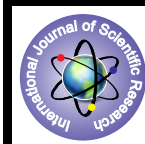


## A Comparative study of Thoracic epidural Clonidine hydrochloride and IV Fentanyl hydrochloride + IV Lignocaine hydrochloride to attenuate hemodynamic response induced by endobronchial intubation



### Medical Science

**KEYWORDS :** Thoracic epidural ,endobronchial intubation,Cardiovascular response

<b>DR. Dipika Patel</b>	Associate Professor Department of Anaesthesia, Gujarat Cancer And Research Institute Ahmedabad, Gujarat, India
<b>DR. Yatrik Ganatra</b>	(3rd Year Resident ) Department of Anaesthesia Gujarat Cancer And Research Institute Ahmedabad, Gujarat, India
<b>DR. Neeta Gosai</b>	(Associate Professor) Department of Anaesthesia Gujarat Cancer And Research Institute Ahmedabad, Gujarat, India
<b>DR. Bijal Shah</b>	(Assistant Professor) Department of Anaesthesia Gujarat Cancer And Research Institute Ahmedabad, Gujarat, India
<b>DR.Rashmi Anand</b>	(Senior Resident) Department of Anaesthesia Gujarat Cancer And Research Institute Ahmedabad, Gujarat, India
<b>DR. Bipin Patel</b>	(HOD And Professor) Department of Anaesthesia Gujarat Cancer And Research Institute Ahmedabad, Gujarat, India

### ABSTRACT

*Objective: To compare the effect of Thoracic epidural Clonidine hydrochloride and IV Fentanyl citrate + IV Lignocaine hydrochloride to attenuate hemodynamic response to endobronchial intubation in thoracotomy.*

*Method: 60 patients with ASA- I & II with age group 20 to 65yrs scheduled for elective thoracotomies were randomly allocated in two groups. General anesthesia was provided with endobronchial intubation. Group A :Clonidine 3mcg/kg diluted with 10ml saline given as epidural bolus 20 minutes before induction. Group B:10ml of NS as epidural bolus 20 min before induction & Iv fentanyl citrate(2 mcg/kg) and lignocaine hydrochloride(2 mg/kg) during induction. Haemodynamic variables were continuously recorded. Results:*

*After Induction, In group A, decrease in Mean BP and HR from baseline were statistically significant compared to group B. After Endobronchial intubation, haemodynamic change in Group A showed very less haemodynamic variation as compared to Group B. (P<0.005)*

*Summary: Clonidine at high thoracic epidural effectively blunted the CVR associated with laryngoscopy and Endobronchial intubation as compared to IV Fentanyl +IV Lignocaine.*

### Introduction

Laryngoscopy and intubation usually results in increased blood pressure and heart rate. This occurs partly due to reflex sympathetic discharge. These responses are particularly deleterious in patient with limited cardiac reserve.

Since the classic description of laryngospasm by Fink in 1956, anaesthesiologists were constantly trying to unlock the mechanism and pathway of airway reflexes and methods to prevent these unwanted side effects.<sup>5</sup> Many anaesthetic adjuvants have been used to blunt these haemodynamic responses. Amongst them, Opioids and lidocaine have been most commonly used adjuvants, but studies have revealed their less effectiveness in blunting CVR.<sup>7</sup>

Clonidine hydrochloride, an alpha 2 adrenoreceptor agonist, is used as an antihypertensive and as an analgesic drug, can be administered via various routes e.g. oral, intravenous, spinal and epidural. High thoracic Clonidine has been seen to decrease blood pressure and heart rate by its spinal sympatholytic action.

So, we designed the present study to compare the attenuation of haemodynamic responses to laryngoscopy and intubation by high thoracic epidural Clonidine HCl (3mcg/kg) and by i.v. Fentanyl (2mcg/kg) plus i.v. Lidocaine (2 mg/kg).

### Materials and Methods

With the approval of our institutional ethical committee and obtaining written informed consent from all patients, this prospective randomized control study was conducted. In our study, we included 60 patients of ASA class I & II of either sex, with Mallampati grade I and II, age group between 20 and 65 yr undergoing thoracotomy for lung, oesophageal and mediastinal surgeries under general anaesthesia and epidural analgesia.

