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Original Research Article

Time-Dependent Hemodynamic Changes Following Administration of Esmolol, Labetalol, and Lignocaine During Endotracheal Intubation

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Abstract:

Background: Direct laryngoscopy and endotracheal intubation are associated with significant sympathetic stimulation resulting in tachycardia, hypertension, and increased myocardial oxygen demand. Attenuation of this cardiovascular response is an important anesthetic consideration, especially in patients with limited cardiovascular reserve.

Aim: To study and compare the effects of intravenous esmolol hydrochloride (0.5 mg/kg), labetalol hydrochloride (0.25 mg/kg), and lignocaine hydrochloride (1 mg/kg) in attenuation of the cardiovascular response to direct laryngoscopy and endotracheal intubation.

Materials and Methods: This prospective, randomized, comparative clinical study was conducted on 90 adult patients belonging to ASA physical status I and II, scheduled for elective surgical procedures under general anaesthesia. Patients were randomly allocated into three groups of 30 each. Group L received intravenous lignocaine (1 mg/kg), Group E received intravenous esmolol (0.5 mg/kg), and Group B received intravenous labetalol (0.25 mg/kg), administered two minutes prior to laryngoscopy. Heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, and rate pressure product were recorded at baseline, immediately before laryngoscopy, and at 1, 3, 5, 7, and 10 minutes following endotracheal intubation. Data were statistically analyzed using appropriate tests.

Results: Demographic parameters and baseline hemodynamic variables were comparable among the three groups. Following laryngoscopy and intubation, all groups showed an increase in heart rate and blood pressure. The lignocaine group demonstrated the maximum increase in hemodynamic parameters. Esmolol effectively attenuated the heart rate response but provided partial control of blood pressure. Labetalol demonstrated the most effective attenuation of both heart rate and blood pressure, with better control of rate pressure product. All drugs were well tolerated with no serious adverse effects.

Conclusion: Intravenous labetalol hydrochloride at a dose of 0.25 mg/kg is more effective than esmolol and lignocaine in attenuating the cardiovascular response to laryngoscopy and endotracheal intubation. Labetalol provides superior hemodynamic stability with minimal adverse effects and can be safely recommended for routine clinical use in ASA I and II patients.

Introduction

General Overview of Airway Management in Anaesthesia: Airway management is the cornerstone of modern anaesthetic practice. Safe maintenance of a patent airway and adequate ventilation is essential for the conduct of general anaesthesia and for the prevention of perioperative morbidity and mortality. Among the various airway management techniques available, direct laryngoscopy followed by endotracheal intubation remains the most reliable and widely practiced method for securing the airway during elective and emergency surgical procedures [1].

Despite significant advancements in supraglottic airway devices and video laryngoscopy, direct laryngoscopy continues to be routinely employed due to its simplicity, availability, and effectiveness. However, laryngoscopy and endotracheal intubation are associated with intense mechanical stimulation of the upper airway, leading to pronounced autonomic responses [2].

Historical Perspective of Cardiovascular Response: The cardiovascular response to airway manipulation was first systematically described by Reid and Brace**,** who observed marked increases in heart rate and arterial blood pressure following laryngoscopy and tracheal intubation [3]. These early observations highlighted the potential clinical significance of airway-induced sympathetic stimulation.

Subsequently, King et al. demonstrated that the act of laryngoscopy itself**,** rather than tracheal intubation, was the primary stimulus responsible for the pressor response [4]. This finding redirected research toward understanding the physiological mechanisms underlying laryngoscopy-induced cardiovascular changes.

Physiological Basis of the Pressor Response: Direct laryngoscopy involves stimulation of highly sensitive areas of the oropharynx, epiglottis, vocal cords, and trachea. This mechanical stimulation activates afferent neural pathways transmitted primarily through the glossopharyngeal and vagus nerves to the medullary centers of the brainstem [5].

Activation of the vasomotor center results in increased sympathetic outflow, leading to release of catecholamines—epinephrine and norepinephrine—from the adrenal medulla. This catecholamine surge produces tachycardia, increased myocardial contractility, peripheral vasoconstriction, and elevation of systemic arterial pressure [6].

