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# Comparison of efficacy of oral clonidine and intravenous fentanyl in attenuation of hemodynamic stress response to laryngoscopy and tracheal intubation

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## Abstract
**Background:** Direct laryngoscopy and tracheal intubation after induction of anesthesia are nearly always associated with sympathetic hyperactivity. To attenuate the pressor response, various drugs have been tried, but very few studies have been done to assess the effect of oral clonidine and IV fentanyl on the hemodynamic response during laryngoscopy and tracheal intubation.
**Aims and objectives:** This study was conducted to assess and to compare the effect of oral clonidine and intravenous fentanyl for the attenuation of the pressor response during direct laryngoscopy and intubation.
**Materials and methods:** Prospective, randomised, double blind, comparative study conducted at KVG Medical college and hospital, Sullia on 60 patients randomly allocated into two groups of 30 each. The patients in group C were given 150mcg of tab clonidine and group F were given inj. fentanyl 2mcg/kg respectively. Cardiovascular parameters (heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure,) were recorded at the following intervals: Baseline, pre-induction, after induction, at endotracheal intubation, one minute, three minutes and five minutes after intubation.
**Stastistical analysis:** Analysed by mean, standard deviation and analysis of variance and chi square test. P value of <0.05 was cosidered significant.
**Results:** The hemodynamic variables in clonidine group significantly lower than fentanyl group for first five minutes after laryngoscopy and intubation.
**Conclusion:** Both clonidine and fentanyl were able to attenuate the hemodynamic response to laryngoscopy and intubation, however, Tab clonidine 150mcg given 90 minutes prior to intubation kept the hemodynamic variables significantly lower than those seen in fentanyl 2 mcg/kg I.V given 5 min prior to intubation.

**Keywords:** attenuation, endotracheal intubation, clonidine, fentanyl, hemodynamic responses, laryngoscopy

## Introduction
General anaesthesia is commonly used in procedures of the head and neck, upper limb, and prolonged surgeries. Tracheal intubation is the traditional technique used to secure the airway during general anaesthesia. Direct laryngoscopy is done to facilitate endotracheal intubation under vision.
Direct laryngoscopy and endotracheal intubation is known to cause epipharyngeal and laryngopharyngeal stimulation. This stimulus is associated with reflex sympathetic discharge and rise in plasma catecholamine concentration, which can lead to increased heart rate, blood pressure and arrhythmia [1].
These changes are transient and usually well tolerated by healthy patients. Some patients with co-morbidities like hypertension, coronary heart disease and cerebrovascular accident, may develop fatal complications [2].
Various sympathetic agonist and anaesthetic agents have been used to attenuate this reflex sympathetic response to direct laryngoscopy and tracheal intubation, such as; opioids, calcium channel blockers, local anaesthetics, beta-blockers, magnesium sulphate etc [3].
No single anaesthetic technique has been accepted to be completely effective in preventing or attenuating this sympathetic response. The methods being used are either partially effective or produce undesirable side effects [4].
Opioids may limit this hemodynamic response to a certain extent by deepening the level of anaesthesia, thereby decreasing sympathetic outflow. Fentanyl at a dose of 2mcg/kg has been shown to be effective in attenuating the sympathetic response to direct laryngoscopy and tracheal intubation [5].
Clonidine is a alpha-2 adrenergic agonist. Premedication with clonidine was shown to blunt the stress response to the surgical stimuli and it reduces the narcotic and anaesthetic requirements. It also increases the cardiac baroreceptor reflex sensitivity to rise in systolic blood pressure and thus it stabilizes the blood pressure [6].
The purpose of our study was to compare the effect of clonidine and fentanyl for the attenuation of hemodynamic response to direct laryngoscopy and endotracheal intubation.

## Materials and methods
### Source of Data
The study was conducted on patients admitted in KVG Medical College and Hospital, Sullia, DK, Karnataka, for elective procedures under general anaesthesia from November 2019 to April 2021.

**Inclusion criteria**

1. Age – 18 to 50years.
2. Gender - both male and female
3. ASA class I & II.
4. Patients posted for elective surgeries under general anaesthesia.

