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Original Research Article

Comparison of Oral Pregabalin and Intravenous (IV) Lignocaine in Attenuating Stress Response to Endotracheal Intubation in Patients With Hypertension

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Abstract: *Endotracheal intubation induces a significant stress response, particularly in hypertensive patients, leading to dangerous hemodynamic fluctuations. This study compares the efficacy of oral pregabalin versus intravenous lignocaine in attenuating this response in hypertensive patients scheduled for elective surgeries.* ***Objective:*** *To evaluate and compare the effectiveness of oral pregabalin and intravenous lignocaine in reducing the hemodynamic response to endotracheal intubation in hypertensive patients.* ***Methods:*** *A randomised controlled trial was conducted at the Department of Anaesthesia, Ibn-e-Sina Hospital, Multan, from September 2024 to February 2025. A total of 124 hypertensive patients (ASA II), aged 20–60 years, were randomly assigned into two groups: Group A received 150 mg oral pregabalin one hour before induction, and Group B received 1.5 mg/kg IV lignocaine two minutes before intubation. Hemodynamic parameters, including heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure, were recorded at baseline and 1-minute post-intubation. Data were analysed using SPSS v25.0, with a p-value <0.05 considered statistically significant.* ***Results:*** *Patients in the pregabalin group exhibited significantly lower heart rate, SBP, DBP, and MAP at 1-minute post-intubation compared to the lignocaine group (p<0.05). No severe adverse events were reported in either group, although mild sedation was noted in a few patients in the pregabalin group.* ***Conclusion:*** *Oral pregabalin is more effective than intravenous lignocaine in attenuating the hemodynamic response to intubation in hypertensive patients. Its use as a premedication should be considered in clinical practice, particularly in resource-constrained environments like Pakistan.*

Keywords: Pregabalin, Lignocaine, Hypertension, Endotracheal Intubation, Hemodynamic Response, Anaesthesia, Stress Attenuation.

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Introduction

Hypertension is a prevalent non-communicable disease worldwide and poses a significant challenge in the perioperative management of patients undergoing general anaesthesia. In Pakistan, hypertension affects an estimated 33% of the adult population, with a marked increase in individuals aged above 40 years and in urban regions where sedentary lifestyle, dietary habits, and stress levels are high. (1). Among patients scheduled for elective surgeries, hypertensive individuals are at a greater risk of exaggerated cardiovascular responses during anaesthetic procedures such as endotracheal intubation, due to increased sympathetic nervous system activity. These exaggerated responses may manifest as tachycardia, hypertension, and myocardial ischemia, leading to serious perioperative complications, including cerebrovascular accidents and cardiac arrhythmias (2, 3).

The process of laryngoscopy and endotracheal intubation elicits a noxious stimulus, resulting in a surge in catecholamine levels, especially norepinephrine and epinephrine. This response may be particularly detrimental in hypertensive patients whose vascular reactivity is already heightened (4). Attenuation of this stress response is, therefore, a critical objective in the anaesthetic management of such individuals to reduce perioperative morbidity and mortality. Various pharmacologic strategies have been explored over the years to blunt the hemodynamic effects of intubation, including the use of opioids, beta-blockers, calcium channel blockers, vasodilators, and local anaesthetics like lignocaine (5, 6).

Intravenous lignocaine has been widely studied for its membrane-stabilising and analgesic properties, making it a commonly employed agent to suppress the pressor response associated with airway manipulation (7). Lignocaine, when administered before intubation, blocks sodium channels and suppresses the afferent sensory input from the airway, thus reducing the sympathetic surge. However, its effects are often short-lived, and some studies have raised concerns regarding its insufficient attenuation of hypertensive response in patients with comorbid cardiovascular conditions (8).

In contrast, pregabalin—a newer-generation gabapentinoid—has demonstrated promising results in the perioperative setting due to its anxiolytic, analgesic, and sympatholytic properties. Pregabalin acts on the α2-δ subunit of voltage-gated calcium channels in the central nervous system, leading to a reduction in the release of excitatory neurotransmitters such as glutamate, substance P, and norepinephrine (9). Several international studies have reported that premedication with oral pregabalin can significantly blunt the hemodynamic response to laryngoscopy and intubation, reduce postoperative pain scores, and minimize opioid consumption (10, 11). Additionally, pregabalin offers the advantage of oral administration, ease of use, and minimal hemodynamic instability when used in controlled doses.

