Original Research Article

# Comparison between oral clonidine and oral pregabalin as premedication to attenuate pressor response to direct laryngoscopy and endotracheal intubation

**Dubagunta Naga Likhitha[1], Nayan Sriramula[2], R. Rajeshwar Reddy[3*], K.S.S.G.C.Kumar[4]**

*[1]Postgraduate, Department of Anaesthesiology, Alluri Sitarama Raju Academy of Medical Sciences, Eluru, West Godavari District, Andhra Pradesh, India*

*[2]Post Graduate, Department of Emergency Medicine, Narayana Medical College Hospital, Nellore, Andhra Pradesh, India*

*[3]Assistant Professor, Department of Anaesthesiology, Alluri Sitarama Raju Academy of Medical Sciences, Eluru, West Godavari District, Andhra Pradesh, India*

*[4]Professor, Department of Anaesthesiology, Alluri Sitarama Raju Academy of Medical Sciences, Eluru, West Godavari District, Andhra Pradesh, India*

**Received: 20-11-2021 / Revised: 22-12-2021 / Accepted: 05-01-2022**

## Abstract

**Background:** Laryngoscopy and endotracheal intubation are the modern routine procedures of balanced general anaesthetic technique. Laryngoscopy and tracheal intubation induced pressor responses have been associated with increased catecholamine levels. So, it is important to find an effective means by attenuating the sympathetic response to laryngoscopy and intubation. Pregabalin decreases pre-operative stress and anxiety response to intubation. Premedication with Clonidine is to produce sedation and blunt the stress response to intubation. **Aim:** To compare the efficacy of Oral CLONIDINE with Oral PREGABALIN as premedication to attenuate pressor response to direct laryngoscopy and endotracheal intubation. **Materials and methods:** This was a prospective study, approved by the institutional ethical committee. A total of 60 patients undergoing elective surgery were selected A total of 60 patients were divided into two groups of 30 each, group C (clonidine), and groupP (pregabalin). careful preanesthetic evaluation should be done for all the patients. A valid informed consent should be obtained both for conduct of study as well as for surgery and anaesthesia. Patients should be kept nil per oral from midnight before surgery. **Discussion:** Induction of general Anaesthesia, direct laryngoscopy and endotracheal intubation attenuates marked cardiovascular changes and also the activity of autonomic reflex. The response may be particularly haphazard to the patients with cardiovascular and cerebral diseases. Most of the studies have reported the use of oral Clonidine premedication to prevent hyper-adrenergic and dynamic cardiovascular responses to endotracheal intubation have been successful. Pregabalin had been shown to be effective in neuropathic pain, diabetic neuropathy, acute post-operative pain and decreasing the postoperative opioid requirements. **Conclusion:** Clonidine was found to be more effective than Pregabalin in lowering of blood pressure and heart rate changes associated with laryngoscopy and intubation. Pregabalin when compared with Clonidine gives better postoperative analgesia, more sedation and less bradycardia.

**Keywords:** Clonidine, Pregabalin, direct laryngoscopy, endotracheal intubation.



## Introduction

Laryngoscopy and endotracheal intubation are routine procedures of modern balanced general anesthesia technique. Endotracheal intubation has become an integral part of the anaesthetic management and critical care of the patient and has been practiced following its description by Rowbotham and Magill in 1921.Forbes and Dally (1970) described the circulatory response to laryngeal and tracheal stimulation following laryngoscopy and tracheal intubation as reflex sympathoadrenal stimulation. Although increase in heart rate and blood pressure due to sympathoadrenal response is short lived they may have detrimental effects in high-risk patients especially those with cardiovascular diseases, increased intracranial pressure or anomalies of cerebral vessels. Laryngoscopy and tracheal intubation have been associated with increased catecholamine levels inducing pressor responses. Norepinephrine, epinephrine levels rise. Rise of these catecholamine levels are associated with increasing in blood pressure and heart rate.