Neuroendocrine Response to Laryngoscopy: Prys-Roberts et al. provided biochemical evidence for sympathetic activation by demonstrating significant elevations in plasma catecholamine levels during laryngoscopy and endotracheal intubation [7]. The increase in circulating catecholamines correlates with the magnitude of hemodynamic changes observed.

The neuroendocrine response is influenced by multiple factors including the depth of anaesthesia, duration of laryngoscopy, patient anxiety, and underlying systemic disease [8].

Temporal Profile of Hemodynamic Changes: The cardiovascular response to laryngoscopy and intubation follows a characteristic temporal pattern. Hemodynamic changes typically begin within seconds of laryngoscopy, peak within the first minute after intubation, and gradually return toward baseline over the next 5–10 minutes in normotensive individuals [9].

However, in patients with hypertension or ischemic heart disease, these changes may be more pronounced and prolonged, increasing the risk of adverse events [10].

Factors Influencing the Magnitude of Response

Several patient-related and procedural factors influence the magnitude of the pressor response:

- Age and baseline sympathetic tone
- Presence of hypertension or coronary artery disease
- Anxiety and pain perception
- Depth of anaesthesia
- Duration and force of laryngoscopy
- Repeated intubation attempts

Stoelting emphasized that inadequate depth of anaesthesia is one of the most important contributors to exaggerated cardiovascular responses [11].

Clinical Significance of Cardiovascular Response: In healthy individuals, the pressor response is usually transient and clinically insignificant. However, in patients with compromised cardiovascular reserve, exaggerated responses may precipitate serious complications.

Fox et al. reported electrocardiographic evidence of myocardial ischemia following intubation-induced tachycardia in patients with coronary artery disease [12]. Sudden increases in blood pressure may lead to arrhythmias, myocardial infarction, left ventricular failure, or cerebrovascular accidents [13].

Rate Pressure Product and Myocardial Oxygen Consumption: Rate pressure product (RPP), calculated as the product of heart rate and systolic blood pressure, is a widely accepted indirect index of myocardial oxygen consumption.

Gobel et al. demonstrated a strong correlation between RPP and myocardial oxygen demand [14]. Studies have shown that myocardial ischemia is more likely to occur when RPP exceeds critical thresholds, particularly in patients with coronary artery disease [15].

Importance of Attenuation of Pressor Response: Given the potential for serious adverse events, attenuation of the pressor response to laryngoscopy and intubation is considered an essential component of balanced anaesthesia, especially in high-risk patients [16].

Both non-pharmacological and pharmacological strategies have been employed to achieve hemodynamic stability during airway manipulation.

Non-Pharmacological Measures: Non-pharmacological techniques include gentle laryngoscopy, minimizing the duration of airway manipulation, use of appropriate laryngoscope blades, and ensuring adequate depth of anaesthesia [17]. While helpful, these measures alone are often insufficient in preventing significant hemodynamic responses.

Pharmacological Approaches: Numerous pharmacological agents have been evaluated for attenuation of cardiovascular responses, including

opioids, vasodilators, calcium channel blockers, alpha-2 agonists, beta-adrenergic blockers, and local anaesthetics [18].

Among these, lignocaine, esmolol, and labetalol have gained widespread acceptance due to their predictable pharmacological effects and favorable safety profiles [19].

Rationale for Drug Comparison

Each of the above agents acts through different mechanisms:

- Lignocaine suppresses airway reflexes
- Esmolol selectively controls heart rate
- Labetalol provides combined alpha and beta blockade

However, the optimal drug and dosage for effective attenuation with minimal adverse effects remains controversial [20].

Need for the Present Study: There is limited literature directly comparing low doses of intravenous esmolol (0.5 mg/kg), labetalol (0.25 mg/kg), and lignocaine (1 mg/kg) under standardized anaesthetic conditions with time-based hemodynamic analysis.

Therefore, the present study was undertaken to compare the efficacy of these agents in attenuating the cardiovascular response to direct laryngoscopy and endotracheal intubation.

Aims And Objectives

Aim of the Study: The aim of the present study is to study and compare the effects of intravenous esmolol hydrochloride (0.5 mg/kg), intravenous labetalol hydrochloride (0.25 mg/kg), and intravenous lignocaine hydrochloride (1 mg/kg) in attenuating the cardiovascular response to direct laryngoscopy and endotracheal intubation in patients undergoing elective surgical procedures under general anaesthesia, and to analyze the resultant hemodynamic changes.

