

# **A comparative study of fentanyl –clonidine and fentanyl - lidocaine on attenuation of haemodynamic stress response to laryngoscopy and tracheal intubation in hypertensive patients**

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**Abstract:** Introduction: Endotracheal intubation may create a period of hemodynamic instability in normotensive patients but more so in hypertensive patients. Endotracheal intubation produces stimulation of laryngeal and tracheal sensory receptors, resulting in a marked increase in the elaboration of sympathetic amines leading to hypertensive crisis. Objectives: The objective of study is to evaluate and compare the efficacy of fentanyl- clonidine and fentanyl – lidocaine combine in attenuating the stress responses to laryngoscopy and endotracheal intubation in hypertensive patients. Material and Methods: We conducted a prospective, randomized, double-blind study in 40 patients with controlled hypertension. All patients were randomly divided into two groups, fentanyl-clonidine (FC) group and fentanyl – lidocaine (FL) group. The FC group received Fentanyl 2 mcg/kg and clonidine 2mcg/kg and the FL group received lidocaine1.5mg/kg and fentanyl 2mcg/kg , 3 min prior to intubation. Hemodynamic parameters were recorded at baseline, before giving induction agents, and 1, 3 and 5 minutes after endotracheal intubation. Results: There were no significant differences between the two groups regarding hemodynamic parameters like heart rate, systolic blood pressure, diastolic and mean arterial blood pressure at before induction, 1, 3 and 5 minutes after intubation. Conclusions: Both fentanyl – clonidine and fentanyl – lidocaine combine effectively decreased the stress response to endotracheal intubation.

**Keywords:** Fentanyl, Hemodynamic Stress, Intubation, Lidocaine, Clonidine

## **1. Introduction**

Endotracheal intubation can induce hypertension, tachycardia, in normotensive patients and more so in hypertensive patients. These tracheal responses are mediated by sympathoadrenal responses and are normally well tolerated by normotensive patients. However, endotracheal intubation may produce an exaggerated hypertensive response in hypertensive patients which may lead to cardiac or cerebral stroke. Endotracheal intubation of the trachea stimulates laryngeal and tracheal sensory receptors, resulting in a marked increase in the elaboration of sympathetic amines. This sympathetic stimulation results in tachycardia and elevation of blood pressure[1-5]. Thus different drugs

such as local anesthetics, opioids, calcium channel blockers, short acting  $\beta$ -adrenergic blockers, and their combinations have been used to prevent this hemodynamic responses but none was found to be most effective. [6-12] Fentanyl, a commonly used opioid along with hypnotic agents have been used to diminish hemodynamic responses to tracheal intubation.[13-15] Furthermore, lidocaine has a suppressive effect on the circulatory responses in patients undergoing laryngoscopy and tracheal intubation [16,17] Clonidine also has been used as a premedicant to prevent stress response to laryngoscopy and intubation [18-20] But no single drug is adequate enough to prevent stress response to laryngoscopy and tracheal intubation in hypertensive patients

There was no study available to compare the attenuation of of stress response to laryngoscopy by combination of two

drugs particularly in hypertensive patients. So this study aimed to evaluate and to compare the efficacy of fentanyl – clonidine and fentanyl - lidocaine combine in attenuating haemodynamic stress responses to laryngoscopy and endotracheal intubation in hypertensive patients.

## 2. Material and Methods

We conducted a prospective, randomized, double-blind trial in 40 patients with controlled hypertension in the SCB medical college from March to September 2014. The study protocol was approved by the hospital ethical committee. Written informed consent was obtained from all patients. All patients were posted for elective surgery under general anaesthesia.

Inclusion criteria; Age < 65yrs and > 30yrs, ASA class II patients (hypertensive patients).

Exclusion criteria; Patients undergoing heart surgery, ASA III or above, CHF (congestive heart failure), arrhythmia, difficult airway, intubation time greater than 15 seconds.

