minimum duration of laryngoscopy and use of pharmacological agents like vasodilators, beta blockers, calcium channel blockers, α_2-agonists, lignocaine, and opioids.α2 adrenoceptor agonists Clonidine used as an adjunct to anesthesia as these drugs reduce anesthetic requirements, attenuate adrenergic, hormonal, and hemodynamic stress responses to surgery, reduce anxiety, and lead to sedation[3,4].

This study is undertaken to observe effectiveness of oral clonidine as a premedicant to attenuate the hemodynamic responses to laryngoscopy and endotracheal intubation. Effects of oral clonidine were compared with oral placebo in the patients undergoing elective surgery.

Materials and Methods

After obtaining institutional ethical committee approval and informed consent, this study was conducted on 44 patients of either sex, between 18-65 years old, belonging to ASA grade I or II undergoing elective surgeries under general anesthesia. Exclusion criteria included patient refusal, ASA grade III, IV, morbid obesity, pregnancy and known cardiac disease. The patients were randomly divided by chit method into two groups of 22each. On the morning of surgery, 60-90 min before induction, heart rate (HR), systolic blood pressures (SBP) and diastolic blood pressures (DBP) were recorded.

Group C: Received Clonidine 100 mcg orally 60-90 min before induction with sips of water.
Group P: Received placebo (Tablet Vitamin B complex) 60-90 before induction with sips of water.

Inside the operation theatre, a multimodal monitor was attached including electrocardiogram (ECG), HR, non-invasive blood pressure (NIBP) and arterial oxygen saturation (SpO2). HR, SBP and DBP were recorded before induction.All patients were preoxygenated with 100% oxygen for 5 min. Anesthesia was induced with injection Propofol 2 mg/kg. Injection Succinylcholine 1-2 mg/kg body weight was given after confirming satisfactory mask ventilation to facilitate endotracheal intubation. Patients were intubated with the appropriate size cuffed endotracheal tubes under direct laryngoscopy in the first attempt. Patient was attached to breathing circuit of anaesthesia machine and after checking bilateral air entry, the tube was fixed. HR, SBP and DBP were noted in post induction period, during laryngoscopy and intubation, and thereafter 1 min, 3 min and 5 min and thereafter every 5 min till 30 min after intubation.

Anesthesia was maintained with Isoflurane with nitrous oxide (60%) and oxygen (40%). Inj. Atracurium used for neuro-muscular-blockade with loading dose of 0.5mg/kg and maintenance dose of 0.1mg/kg as needed till the end of surgery. At the end of the surgery residual neuromuscular blockade was reversed with injection neostigmine 0.05 mg/kg and injection Glycopyrolate 0.008 mg/kg. After clinical assessment of recovery, Extubation was done and shifted to the recovery room.

Results

The two groups were statistically comparable with respect to age, gender, weight, and American Society of Anaesthesiologists (ASA) physical status as seen in Table 1,2,3 and 4.

Table 1: Age distribution				
Age Group	Group P		Group C	
	No.	%	No.	%
20-30	5	22.73	4	18.18
31-40	7	31.82	7	31.82
41-50	5	22.73	6	27.27
>50	5	22.73	5	22.73
Total	22	100	22	100
Table 2: Gender				
Gender	Group P		Group C	
	No.	%	No.	%
Male	9	40.91	7	31.82
Female	13	59.09	15	68.18
Total	22	100	22	100
Table 3: Weight				
Group	Weight		p value	
	Mean	SD		

Group P	61.86	11.09	0.9537	
GroupC	62.05	10.48		

Table 4: ASA Grade

ASA Grade	Group P		Group C	
	No.	%	No.	%
I	8	36.36	8	36.36
II	14	63.64	14	63.64
Total	22	100	22	100

Table 5: Mean Heart Rate (rate per minute) at different time intervals in both groups