**Exclusion criteria**

1. Patients with disorder of cardiovascular, respiratory, hepatic, renal or neuromuscular systems.
2. Patients belonging to ASA class III and IV.
3. Patients on calcium channel blockers, beta blockers and chronic use of opioids.
4. Patients with BMI>35.
5. Patients receiving drugs known to interact with study drugs.
6. Anticipated difficult airway.
7. History suggestive of sensitivity to fentanyl or clonidine.

**Sampling Procedure**

Patients were randomly allocated into 2 groups of 30 each by sealed envelope method.

Group C - Received 150mcg of Tab. Clonidine 90min prior to surgery and Inj Normal saline 5ml, 5 min before induction of anaesthesia.

Group F –received Multivitamin tablet 90 min prior to surgery and Inj fentanyl 2mcg/kg IV, diluted with normal saline made upto 5ml, 5 min before induction of anaesthesia.

**Study Procedure**

After approval from institutional ethics committee, 60 patients were selected for the study. Preanaesthetic evaluation was done and written informed consent was taken from all the patients.

Patients were kept NPO from midnight and premedicated with tab Alprazolam 0.5mg on the previous day of surgery.

On the day of the surgery, after arrival to the operation theatre, 18G cannula was secured and an IV fluid (Ringer lactate) was started. Standard monitor with electrocardiogram, non-invasive blood pressure, and pulse oximeter was connected.

Base line blood pressure, pulse rate and SpO2 were recorded. The study drug, either tab clonidine 150mcg or inj fentanyl 2mcg/kg diluted up to 5cc was given.

Patients were then preoxygenated for three minutes. Anaesthesia was induced using inj propofol 2mg/kg over 20 seconds intravenous along with rocuronium 0.6mg/kg to facilitate tracheal intubation. Ventilation was assisted following the injection of rocuronium, and after two minutes direct laryngoscopy was attempted. Intubation was done under direct vision using a Macintosh blade size 3 by the same experienced anaesthesiologist. Positioning of tube was confirmed by bilateral equal air entry and capnometry.

Heart rate, systolic and diastolic pressures, mean arterial pressure and SpO2 were documented by an independent observer who was blinded to the nature of the study. Intubation response was graded and recorded.

T0- Baseline readings
T1- Just before injection of study drug
T2- Just before induction
T3- Just before intubation
T4- 1 minute after intubation
T5- 2 minutes after intubation
T6- 3 minutes after intubation
T7- 5 minutes after intubation

Surgical stimulus was allowed only after 5 minutes following intubation.

Any episode of bradycardia (heart rate less than 50) was recorded.

**Statistical analysis**

Collected data was entered in SPSS 10.0 and analysed by mean, standard deviation and analysis of variance for repeated measures and chi-square test. P value of <0.05 was considered as significant.

**Results**

Sixty patients, undergoing various surgeries under general anaesthesia, aged between

18 and 50, were studied. Thirty patients received Tab clonidine 150mcg (group C) and the remaining thirty received fentanyl 2mcg/kg (group F) prior to intubation. Hemodynamic parameters following intubation were observed.

Descriptive data which includes mean, standard deviation, minimum and maximum values were calculated for each group.

**Table 1**

| Baseline characteristics | Clonidine group (N=30) | Fentanyl group (N=30) | P value |
|---|---|---|---|
| Mean age (years) | 32.53±10.21 | 31.43±9.000 | 0.621 |
| Mean weight (kg) | 63.33 ± 7.59 | 63.00 ± 5.43 | 0.169 |

**Table 2**

| Time interval Heart rate | Group C | Group F | P value |
|---|---|---|---|
| Baseline(T0) | 79.93± 12.12 | 82.60± 13.5 | 0.434 |
| just before study drug(T1) | 79.36 ± 10.44 | 79.33± 11.21 | 0.991 |
| Just before induction(T2) | 69.16 ± 9.10 | 75.06 ± 10.16 | 0.029 |
| Just before intubation (T3) | 64.90 ± 6.26 | 72.13 ±9.04 | 0.003 |
| 1 min post intubation (T4) | 78.96 ±10.67 | 88.36±11.05 | 0.002 |
| 2 min post intubation (T5) | 76.63±10.37 | 88.36±11.05 | <0.001 |
| 3 min post intubatiom(T6) | 76.13±10.75 | 83.56 ±11.07 | 0.014 |
| 5 min post intubation (T7) | 73.03±12.03 | 79.5± 10.34 | 0.028 |