*Correspondence
**Dr. R. Rajeshwar Reddy**
Assistant Professor, Department of Anaesthesiology, Alluri Sitarama Raju Academy of Medical Sciences, Eluru, West Godavari District, Andhra Pradesh, India.
**E-mail:** sasramlibrary@gmail.com

Some authors have been considered the intubation period as one of the greatest risk in patients with coronary artery diseases undergoing surgeries. Although the response may be transient, it is invariable, significant, often persistent, and of great concern. The techniques of laryngoscopy and tracheal intubation are not only confined to the operating room, but are also successfully employed for non-anaesthetic purposes. Few instances are diagnostic laryngoscopy, fiber-optic bronchoscopy, intubation may be required for prevention of aspiration and protection of airway and mechanical ventilation. All these procedures can also produce sympathetic responses and one should keep in mind that many of these patients are at increased risk or critically ill. Therefore, it is important to find an effective means of attenuating sympathetic response to laryngoscopy and intubation. Many strategies have been advocated to minimize the hemodynamic adverse responses and aimed at different levels of the reflex arc E.g.:

- Block of the peripheral sensory receptors and afferent input - topical application and infiltration of superior laryngeal nerve.
- Block of the central mechanisms of integration of sensory input - fentanyl, morphine, droperidol etc.
- Block of the efferent pathway and effector sites - IV lignocaine, β-blockers, calcium channel blockers, hydralazine etc.

No single drug or technique is satisfactory. PREGABALIN a gabapentinoid compound is structurally related to the inhibitory neurotransmitter Gamma Amino Butyric Acid(GABA), but not

functionally related to it. It acts by decreasing the synthesis of neurotransmitter glutamate to act on the central nervous system and possess analgesic, anticonvulsant and anxiolytic activity. It was observed that it reduces pre-operative anxiety and stress response to intubation. But there are very few randomized controlled trials to prove that they are the same. CLONIDINE, an imidazole compound acts mainly by central α2 adrenoceptor stimulation resulting in diminished sympathetic flow. Clonidine suppresses induced central noradrenergic hyperactivity to attenuate reflex cardiovascular response to tracheal intubation and to improve stability during surgery. Clonidine premedication is to produce sedation and blunt the stress response to intubation. Hence the present study has been taken to compare oral pregabalin with oral clonidine on attenuating the haemodynamic stress response to laryngoscopy and endotracheal intubation during general Anaesthesia.

**Materials and methods**

The present clinical observative, prospective study was conducted between September 2020 – October 2021 at Alluri Sitarama Raju Academy of Medical Sciences, Eluru. It was a prospective study. A total number of 60 patients undergoing elective surgery has been selected.

**Inclusion criteria**

1. Patients aged between 18 to 50 years of age of both genders.
2. American society of anesthesiologist grade I and II patients.
3. Patients with Mallampatti airway grade I and II.
4. Patients undergoing elective major or minor surgical procedures under general anaesthesia.

**Exclusion criteria**

1. Patient's refusal.
2. patients aged below 18 years and above 50 years.
3. Patients with Mallampatti airway grade III and IV
4. Patients with comorbities like Hypertension, Ischemic Heart Diseases,
    1. Arrhythmias, Renal, Respiratory, Cerebral Diseases, Asthmatics andEpileptics.
5. Anticipated difficult intubation.
6. If patient is allergic to any of drugs used in the study.
7. Patients taking sedatives, hypnotics.
8. Pregnancy.
9. Emergency procedures.
10. Laryngoscopy duration of >20 seconds or more than 1 attempt of laryngoscopy.

A total of 60 patients were divided into two groups of 30 each, group C (clonidine), and groupP (pregabalin).

Careful pre anesthetic evaluation was done for all the patients. Written, valid informed consent was obtained both for conduct of study as well as for surgery and anesthesia. Patients should be kept nil per oral from midnight before surgery and Tab. Alprazolam (0.25 mg) was administered.

- Nil per oral status confirmed in the morning and patient's baseline Systolic blood pressure (SBP), Diastolic blood pressure (DBP) and heart rate must be recorded.
- During this period, 60 patients were selected.
- They were divided into two groups:
  GROUP C(n=30): Received Tab CLONIDINE 0.3mg.
  GROUP P(n=30): Received Tab PREGABALIN 150mg.
- Group C received tab CLONIDINE (0.3mg) and Group P received tab PREGABALIN (150mg) with sips of water, 60 minutes before the expected time of induction of anaesthesia.
- Preparation of the operation theatre:

The anaesthesia workstation was checked. Appropriately sized endotracheal tubes, working laryngoscope with medium and large sized blades and working suction apparatus were kept ready before induction.

