International Journal of Medical and Pharmaceutical Research

Online ISSN-2958-3683 | Print ISSN-2958-3675
Frequency: Bi-Monthly
Available online on: https://ijmpr.in/

Original Article

A Comparative Study of Oral Clonidine and Oral Pregabalin in Attenuating Hemodynamic Pressor Response during Laryngoscopy and Tracheal Intubation

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OPEN ACCESS

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Received: 15-12-2025
Accepted: 11-01-2026
Available online: 01-02-2026

ABSTRACT

Background: Strong unpleasant stimuli like laryngoscopy and endotracheal intubation cause sympathetic reactions that raise myocardial oxygen demand, cause tachycardia, and raise blood pressure. Particularly in people with cardiovascular problems, these brief haemodynamic alterations may be harmful. Numerous pharmaceutical substances have been investigated to reduce this reaction. Pregabalin, a gabapentinoid with analgesic and anxiolytic effects, and clonidine, an α2-adrenergic agonist, have demonstrated promise as oral premedications.

Methods: This prospective, randomized study was conducted on 90 adult patients aged 18–60 years, belonging to ASA physical status I and II, scheduled for elective surgeries under general anesthesia. Patients were randomly allocated into two groups of 45 each. Oral pregabalin 75 mg and clonidine 300 µg were given to Group P and Group C, respectively, 120 minutes prior to induction. HR (Heart Rate), SBP (Systolic Blood Pressure), DBP (Diastolic Blood Pressure), MAP (Mean Arterial Pressure), and RPP (Rate Pressure Product) were measured at baseline, following medication administration, prior to induction, during laryngoscopy, and 1, 5, 10, and 15 minutes following intubation. Both parametric and non-parametric tests were used in the statistical analysis.

Results: Pregabalin and clonidine both markedly reduced the haemodynamic pressor response to intubation and laryngoscopy. But at most time intervals, especially during and after intubation, clonidine showed better control over HR, SBP, DBP, MAP, and RPP. At a number of important observation points, the two groups' differences were statistically significant ($p < 0.05$). No significant adverse effects such as bradycardia, hypotension, or respiratory depression were observed in either group.

Conclusion: When it comes to reducing the haemodynamic pressor response related to laryngoscopy and endotracheal intubation, oral clonidine 300 µg works better than oral pregabalin 75 mg. This results in improved perioperative haemodynamic stability with minimal adverse effects.

Keywords: *Hemodynamic Pressor Response, Laryngoscopy, Endotracheal Intubation, Clonidine, Pregabalin.*

INTRODUCTION

Before endotracheal intubation, laryngoscopy is a highly invasive and unpleasant stimulation.[1] Increased circulating catecholamines, tachycardia, hypertension, increased myocardial oxygen consumption, and the emergence of cardiac dysrhythmias are all signs of a significant sympathetic reaction brought on by manipulation of the respiratory tract during laryngoscopy and tracheal intubation.[2] An essential measure of cardiac workload and haemodynamic stress is the rate pressure product, which is computed as the product of heart rate and systolic blood pressure.

The force used and the length of the laryngoscopy are directly correlated with the size of this pressor response. In patients with underlying cardiovascular or cerebrovascular disease, these transient but pronounced hemodynamic changes may precipitate serious complications such as myocardial ischemia, arrhythmias, cerebrovascular accidents, and increased perioperative morbidity and mortality. Consequently, several pharmacological strategies have been explored to attenuate this response.

A few strategies to reduce the pressor response include making sure that the anaesthesia is deep enough, keeping the laryngoscopy time under 15 seconds, and using pharmacological agents like vasodilators (nitroglycerine and sodium nitroprusside)[3] calcium channel blockers (diltiazem),[4] local anaesthetics (lignocaine,[5] applied topically or intravenously),[6] opioids (fentanyl,[7] and remifentanil[8] and beta-adrenergic blockers (esmolol,[9] and metoprolol).[10] However, each of these methods has inherent limitations. Deep planes of anesthesia may cause myocardial depression and hypotension, particularly in patients with ischemic heart disease. Vasodilators and calcium channel blockers can produce reflex tachycardia, while beta blockers may be associated with bronchospasm or bradycardia.