All patients were randomly divided into two groups, fentanyl –clonidine (FC) group and fentanyl -lidocaine (FL) group of 20 each. Patients received their morning dose of anti-hypertensive medication before surgery. A routine pre-operative check-up was done in all patients and baseline vitals were noted. All patients were given 0.2 mg Glycopyrrolate bromide intramuscularly 30 min prior to surgery. Then patients received ringer's lactate 5ml/kg after starting an intravenous line. Patients were attached to the following monitors; ECG, noninvasive blood pressure monitor, pulse oximetry. The baseline mean arterial pressure

(MAP), systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR) were recorded. All the patients were premedicated with Inj. Midazolam 0.03 mg/kg i.v and were preoxygenated. The FC group received 2 mcg/kg fentanyl and 2mcg/kg clonidine. FL group received 2mcg/kg fentanyl and 1.5mg/kg lidocaine. Observer was blind to the drugs like clonidine and lidocaine which were administered by another anaesthesiologist. After 3 minutes anaesthesia was induced by propofol given in a dose of 2 mg/kg and rocuronium was given in a dose of 1 mg/kg. Then a laryngoscopy was performed by an anaesthesiologist with a standard Macintosh laryngoscope and the trachea was intubated with an appropriate size cuffed endotracheal tube. Hemodynamic variables; MAP, SBP, DBP, and HR were recorded at 1, 3 and 5 minutes after performing endotracheal intubation. We also recorded any possible complications such as; bradycardia (HR < 50) and hypotension (SBP < 90). All results were expressed as mean  $\pm$  SD. Hemodynamic variables in the present study were analyzed statistically by using by using the analysis of variance (ANOVA) and Student's t-test. *P* values  $\leq$  0.05 were considered significant.

## 3. Results

We evaluated 40 patients including 20 males (50%) and 20 females (50%) with a mean age of  $54.08 \pm 10.25$  years. There was no significant difference between the two groups regarding HR, SBP, DBP and MAP in the patients before induction (base line), 1, 3 and 5 minutes after intubation. Table no 1, 2, 3 and 4 show changes in the hemodynamic variables in both groups.

**Table 1.** Mean Heart Rate in Fentanyl –clonidine and Fentanyl - Lidocaine Groups.

Heart Rate Groups	Fentanyl+clonidine, Mean $\pm$ SD	Fentanyl+Lidocaine, Mean $\pm$ SD	P value
Before induction(baseline)	82.34 $\pm$ 12.42	80.35 $\pm$ 9.4	0.33
1 minutes after intubation	78.26 $\pm$ 8.92	72.16 $\pm$ 8.94	0.08
3 minutes after intubation	72.54 $\pm$ 9.59	71.53 $\pm$ 10.86	0.68
5 minutes after intubation	67.34 $\pm$ 10.24	66.56 $\pm$ 9.86	0.80

There was no significant difference in mean heart rate between the two groups (as shown in Table 1)

**Table 2.** Systolic Blood Pressure in Fentanyl-clonidine and Fentanyl - Lidocaine Groups.

Systolic Blood Pressure Groups	Fentanyl+clonidine ( Mean $\pm$ SD)	Fentanyl+Lidocaine, ( Mean $\pm$ SD)	P value
Before induction	147.46 $\pm$ 22.46	160.30 $\pm$ 24.78	0.15
1 minutes after intubation	121.48 $\pm$ 21.25	122.28 $\pm$ 13.76	0.95
3 minutes after intubation	115.56 $\pm$ 23.24	112.76 $\pm$ 23.18	0.74
5 minutes after intubation	106.24 $\pm$ 20.68	112.34 $\pm$ 28.84	0.52

There was no significant difference between two groups for systolic blood pressure (as shown in table 2)

**Table 3.** Diastolic Blood Pressure in Fentanyl- clonidine and Fentanyl - Lidocaine Groups.

Diastolic Blood Pressure Groups	Fentanyl+clonidine, Mean $\pm$ SD	Fentanyl+Lidocaine, Mean $\pm$ SD	P value.
Before Induction	85.30 $\pm$ 11.26	92.35 $\pm$ 11.64	0.63
1 minutes after intubation	72.38 $\pm$ 10.76	77.34 $\pm$ 12.58	0.28
3 minutes after intubation	72.37 $\pm$ 13.64	72.75 $\pm$ 16.27	0.28
5 minutes after intubation	76.24 $\pm$ 18.68	72.34 $\pm$ 13.84	0.62

There was no significant difference between two groups for diastolic blood pressure (as shown in table 3)

**Table 4.** Mean arterial Pressure in Fentanyl - clonidine and Fentanyl - Lidocaine Groups.

Mean Arterial Pressure Groups	Fentanyl+ clonidine, Mean± SD	Fentanyl+Lidocaine, Mean±SD	P value.
Before Induction	95.40±12.34	99.54±13.46	0.54
1 minutes after intubation	84.46±11.68	87.42±11.82	0.34
3 minutes after intubation	82.72±12.48	83.57±15.27	0.26
5 minutes after intubation	86.24±16.74	82.46±13.64	0.42

There was no significant difference between two groups for mean blood pressure (as shown in table 4)