### Exclusion criteria were

1) Patients with contraindication for central neuraxial block-

ade.

- 2) Patients with cardiovascular disease, renal and hepatic disease.
- 3) Patients with diabetes mellitus.
- 4) Obese and cachectic patients.
- 5) Expected difficult intubation.

Patients were randomly allocated into two groups of 30 patients in each by computer generated numbers.

All patients were pre-medicated with tab Lorazepam 1 mg PO on the night before surgery, tab Diazepam 5 mg PO on the day of surgery, Inj Atropine Hydrochloride 0.02 mg/kg IM 60 min before induction of GA.

All patients were preloaded with 500 ml of lactated ringer solution, given over 10 min, 20 min prior to induction of GA. In all patients, under all aseptic and antiseptic precautions, epidural puncture was made via median approach at T6-T7 or T7-T8 intervertebral space using 18G Tuohy needle with loss of resistance technique and 20G epidural catheter was advanced 3cm cephalic. Aspiration test done for blood and cerebrospinal fluid.

Group A (Clonidine group, n=30) 3 mcg/kg of clonidine diluted in 10 ml of normal saline was injected as epidural bolus 20 min prior to induction of GA.

Group B (Fentanyl + Lidocaine group, n=30) 10 ml of normal saline was injected as epidural bolus 20 min prior to induction of GA but received i.v. Fentanyl (2mcg/kg) plus Lidocaine (2 mg/kg)

In the operating room, standard 5 lead ECG, non-invasive blood pressure and pulse oximetry were attached and baseline haemodynamic parameters were noted.

Anaesthesia was induced with i.v. Thiopentone 5mg/kg and en-

dobronchial intubation was facilitated with i.v. Vecuronium 0.1 mg/kg. After 3 min of oxygenation. Intubation was done with double lumen tube, either right or left Broncho-cath as per requirement of surgery . Duration of laryngoscopy and intubation were limited to less than 30 sec and cases with single attempt intubation were included in the study. Tube placement was confirmed within 3 min by inspection and auscultation. Ventilation was controlled and anaesthesia was maintained with Isoflurane (2%) in a mixture of 50% of Oxygen and 50% of Nitrous oxide + vecuronium bromide.

Mean blood pressure and heart rate was measured and recorded at following intervals.

- T1- Base line value.
- T2- 20 min after epidural bolus.
- T3- Immediately after induction of anaesthesia.
- T4- 1 min after intubation.
- T5- 3 min after intubation.
- T6- 5 min after intubation.
- T7- 10 min after intubation.
- T8- 20 min after intubation

Statistical analysis were performed using the software SAS version 8.1. Data were expressed as mean ± SD. Patients characteristics were analysed using Chi square test and analysis of variance (ANOVA) for continuous variables. Intergroup comparison were performed using ANOVA. P<0.05 was considered significant, P<0.001 was taken as highly significant and P>0.05 was regarded as non-significant.

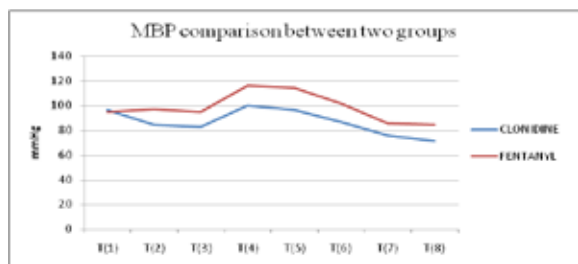
**Results**

**Table 1[Demographic data]**

GROUP	AGE(years)	WEIGHT(kg)	SEX(M:F)
Group A	44.6±12.38	47.08±9.14	19:6
Group B	44.4±12.75	47±7.47	19:6

Sixty patients were enrolled in our study. The two groups were comparable with respect to age, sex and weight [ table 1] with no statistically significant difference.