Specific Objectives

1. To observe and record the hemodynamic responses**,** including heart rate and blood pressure parameters, following direct laryngoscopy and endotracheal intubation at 1, 3, 5, 7, and 10 minutes after intubation.
2. To study and compare the efficacy of intravenous labetalol hydrochloride (0.25 mg/kg), intravenous esmolol hydrochloride (0.5 mg/kg), and intravenous lignocaine hydrochloride (1 mg/kg) in attenuating the hemodynamic response to laryngoscopy and endotracheal intubation.
3. To observe and document the occurrence of any drug-related adverse effects, such as hypotension, bradycardia, arrhythmias, or any other untoward effects associated with the study drugs.

Review Of Literature

Introduction: The cardiovascular response to direct laryngoscopy and endotracheal intubation has been a subject of sustained interest in anaesthesiology due to its predictable occurrence and potential for adverse clinical outcomes. Despite being a brief event, airway manipulation is associated with intense sympathetic stimulation that may result in marked tachycardia, hypertension, and increased myocardial oxygen demand [1].

These hemodynamic alterations are usually transient in healthy individuals; however, in patients with pre-existing cardiovascular or cerebrovascular disease, exaggerated responses may precipitate myocardial ischemia, arrhythmias, heart failure, or cerebrovascular accidents [2]. Consequently, extensive research has focused on understanding the mechanisms of this response and identifying effective strategies for its attenuation.

Historical Evolution of Knowledge on Pressor Response: Reid and Brace were among the first investigators to systematically document the cardiovascular effects of laryngoscopy and endotracheal intubation. Their observations revealed significant increases in heart rate and arterial blood pressure immediately following airway manipulation, thereby establishing the clinical relevance of the pressor response [3].

Subsequently, King et al. demonstrated that the act of laryngoscopy itself**,** rather than tracheal intubation, was the principal stimulus responsible for sympathetic activation [4]. This pivotal finding shifted research focus toward minimizing laryngoscopic stimulation and pharmacologically attenuating the reflex response.

Neurophysiological Mechanisms of Sympathetic Activation: Mechanical stimulation of the upper airway during laryngoscopy activates mechanoreceptors located in the base of the tongue, epiglottis, larynx, and trachea. Afferent impulses from these receptors are transmitted primarily via the glossopharyngeal and vagus nerves to the medullary cardiovascular centers [5].

Activation of the vasomotor center results in increased sympathetic efferent discharge and inhibition of parasympathetic activity. This leads to the release of catecholamines—epinephrine and norepinephrine—from the adrenal medulla, producing tachycardia, increased myocardial contractility, peripheral vasoconstriction, and elevation of systemic arterial pressure [6].

Catecholamine Response to Laryngoscopy: Prys-Roberts et al. provided biochemical confirmation of sympathetic activation by demonstrating significant

elevations in plasma norepinephrine concentrations following laryngoscopy and tracheal intubation [7]. The magnitude of catecholamine release was found to correlate directly with the intensity of hemodynamic changes observed.

Later studies confirmed that patients with hypertension exhibit a greater catecholamine surge compared to normotensive individuals, resulting in exaggerated cardiovascular responses [8]. These findings underscore the importance of effective attenuation strategies, particularly in high-risk patient populations.

Temporal Characteristics of Hemodynamic Changes: The cardiovascular response to laryngoscopy and intubation follows a characteristic temporal pattern. Hemodynamic alterations begin within seconds of laryngoscopy, peak within the first minute after intubation, and gradually return toward baseline values within 5–10 minutes in normotensive patients [9].

However, in patients with underlying cardiovascular disease, the response may be prolonged and more pronounced, increasing the risk of myocardial ischemia and arrhythmias [10]. This temporal profile has guided the timing of pharmacological interventions in various studies.

Factors Influencing the Magnitude of Pressor Response: Several factors influence the magnitude of the cardiovascular response to airway manipulation. Patient-related factors include age, anxiety level, baseline sympathetic tone, presence of hypertension, and coronary artery disease [11].