**Table 3**

| SBP | Group C | Group F | P value |
|---|---|---|---|
| Baseline(T0) | 130.43± 9.22 | 130.96 ± 7.74 | 0.802 |
| just before study drug(T1) | 132.06 ± 9.52 | 129.66 ± 8.85 | 0.278 |
| Just before induction(T2) | 124.53± 23.23 | 123.93 ± 7.55 | 0.885 |
| Just before intubation (T3) | 114.96 ± 10.08 | 121.30 ±7.47 | 0.005 |
| 1 min post intubation (T4) | 134.43± 10.15 | 142.26±11.44 | 0.011 |
| 2 min post intubation (T5) | 129.73±9.32 | 143.3 ± 12.97 | <0.001 |
| 3 min post intubatiom(T6) | 124.66 ±10.38 | 134.13 ± 10.23 | 0.003 |
| 5 min post intubation (T7) | 114.36 ±7.57 | 125.60± 9.91 | <0.001 |

**Table 4**

| Time interval DBP | Group C | Group F | P value |
|---|---|---|---|
| Baseline (T0) | 80.66± 6.24 | 77.23 ± 7.064 | 0.095 |
| just before study drug (T1) | 81.43 ± 6.25 | 77.76 ± 7.605 | 0.087 |
| Just before induction (T2) | 80.60 ± 6.066 | 73.500 ± 7.45 | 0.001 |
| Just before intubation (T3) | 73.06 ± 7.76 | 70.66 ±7.76 | 0.234 |
| 1 min post intubation (T4) | 86.26 ± 9.28 | 89.73 ±7.45 | 0.128 |
| 2 min post intubation (T5) | 84.90±10.51 | 89.03 ± 7.752 | 0.113 |
| 3 min post intubatiom (T6) | 84.0 ±10.17 | 83.93 ± 8.008 | 0.980 |
| 5 min post intubation (T7) | 74.67 ±7.73 | 79.96± 7.31 | 0.008 |

**Table 5**

| Time interval MAP | Group C | Group F | P value |
|---|---|---|---|
| Baseline (T0) | 97.76± 7.44 | 96.33 ± 7.29 | 0.498 |
| just before study drug (T1) | 98.86 ± 8.03 | 95.86 ± 8.024 | 0.204 |
| Just before induction (T2) | 97.66 ± 9.12 | 92.03 ± 7.82 | 0.017 |
| Just before intubation (T3) | 88.26 ± 8.68 | 89.36 ±7.93 | 0.589 |
| 1 min post intubation (T4) | 102.73 ±9.38 | 107.56±9.021 | 0.074 |
| 2 min post intubation (T5) | 100.40±9.69 | 107.56± 9.90 | 0.014 |
| 3 min post intubatiom (T6) | 96.50±10.79 | 100.53±9.0391 | 0.186 |
| 5 min post intubation (T7) | 88.40±8.38 | 96.53± 10.36 | 0.006 |