## 4. Discussion

We found that fentanyl- clonidine and fentanyl – lidocaine combine were equally effective in decreasing hemodynamic stress responses (HR, SBP and DBP) in hypertensive patients. Endotracheal intubation is a stressful noxious stimulus, which result in a marked increase in the release of sympathetic amines (adrenaline and noradrenaline) by stimulating laryngeal and tracheal sensory receptors. This increase in the sympathetic amines leads to complications especially in patient with hypertension. In response to endotracheal intubation, there is increase in blood pressure, increases in heart rate and tachyarrhythmia arising essentially due to sympathetic stimulation. These responses are significantly high, but they are generally well tolerated in normotensive patients, but in patients with hypertension many complications like cerebral hemorrhage/infarction, myocardial ischemia/infarction, left ventricular failure, may occur.[21-24] These hemodynamic responses to intubation were controlled effectively in our patients by using two drugs combine like fentanyl – clonidine and fentanyl- lidocaine. Different previous studies have proved the efficacy of single study drug administration before intubation in normotensive patients. Neither any combination of drug nor any study in hypertensive patients has been done before. Tripathi et al had studied that Clonidine, 2 µg/ kg intravenously, 30 min before induction was safe and effective in preventing the hemodynamic stress response during laparoscopic cholecystectomy.[19] According to Ali et al. pre-treatment with lidocaine improved intra- and post-operative hemodynamic stability during laparoscopic surgery without prolonging recovery.[25] Our study was in line with some previous studies such as Shin et al. that compared the effects of lidocaine, fentanyl, Nicardipine and Esmolol, on the hemodynamic response during intubation and those studies showed that all the agents were effective in producing hemodynamic stability[26] According to Levitt et al. Esmolol and lidocaine had similar efficacies to attenuate moderate hemodynamic responses to intubation in patients with isolated head trauma.[27] Additionally, Malde and Sarode compared lignocaine and fentanyl efficacy on hemodynamic stability and revealed that lignocaine and fentanyl both attenuated the rise in heart rate, however, fentanyl produced better results. Lignocaine attenuated the rise in blood pressure with intubation while fentanyl inhibited it totally.[28] Feng CK et al showed that only

esmolol could reliably offer protection against the increase in both HR and SBP. Low dose of fentanyl (3 micrograms/kg) prevented hypertension but not tachycardia, and 2 mg/kg lidocaine had no effect to blunt adverse hemodynamic responses during laryngoscopy and tracheal intubation.[29] Kulka et al shown that Intravenous Clonidine was effective in reducing Stress Response During Induction of Anesthesia in Coronary Artery Bypass Graft Patients. Marco P et al [30] and Gurulingappa et al in their study found that attenuation of pressor response was seen both with lignocaine and fentanyl upto different extent. Of the two drugs fentanyl 4microgram i.v. bolus provided a consistent, reliable and effective attenuation as compared to lignocaine 1.5mg/kg iv. bolus.[31] So fentanyl at 2mcg/kg might not be sufficient to blunt the stress response alone. Marco P et al also studied that preoperative clonidine attenuated stress response during emergence from anesthesia[32] Matot et al studied the effect of clonidine premedication on hemodynamic responses to microlaryngoscopy and rigid bronchoscopy and found its effectiveness[33] Sameena kousar et al compared effect of Fentanyl and Clonidine for Attenuation of the Haemodynamic Response to Laryngocopy and Endotracheal Intubation and found that Clonidine showed better attenuation of the sympathetic response.[34] Valiallah et al compared Fentanyl and Fentanyl Plus Lidocaine on attenuation of hemodynamic responses to Tracheal Intubation in controlled hypertensive patients undergoing general anesthesia and found that fentanyl and fentanyl plus lidocaine effectively decreased the hemodynamic response to tracheal intubation and fentanyl plus lidocaine was not more effective than fentanyl alone.[35] Our study shown that both FC and FL combine effectively prevented hemodynamic responses to tracheal intubation.

## 5. Conclusion

Our results were limited by the fact that we did not monitor the depth of anesthesia and we did not compare the intragroup hemodynamic variables as our aim was achieved in the study. Fentanyl-clonidine and fentanyl - lidocaine combine are equally effective in decreasing the hemodynamic stress response to tracheal intubation particularly in hypertensive patients. Perioperative haemodynamic stability was an added advantage in both the groups. Study has been limited in choosing the best single drug to prevent stress response particularly in hypertensive patients. So more studies should be taken up wheather combination of drug may be more effective than a single drug.

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