http://doi.org/10.48165/ijabms.2021.23118

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COMPARISON OF FENTANYL AND CLONIDINE IN ATTENUATION OF HAEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION

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Abstract:

Background: Laryngoscopy and endotracheal intubation has led to provision of safer anaesthesia due to better control of airway and ventilation. It is associated with reflex sympathetic stimulation resulting in an increase in heart-rate and blood-pressure, which is known as pressor response to laryngoscopy and intubation.

Various drugs have been used to avoid this pressor response. This study was aimed to assess the effects of IV Fentanyl and IV Clonidine on pressor responses occurring due to laryngoscopy and intubation in normotensive patients posted for a planned surgical procedure under general anaesthesia.

Methods: Approval from the institutional ethical committee was taken for the study. We conducted this study in 60 patients belonging to ASA grade I and II, of 18 to 65 years of age, of either sex, scheduled for planned surgical procedures under general anaesthesia.

Patients were randomly allocated into 2 groups; the study drug was injected IV slowly 10 mins before induction.

Group-F: received Inj Fentanyl 2mcg/kg

Group-C: received Inj. Clonidine 2mcg/kg

Observations were noted in terms of heart-rate, systolic-BP, diastolic-BP, mean-BP and spO2.

Results: We observed that Clonidine pre-treatment provided better blunting of stress response during laryngoscopy and intubation without causing clinically significant sedation, respiratory depression, bradycardia or hypotension compare to Fentanyl.

Conclusion:

We came to a conclusion that Clonidine provided better response compare to Fenatanyl in obliterating the rise in heart-rate and blood pressure on laryngoscopy and intubation.

Keywords:

Laryngoscpoy, endotracheal intubation, pressor response, Clonidine, Fentanyl

Introduction:

Laryngoscopy and endotracheal intubation guarantee better control of airway and ventilation. Pressor response due to reflex sympathetic stimulation is the biggest drawback of this procedure, resulting in tachycardia and hypertension, in 1940, **Reid and Brace**[9] described hemodynamic response to laryngoscopy and intubation for the first time which was also documented by **King BD, HarrisLC**[3] et al in 1951. It occurs due to reflex sympathetic discharge caused by mechanical stimulation of pharynx and larynx. Though it is transient, it may lead to detrimental effects in patients with primary or secondary hypertension, ischemic heart disease, poor cardiovascular reserve and cerebrovascular diseases.

Various anaesthetic techniques and drugs are used to blunt this effect.

Fentanyl is synthetic opioid agonist(μ-receptor), commonly used as an Intravenous (IV) analgesic component of balanced anaesthesia. Fentanyl in small doses (2 to 5mcg/kg) infrequently causes significant hypotension when given as a single drug, even in patients with decreased left ventricular function, causes little or no change in myocardial contractility[7].

Clonidine, an imidazoline derivative, is centrally acting α2-adrenoceptor agonist[6]. It decreases the central sympathetic outflow by increasing the reuptake of nor-adrenaline by stimulation of pre-synaptic α2-

adrenoceptors. Thus, it results in less nor-adrenaline to act on post-synaptic membrane, in Nucleus Tractus Soliterious (NTS) and vasomotor centre of brainstem[2]. Clonidine premedication was associated with decreasing the stress response to surgical stimuli and reduced anaesthetic requirements[1]. It also increases the cardiac baroreceptor reflex sensitivity to an increase in the systolic blood pressure[4,5].

IV Fentanyl and IV Clonidine have become favoured drugs to blunt the haemodynamic stress response to laryngoscopy and endotracheal intubation. So, this study was carried out to compare the efficacy of IV Fentanyl (2mcg/kg) and IV Clonidine (2mcg/kg) in attenuating the haemodynamic responses to larygoscopy and endotracheal intubation.

Materials and Methodology:

We conducted this study once the approval from the institutional ethical committee was granted. This study was conducted in 60 patients posted for planned surgeries under general anesthesia.

Inclusion criteria:

1. Patients scheduled for planned surgery.
2. Age between 18-65 years of both sexes.
3. Patients with ASA grade-I/II.
4. Mallampati airway assessment of grade-1.
5. Normotensive patients.

Anesthesia protocol:

After thorough pre-operative evaluation, informed written consent was taken from each patient. Patients were kept NBM overnight. After arriving to the operation theatre, large bore venous access was secured, monitors were attached. Baseline values of Heart-rate, mean arterial pressure (MAP), Rate pressure product (RRP= heart-rate*SBP), Respiratory rate, Arterial oxygen saturation (SpO2) and sedation score were noted. All patients were premedicated with inj. Glycopyrrolate 0.004mg/kgIV and in Ondansetron 0.08 mg/kgIV 30 mins before induction.

