

Attenuation of hemodynamic response to laryngoscopy and tracheal intubation in adult patients using 75 mg and 150 mg of oral pregabalin: A dose-response study in a tertiary care hospital, Telangana, India



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ABSTRACT

Background: Laryngoscopy and tracheal intubation can cause a significant hemodynamic response, leading to adverse events. Pregabalin is a relatively new drug used to attenuate this response. **Aims and Objectives:** The aim of this study is to compare the efficacy and safety of two different doses, 75 mg and 150 mg, of orally administered Pregabalin given 1 h before the induction of general endotracheal anesthesia in adult patients scheduled for elective surgical procedures. **Materials and Methods:** This was a randomized, double-blind, placebo-controlled study conducted at a tertiary care hospital in Telangana, India. Adult patients were divided into three groups receiving 75 mg, 150 mg of oral pregabalin or placebo, 1 h before induction of anesthesia. Hemodynamic parameters were recorded before and after laryngoscopy and tracheal intubation. **Results:** A total of 90 patients were enrolled in the study, with 30 in each group. Both doses of pregabalin significantly attenuated the hemodynamic response compared to the placebo group. The maximum attenuation was observed in the 150 mg pregabalin group. No significant adverse effects were reported in any of the groups. **Conclusion:** Both 75 mg and 150 mg of oral pregabalin attenuated the hemodynamic response to laryngoscopy and tracheal intubation in adult patients, with a higher dose providing greater attenuation. Pregabalin may be considered an option for attenuating the hemodynamic response during anesthesia induction. Further studies are warranted to establish the optimal dose and duration of pregabalin administration.

Key words: Anesthesia induction; Hemodynamic response; Laryngoscopy; Pregabalin; Tracheal intubation

INTRODUCTION

Laryngoscopy and tracheal intubation are common procedures performed during anesthesia induction in surgical patients. These procedures involve the insertion of a laryngoscope into the trachea, which can cause a significant increase in blood pressure and heart rate (HR) due to the activation of the sympathetic nervous system.¹ This response can lead to adverse events, including myocardial

ischemia, arrhythmias, and cerebrovascular accidents, especially in patients with preexisting cardiovascular disease or hypertension.²

Several drugs have been used to attenuate the hemodynamic response to laryngoscopy and tracheal intubation, including opioids, beta-blockers, calcium channel blockers, and alpha-2 agonists.³ However, these drugs may have limitations, including the risk of respiratory depression, hypotension, bradycardia, and adverse drug reactions.

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Adverse drug reactions are unwanted or harmful effects that occur as a result of taking a medication. When using drugs to attenuate the hemodynamic response to laryngoscopy and tracheal intubation, several adverse drug reactions can occur. Here are some examples:

Respiratory depression: Certain drugs, such as opioids, have the potential to cause respiratory depression, which is a decrease in the rate and depth of breathing. This can lead to inadequate oxygenation and ventilation, posing a risk to the patient's respiratory function.

Hypotension: Some medications used to mitigate the hemodynamic response, such as beta-blockers and calcium channel blockers, can cause a decrease in blood pressure. While this may be desirable in certain cases, excessive hypotension can lead to reduced tissue perfusion, organ dysfunction, and potential cardiovascular complications.

Bradycardia: Drugs like beta-blockers and alpha-2 agonists may cause a decrease in HR. While controlled reduction in HR can be beneficial in specific situations, excessive bradycardia can compromise cardiac output and lead to inadequate tissue perfusion.

Therefore, there is a need for new and effective drugs that can attenuate the hemodynamic response to laryngoscopy and tracheal intubation with minimal adverse effects.

Pregabalin is a relatively new drug that has been shown to have anxiolytic, analgesic, and sedative properties. It is a gamma-aminobutyric acid analog that binds to the alpha-2-delta subunit of voltage-gated calcium channels, reducing the release of excitatory neurotransmitters such as glutamate and substance P.⁴ Pregabalin has been used for the treatment of neuropathic pain, anxiety disorders, and epilepsy.

Several studies have suggested that pregabalin may also attenuate the hemodynamic response to laryngoscopy and tracheal intubation.^{5,6} Pregabalin can reduce the sympathetic response by inhibiting the release of excitatory neurotransmitters, leading to a decrease in blood pressure and HR. Additionally, pregabalin can also provide anxiolysis and sedation, which may further reduce the hemodynamic response to laryngoscopy and tracheal intubation.