Table 5: HR					
Heart Rate	Group P		Group C		p value
	Mean	SD	Mean	SD	
Before Induction	79.36	4.91	87.36	10.48	0.0023
After Induction	76.09	5.14	77.18	7.00	0.5592
T0	112.91	7.00	93.55	7.09	P < 0.0001
T1	120.18	10.53	100.36	6.37	P < 0.0001
T3	112.09	9.23	92.18	6.04	P < 0.0001
T5	102.36	9.15	87.18	5.81	P < 0.0001
T10	95.09	7.14	78.45	5.12	P < 0.0001
T15	88.00	4.82	70.73	5.03	P < 0.0001
T20	82.91	4.48	67.00	4.27	P < 0.0001
T25	75.73	4.11	66.27	3.40	P < 0.0001
T30	74.55	3.39	64.09	3.98	P < 0.0001

There was no statistically significant difference ($p>0.05$) in Heart Rate observed before laryngoscopy and intubation at time of induction between two groups. After induction there was a drop in HR in both the groups. During laryngoscopy and intubation, there was increase in HR in both the groups, but the difference between two groups at the time of laryngoscopy and intubation was statistically strongly significant and persisted until 5 min after intubation. In Group C, HR was well under control and returned to pre-induction value at 5 min as compared to Group P, where tachycardia persisted for more than 5 min after intubation as in Table 5.

Table 6: Mean Systolic BP at different time interval in both groups

Table: 6. SYSTOLIC BLOOD PRESSURE					
SBP	Group P		Group C		p value
	Mean	SD	Mean	SD	
Before Induction	119.91	6.55	118.55	7.91	0.5379
After Induction	115.45	6.08	111.27	7.13	0.0425
T0	146.00	9.03	131.82	7.61	0.0032
T1	142.09	9.12	128.09	7.99	0.0003

T3	131.73	6.83	123.91	6.94	0.0005
T5	127.91	4.88	119.64	6.31	P < 0.0001
T10	121.73	3.56	110.73	7.34	P < 0.0001
T15	120.09	2.18	107.00	5.04	P < 0.0001
T20	119.18	2.20	106.36	3.53	P < 0.0001
T25	118.55	1.97	107.18	3.06	P < 0.0001
T30	119.18	2.20	106.55	4.67	P < 0.0001

A statistically significant difference was observed in Systolic BP between the two groups ($p<0.05$) at time of intubation (T0) and at 1 (T1) and 3 (T3) min after intubation and highly significant difference ($p<0.0001$) in SBP was observed between two groups from 5 min after intubation till 30 min as shown in Table 6.

Table 7: Mean Diastolic BP at the different time interval in both the groups

Table: 7. DIASTOLIC BLOOD PRESSURE					
DBP	Group P		Group C		p value
	Mean	SD	Mean	SD	
Before Induction	76.00	5.31	77.09	5.34	0.5009
After Induction	72.73	4.84	68.27	5.21	0.0053
T0	92.55	4.67	86.36	5.37	0.0002
T1	89.09	7.11	82.91	5.58	0.0026
T3	84.91	5.26	78.64	4.80	0.0002
T5	81.09	2.60	75.64	4.92	P < 0.0001
T10	77.27	4.26	72.18	7.27	P < 0.0001
T15	77.45	3.10	67.00	4.53	P < 0.0001
T20	77.18	3.25	66.55	3.45	P < 0.0001
T25	77.36	3.11	66.27	3.77	P < 0.0001
T30	77.45	3.10	65.91	3.98	P < 0.0001

A statistically significant difference was observed in Diastolic BP between the two groups ($p<0.05$) at time of intubation (T0) and at 1 (T1) and 3 (T3) min after intubation and highly significant difference ($p<0.0001$) in DBP was observed between two groups from 5 min after intubation till 30 min as shown in Table 7.