The degree of sedation was graded as follows:

Sedation score 0	Patient awake and talkative
Sedation score 1	patient sedated but arousable
Sedation score 2	Patient asleep but responding to oral commands.
Sedation score 3	Patient asleep, responding to oral commands with delay
Sedation score 4	Patient asleep, not responding to oral commands

Any other complaints like nausea, vomiting, headache, restlessness, pruritus, bradycardia (pulse-rate<60/minute), hypotension (decrease in SBP by>20% of baseline) and allergic reaction were noted.

Method of study:

Patients were randomly allocated into 2 groups, both groups were injected the study drug slowly 10 min before induction. Group-F: received Inj. Fentanyl 2mcg/kg IV. Group-C: received Inj. Clonidine 2mcg/kg IV. Pre-oxygenation with 100% oxygen was done in all patients. Patients were observed for 10 mins and vitals were recorded. After that induction was done with Inj. Xylocard 2% 1.5mg/kg IV and Inj. Thiopentone Sodium 2.5% IV 5mg/kg. muscle relaxation was done by Inj. Suxamethonium 2mg/kg IV to facilitate laryngoscopy and intubation. Patients were intubated with appropriately sized endotracheal tube and was maintained with O_2(50%), N_2O (50%), Sevoflurane1.5% and Inj. Vecuronium bromide 0.06-0.08mg/kg. All intubations were accomplished within 15 seconds of laryngoscopy in single attempt. Monitoring was done with respect to Heart-rate(pulse-rate), Mean arterial blood pressure (MAP) and Rate pressure product (RPP) at baseline value, 10-mins after study drug administration, during intubation, at 1-min, 3-min 5-min, 7min, 10-min after intubation.

Method of statiscal analysis: Descriptive data of both groups were compared by unpaired "t"-test with P value<0.05-significant(S), P value>0.05-non-significant (NS), P value<0.001-highly significant (HS).

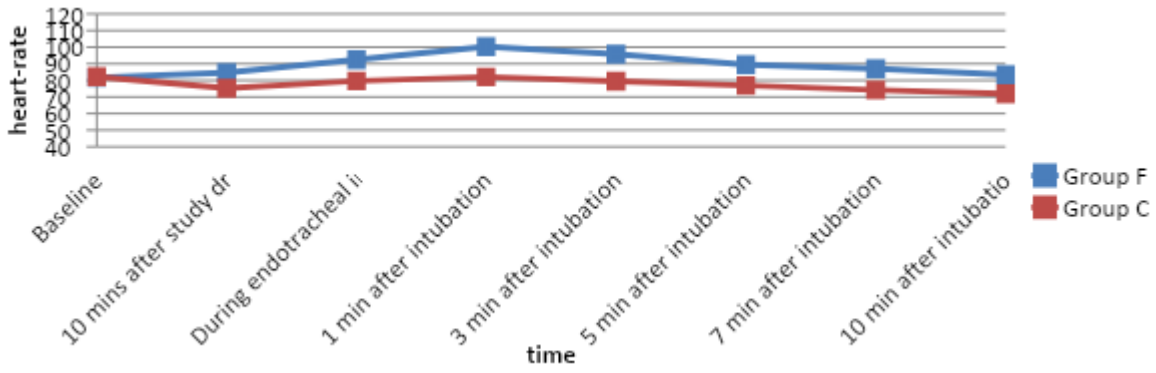
Results: In the present study all patients were between 18-65yrs of age with mean age of 38yrs in group-F and 39 yrs in group-C. Sex ratio of group-F is 16:14(M: F) while that of group-C is 15:15(M: F).

In present study, there was no significant difference observed between 2 groups regarding respiratory-rate at baseline and 10-mins after study drug, sedation score and SpO2($p>0.05$).

Pulse-Rate:

In present study, preoperative baseline mean pulse-rate were comparable in both groups with no significant difference. During laryngoscopy and endotracheal intubation, 13.14% rise from baseline in group-F and 3.09% fall from baseline value in group-C was noted. ($p<0.001$). Mean heart-rate returned to near baseline values at 10 mins after intubation in group-F whereas in group-C mean heart-rate was almost near baseline at 1-min after intubation($p<0.001$).