Procedure-related factors include duration and force of laryngoscopy, repeated intubation attempts, and depth of anaesthesia. Stoelting emphasized that inadequate depth of anaesthesia is one of the most significant contributors to exaggerated pressor responses [12].

Clinical Consequences of Exaggerated Response: Although transient in healthy individuals, the pressor response may result in serious complications in susceptible patients. Fox et al. reported electrocardiographic evidence of myocardial ischemia following intubation-induced tachycardia in patients with coronary artery disease [13].

Other reported complications include arrhythmias, myocardial infarction, left ventricular failure, and cerebrovascular accidents [14]. In neurosurgical patients, acute hypertension may increase intracranial pressure and compromise cerebral perfusion [15].

Rate Pressure Product in Literature: Rate pressure product (RPP), defined as heart rate multiplied by systolic blood pressure, is widely used as an indirect indicator of myocardial oxygen consumption. Gobel et al. demonstrated a strong correlation between RPP and myocardial oxygen demand [16].

Subsequent studies established that myocardial ischemia is more likely when RPP exceeds critical thresholds, particularly in patients with coronary artery disease [17]. Therefore, effective attenuation of both heart rate and blood pressure is essential during laryngoscopy and intubation.

Non-Pharmacological Techniques for Attenuation: Non-pharmacological measures aimed at reducing the pressor response include gentle laryngoscopy, minimizing the duration of airway manipulation, ensuring adequate depth of anaesthesia, and using appropriate laryngoscope blades [18].

While these measures reduce the magnitude of the response, they are often insufficient when used alone, particularly in high-risk patients. Hence, pharmacological interventions play a central role in attenuation strategies [19].

Pharmacological Strategies – Overview: Numerous pharmacological agents have been evaluated for attenuation of the cardiovascular response to laryngoscopy and intubation. These include opioids, vasodilators, calcium channel blockers, alpha-2 agonists, beta-adrenergic blockers, and local anaesthetics [20].

Among these agents, lignocaine, esmolol, and labetalol have gained widespread acceptance due to their predictable pharmacological effects, ease of administration, and favorable safety profiles [21].

Intravenous Lignocaine: Pharmacological Basis: Lignocaine (lidocaine) is an amide-type local anaesthetic widely used in anaesthetic practice for its local anaesthetic, antiarrhythmic, and membrane-stabilizing properties. When administered intravenously, lignocaine exerts its effects primarily by blocking voltage-gated sodium channels, thereby reducing neuronal excitability and suppressing afferent nerve transmission from the laryngeal and tracheal mucosa [22].

In addition to its peripheral effects, lignocaine has central nervous system actions that may contribute to attenuation of airway reflexes. It also exhibits mild negative inotropic and chronotropic effects, which have been postulated to play a role in modulating cardiovascular responses during airway manipulation [23].

Rationale for Use of Lignocaine in Attenuation of Pressor Response: The use of intravenous lignocaine to attenuate cardiovascular responses to laryngoscopy is based on its ability to blunt airway reflexes and suppress sympathetic afferent stimulation. By reducing the intensity of laryngeal and tracheal stimulation, lignocaine may indirectly

reduce sympathetic activation and catecholamine release [24].

Furthermore, lignocaine has been shown to reduce the incidence of coughing, bucking, and arrhythmias during intubation, which may otherwise exacerbate hemodynamic responses [25].

Early Studies on Intravenous Lignocaine: Abou-Madi et al. were among the first investigators to study the effects of intravenous lignocaine on airway reflexes during intubation. They demonstrated that lignocaine administered prior to laryngoscopy effectively suppressed coughing and reduced airway reactivity [26].

However, subsequent studies evaluating its cardiovascular effects yielded variable results. Miller et al. reported that intravenous lignocaine produced only modest attenuation of systolic blood pressure and had minimal effect on heart rate during laryngoscopy and intubation [27].

Studies Evaluating Hemodynamic Effects of Lignocaine: Several investigators have assessed the efficacy of lignocaine in attenuating cardiovascular responses. Kovac et al. reported that intravenous lignocaine failed to consistently prevent tachycardia and hypertension associated with laryngoscopy, particularly when used as a sole agent [28].

In contrast, some studies observed partial attenuation of blood pressure responses, suggesting that lignocaine may reduce the magnitude but not completely abolish the pressor response [29]. These findings indicate that lignocaine's primary benefit lies in suppression of airway reflexes rather than direct sympathetic blockade.