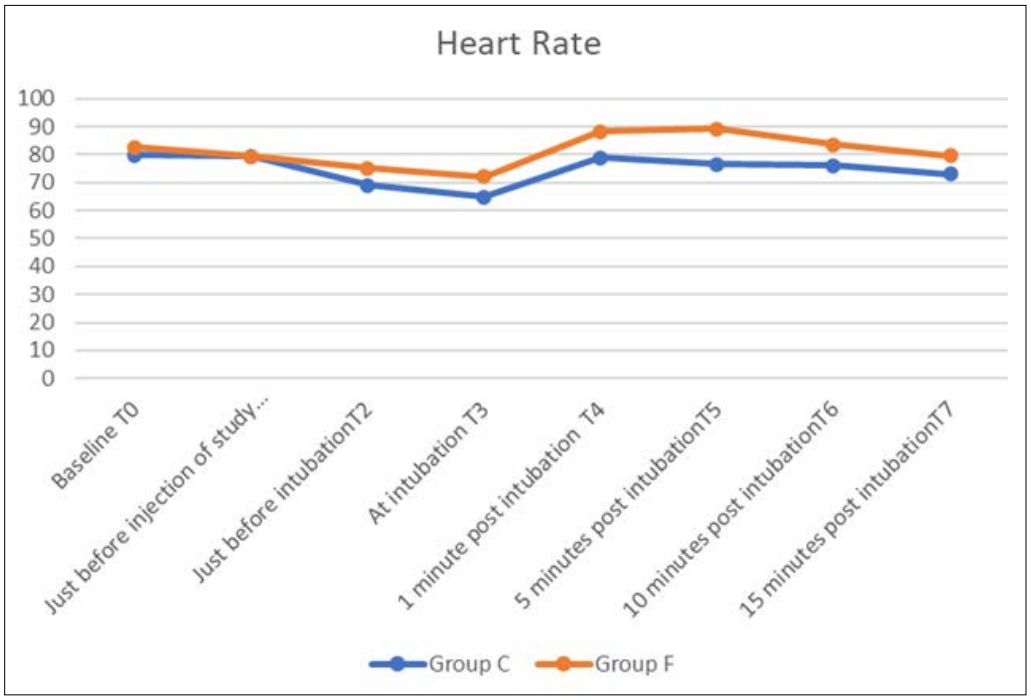


**Fig 1**

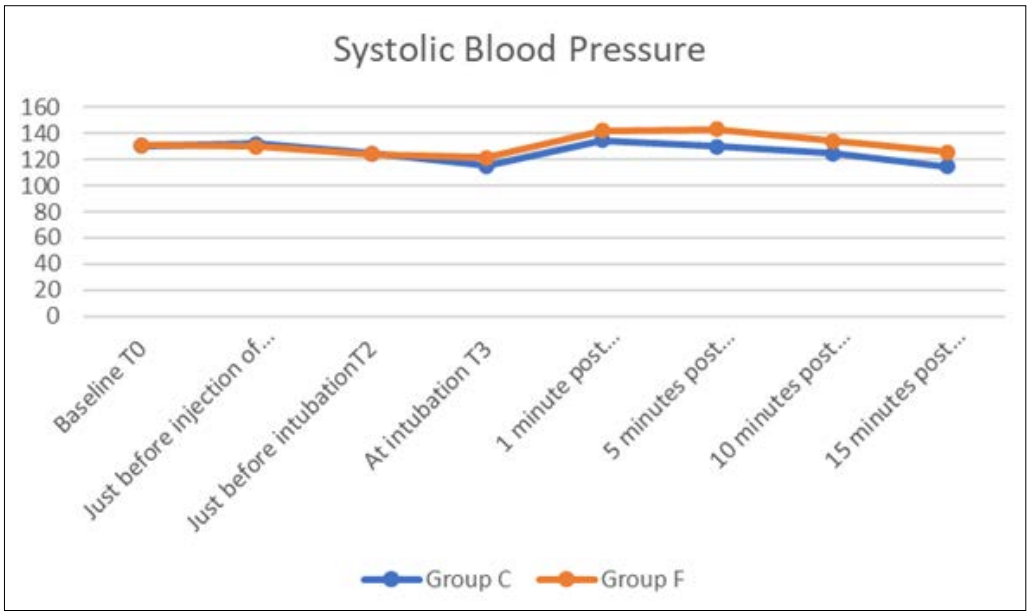


**Fig 2**

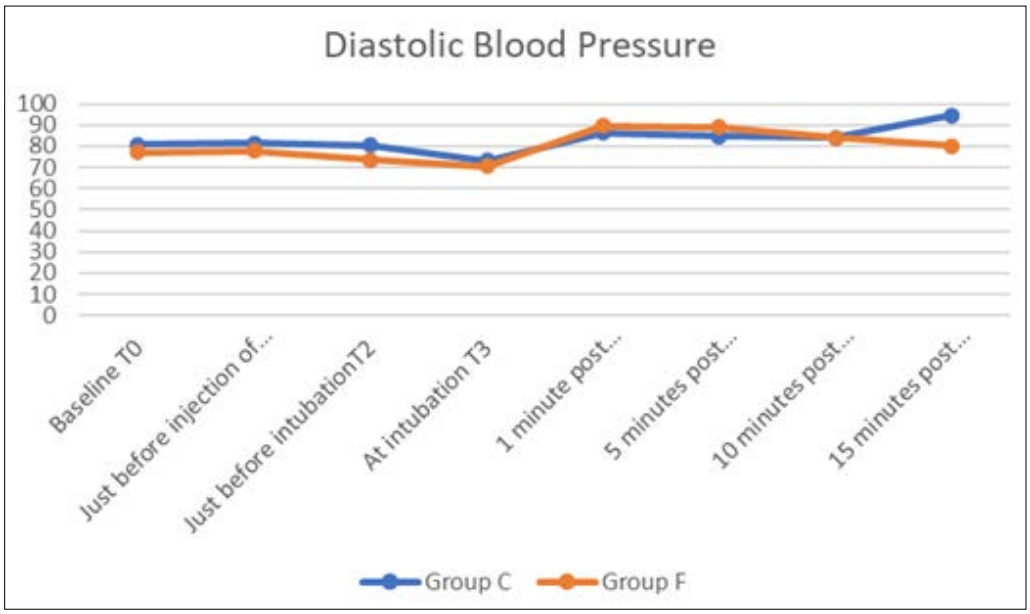


**Fig 3**

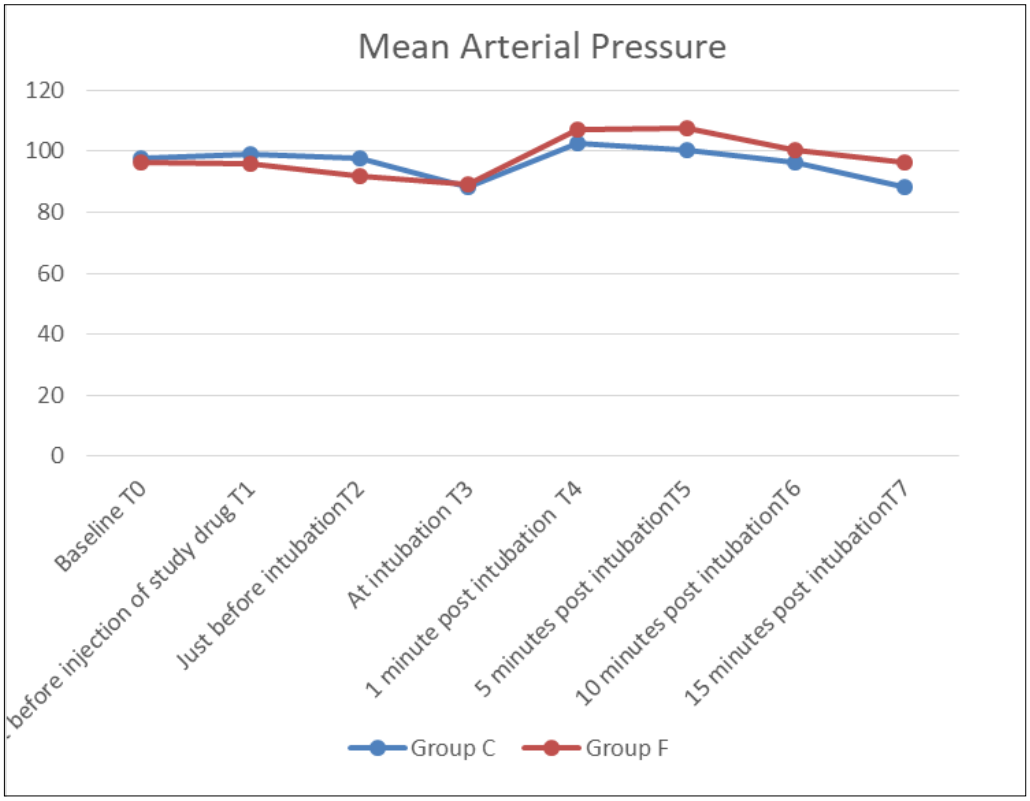


**Fig 4**

Table 1 shows comparision of mean heart rate at various time intervals compared to pre-induction. There was no statistical difference in the heart rate at baseline (p=0.434).Following oral clonidine, the heart rate dropped to 68.57±8.22bpm and 64.87±6.29bpm, before induction and before intubation respectively.

The lower heart rate among the clonidine group patients, just before intubation, was statistically significant (p=0.003).The heart rate did not rise in the clonidine group following intubation. The heart rate at 1 minute post intubation was 78.96±10.67bpm, which further fell to 73.03±12.03bpm at 5 minutes post intubation. In comparison with fentanyl group, there was a rise in heart rate post intubation, which was highest 2 minutes post intubation (89.16±12.42bpm). There was a fall in heart rate over time, and the heart rate at 5 minutes post intubation was 79.57±10.34bpm.

Table 2 shows comparision of systolic blood pressure at various time intervals compared to pre induction values. The