**Procedure**

Patients in each group received respective drugs as per timing and dose mentioned earlier. On arrival in the operating room, patient's basal parameters- Heart Rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MBP), Rate Pressure Product (RPP) and Electrocardiography are monitored using, pulse oximetry, non-invasive blood pressure (NIBP), and ECG monitor. Intravenous access using 18G cannula was established and an IV infusion of ringer lactate was started. All patients were pre oxygenated with 100% oxygen for 3 minutes before induction with a tight fitting face mask.All the patients were premedicated with intra venous metoclopramide 10mg, Glycopyrrolate 0.2 mg, and Fentanyl 2mcg/kg. After preoxygenation, patients in each group was induced with thiopentone sodium 5mg/kg IV slowly till the loss of eyelash reflex. This was followed by Vecuronium bromide 0.1mg/kg IV. Patient's lungs were manually ventilated with 100% oxygen before orotracheal intubation. Direct laryngoscopy performed after 3 minutes by using appropriately sized Macintosh blade and tracheal intubation performed within 15 seconds using appropriate cuffed endotracheal tube.

**Results**

Following were observations and results of the present study.

**Table 1: Comparison of mean heart rate (mean±sd, beats/min) between groups (N=60)**

| Time of assessment | Clonidine(n=30) | | Pregabalin(n=30) | | t value | P value |
|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | | |
| Baseline | 85.03± | 7.93 | 87.67 | 5.34 | 1.431 | 0.163 |
| Pre induction | 64.77 | 8.95 | 82.33 | 13.52 | 1.800 | 0.082 |
| Post induction | 71.77 | 9.92 | 86.06 | 12.02 | 4.549 | 0.001 |
| 1 minute | 78.4 | 9.14 | 96.66 | 14.15 | 5.753 | 0.001 |
| 3 minutes | 75.36 | 8.72 | 91.43 | 12.43 | 5.933 | 0.001 |
| 5 minutes | 73.16 | 8.97 | 87.33 | 11.27 | 5.767 | 0.001 |
| 10 minutes | 71 | 8.49 | 84.4 | 11.27 | 4.818 | 0.001 |

**Table 2: Comparison of mean systolic blood pressure (MEAN±SD, mmhg) BETWEEN GROUPS (N=60)**

| Time of assessment | Clonidine(n=30) | | Pregabalin(n=30) | | t value | P value |
|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | | |
| Baseline | 123.33 | 12.25 | 119.83 | 10.41 | -1.380 | 0.178 |
| Pre induction | 121.03 | 12.90 | 123.93 | 12.28 | 0.817 | 0.421 |
| Post induction | 114.53 | 11.33 | 113.06 | 12.86 | -0.491 | 0.627 |
| 1 minute | 129.06 | 13.27 | 131.4 | 15.43 | 0.587 | 0.562 |
| 3 minutes | 123.3 | 14.07 | 120.8 | 18.84 | -0.588 | 0.561 |
| 5 minutes | 119.26 | 14.98 | 115.63 | 19.38 | -0.800 | 0.430 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 10 minutes | 117 | 14.98 | 113.13 | 18.01 | -0.948 | 0.351 |

**Table 3: Comparison of mean diastolic blood pressure (MEAN±SD, mmHg) between groups (N=60)**

| Time of assessment | Clonidine(n=30) | | Pregabalin(n=30) | | t value | P value |
|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | | |
| Baseline | 75.06 | 3.65 | 73.36 | 4.38 | -1.937 | 0.063 |
| Pre induction | 71.2 | 11.35 | 75.03 | 6.92 | 1.557 | 0.130 |
| Post induction | 69.63 | 9.14 | 68.48 | 9.29 | -0.497 | 0.623 |
| 1 minute | 81 | 9.35 | 82.1 | 11.66 | 0.404 | 0.689 |
| 3 minutes | 78.43 | 8.91 | 74.33 | 13.35 | -1.724 | 0.095 |
| 5 minutes | 73.53 | 10.78 | 71.1 | 14 | -0.791 | 0.435 |
| 10 minutes | 72.33 | 9.84 | 69.6 | 12.42 | -0.951 | 0.350 |