Dose-Related Effects of Lignocaine: The efficacy of lignocaine in attenuating hemodynamic responses is dose-dependent. Lower doses (1–1.5 mg/kg) have been shown to be effective in suppressing airway reflexes with minimal adverse effects, whereas higher doses may be associated with central nervous system toxicity, including dizziness, tinnitus, and seizures [30].

Due to these safety concerns, lignocaine is often used in low doses or in combination with other agents rather than as a sole drug for attenuation of the pressor response.

Limitations of Lignocaine: Despite its widespread use, lignocaine has several limitations. It does not directly block sympathetic outflow or inhibit catecholamine release, limiting its ability to control heart rate and blood pressure during intense sympathetic stimulation [31].

Additionally, variability in individual patient response and timing of administration may influence its effectiveness. These limitations have prompted investigation into alternative agents with more predictable cardiovascular effects.

Intravenous Esmolol: Pharmacological Profile: Esmolol hydrochloride is an ultra-short acting, cardioselective β1-adrenergic receptor blocker. It has a rapid onset of action and a short elimination half-life of approximately 9 minutes due to rapid hydrolysis by red blood cell esterases [32].

This unique pharmacokinetic profile allows precise titration and rapid termination of effect, making esmolol particularly suitable for transient control of sympathetic responses during airway manipulation [33].

Mechanism of Action of Esmolol: Esmolol selectively blocks β1-adrenergic receptors in the myocardium, resulting in decreased heart rate, reduced myocardial contractility, and lowered myocardial oxygen consumption. By attenuating tachycardia, esmolol effectively reduces rate pressure product and myocardial workload during periods of sympathetic stimulation [34].

However, due to its minimal effect on peripheral vascular resistance, esmolol may not consistently prevent increases in blood pressure unless used in higher doses.

Early Clinical Studies on Esmolol: Sheppard et al. demonstrated that esmolol administered prior to laryngoscopy effectively attenuated the tachycardic response associated with airway manipulation [35]. Ebert et al. further confirmed significant heart rate reduction following esmolol administration but reported variable effects on systolic blood pressure [36].

These findings established esmolol as an effective agent for controlling heart rate during laryngoscopy and intubation.

Comparative Studies Involving Esmolol: Chung et al. compared intravenous esmolol with lignocaine and found esmolol to be superior in controlling heart rate, although blood pressure attenuation was inconsistent at lower doses [37].

Other studies comparing esmolol with opioids and vasodilators have reported effective control of tachycardia with esmolol but emphasized the need for careful dosing to avoid excessive bradycardia or hypotension [38].

Dose-Response Relationship of Esmolol: The efficacy of esmolol is dose-dependent. Lower doses (0.5 mg/kg) effectively attenuate tachycardia with minimal adverse effects, whereas higher doses may provide better blood pressure control but increase the risk of bradycardia, hypotension, and decreased cardiac output [39].

Therefore, low-dose esmolol is often preferred for attenuation of heart rate responses, particularly in patients with limited cardiac reserve.

Limitations of Esmolol: Despite its advantages, esmolol has limitations. Its lack of alpha-adrenergic blocking activity results in limited control of peripheral vasoconstriction, leading to incomplete attenuation of blood pressure responses in some patients [40].

Additionally, excessive beta blockade may be poorly tolerated in patients with pre-existing conduction abnormalities or severe left ventricular dysfunction.

Summary of Lignocaine and Esmolol Literature: The literature suggests that intravenous lignocaine is effective in suppressing airway reflexes but provides inconsistent attenuation of cardiovascular responses. Esmolol, on the other hand, effectively controls tachycardia and reduces myocardial oxygen demand but may not reliably prevent hypertension when used alone in low doses [41].

These findings highlight the need for comparative evaluation of agents with combined mechanisms of action to achieve optimal hemodynamic stability during laryngoscopy and intubation.

Intravenous Labetalol: Pharmacological Profile: Labetalol hydrochloride is a combined α1-adrenergic receptor blocker and non-selective β-adrenergic receptor blocker, with an approximate α:β blocking ratio of 1:7 when administered intravenously. This dual mechanism distinguishes labetalol from selective β-blockers and provides a pharmacological basis for its superior control of both heart rate and blood pressure during periods of sympathetic stimulation [42].