comparison between the two groups show no significant difference in systolic blood pressure at baseline (p=0.802), before injection of the drugs (p=0.278) or before induction (p=0.885). Just before intubation, the SBP in the Oral clonidine group (114.96 ± 10.084mmHg) was lower than in the fentanyl group (121.30±7.47mmHg). This was statistically significant (p = 0.005).

As seen in the graph, both Oral clonidine and fentanyl did attenuate the hemodynamic response following intubation, but the mean rise in systolic pressure was lower in the Oral clonidine group as compared the fentanyl group at post intubation intervals of 1, 2, 3 and 5 minutes, which was significant (p<0.05).

Table 3 shows comparision of mean diastolic blood pressure at various time intervals compared to pre induction values. With regards to DBP, the base line value in the clonidine group was 80.66±6.24mmHg. The DBP reduced, following oral clonidine to 73.06±7.76mmHg just before intubation. The values of diastolic pressure at 1 and 2 minutes post intubation were 86.26±9.28 and 84.90±10.51mmHg. This then reduced to 74.67 at the end of 5 minutes.

The baseline DBP in the fentanyl group was 77.23±7.06 and following the injection of fentanyl, the pressure reduced to 73.50±7.45 and 70.66±7.76mmHg, just before induction and intubation respectively. One minute after intubation, the diastolic pressure went up by 15%, which was the maximum rise in DBP recorded. Gradually, the DBP came down to 79.96±7.31 mmHg at 5 minutes post intubation.

Table 4 shows comparision of mean of mean blood pressures at various time intervals compared to pre-induction values. The base value of mean arterial pressure in the clonidine group was 97.76±7.44mmHg as compared to 96.33±7.29mmHg seen in the fentanyl group (p=0.49).The mean arterial pressure was 5mmHg higher in the clonidine group just before induction when compared to the fentanyl group at the same time.

The highest MAP reading was seen at 1 minute post intubation in both the groups, 102.73±9.38mmHg in the clonidine group and 107.56±9.02mmHg in the fentanyl group. The MAP difference was 7mmHg lower in the clonidine group at 2 minutes post intubation and 8 mmHg lower at 5 minutes post intubation.

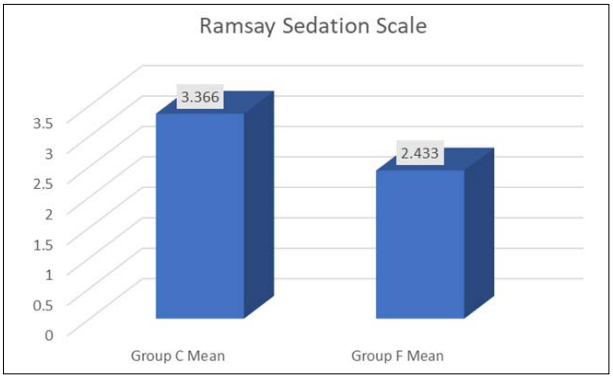


**Fig 5**

Above graph shows comparision of sedation according to ramsay sedation score in both clonidine and Fentanyl group when patient was received in PACU.