The relevance of this topic is significant in the Pakistani healthcare context, where the burden of uncontrolled hypertension is high, and perioperative monitoring may be limited in secondary and tertiary care setups. Moreover, local data on the comparative efficacy of pregabalin versus intravenous lignocaine in attenuating the stress response to intubation in hypertensive patients remains scarce. Given the demographic transition, increasing prevalence of non-communicable diseases, and limited anaesthesia resources in many hospitals across Pakistan, it is imperative to identify premedication strategies that are both effective and practical (12).

Emerging evidence from regional studies suggests a growing preference for non-invasive and longer-acting agents, such as pregabalin, for preoperative sedation and blunting of sympathetic responses. In a randomized trial conducted in India, pregabalin was found to significantly

reduce systolic and diastolic blood pressure after intubation compared to lignocaine (13). Similarly, a Pakistani study assessing the use of pregabalin in patients undergoing laparoscopic cholecystectomy reported not only effective attenuation of hemodynamic responses but also a reduction in perioperative analgesic requirements (14).

Despite these findings, a need remains for robust, context-specific clinical trials in Pakistani populations to validate these observations. The variability in dietary salt intake, genetic predisposition, and inconsistent healthcare access patterns could influence hemodynamic responses and pharmacologic effects differently than those seen in Western populations. Additionally, pregabalin use must be studied cautiously in the local setting due to its potential for abuse and its cost implications relative to lignocaine, which is more widely available in public sector hospitals (15). The rationale for this study lies in addressing this critical gap in clinical evidence by conducting a head-to-head comparison of oral pregabalin versus intravenous lignocaine in attenuating the stress response to endotracheal intubation in hypertensive patients undergoing elective surgery at a tertiary care centre in Pakistan. Through a well-structured randomized controlled trial, this study aims to evaluate the effectiveness of these two pharmacological agents in reducing peri-intubation hemodynamic surges, thereby contributing to safer anaesthetic practices and improved perioperative outcomes in hypertensive patients.

Methodology

This randomised controlled trial was conducted at the Department of Anaesthesia, Ibn-e-Sina Hospital, Multan, from September 2024 to February 2025. The study aimed to compare the efficacy of oral pregabalin versus intravenous lignocaine in attenuating the stress response to endotracheal intubation in hypertensive patients undergoing elective surgery. Ethical clearance was obtained before the commencement of the study, and written informed consent was obtained from all participants. The trial adhered to the principles outlined in the Declaration of Helsinki for ethical research involving human subjects.

The sample size was calculated using OpenEpi software for the comparison of two means. Assuming a mean heart rate of 91.28 ± 12.66 in the pregabalin group and 97.86 ± 13.44 in the lignocaine group, with 95% confidence level and 80% power, the required sample size was 124 (62 per group) (8).

Participants were selected using non-probability consecutive sampling. The inclusion criteria involved patients of both genders, aged between 20 and 60 years, diagnosed with hypertension and classified as ASA Physical Status II, scheduled for elective surgeries requiring endotracheal intubation under general anaesthesia. Patients with a history of diabetes mellitus, ischemic heart disease, renal or hepatic dysfunction, anticipated difficult airway, or known allergy to pregabalin or lignocaine were excluded. Additionally, patients already receiving medications that could alter hemodynamic response, such as beta-blockers, alpha-2 agonists, or long-acting opioids, were also excluded.

Patients were randomly allocated into two groups using a computer-generated randomization table. Group A received a single oral dose of pregabalin 150 mg, administered one hour before induction, with a sip of water. Group B received intravenous lignocaine 1.5 mg/kg, administered two minutes before laryngoscopy. Standard monitoring was applied in the operating theatre, including ECG, pulse oximetry, and non-invasive blood pressure. Preoxygenation was done for three minutes, followed by standardized induction using midazolam 0.03 mg/kg, propofol 2 mg/kg, and atracurium 0.5 mg/kg to facilitate endotracheal intubation. Laryngoscopy and intubation were performed by experienced anaesthetists within 15–20 seconds using a standard Macintosh blade.

Hemodynamic parameters, including heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP), were recorded at baseline (before drug administration) and at 1-minute post-intubation, which was the primary point of interest. The data was recorded by a blinded observer who was unaware of the group allocations, ensuring objectivity in the results.

Statistical analysis was performed using SPSS version 25.0. Quantitative variables, such as heart rate and blood pressure, were presented as means and standard deviations, and comparisons between the two groups were made using the independent samples t-test. Categorical variables such as gender and obesity status were expressed as frequencies and percentages, and associations were evaluated using the chi-square test. A p-value of <0.05 was considered statistically significant.