Clonidine, an imidazoline derivative and selective α_2-adrenergic agonist, reduces sympathetic outflow by inhibiting catecholamine release, thereby effectively attenuating the hemodynamic response to laryngoscopy and tracheal intubation.[11]Pregabalin, a gabapentinoid structurally described as (S)-3-aminomethyl-5-methylhexanoic acid, exerts analgesic, anticonvulsant, and anxiolytic effects by modulating neurotransmitter release within the central nervous system and reducing acute nociceptive pain.

AIMS AND OBJECTIVES

The study aimed to assess and contrast the efficacy of oral pregabalin and clonidine in reducing the haemodynamic pressor response linked to tracheal intubation and laryngoscopy. During the peri-intubation period, the goals were to evaluate and compare their impact on important haemodynamic parameters, such as heart rate, systolic and diastolic blood pressure, mean arterial pressure, and rate pressure product.

MATERIALS AND METHODS

Study Design

This study was a randomized, prospective clinical study conducted in the Department of Anaesthesiology over a period of one and a half years, from December 2017 to August 2019. Data were methodically collected from eligible patients undergoing elective surgical operations under general anaesthesia in order to evaluate and compare the effects of oral clonidine and oral pregabalin on the haemodynamic pressor response during laryngoscopy and tracheal intubation. Study groups were formed by random assignment of participants.

Inclusion and Exclusion Criteria

Adults between the ages of 18 and 60 who were scheduled for elective surgery under general anaesthesia, had ASA physical status I or II, had a body mass index between 18 and 25, had stable baseline haemodynamics, and had no history of allergy to the study medications were included in the study. Exclusion criteria comprised patients with a history of severe hypertension, diabetes mellitus, cardiovascular, respiratory, cerebrovascular, renal, or hepatic disease; pregnant patients; patients had a baseline pulse rate of less than 60 beats per minute or a systolic blood pressure of less than 90 mmHg at the time the trial medicine was administered, as well as those who were obese or expected to have problematic airways.

Sample Size Calculation

With a 95% confidence level and 80% power, the expected percentage of stress response across the two study groups is 29.9% and 12.7%. Using the method, the minimal sample size for each group is 44,

$$n = \frac{(Z_\alpha + Z_\beta)^2 * p * q}{D^2}$$

Where,
Z_α=Z value at α level = 95%
Z_β= Z value at β level = 80%
D = Difference between two parameters
P = Proportion value
q = 100-p
Hence, 45 cases were included in each group.

Data Collection Procedure

Ninety patients scheduled for elective surgery under general anesthesia were randomly divided into two groups of 45 each using computer-generated randomization. All patients were evaluated preoperatively, investigated as per institutional protocol, counselled, and written informed consent was obtained, with overnight fasting advised. On the day of surgery, baseline heart rate, mean arterial pressure, systolic blood pressure, and diastolic blood pressure were

measured. 120 minutes before induction, Group P got 75 mg of oral pregabalin and Group C received 300 µg of oral clonidine. All patients received intravenous glycopyrrolate, ondansetron, midazolam, and fentanyl as premedication while standard monitoring was in place. Following 100% oxygen preoxygenation, propofol was used to produce anaesthesia, succinylcholine was used to accomplish neuromuscular blockade, laryngoscopy, and endotracheal intubation were performed. Oxygen, nitrous oxide, and isoflurane were used to maintain anaesthesia. Haemodynamic parameters were measured prior to induction, during laryngoscopy, at 1, 5, 10, and 15 minutes after intubation, and at baseline, 30, 60, and 90 minutes following drug delivery. Heart rate multiplied by systolic blood pressure was used to get the rate pressure product.