It shows sedation was more in clonidine group with a score of 3.366 ± 0.4901 and 2.433 ± 0.5040 in Fentanyl group which was statistically significant(p<0.001).

**Table 6**

| Bradycardia | Group C | | Group F | | P value |
|---|---|---|---|---|---|
| | Number | % | Number | % | |
| Yes | 1 | 3.3 | 0 | 0 | 0.33 |
| No | 29 | 97.7 | 30 | 100 | |
| Total | 30 | 100 | 30 | 100 | |

Among the patients included in this study, one patient developed bradycardia and that patient belonged to the clonidine group. This incidence was shown not to have statistical significance. (p =0.33).

## Discussion

From the present study overall we found that oral clonidine is better though not complete over IV fentanyl. Ko SH *et al*, showed that when they used fentanyl in the dose of 2mcg/kg 5 min before intubation was found to be good in controlling the hemodynamic parameters [7].

Chadha R *et al*, in their study used oral clonidine in the dose of 3.6mcg/kg, 90-110min before the operation and they compared with diazepam given in the dose of 0.2mcg/kg. they observed that blood pressure and the heart rate were significantly controlled in the clonidine group patients as compared to the diazepam group patients [8].

Laurito CL *et al*, in their study found that oral clonidine blunts the hemodynamic response for brief period (15seconds) but not for prolonged laryngoscopy (45seconds), when used in dose of 300mg given 90minutes prior to laryngoscopy [9].

Mikawa K *et al*, studied efficacy of oral clonidine in children of age 4-12 years. They used oral clonidine in two different doses like 2mcg/kg and 4mcg/kg. This was given to children in two difference doses one hour before the surgery, which was related to eyes. They noted that a good amount of sedation was given by clonidine and more the dose, more sedation was there. It also attenuated rise in the heart rate and the blood pressure. There were no side effects observed during this study [10].

Raval DL *et al*, compared the oral clonidine which they gave in the dose of 4mcg/kg with that of diazepam which was given in the dose of 0.2mg/kg body weight. The authors noted that oral clonidine when given in the above said doses was more effective than diazepam [11].

Pawlik MT *et al*, studied about benefit of clonidine premedication in patients with obstructive sleep apnea syndrome,found that oral clonidine premedication stabilizes hemodynamic variables during induction, maintenance and emergence from anaesthesia and reduces the amount of intraoperative anesthetic and postoperative opioids without deterioration of ventilation [12].

Sameenakousar *et al*. studied the effect of intravenous fentanyl with intravenous clonidine on hemodynamic responses to laryngoscopy and tracheal intubation on 150 patients and they found that clonidine was better than fentanyl for attenuating the hemodynamic responses, and it remained till the end of 10 minutes. So, they recommended intravenous

clonidine 2microgram /kg 5 minutes before the laryngoscopy and the intubation [13].

Smita Joshi, Harshi SS, Rakesh Dconducted a study to compare between IV clonidine and IV fentanyl to attenuate hemodynamic response to endotracheal intubation on 60 patients concluded that both IV fentanyl and IV clonidine were able to attenuate the pressorresponse, however iv fentanyl 2mcg/kg given 5 min prior to intubation was better than iv clonidine 2mcg /kg given 5 min prior to intubation as fentanyl did not allow marked fluctuations in SBP, DBP and MAP [14].

Rukmini G, Reddy MS conducted a study on oral clonidine 150mcgversus IV fentanyl on 60 patients and found that clonidine was more effective than IV fentanyl in stabilizing the cardiovascular parameters [15].