Graph No.-1 Mean Heart-rate (beats/min)



Mean arterial pressure:

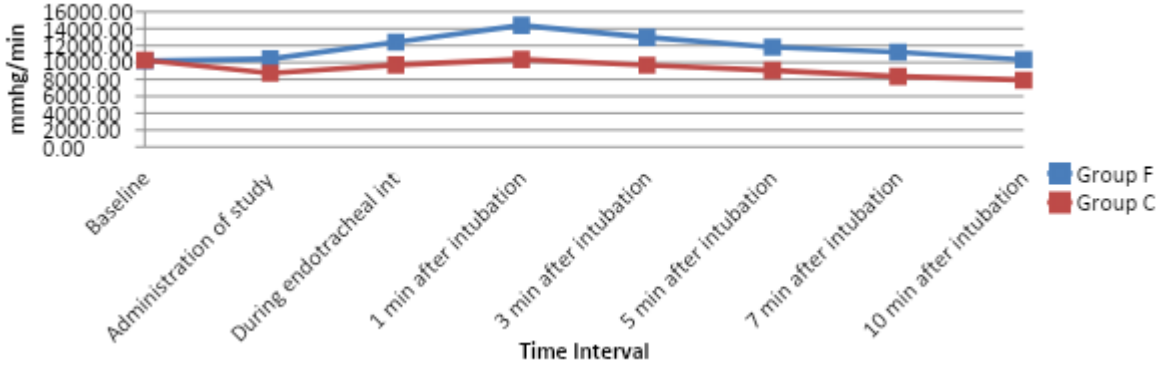
TABLE - 1: MEAN ARTERIAL PRESSURE (Mean ± SD)

TIME	GROUP - F		GROUP – C		P-VALUE	INFERENCE
	mmHg	%	mmHg	%		
Baseline	94.01 ± 6.47	-	93.22 ± 5.44	-	> 0.05	NS
10 mins after study drug administration	91.92 ± 4.96	2.23 ↓	83.79 ± 7.07	10.13 ↓	< 0.001	HS
During intubation	99.30 ± 4.91	5.62 ↑	88.38 ± 7.13	5.20 ↓	< 0.001	HS
1 min after intubation	106.42 ± 4.81	13.20 ↑	92.24 ± 7.94	1.05 ↓	< 0.001	HS
3 mins after intubation	100.06 ± 4.90	6.43 ↑	89.13 ± 7.78	4.39 ↓	< 0.001	HS
5 mins after intubation	97.71 ± 6.47	3.93 ↑	86.51 ± 7.60	7.21 ↓	< 0.001	HS
7 mins after intubation	94.53 ± 5.84	-	83.09 ± 6.91	10.89 ↓	< 0.001	HS
10 mins after intubation	91.47 ± 5.37	2.70 ↓	81.14 ± 6.99	12.98 ↓	< 0.001	HS

In present study, preoperative baseline MAP was comparable in both the groups. During laryngoscopy and endotracheal intubation MAP rise 5.62% from baseline in group-F while it falls 5.20% from baseline in group-C.($p<0.001$). Return of MAP to near-baseline values was noted at 10mins after intubation in group-F while it remained to near to baseline values even at 1 min after intubation in group-C.($p<0.001$).

Rate pressure product:

GRAPH-2: RATE PRESSURE PRODUCT (Mean ± SD)



In present study, preoperative baseline RPP were comparable in both groups. During laryngoscopy and endotracheal intubation RPP increased by 21.74% from baseline in group-F while it decreased by 5.49% from baseline in group-C.($p<0.001$). Return of RPP to near its baseline values was noted at 10-mins after intubation in group-F whereas in group-C RPP was near basline values at 1-min after intubation($p<0.001$).

DISCUSSION:

Respiratory Parameters: The mean sedation score in our study10-mins after study drug in Group-F (1.17±0.38) and Group-C (1.23±0.42) were comparable. None of the patients in both groups had respiratory

depression at 10-mins after study drug administration. RR and SpO2 in our study were comparable in both the groups at baseline value and at 10 mins after administration of study drugs($p>0.05$). None of the patients in our study became apnoeic after receiving Fentanyl or Clonidine in the study dose and didn't require assisted ventilation before induction. **Swati Chattrapati et al**[14] in her study observed that the mean sedation score at the end of infusion in Clonidine(3mcg/kg) group was 1.87±0.587 as compared to 0 in control group ($p<0.001$). They did not observe any respiratory depression in Clonidine group. They observed sedation score-3 in only 10 % of patients, sedation score-2 was noted in 66.66% of patients and 23.33% patients had sedation score-1.