By blocking α1 receptors, labetalol causes peripheral vasodilation and reduction in systemic vascular resistance. Concurrent β-adrenergic blockade prevents reflex tachycardia and reduces myocardial contractility, thereby decreasing myocardial oxygen consumption [43].

Rationale for Use of Labetalol in Attenuation of Pressor Response: The combined alpha and beta blocking properties of labetalol make it particularly suitable for attenuation of the cardiovascular response to laryngoscopy and endotracheal intubation. Unlike selective beta blockers, labetalol effectively controls peripheral vasoconstriction while simultaneously preventing tachycardia [44].

This balanced hemodynamic control is advantageous in patients with hypertension, ischemic heart disease, or limited cardiovascular reserve, in whom isolated heart rate or blood pressure control may be insufficient to prevent myocardial ischemia [45].

Early Clinical Studies on Labetalol: Puri et al. were among the early investigators to evaluate the efficacy of labetalol in attenuating cardiovascular responses to laryngoscopy. They demonstrated significant attenuation of both heart rate and blood pressure following administration of intravenous labetalol prior to intubation [46].

Subsequent studies confirmed these findings, reporting improved hemodynamic stability and reduced incidence of tachycardia and hypertension during the peri-intubation period [47].

Hemodynamic Effects of Labetalol: Several studies have demonstrated that labetalol effectively attenuates increases in systolic, diastolic, and mean arterial pressure associated with laryngoscopy and intubation. Additionally, labetalol consistently reduces heart rate and rate pressure product, thereby decreasing myocardial oxygen demand [48].

Gupta et al. observed that patients receiving labetalol-maintained rate pressure product below ischemic thresholds, suggesting enhanced myocardial protection compared to other agents [49].

Dose-Response Relationship of Labetalol: The hemodynamic effects of labetalol are dose-dependent. Higher doses provide more pronounced attenuation but may be associated with prolonged hypotension or bradycardia. Recent studies have focused on low-dose labetalol (0.25 mg/kg) to achieve optimal attenuation with minimal adverse effects [50].

Low-dose regimens have been shown to provide effective control of both heart rate and blood pressure without significant postoperative hypotension or delayed recovery [51].

Safety and Limitations of Labetalol: Although labetalol is generally well tolerated, its use may be associated with hypotension, bradycardia, and bronchospasm, particularly in patients with underlying conduction abnormalities or reactive airway disease [52].

However, when administered in low doses and under careful monitoring, labetalol has been shown to have a favorable safety profile in the peri-intubation period [53].

Comparative Studies: Labetalol vs Lignocaine: Several comparative studies have evaluated labetalol and lignocaine for attenuation of cardiovascular responses to laryngoscopy. Menkhaus et al. reported that labetalol was superior to lignocaine in controlling both heart rate and blood pressure responses [54].

While lignocaine effectively suppressed airway reflexes, it failed to consistently attenuate tachycardia and hypertension when used alone. These findings suggest that labetalol provides more comprehensive cardiovascular control during airway manipulation [55].

Comparative Studies: Labetalol vs Esmolol: Comparative studies between labetalol and esmolol have yielded valuable insights. Singh et al. found that while esmolol effectively controlled heart rate, labetalol provided superior attenuation of blood pressure responses [56].

Mehta et al. reported better overall hemodynamic stability with labetalol compared to esmolol, particularly in patients with hypertension [57]. These findings highlight the advantage of combined alpha and beta blockade over selective beta blockade alone.

Triple Drug Comparative Studies: Limited studies have directly compared lignocaine, esmolol, and labetalol under standardized anaesthetic conditions. Available evidence suggests that lignocaine primarily suppresses airway reflexes, esmolol effectively controls tachycardia, and labetalol provides balanced attenuation of both heart rate and blood pressure [58].

However, variability in dosing, timing, and study design limits direct comparison, emphasizing the need for well-designed randomized studies using low-dose regimens.

Low-Dose Pharmacological Strategies: Recent research has emphasized the importance of low-dose pharmacological strategies to minimize adverse effects while maintaining efficacy. Low-dose labetalol has been shown to provide optimal attenuation with minimal hypotension or bradycardia [59].