## Conclusion

Clonidine is easily available, cheap, orally administered and does not produce any untoward effects in the perianesthetic therapeutic range. When administered 90min prior to surgery its effect is similar to IV clonidine. The ease of administration and the hemodynamic stability it offers makes clonidine as a useful drug to use in any clinical set up.

## References


1. Sulaiman S, Karthekeyan RB, Vakamudi M, Sundar AS, Ravullapalli H, Gandham R. The effects of dexmedetomidine on attenuation of stress response to endotracheal intubation in patients undergoing elective off-pump coronary artery bypass grafting. Ann Card Anaesth,2012:15:39-43.
2. Mikawa K, Nishina K, Maekawa N, Obara H. Comparison of nicardipine, diltiazem and verapamil for controlling the cardiovascular response to tracheal intubation. Br J Anaesth,1996:76(2):221-6.
3. Kovac AL. Controlling the Hemodynamic Response to Laryngoscopy and Endotracheal Intubation. J Clin Anesth,1996:8:63-79.
4. Mondal S, Mondal H, Sarkar R, Rahaman M. Comparison of dexmedetomidine and clonidine for attenuation of sympathoadrenal responses and anesthetic requirements to laryngoscopy and endotracheal intubation. Int J Basic ClinPharmacol,2014:3(3):501.
5. HoonKo S, Kim DC, Han YJ, Song HS. Small-Dose Fentanyl: Optimal Time of Injection for Blunting the Circulatory Responses to Tracheal Intubation. Anesth Analg,1998:86:6.
6. Stoelting RK, Hiller SC. Antihypertensive Drugs. In: Pharmacology and Physiology in Anesthetic Practice 4thedition. Brown B, editor. Lippincott Williams and Wilkins; Philadelphia, 2006, 340-4.
7. Ko SH, Kim DC, Han YJ, Song HS. Small-dose fentanyl: optimal time of injection for blunting the circulatory responses to tracheal intubation. Anesth Analg,1998:86(3):658-61.
8. Chadha R, Padmanabhan V, Joseph A, Mohandas K. Oral clonidine pretreatment for hemodynamic stability during craniotomy. Anaesth Intensive Care,1992:20(3):341-4.
9. Laurito CE, Baughman VL, Becker GL, Cunningham F, Pygon BH, Citron GM. Oral clonidine blunts the hemodynamic responses to brief but not prolonged laryngoscopy. J Clin Anaesth,1993:5(1):54-7.
10. Mikawa K, Maekawa N, Nishina K, Takao Y, Yaku H, Obara H. Efficacy of oral clonidine premedication in children. Anesthesiol,1993:79:926-931.
11. Raval DL, Mehta MK. Oral clonidine premedication for attenuation of hemodynamic response to laryngoscopy and intubation. Indian J Anaesth,2002:46(2):124-9.
12. Pawlik MT, Hansen E, Waldhauser D, Selig C, Kuehnel TS. Clonidine premedication in patients with sleep apnea syndrome: a randomized, doubleblind, placebo-controlled study. Anesthesia Analgesia,2005:101(5):1374-80.
13. Sameenakousar Mahesh, Srinivasan KV. Comparison of Fentanyl and clonidine for Attenuation of the Haemodynamic Response to Laryngoscopy and Endotracheal Intubation.Journal of Clinical and Diagnostic Research,2013:7(1):106-11.
14. Routray SS, Raut K, Biswal D, Pradhan K, Mishra DA. Comparative Study of Fentanyl- Clonidine and fentanyl - lidocaine on attenuation of Hemodynamic Stress Response to Laryngoscopy and Tracheal Intubation in Hypertensive Patients,2014:4:27-31.
15. Smita Joshi, Harshi S, Shah, Rakesh D. Comparative Study between Intravenous Clonidine And Intravenous Fentanyl to Attenuate Hemodynamic Response to Laryngoscopy and Tracheal Intubation. Indian J Anesth Analg,2019:6(1):122-134.
16. Rukmini G, Reddy MS. Oral clonidine versus Intravenous fentanyl in attenuation of Hemodynamic responsesto laryngoscopy and endotracheal intubation:a comparative study Int J Adv Med,2019:6:623-7.