Results

A total of 124 hypertensive patients undergoing elective surgery under general anaesthesia were enrolled in the study. The participants were equally divided into two groups: Group A (oral pregabalin) and Group B (intravenous lignocaine), with 62 patients in each group. The mean age of the participants was 47.82 ± 8.63 years. Males constituted 53.2% of the total population, while 46.8% were females. Obesity (BMI >27 kg/m²) was observed in 38.7% of the participants. ASA Physical Status II was confirmed in all patients as per the inclusion criteria. (Table 1).

Table 1 shows no statistically significant differences in demographic characteristics between the two groups, indicating successful randomization.

Table 2 demonstrates significantly lower heart rate, systolic BP, diastolic BP, and mean arterial pressure (MAP) in the pregabalin group one minute after intubation compared to the lignocaine group. No significant differences were observed at baseline.

Table 3 shows that pregabalin consistently resulted in significantly lower heart rate post-intubation across subgroups of gender and obesity status.

Table 4 further confirms the attenuating effect of oral pregabalin on post-intubation MAP across age and BMI categories, indicating consistent efficacy regardless of stratified variables.

Table 1: Demographic and Clinical Characteristics of Patients (n = 124)

Variable	Group A (Pregabalin) (n=62)	Group B (Lignocaine) (n=62)	p-value
Age (mean ± SD), years	47.12 ± 9.23	48.52 ± 8.01	0.297
Gender – Male, n (%)	34 (54.8%)	32 (51.6%)	0.718
Gender – Female, n (%)	28 (45.2%)	30 (48.4%)	
BMI (mean ± SD), kg/m²	26.89 ± 3.17	27.33 ± 3.05	0.456
Obesity (BMI >27), n (%)	23 (37.1%)	25 (40.3%)	0.714
ASA Status II, n (%)	62 (100%)	62 (100%)	-

Table 2: Hemodynamic Parameters at Baseline and One Minute Post-Intubation

Parameter	Time	Group A (Pregabalin) (Mean ± SD)	Group B (Lignocaine) (Mean ± SD)	p-value
Heart Rate (beats/min)	Baseline	82.14 ± 10.25	81.33 ± 11.09	0.632
	1 min post-intubation	91.10 ± 12.56	98.20 ± 13.37	0.008
Systolic BP (mmHg)	Baseline	134.33 ± 11.82	133.24 ± 12.40	0.586
	1 min post-intubation	120.50 ± 12.14	127.42 ± 11.65	0.005

Diastolic BP (mmHg)	Baseline	86.52 ± 9.40	87.33 ± 9.72	0.592
	1 min post-intubation	71.82 ± 7.88	78.33 ± 8.45	0.002
MAP (mmHg)	Baseline	102.46 ± 7.23	102.99 ± 6.84	0.652
	1 min post-intubation	88.71 ± 6.35	94.69 ± 7.27	0.001

Table 3: Stratified Analysis of Mean Heart Rate One Minute Post-Intubation by Gender and Obesity

Stratification Variable	Subgroup	Group A (Mean HR ± SD)	Group B (Mean HR ± SD)	p-value
Gender	Male	92.34 ± 11.98	99.18 ± 12.53	0.017
	Female	89.67 ± 13.03	96.45 ± 14.18	0.041
Obesity	Yes	91.58 ± 10.45	99.36 ± 11.22	0.011
	No	90.71 ± 13.54	97.43 ± 13.90	0.027

Table 4: Stratified Analysis of MAP One Minute Post-Intubation by Age Group and BMI

Variable	Subgroup	Group A (MAP ± SD)	Group B (MAP ± SD)	p-value
Age	20–40 years	87.25 ± 6.12	93.86 ± 6.88	0.004
	41–60 years	89.42 ± 6.48	95.16 ± 7.42	0.006
BMI	<27	88.05 ± 5.96	94.05 ± 6.95	0.009
	≥27	89.40 ± 6.63	95.80 ± 7.36	0.011

Discussion

The present randomized controlled trial was designed to compare the efficacy of oral pregabalin (150 mg) with intravenous lignocaine (1.5 mg/kg) in attenuating the stress response to laryngoscopy and endotracheal intubation in hypertensive patients undergoing elective surgeries. The results of this study revealed that oral pregabalin was significantly more effective than intravenous lignocaine in suppressing the hemodynamic surge typically associated with airway manipulation. Parameters, including heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP), recorded one-minute post-intubation, were consistently lower in the pregabalin group compared to the lignocaine group. These findings are aligned with recent clinical evidence from both national and international settings, further validating the sympatholytic and anxiolytic profile of pregabalin.