**Chart-1**



**Chart 2**

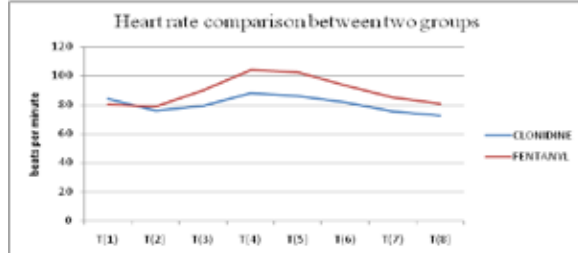


Chart 1 shows comprehensive and statistical changes in Mean Arterial Pressure of patients at fixed time interval in both groups. Baseline MAP (T1) of two groups is not statistically significantly different. After epidural(T2) MAP decreased from baseline in Group A, while in Group B it rose. After intubation (T4) MBP remained near to base line in group A, but in Group B its increased significantly compared to baseline , which was statistically significant. MBP fell at T5, T6 and T7 in both groups but

in Group B, MAP was significantly higher compared to Group A. P value <0.05 shows that there was statistically significant change in mean blood pressure in both groups.

Chart 2 shows comprehensive and statistical changes in Heart Rate per minutes in both groups compared with preoperative in both groups. Base line HR (T1) of two groups are statistically significantly different. After epidural drug(T2)HR decreased from baseline in Group A, and slightly increased in Group B. After induction (T3), HR remained below baseline in Group A, while in Group B it increased significantly, which is statistically significant. After intubation (T4), HR rose in both group but more in Group B as compared to Group A, which was statistically significant. HR fell at T5, T6 and T7 in both groups but in Group B, HR was significantly higher compared to Group A.

**Discussion**

Distribution of airway receptors is richest in larynx and more concentrated in the proximal portion of the tracheo-bronchial tree.<sup>1,2</sup> In addition, characteristics of these receptors become more chemo-sensitive and less mechano-sensitive in distal portion.<sup>3</sup> Afferent inputs from the lung and airways travel along Vagus and sympathetic nerve to upper thoracic segment,<sup>4</sup> where as those from laryngo-pharyngeal area traverse through the 9<sup>th</sup> and 10<sup>th</sup> cranial nerve to Vaso Motor Centre (VMC)<sup>5</sup>. Reflex changes in the cardiovascular system after laryngoscopy and intubation are most marked<sup>6</sup>. They manifest themselves in the form of tachycardia, hypertension and cardiac arrhythmias.<sup>6</sup> Cardiovascular responses to intubation have been attributed to reflex sympathetic discharge caused by stimulation of the upper respiratory tract. Efferent sympathetic outflow to the heart originates from the spinal cord between T1 and T4. So it can be possible to attenuate these harmful haemodynamic responses by blocking these cardiac fibres originating from T1-T4 with the help of high thoracic epidural treatment.<sup>7,8</sup>

High thoracic epidural anaesthesia (TEA) significantly prolongs the action potential duration and refractoriness at higher heart rate, thus TEA may have anti-arrhythmic properties, especially in situations that results in shortening of repolarization, such as ventricular and atrial tachyarrhythmia and increased sympathetic tone and myocardial ischaemia.<sup>7,8</sup>

Traditionally, many drugs have been tried to prevent these haemodynamic responses. Amongst them, i.v. Fentanyl citrate (2 mcg/kg) and i.v. Lidocaine HCl (1.5 mg/kg) pre-treatment has remained as agent of choice for years. But many studies have revealed its little effectiveness for desired response.<sup>9,10</sup>

Licker m,forinelli c et al<sup>7</sup> studied "Cardiovascular reflex during induction and endotracheal intubation in elderly patients -the influence of thoracic epidural anethesia".In their study 10 patients undergone colonic and gastric surgery under thoracic epidural anaesthesia +GA compared with 10 patients under GA without thoracic epidural.In epidural analgesia 1% Lidocaine was used. Epidural group presented attenuation of maximum rise in MAP and HR although not significant.

Klaus kirno et al<sup>11</sup> and Torsten Gordh Jr et al<sup>12</sup> studied that Clonidine can a reduce blood pressure by inhibiting the sympathetic nervous system activity and enhancing the activity of parasympathetic activity in the brain stem. Epidural Clonidine is absorbed by the systemic circulation and CSF thus can affect the brain stem. Epidurally administered Clonidine decreases sympathetic outflow by supraspinal mechanism.