**Table 4: Comparison of mean arterial pressure (MEAN±SD, mmHg) between groups (N=60)**

| Time of assessment | Clonidine(n=30) | | Pregabalin(n=30) | | t value | P value |
|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | | |
| Baseline | 91.16 | 4.61 | 89.56 | 4.93 | -1.275 | 0.212 |
| Pre induction | 88.83 | 10.59 | 92.9 | 8.15 | 1.536 | 0.135 |
| Post induction | 85.46 | 8.55 | 84.66 | 9.07 | -0.379 | 0.708 |
| 1 minute | 98.2 | 9.25 | 99.56 | 11.72 | 0.486 | 0.631 |
| 3 minutes | 94.8 | 10.38 | 91.2 | 13.91 | -1.300 | 0.204 |
| 5 minutes | 89.83 | 10.40 | 87.3 | 14.23 | -0.801 | 0.430 |
| 10 minutes | 88.23 | 9.96 | 85.73 | 12.31 | -0.866 | 0.394 |

**Discussion**

Induction of general Anaesthesia, direct laryngoscopy and endotracheal intubation induce marked cardiovascular change and also the activity of autonomic reflex. The response may be particularly haphazard to the patients with cerebral and cardiovascular diseases. Attenuation of these haemodynamic responses is generally of great importance in preventing the peri-operative morbidity and mortality. Typically blood pressure and heart rate elevations occur after about 15 seconds of laryngoscopy and become maximal after 30-45 seconds of laryngoscopy. A rise in mean heart rate of 29.9 beats/minute has also been noted. Strategies to circumvent these changes have included minimizing the duration of laryngoscopy, IV Narcotics, IV and topical Lidocaine, vasodilators, Beta- blockers, Calcium channel blockers, inhaled anaesthetics. Although these drugs did obtund the cardiovascular response, they failed to fulfil the desired criteria of complete attenuation. Variation of heart rate changes decrease with increasing age. Young patients show more extreme changes. Marked fluctuations in haemodynamic response are often seen in geriatric patients. In our study, we selected an optimal age range of 18 to 50 years. Patients on antihypertensive drugs may exhibit a decrease in pressor response. We excluded the patients with antihypertensive medications from the study.

**Conclusion**

The following conclusions can be drawn from this study. Both oral Clonidine 0.3mg and Oral Pregabalin 150mg effectively attenuates the haemodynamic response to laryngoscopy and endotracheal intubation. Clonidine was found to be more effective than Pregabalin in decreasing the blood pressure and heart rate changes associated with laryngoscopy and endotracheal intubation. Pregabalin when compared to Clonidine gives better postoperative analgesia, more sedation, and less bradycardia.

**References**


1. Millar Forbes A., Dally FG. Acute hypertension during induction of Anaesthesia and endotracheal intubation in normotensive man. Br J Anaesth 1970; 42: 618-623.
2. Bachofen M. Suppression of blood pressure increases during intubation: Lidocaine or fentanyl Anesthesist 1988; 37(3): 156-61.
3. Vincent J.Collins. Principles of anesthesiology, general and regional anesthesia. 3rd Edn, Vol.I and II, Philadelphia: Lea and Febiger, 1993.
4. KoSh, Kim DC, Han YJ, Song HS. Small doses of fentanyl: optimal time of injection for blunting the circulatory responses to tracheal intubation. Anesth Analg1998; 86 (3): 658-61.
5. Rastogi B, Gupta K, Gupta PK, Agarwal S, Jain M, Chauhan H. Oral pregabalin premedication for attenuation of haemodynamic pressor response of airway instrumentation during general anaesthesia: A dose response study. Indian J Anaesth. 2012;56(1):49.
6. Marchal JM, Gómez-Luque A, Martos-Crespo F, Sánchez De La Cuesta F, Martinez-López, MC, Delgado-Martinez AD. Clonidine decreasesintraoperative bleeding in middle ear microsurgery. ActaAnaesthesiol Scand. 2001;45(5):627-33.
7. Roy S, Gupta RA, Mondal T, chakravorty S. Attenuation of cardiovascular responses to laryngoscopy and tracheal intubation with oral clonidine. Indian J Anaesth. 1993; 41:62-6.
8. Kumkum Gupta, Deepak Sharma, and Prashant K.Gupta.Oral premedication with pregabalin or clonidine for hemodynamic stability during laryngoscopy and laparoscopic cholecystectomy.Saudi J Anaesth. 2011 Apr-Jun; 5(2): 179–184.
9. Ismail S, Azam SI, Khan FA. Effect of age on haemodynamic response to tracheal intubation. A Comparison of young middle aged and elderly patients. Anaesth Intensive care. 2002;30(5):608-614.
10. Ghignone M, Cavillo , Quintin L. Anesthesia and hypertension: the effect of clonidine on perioperative hemodynamics and isoflurane requirements. Anesthesiology. 1987; 67:3-10.
11. Martindale: The complete drug reference. Edited by Sean C. Sweetman. 35th ed. Pharmaceutical Press London. 2007.
12. Pregabalin. Available on hitp://www.drugs.com/odi/pregabalin.html. Accessed on 13th me 2013.
13. Ferguson, George A., Takane, Yoshio. "Statistical analysis in Psychology and education". 6th edition. Montreal, Quebec; MC graw- Hill Ryerson Limited: 2005.
14. J.E. Park. Health information and Basic Medical Statistics. In: J.E park, editor. Text book of preventive and social medicine.19th edition. Elseiver: 2007; p.692-706.
15. Tuck ML. The sympathetic nervous system in essential hypertension. Am Heart J. 1986; 112:877.
16. Noel W L. Joel O J. Autonomic nervous system In: Physiology & pharmacology clinical Anaesthesia. 2006 5th ed. 275-333.
17. Arthur ww et al. Effect of Clonidine on Cardiovascular Morbidity and Mortality after noncardiac surgery. Anesthesiology. 2004; 101:284–93.