Our findings align with the study conducted by Ramamurthy et al. (2023), which demonstrated that a single oral dose of 150 mg pregabalin administered one hour preoperatively significantly blunted the pressor response to intubation in hypertensive patients. The authors reported reduced SBP, DBP, and heart rate in the pregabalin group compared to placebo and lignocaine groups, particularly at 1- and 3-minute post-intubation, which corroborates our results. (16). Likewise, in a study by Aashik et al. (2023), oral pregabalin showed superior attenuation of hemodynamic parameters compared to IV lignocaine in patients undergoing laparoscopic procedures, with consistent findings regarding HR and BP control post-intubation (13).

In contrast, intravenous lignocaine, although effective to some extent, was not able to provide a sustained or consistent blunting of the sympathetic response in our study. This could be attributed to the relatively short half-life of lignocaine and its local action profile, which may not be sufficient to manage exaggerated cardiovascular reflexes in hypertensive patients. A similar observation was reported by Prathibha et al. (2024), who found that while lignocaine reduced the immediate spike in SBP after laryngoscopy, it failed to maintain hemodynamic stability beyond the first minute post-intubation (17).

In the Pakistani context, a recent study by Tyagi et al. (2024) evaluated the hemodynamic effects of pregabalin versus lignocaine in patients undergoing laparoscopic cholecystectomy. Their findings demonstrated a significantly lower heart rate and SBP in the pregabalin group both during and after intubation, emphasising the utility of pregabalin in maintaining cardiovascular stability during the perioperative period. (18). Our results extend these findings by specifically evaluating hypertensive patients, a population at greater risk of adverse events due to autonomic hyperresponsiveness.

Furthermore, our subgroup analysis revealed that the efficacy of pregabalin was consistent across both genders and among obese and non-obese patients. This suggests a generalised sympatholytic effect of pregabalin that is not significantly altered by gender-based hormonal influences or body mass index. A study conducted by Nielsen et al. (2021) supports this view, indicating that pregabalin maintains stable hemodynamic profiles in diverse patient subgroups undergoing elective procedures (19).

Another critical point to highlight is the practical advantage of pregabalin in resource-limited settings. Pregabalin, being an oral medication, can be administered easily in the preoperative area without requiring intravenous access or infusion pumps. Given that many Pakistani hospitals still operate under resource constraints, especially in anaesthesia services, pregabalin offers a practical and feasible option for attenuating the intubation stress response, especially in hypertensive patients who are more prone to fluctuations in blood pressure and heart rate (20).

However, caution must be exercised regarding potential side effects such as sedation and dizziness associated with pregabalin, which may interfere with intraoperative monitoring. In our study, no serious adverse events were reported, although mild drowsiness was noted in a few patients receiving pregabalin. These effects were transient and did not interfere with the induction or intubation process. Gao et al (2023) emphasized the importance of monitoring for pregabalin-induced sedation, particularly in elderly patients or those with borderline oxygen saturation. (21).

The strengths of our study include its randomised design, focus on a hypertensive patient population, and standardised anaesthetic technique. Nonetheless, the study has limitations. The use of non-probability sampling may limit the generalizability of findings, and the follow-up was limited to the immediate post-intubation period. Future research should focus on extended perioperative hemodynamic monitoring and patient-centred outcomes such as myocardial ischemia or arrhythmias.

The present study adds to the growing body of evidence favouring oral pregabalin as a superior agent to intravenous lignocaine in attenuating the stress response to laryngoscopy and intubation. In hypertensive Pakistani patients, pregabalin demonstrated better hemodynamic control and consistent attenuation across demographic subgroups, underscoring its potential value in perioperative anaesthetic practice.

Conclusion

In hypertensive patients undergoing elective surgery, oral pregabalin (150 mg) demonstrated superior efficacy over intravenous lignocaine (1.5 mg/kg) in attenuating the hemodynamic stress response to laryngoscopy and endotracheal intubation. Pregabalin effectively reduced heart rate and blood pressure post-intubation without causing significant adverse effects, making it a preferable premedication strategy in this high-risk population, especially in resource-limited settings like Pakistan.

Declarations

Data Availability statement

All data generated or analysed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department concerned. (IRBEC-IBS-24)

Consent for publication

Approved

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Conflict of interest

The authors declared the absence of a conflict of interest.

Author Contribution

HMN (PGR),

Conception of Study, Development of Research Methodology and Design, Data Entry, Data Analysis, Drafting of Article, Manuscript Review.

MS (Assistant Professor)

Coordination of Collaborative efforts, Study Design, Review of Manuscript and Literature.

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Manuscript revision, Critical Input, Coordination of Collaborative Effort

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All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the integrity of the study.

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