Su choi et al<sup>13</sup> compared the effects of epidural clonidine(3 mcg/kg) with fentanyl citrate 2 mcg/kg iv and lignocaine hydrochloride 1 mg/kg iv on hemodynamic responses to endobronchial intubation.In clonidine Group, after 20 min of epidural Clonidine administration Reduction of MBP was 10.7% while HR decreased by 8.33% as compared to baseline . After anaesthetic induction, MBP further reduced by 15.6% compared to baseline, while HR reduced by 7.14% compared to baseline [T1] value. With laryngoscopy and intubation, there was rise of MBP and HR which was 4.9% increment in MBP and 4.16% increment in HR compared to baseline.they concluded that epi-

dural clonidine was more effective in suppressing hemodynamic responses to endobronchial intubation compared to lignocaine fentanyl group.

In our study, in Group A, after 20 min of epidural Clonidine administration [T2]. Reduction of MBP was 12.5% while HR decreased by 10.7% as compared to baseline [T1] while in Group B slight increase in BP but decrease in HR. After anaesthetic induction, MBP further reduced by 17% compared to baseline, while HR increased compared to T2 value but remained reduced by

4.7% compared to baseline [T1] value. With laryngoscopy and intubation, there was rise of MBP and HR which was 5% increment in MBP and 2.4% increment in HR compared to baseline.

### Conclusion

Clonidine injected via a thoracic epidural route is an effective mean of reducing the cardiovascular response to laryngoscopy and intubation as compared to intravenous Fentanyl and Lidocaine .

## REFERENCE

1. Widdicombe JG: Pulmonary and respiratory tract receptors. *J Exp Biol* 1982; 100:41-57 | 2. Sant' Ambrogio G: Nervous receptors of the tracheobronchial tree. *Ann Rev Physiol* 1987; 49:611-27 | 3. Karlsson JA, Hansson L, Wollmer P et al: Regional sensitivity | of the respiratory tract to stimuli causing cough and reflex | bronchoconstriction. *Respiratory Med* 1991; 85(suppl A):47-50 | 4. Randall WC. Sympathetic control of the heart. In: Randall WC, ed. *Neural regulation of the heart*. Oxford: Oxford University Press, 1977: 45-94. | 5. Boles R. Neuroanatomy for the otolaryngologist. In: Paparella MM, Shumrick DA, eds. *Otolaryngology*, vol. 1: basic science and related disciplines. Philadelphia: WB Saunders, 1973: 186-232. | 6. Laryngel reflex. *Anesthesiology* 1998;88: 1433-34 | 7. Licker M, Farinelli C, Klopfenstein CE. Cardiovascular reflexes during anaesthesia induction and tracheal intubation in elderly patients: the influence of thoracic epidural anaesthesia. *J Clin Anesth*. 1995 Jun; 7(4):281-7 | 8. Andreas Meissner, Lars Eckardt, Paulus Kirchhof, Effects of Thoracic Epidural Anesthesia with and without Autonomic Nervous System Blockade on Cardiac Monophasic Action Potentials and Effective Refractoriness in Awake Dogs. *Anesthesiology* 2001; 95:132-8 | 9. Bruder N, Granthil C, Ortega D. Consequences and prevention methods of hemodynamic changes during laryngoscopy and intubation. *Ann Fr Anesth Reanim* 1992; 11(1):57-71. | 10. Steven M, Which Drug Prevents Tachycardia and Hypertension associated with Tracheal Intubation: Lidocaine, Fentanyl, or Esmolol. *Anesth-analg* 1991, 72: 482-486 | 11. Stefan lundin, Mikael elam. Epidural clonidine depresses sympathetic nerve activity in humans by supraspinal mechanism. *Anesthesiology* 78:1021-1027,1993 | 12. Torsten Gordh Jr, Ulla Feuk, Karin Norlen. Effect of Epidural Clonidine on Spinal Cord Blood Flow and Regional and Central Hemodynamics in Pigs. *Anesth Analg* 1986;65: 1312-8 | 13. SU Choi et al, Thoracic epidural clonidine attenuates hemodynamic responses induced by endobronchial intubation. |