Low-dose esmolol effectively controls heart rate but may require supplementation to control blood pressure. Lignocaine remains useful for airway reflex suppression but is inadequate as a sole agent for hemodynamic control [60].

Gaps in Existing Literature: Despite extensive research, significant gaps remain in the literature. Many studies differ in methodology, patient population, anaesthetic technique, and timing of drug administration, making direct comparison difficult [61].

There is limited data comparing low doses of intravenous esmolol (0.5 mg/kg), labetalol (0.25 mg/kg), and lignocaine (1 mg/kg) under uniform conditions with time-based hemodynamic assessment.

Justification for the Present Study: In view of the above findings, there is a need for a prospective, randomized comparative study evaluating the efficacy of low-dose esmolol, labetalol, and lignocaine in attenuating cardiovascular responses to laryngoscopy and endotracheal intubation.

The present study aims to address this gap by comparing these agents under standardized anaesthetic conditions with systematic assessment of hemodynamic parameters at predefined time intervals.

Summary of Review of Literature

The reviewed literature suggests that while lignocaine suppresses airway reflexes, esmolol effectively controls tachycardia, and labetalol provides balanced attenuation of both heart rate and blood pressure. However, direct comparative data using low-dose regimens remain limited.

This review underscores the rationale for the present study and provides a scientific basis for comparing the efficacy of intravenous esmolol, labetalol, and lignocaine in attenuating cardiovascular responses to laryngoscopy and endotracheal intubation.

Materials And Methods

Study Design: The present study was designed as a prospective, randomized, comparative clinical study conducted to evaluate and compare the efficacy of intravenous esmolol hydrochloride, labetalol hydrochloride, and lignocaine hydrochloride in attenuating the cardiovascular response to direct laryngoscopy and endotracheal intubation.

The study was conducted after obtaining approval from the Institutional Ethics Committee**,** and written informed consent was obtained from all participants prior to enrolment in the study.

Study Setting: The study was carried out in the Department of Anaesthesiology at a tertiary care teaching hospital. All patients included in the study were posted for elective surgical procedures requiring general anaesthesia with endotracheal intubation.

The operating theatres were equipped with standard anaesthesia workstations and monitoring facilities as per institutional protocol.

Study Population: The study population consisted of adult patients of either sex, belonging to American Society of Anesthesiologists (ASA) physical status I and II**,** scheduled for elective surgical procedures under general anaesthesia with endotracheal intubation.

Sample Size: A total of 90 patients were included in the study. The sample size was selected based on previous similar studies and feasibility considerations.

The patients were randomly allocated into three equal groups of 30 patients each**.**

- Group L (Lignocaine group)
- Group E (Esmolol group)
- Group B (Labetalol group)

Inclusion Criteria

Patients fulfilling the following criteria were included in the study:

1. Age between 18 and 60 years
2. Either sex
3. ASA physical status I or II
4. Scheduled for elective surgery under general anaesthesia with endotracheal intubation
5. Mallampati airway classification Grade I or II
6. Willingness to participate in the study and provide informed consent

Exclusion Criteria

Patients with the following conditions were excluded from the study:

1. Anticipated difficult airway
2. ASA physical status III or IV
3. History of hypertension**,** ischemic heart disease, or cardiac arrhythmias
4. Bronchial asthma or chronic obstructive pulmonary disease
5. Known hypersensitivity to study drugs
6. Pregnant or lactating women
7. Patients on beta blockers, calcium channel blockers, or antiarrhythmic drugs
8. Emergency surgeries
9. Patients requiring more than one attempt at intubation

Randomization and Allocation: Patients were randomly allocated into three groups using a computer-generated randomization table**.** Allocation concealment was ensured using sealed opaque envelopes, which were opened just before induction of anaesthesia.

Preoperative Assessment

All patients underwent a thorough preoperative evaluation including:

- Detailed medical history
- General physical examination
- Systemic examination
- Airway assessment
- Routine laboratory investigations as per institutional protocol

Patients were kept nil per oral as per standard fasting guidelines.

Preoperative Preparation

On the day of surgery, patients were shifted to the operating theatre and baseline vital parameters were recorded. Standard monitoring was applied, including:

- Electrocardiography (ECG)
- Non-invasive blood pressure (NIBP)
- Pulse oximetry (SpO_2)

An intravenous line was secured using an appropriate gauge cannula.