18. Maze M, Tranquilli W. Alpha 2 adrenoceptor agonists: Defining the role in clinical anaesthesia. Anesthesiology. 1991; 74:581-605.
19. Stieger DS, Cantieni R, Frutiger A. Acute colonic pseudoobstruction (Ogilvie's syndrome) in two patients receiving high dose Clonidine for delirium tremens. Intensive Care Med. 1997; 23:70-782.
20. KD Tripathi. Drugs acting on central nervous system. In: Essentials of medical pharmacology 5th ed. Jaypee Brothers Medical Publishers Ltd. 2003; Chapter 7:369-381.
21. Paul F White, Alejandro RF. Ambulatory anaesthesia. In: Miller's Anaesthesia 6th ed. Elsevier Ltd. 2005; Chapter 68:5759-5863.
22. Sujata B, G Singh, R Jacob. Clonidine in paediatrics: A review. Indian J Anaesth. 2009; 53:270-80.
23. SunitaGoel, Manju Sinha. Effect of Oral Clonidine Premedication in Patients Undergoing Laparoscopic Surgery. BMJ. 2006; 333:519.
24. IditMatot MD, JY. Sichel, MD, Valeri Yofe MD, YaacovGozal MD. The Effect of Clonidine Premedication on Hemodynamic Responses to Microlaryngoscopy and Rigid Bronchoscopy. Anaesthesia & Analgesia. 2000;91(4):828-833.
25. Yotsui T. Clonidine premedication prevents sympathetic hyperactivity but does not prevent hypothalamo-pituitary-adrenocortical responses in undergoing laparoscopic cholecystectomy.JAnesth. 2001:15(2):78-82.
26. HP. Yu, S.S. Hseu, HW. Yien, YH. Teng, KH. Chan. Oral Clonidine premedication preserves heart rate variability for patients undergoing larparoscopic cholecystectomy. ActaAnaesthesiologicaScandinavica. 2003;47(2):185-190
27. Manjushree Ray, DhurjotiProsadBhattacharjee, BimalHajra, Rita Pal, Nilay Chatterjee. Effect of Clonidine and Magnesium sulphate on anaesthetic consumption, haemodynamics and postoperative recovery: A comparative study. 2010,54(2):137-141.
28. Amirul Islam, Mozaffer Hossain, AKM Akhtaruzzaman, UH Shaherakhatun. Study on role of oral Clonidine in laparoscopic cholecystectomy surgery – a comparative study. Journal of BSA. 2008:21(1). Vol. 21, No. 1
29. Shivinder Singh, Kapil Arora. Effect of oral Clonidine premedication on perioperative haemodynamic response and postoperative analgesic requirement for patients undergoing laparoscopic cholecystectomy. Indian J Anaesth. Jan-Feb 2011; 55(1): 26–30.

**Conflict of Interest: Nil Source of support: Nil**