Statistical Analysis

Data were expressed using frequencies, percentages, and appropriate diagrams. Fisher's exact test or the chi-square test were used to examine relationships between qualitative variables. The unpaired t-test for normally distributed data and the Mann-Whitney U test for non-normally distributed data were used to compare quantitative variables between the two groups. Statistical significance was defined as a p-value of less than 0.05, and high significance as a p-value of less than 0.001.

RESULTS

Table 1. Demographic Profile of Study Population

Parameter	Group C (Clonidine) n=45	Group P (Pregabalin) n=45	p-value
Age (years, mean ± SD)	33 ± 13	34 ± 11	0.852
Male n (%)	15 (33.3%)	18 (40%)	NS
Female n (%)	30 (66.7%)	27 (60%)	NS

Table 1 shows that both groups were comparable with respect to age and gender distribution, with no statistically significant difference.

Table 2. Comparison of Heart Rate (beats/min)

Time Point	Group C (Mean ± SD)	Group P (Mean ± SD)	p-value
Baseline	81.07 ± 9.16	84.27 ± 10.43	0.126
Before induction	75.78 ± 5.53	80.87 ± 6.37	0.001*
1 min post-intubation	91.82 ± 11.36	95.71 ± 9.82	0.086
15 min post-intubation	76.16 ± 7.24	80.36 ± 7.61	0.009*

Table 2 illustrates that clonidine produced a greater reduction in heart rate compared to pregabalin, with statistically significant differences at several time points.

Table 3. Comparison of Systolic Blood Pressure (mmHg)

Time Point	Group C	Group P	p-value
Baseline	119 ± 9.52	120.5 ± 8.71	0.434
Before induction	114.98 ± 6.99	116.56 ± 6.95	NS
1 min post-intubation	133.47 ± 8.54	137.36 ± 7.39	0.023*
15 min post-intubation	101.18 ± 6.14	107.18 ± 10.48	0.001*

Table 3 shows a significantly better attenuation of systolic blood pressure in the clonidine group following intubation.

Table 4. Comparison of Diastolic Blood Pressure (mmHg)

Time Point	Group C	Group P	p-value
Baseline	75.51 ± 7.14	76.09 ± 7.34	NS
Before induction	73.91 ± 5.31	75.56 ± 5.01	0.005*
1 min post-intubation	84.53 ± 4.96	88.09 ± 4.11	0.000*
15 min post-intubation	73.16 ± 4.12	75.47 ± 4.98	0.019*

Table 4 illustrates significantly lower diastolic blood pressure values in the clonidine group at most peri-intubation intervals.

Table 5. Comparison of Mean Arterial Pressure (mmHg)

Time Point	Group C	Group P	p-value
Baseline	89.96 ± 7.64	90.91 ± 7.40	NS
Before induction	87.60 ± 5.39	89.22 ± 5.21	NS
1 min post-intubation	100.84 ± 5.74	104.51 ± 4.70	0.001*
15 min post-intubation	86.04 ± 6.08	90.20 ± 6.16	0.002*

Table 5 shows superior control of mean arterial pressure with clonidine during and after intubation.

Table 6. Comparison of Rate Pressure Product (RPP)

Time Point	Group C	Group P	p-value
Baseline	9640 ± 1279	10181 ± 1692	NS
Before induction	8717 ± 886	9424 ± 932	0.000*
1 min post-intubation	12319 ± 2163	13176 ± 1787	0.044*
15 min post-intubation	7739 ± 1142	8649 ± 1453	0.001*

Table 6 illustrates a significantly lower myocardial workload in the clonidine group, as reflected by reduced RPP values.

Table 7. Hemodynamic Attenuation

Parameter	Better Attenuation
Heart Rate	Clonidine
SBP	Clonidine
DBP	Clonidine
MAP	Clonidine
RPP	Clonidine

Table 7 summarizes that oral clonidine consistently provided superior attenuation of the hemodynamic pressor response compared to oral pregabalin.