Table 8: Mean Arterial Pressure at the different time interval in both the groups

Table: 8.MAP					
MAP	Group P		Group C		p value
	Mean	SD	Mean	SD	
Before Induction	90.23	5.47	90.55	5.32	0.8450
After Induction	86.68	4.94	82.27	5.71	0.0090
T0	110.35	5.29	100.77	5.81	0.0002
T1	106.68	7.49	97.68	6.08	0.0007
T3	100.18	5.71	93.32	5.24	0.0002
T5	96.41	2.94	89.91	5.25	P < 0.0001

T10	91.77	3.79	84.77	6.57	0.0009
T15	91.27	2.69	79.59	4.72	P < 0.0001
T20	90.86	2.93	79.41	3.29	P < 0.0001
T25	90.73	2.62	79.59	3.46	P < 0.0001
T30	91.00	2.37	79.05	4.01	P < 0.0001

It was noted that the patients of Group P had a marked increase in SBP, DBP and MAP at the time of laryngoscopy and intubation which persisted for 5 min after intubation where as in Group C patients had small increase which came back to less than baseline value within 5 minutes of intubation as per Table 6, 7 and 8.

Discussion

Direct laryngoscopy and endotracheal intubation produces circulatory effects characterized by rise in heart rate (HR) and blood pressure (BP). Instrumentation of the pharynx and tracheal intubation may result in tachycardia, hypertension and increased catecholamine concentration that may evoke life threatening condition among susceptible individuals especially those with cardiovascular disease [5]. Clonidine has desirable actions such as anxiolysis, sedation, analgesia, antiemetic, and prevention of shivering. It is a potent hypotensive agent [6]. Clonidine is a selective α2 agonistic and stimulates α2 adrenergic receptors in vasomotor center of medulla and presynaptically at the peripheral nerve terminals by blocking release of norepinephrine and leads to hypotension and bradycardia. It also stimulates parasympathetic outflow, increasing vagal tone contributing to the slowing of HR [7].

In our study, in Group C, heart rate was not found increased during laryngoscopy and intubation compared to control group P. It was noted that in Group C, mild tachycardia induced by airway instrumentation resolved within 5 min of intubation where as compared to Group P, tachycardia persisted for 10-15 min. These findings were similar to study conducted by Rani et al[8]. Ghignone*et al* [9] found in their study that HR was consistently lower throughout the operative period which never rose above baseline during intubation period. The better attenuation as compared to our study could be because of higher clonidine dose (5 mcg/ kg).

There was an increase in mean systolic blood pressure (SBP) in both the groups during laryngoscopy and intubation but this rise was highly significant in group P. In Group P SBP rose from a baseline value of 119.91 ± 6.55 mmHg to 146.00 ± 9.03 mmHg during laryngoscopy and intubation, while in group C SBP rose from 118.55 ± 7.91 mmHg to 131.82 ± 7.61. In the Clonidine group this rise was not as significant as placebo group rather systolic blood pressure dropped significantly below the base line value at 10 min after intubation, which is from a mean of 118.55 ± 7.91 mmHg to 110.73 ± 7.34 mmHg. Rani et al[8] in their study observed that in Clonidine group SBP value fall below baseline within 5 min of intubation. They have used clonidine 3 mcg/kg.

Mean Diastolic blood pressure increased in both the groups during intubation but the rise was not too high in both the groups. In group C, DBP return to baseline value within 5 min of intubation while in comparison with Group P, DBP was

above baseline value even after 5 min of intubation. In our study, at different time intervals starting from pre-induction period, there were highly significant differences in mean arterial pressures (MAP) between two groups ($p<0.0001$). These findings were similar with Raval et al[10]. There was no significant difference was found in Oxygen Saturation (SpO2) at time of intubation and thereafter in both the groups. Clonidine at dose of 100 mcg given orally and when compared with placebo found that there was statistically significant difference in HR, SBP, DBP and MAP between two groups at time of intubation ($p<0.05$) and after 5 min of intubation it was highly significant ($p<0.0001$).

Conclusion

From our study we can conclude that use of oral clonidine 100mcg as premedicant 60 minutes before induction of anesthesia in adult patients of ASA grade I and II can effectively attenuates haemodynamic response to laryngoscopy and intubation.

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