Heart-Rate: In our study, at 1-min after intubation there is maximum increase in heart-rate of 22.76% (100.33±7.64)/min from baseline (81.73±9.40)/min with group-F while there is no significant increase in heart-rate with group-C, instead there is 0.17% fall (82.03±9.67)/min at 1-min after intubation as compared to baseline (82.17±9.26)/min. The group-C showed better attenuation of heart-rate than group-F($p<0.001$). Heart-rate returned to normal baseline values at 10mins in groupF (83.37±6.12)/min. However, the heart-rate remained lower than the basal value in group-C, with minimum of (71.93±7.11)/min that is 12.48% less than baseline value, in whole study($p<0.001$). **Sameena Kousar et al**[13] compared Fentanyl and Clonidine for diminishing the haemodynamic response to laryngocopy and endotracheal intubation. They observed 48.07% rise in heart-rate in the control group, whereas heart-rate rise in fentanyl group was 27.75% and in clonidine group was 12.57% which was significantly lower ($p<0.001$). **Sakshi Arora et al**[12] observed that in control group fentanyl 2μg/kg did not reduce the hemodynamic response to laryngoscopy and intubation. Heart rate in fentanyl group showed 11.62% rise from baseline whereas Clonidine 1.0μg/kg and 2.0μg/kg significantly attenuated the pressor response to laryngoscopy and intubation. In group-B (Clonidine-1μg/kg) HR decreased 2.81% below baseline; and in group-C(Clonidine-2μg/kg) HR decreased 8.1% below baseline during the time of intubation.

Mean Arterial Pressure: At 1min after intubation there is maximum increase in MAP of 13.2% (106.42±4.81) mmHg from baseline value (94.01±6.47) mmHg with group-F whereas in group-C there was 1.05% (92.24±7.94) mmHg fall at 1-min after intubation than baseline value (93.22±5.44) mmHg. The group-C showed better attenuation of MAP than group-F($p<0.001$). MAP returned to normal baseline values at 10mins in group-F (91.47±5.37) mmHg. In group-C, MAP remained lower than basal values, with minimum of (81.14±6.99) mmHg that is 12.98% less than baseline value, in whole study($p<0.001$). **Swati Chhatrapati et al**[14] in her study observed a peak rise in MAP was 4.39% (101.11±6.17 mmHg) from baseline (96.86±3.17mmHg) at 1-min after intubation in Clonidine group significantly low compared to rise in the control group which showed rise of 16.60% (112.15±1.87mmHg) from baseline (96.18±1.76 mmHg) in control group noted at the time of intubation ($p<0.05$). MAP reached near pre-study values within 3-min of intubation in Group A as opposed to 7-min in control group. Following this, MAP was significantly low compared to the pre-study values in both the groups. **Sameena koushar et al**[13] observed that the maximum rise in MAP was 35.77% (121.31±14.26) in the control group whereas 18.78% (106.13±8.78) in the Fentanyl group, while in Clonidine group, it was 6.69% (94.47±9.03) (p value < 0.001).

Rate Pressure product: At 1-min after intubation there is maximum increase in Rate pressure product (RPP) of 41.27% (14406.27±1282.31) mmHg/min from baseline value (10197.03 ±1396.72) mmHg/min with group-F while there is no significant increase in RPP with group-C, 0.87% (10369.97±1369.22) mmHg/min rise at 1-min after intubation than baseline value (10279.03±1278.82) mmHg/min. The group-C showed better attenuation of RPP than group-F($p<0.001$). RPP returned to normal baseline values at 10-mins in group-F (10336.73±966.05) mmHg/min. In group-C the RPP remained lower than basal values, with minimum of (7914.23±909.32) mmHg that is 23% less than baseline value, in whole study which is highly significant ($p<0.001$). **Swati Chhatrapati et al**[14] observed maximum rise in RPP was 17.02% (12544.67±1685.06) from baseline (10719.87±779.01) at 1-minute after intubation in Clonidine group as compared to 77.32% (18388.13±567.94) from baseline (10369.87±591.16) in control group which occurred at the time of intubation ($p<0.05$). Clonidine did not allow the RPP to rise above 12544.67±1685.06, providing protection against angina or unwanted cardiac event in perioperative period.

Both the BP response and the heart-rate were attenuated more effectively in the group-C as compared to those in the group-F.

Complications: No complications like nausea, vomiting, headache, restlessness, pruritus, bradycardia, hypotension, ischaemic changes and allergy were noted.

Conclusion:

From observations of our study, while comparing IV Fentanyl (2mcg/kg) with IV Clonidine (2 mcg/kg) given 10-mins prior to induction for attenuating the pressure response to laryngoscopy and intubation, we found that Clonidine pre-treatment proved better in blunting the stress response during the procedure of laryngoscopy and intubation without any occurrence of clinically significant sedation, respiratory depression, bradycardia or hypotension. In conclusion Clonidine was found to be superior to Fentanyl for attenuation of pressor response without any adverse effects.

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Conflict of Interest:

Nil

Funding:

Nil

Acknowledgement:

Nil