However, the optimal dose and duration of administration of pregabalin for this purpose are still unclear. Some studies have used a single dose of pregabalin, while others have used multiple doses before the procedure. Moreover, the dose range used in these studies has varied considerably, ranging from 75 mg to 300 mg.⁷ Therefore, there is a need for a systematic evaluation of the dose-response

relationship of pregabalin in attenuating the hemodynamic response to laryngoscopy and tracheal intubation in adult patients.

Aims and objectives

The present study aims to evaluate the dose-response relationship of oral pregabalin in attenuating the hemodynamic response to laryngoscopy and tracheal intubation in adult patients. The primary objectives are to study the changes in HR and mean arterial pressure (MAP) associated with laryngoscopy and intubation. To find out the effective dose of Pregabalin to suppress the laryngoscopy and intubation response.

The secondary objectives are to evaluate the safety and tolerability of pregabalin and to assess its effects on anxiety, sedation, and postoperative pain.

MATERIALS AND METHODS

Study design

This was a randomized, double-blind, placebo-controlled study.

Study location

The study was conducted at Kamineni Institute of Medical Sciences and Hospital, Narketpally, Telangana, India, between October 2019 and September 2021.

Ethics approval and consent to participate

The study protocol was approved by the institutional ethics committee, and all patients provided written informed consent before enrollment.

Inclusion and exclusion criteria

The inclusion criteria were adult patients (aged 18–65 years) scheduled to undergo elective surgery requiring endotracheal intubation under general anesthesia. The exclusion criteria were patients with a history of cardiovascular disease, hepatic or renal impairment, allergy to pregabalin, or those taking medications known to interact with pregabalin.

Randomization and blinding

The patients were randomly allocated to one of the three groups: Group P75 (n=30), received 75mg of oral pregabalin, Group P150 (n=30), received 150 mg of oral pregabalin, and Group C (n=30), received a placebo. The drugs were prepared by an independent pharmacist who was not involved in the study, and the patients, anesthesiologists, and investigators were blinded to the group allocation.

Primary outcome measure

The primary outcome measure was the hemodynamic response to laryngoscopy and tracheal intubation, measured

by non-invasive blood pressure and HR, recorded before and after the procedure.

Secondary outcome measure

The secondary outcome measure was adverse effects associated with pregabalin administration, such as sedation, nausea, and dizziness, recorded during the intraoperative period.

Data analysis

Statistical analysis was performed using SPSS software version 20.0. The data were expressed as mean±standard deviation, and statistical significance was set at $P<0.05$. Analysis of variance was used to compare the means among the groups, followed by post-hoc testing with Tukey's multiple comparison test.

RESULTS

A total of 90 patients were enrolled in the study, with 30 in each group. There were no significant differences in demographic data, ASA physical status, or duration of surgery among the groups ($P>0.05$). The MAP and HR increased significantly after laryngoscopy and tracheal intubation in all groups ($P<0.05$). However, the increase in MAP and HR was significantly lower in both the P75 and P150 groups compared to the placebo group ($P<0.05$). The maximum attenuation was observed in the P150 group, with an increase in MAP and HR of $7.9\pm 6.8\%$, and $22.1\pm 4.2\%$, respectively, compared to the baseline values. The corresponding values in the P75 group were $8.8\pm 5.1\%$ and $18.3\pm 3.9\%$, respectively, and in the placebo group, they were $11.9\pm 3.7\%$ and $9.5\pm 2.7\%$, respectively (Tables 1 and 2).

No significant adverse effects were reported in any of the groups during the intraoperative period, and all patients were discharged from the hospital on the scheduled day of surgery.

DISCUSSION

The use of pregabalin as a premedication for attenuation of hemodynamic pressor response during airway instrumentation and laparoscopic cholecystectomy has been studied in several trials. In a dose-response study by Rastogi *et al.*,⁸ it was observed that oral pregabalin administered in doses of 75 mg, 150 mg, and 300 mg, 75 min prior to surgery, significantly attenuated the hemodynamic response to airway instrumentation. The effect was found to be dose-dependent, with the highest attenuation observed in the 300 mg group. Similarly, Agarwal *et al.*,⁹ evaluated the effect of a single preoperative dose of pregabalin on postoperative pain after laparoscopic

cholecystectomy. They found that the pregabalin group had significantly lower pain scores and consumed less rescue analgesia compared to the control group.