DISCUSSION

The goal of the current study was to examine and assess how well oral pregabalin and clonidine work as pre-medicants to reduce the haemodynamic pressor response to endotracheal intubation and laryngoscopy. Both drugs possess anxiolytic, sedative, and analgesic properties and have been previously studied for their role in maintaining perioperative hemodynamic stability.

Laryngoscopy and tracheal intubation are known to produce intense sympathetic stimulation resulting in tachycardia, hypertension, and increased circulating catecholamines. Shribman et al.[12] demonstrated significant elevations in heart rate, blood pressure, and catecholamine levels during airway manipulation, while Hassan et al.[13] reported an increased incidence of arrhythmias, myocardial ischemia, and acute left ventricular failure during these procedures. Reid and Brace[14] attributed these changes to sympathetic discharge triggered by stimulation of the epipharynx and larynx.

Numerous pharmaceutical substances, such as beta blockers, vasodilators, calcium channel blockers, and opioids, have been used to reduce these reactions. However, side effects like bradycardia, hypotension, and postoperative respiratory depression frequently restrict their use. As a result, oral premedicantions like pregabalin and clonidine that are safer and more effective have drawn interest.

In the current investigation, oral clonidine outperformed oral pregabalin in terms of attenuating heart rate, systolic and diastolic blood pressure, mean arterial pressure, and rate pressure product. The hemodynamic stability observed with clonidine can be attributed to its central α_2-adrenergic agonist action, which reduces sympathetic outflow and enhances vagal tone, along with inhibition of norepinephrine release at peripheral presynaptic receptors.[11] These mechanisms collectively result in reduced myocardial workload and improved cardiovascular stability.

Pregabalin reduces excitatory neurotransmitter release and modifies central sensitisation via binding to the α_2-delta subunit of voltage-gated calcium channels. Although pregabalin effectively attenuated the pressor response, its effect was less pronounced than clonidine, possibly due to relatively lower sedative and sympatholytic action at the administered dose.

Our findings are consistent with studies by Gupta et al.[15] Khan et al.[16] and Parveen et al.[17] which reported clonidine to be superior to pregabalin in attenuating hemodynamic responses to laryngoscopy and intubation. Archana et al.[18] also demonstrated better heart rate control with clonidine, while Rastogi et al.[19] and AyyaSyamaSundar et al.[20] confirmed the efficacy of pregabalin in dose-dependent attenuation of pressor responses.

Importantly, no significant adverse effects such as bradycardia, hypotension, or respiratory depression were observed in either group in the present study, indicating the safety of both drugs at the studied doses.

With a positive safety profile, this study demonstrates that oral clonidine is a more effective pre-medication than oral pregabalin at reducing the haemodynamic stress response to laryngoscopy and endotracheal intubation.

Limitations

The present study has certain limitations. Biochemical stress mediators such as endogenous plasma catecholamines and cortisol were not measured; assessment of these parameters could have provided a more objective correlation with the observed hemodynamic responses and aided in elucidating the precise mechanism of action of pregabalin in attenuating stress responses. Additionally, the study did not specifically evaluate or compare the adverse effects of clonidine and pregabalin. Furthermore, potential interactions of these study drugs with other anesthetic agents and concomitant medications were not assessed, which may influence perioperative hemodynamic outcomes.

CONCLUSION

Pregabalin and clonidine are both affordable, safe, and efficient oral pre-medicantions that can be used to reduce the haemodynamic pressor response brought on by tracheal intubation and laryngoscopy. However, compared to oral pregabalin 75 mg, the results of this trial show that a single oral dose of clonidine 300 µg given 120 minutes prior to surgery produces improved attenuation of heart rate, blood pressure, mean arterial pressure, and rate pressure product. Therefore, with direct laryngoscopy and endotracheal intubation, oral clonidine provides improved perioperative haemodynamic stability without major side effects.