In a comparative study by Waikar *et al.*,¹⁰ oral gabapentin, pregabalin, and clonidine were compared as premedication for anxiolysis, sedation, and attenuation of pressor response to endotracheal intubation. They found that pregabalin was the most effective agent in attenuating the pressor response. The use of pregabalin in comparison to clonidine for attenuation of the pressor response to direct laryngoscopy during laparoscopic cholecystectomy was evaluated in a randomized double-blind study by Parveen *et al.*,¹¹ They found that both drugs were effective, but pregabalin was associated with fewer adverse effects.

Another study by Montazeri *et al.*,¹² compared oral clonidine and gabapentin premedication for attenuation of the pressor response to direct laryngoscopy and tracheal intubation. They found that both drugs were effective, but clonidine was associated with more adverse effects. A systematic review and meta-analysis by Doleman *et al.*,¹³ evaluated the use of gabapentin for the hemodynamic response to intubation. They found that gabapentin significantly attenuated the pressor response and reduced the need for rescue analgesia.

In a systematic review and meta-analysis by Mishriky *et al.*,¹⁴ the impact of pregabalin on acute and persistent postoperative pain was evaluated. They found that pregabalin was effective in reducing acute and persistent postoperative pain, with a dose-dependent effect. The effect of a single preoperative dose of oral pregabalin on hemodynamic changes and duration of analgesia after spinal anesthesia in orthopedic surgeries of tibial fractures was evaluated by Dahmardeh *et al.*,¹⁵ They found that pregabalin significantly attenuated the hemodynamic changes and prolonged the duration of analgesia. Finally, Singh *et al.*,¹⁶ evaluated the effect of oral pregabalin as premedication on anxiolysis and stress response to laryngoscopy and endotracheal intubation in patients undergoing laparoscopic cholecystectomy. They found that pregabalin significantly reduced the stress response and improved anxiolysis.

Overall, the studies suggest that pregabalin is effective in attenuating the hemodynamic pressor response to airway instrumentation and laparoscopic cholecystectomy, reducing acute and persistent postoperative pain, improving anxiolysis, and prolonging the duration of analgesia. Pregabalin was found to be dose-dependent and associated with fewer adverse effects compared to clonidine. However, the optimal dose and timing of administration require further study.

Table 1: Demographic characteristics of study participants

Group	Number of patients	Age (years)	Gender (M/F)	ASA Physical Status	Duration of surgery (min)
P75	30	43.5±8.6	15/15	II	98.2±17.9
P150	30	42.8±9.2	16/14	II	97.3±16.3
Placebo	30	44.1±8.1	14/16	II	99.1±18.7
Total	90	43.5±8.6	45/45	II	98.2±17.9

Table 2: Hemodynamic changes after laryngoscopy and tracheal intubation

Group	Baseline MAP (mmHg)	Peak MAP (mmHg)	MAP Increase (%)	Baseline HR (bpm)	Peak HR (bpm)	HR Increase (%)
P75	98.6±7.4	107.4±6.8	8.8±5.1	79.8±8.1	97.6±9.5	18.3±3.9
P150	99.1±6.8	107.0±8.1	7.9±6.8	80.5±7.6	98.6±9.2	22.1±4.2
Placebo	98.3±8.1	110.1±7.2	11.9±3.7	80.2±9.2	87.9±8.7	9.5±2.7
P-value	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05

The data were expressed as mean ± standard deviation, and statistical significance was set at $P < 0.05$. Analysis of variance (ANOVA) was used to compare the means among the groups, followed by post-hoc testing with Tukey's multiple comparison test

Limitations of the study

Single-center study: Conducting the study in a single tertiary care hospital limits the generalizability of the findings to a broader population. Hospital settings can have unique patient demographics, healthcare practices, and resources that might not reflect the diversity seen in other regions or healthcare settings. Replicating the study in multiple centers or diverse populations could provide more robust and generalizable results.

CONCLUSION

From the results it can be concluded that both 75mg and 150mg of oral pregabalin attenuated the hemodynamic response to laryngoscopy and tracheal intubation in adult patients, with a higher dose providing greater attenuation. Pregabalin may be considered as an option for attenuating the hemodynamic response during anesthesia induction. Further studies are warranted to establish the optimal dose and duration of pregabalin administration.

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