REFERENCES

1. Kovac AL. Controlling the hemodynamic response to laryngoscopy and endotracheal intubation. Journal of Clinical Anesthesia 1996;8(1):63-79.
2. Wycoff CO. Endotracheal intubation: effects on blood pressure and pulse rate. Anesthesiology 1960;21:153-8.
3. Fassoulaki A, Kaniasis P. Intranasal administration of nitroglycerine attenuatesthe pressor response to laryngoscopy & intubation of trachea. Br J Anaesth 1983;55:49-52.
4. Mikawa K, Ikegaki J, Maekawa N, et al. The effect of diltiazem on the cardiovascular response to tracheal intubation. Anaesthesia 1990;45(4):289-93.
5. Stoelting RK. Circulatory changes during direct laryngoscopy and tracheal intubation: influence of duration of laryngoscopy with or without prior lidocaine. Anesthesiology 1977;47(4):381-4.
6. Stoelting RK: Blood pressure and heart rate changes during short duration laryngoscopy for tracheal intubation: influence of viscous or intravenous lignocaine. Anaesth Analg 1978;57:197-9.
7. Ghignone M, Quintin L, Duke PC, et al. Effects of Clonidine on narcotic requirements and hemodynamic response during induction of fentanyl anesthesia and endotracheal intubation. Anesthesiology 1986;64(1):36-42.
8. Thompson JP, Hall AP, Russell J, et al. Effect of remifentanil on the haemodynamic response to orotracheal intubation. Br J Anaesth 1998;80:467-9.
9. Vucevic M, Durdy GM, Ellis FR. Esmolol hydrochloride for management of thecardiovascular stress responses to laryngoscopy & tracheal intubation. Br J Anaesth 1992;68(5):529-30.
10. Coleman AJ, Jordan C. Cardiovascular responses to anaesthesia: Influence of beta-adrenoreceptor blockade with metoprolol. Anaesthesia 1980;35(10):972-8.
11. Zalunardo MP, Zollinger A, Spahn DR, et al. Effect of intravenous and oral Clonidine on hemodynamic and plasmacatecholamine response due toendotracheal intubation. J Clin Anesth 1997;9:143-7.
12. Shribman AJ, Smith G, Achola KJ. Cardiovascular and catecholamine responses to laryngoscopy with and without tracheal intubation. Br J Anaesth 1987;59(3):295-9.
13. Hassan HG, El-Sharkawy TY, Renck H, et al. Hemodynamic and catecholamine responses to laryngoscopy with vs. without endotracheal intubation. Acta Anaesthesiol Scand 1991;35(5):442-7.
14. Reid LC, Brace DE. Irritation of the respiratory tract and its reflex effect upon the heart. Surg Gynecol Obstet 1940;70:157-62.
15. Gupta K, Sharma D, Gupta PK. Oral premedication with Pregabalin or Clonidine for hemodynamic stability during laryngoscopy and laparoscopic cholecystectomy: a comparative evaluation. Saudi J Anaesth 2011;5(2):179-84.
16. Khan AA, Gani S, Munshi FA, et al. A comparative trial studying the effectiveness of oral Clonidine and Pregabalin premedication in attenuation of haemodynamic response following laryngoscopy and endotracheal intubation. Journal of Evolution of Medical Science 2015;4(41):7134-44.
17. Parveen S, Negi DS, Kumar R, et al. Oral Clonidine vs oral Pregabalin premedication to attenuate pressor response to direct laryngoscopy in patients undergoing laparoscopic cholecystectomy: a randomized double blind study. Journal of Clinical and Diagnostic Research 2016;10(9):UC21.
18. Raichurkar A, Dinesh K, Ravi M, et al. A comparative study of oral Pregabalin and Clonidine for attenuation of hemodynamic responses to laryngoscopy and tracheal intubation. J Clin Biomed Sci 2015;5(1):25-9.
19. Rastogi B, Gupta K, Gupta PK, et al. 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):49-54.
20. Sundar AS, Kodali R, Sulaiman S, et al. The effects of preemptive Pregabalin on attenuation of stress response to endotracheal intubation and opioid-sparing effect in patients undergoing off- pump coronary artery bypass grafting. Ann Card Anaesth 2012;15(1):18-25.