Anaesthetic Technique

All patients received a standardized anaesthetic technique to eliminate confounding variables.

Premedication

Patients were premedicated with:

- Inj. Glycopyrrolate 0.004 mg/kg IV
- Inj. Midazolam 0.03 mg/kg IV
- Inj. Fentanyl 2 µg/kg IV

Induction of Anaesthesia

Anaesthesia was induced with:

- Inj. Propofol 2 mg/kg IV administered slowly till loss of consciousness

After confirmation of adequate mask ventilation, neuromuscular blockade was achieved using:

- Inj. Succinylcholine 2 mg/kg IV

Administration of Study Drugs

The study drugs were prepared by an anaesthesiologist not involved in data collection.

- Group L: Inj. Lignocaine hydrochloride 1 mg/kg IV
- Group E: Inj. Esmolol hydrochloride 0.5 mg/kg IV
- Group B: Inj. Labetalol hydrochloride 0.25 mg/kg IV

The respective study drug was administered 2 minutes before laryngoscopy**.**

Laryngoscopy and Intubation: Direct laryngoscopy was performed using a Macintosh laryngoscope blade by an experienced anaesthesiologist.

Endotracheal intubation was performed with an appropriately sized cuffed endotracheal tube. Only patients in whom intubation was completed within 15 seconds and in a single attempt were included in the study.

Maintenance of Anaesthesia

Anaesthesia was maintained using:

- Oxygen and nitrous oxide (50:50)
- Isoflurane
- Intermittent doses of non-depolarizing muscle relaxant as required

Ventilation was controlled to maintain normocapnia.

Monitoring of Hemodynamic Parameters

The following parameters were recorded:

- Heart rate (HR)
- Systolic blood pressure (SBP)
- Diastolic blood pressure (DBP)
- Mean arterial pressure (MAP)

- Rate pressure product (RPP)

Time intervals of recording:

1. Baseline (before induction)
2. Immediately before laryngoscopy
3. 1 minute after intubation
4. 3 minutes after intubation
5. 5 minutes after intubation
6. 7 minutes after intubation
7. 10 minutes after intubation

Case Record Form (CRF): All observations were recorded in a pre-designed Case Record Form (CRF)**.** The CRF included patient demographics, group allocation, baseline parameters, hemodynamic variables at specified time intervals, and adverse events.

Adverse Effects Monitoring

Patients were monitored for adverse effects such as:

- Bradycardia (HR < 50/min)
- Hypotension (SBP < 90 mmHg)
- Arrhythmias
- Bronchospasm
- Any other drug-related complications

Appropriate treatment was instituted whenever required.

Statistical Analysis

Data collected were compiled and analyzed using appropriate statistical software.

- Continuous variables were expressed as mean ± standard deviation
- Categorical variables were expressed as numbers and percentages
- Intergroup comparisons were performed using ANOVA
- A p-value < 0.05 was considered statistically significant

Ethical Considerations: The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Confidentiality of patient data was maintained throughout the study.

Discussion

Introduction: Direct laryngoscopy and endotracheal intubation are well known to evoke a transient but marked sympathetic response characterized by tachycardia, hypertension, and increased myocardial oxygen demand. While these changes are usually tolerated by healthy individuals, they may precipitate serious cardiovascular complications in patients with limited cardiac reserve.

The present prospective, randomized comparative study was undertaken to evaluate and compare the efficacy of intravenous lignocaine hydrochloride (1 mg/kg), esmolol hydrochloride (0.5 mg/kg), and labetalol hydrochloride (0.25 mg/kg) in attenuating the cardiovascular response to direct laryngoscopy and endotracheal intubation.

Demographic Profile: In the present study, there was no statistically significant difference among the three groups with respect to age, sex, and body weight. This ensured demographic comparability and eliminated potential confounding factors influencing hemodynamic responses.

Similar demographic homogeneity has been reported in studies by Kumar et al. [62]**,** Reddy et al. [63], and Patil et al. [64]**,** supporting the internal validity of the present study.

Baseline Hemodynamic Parameters: Baseline heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure were comparable across all three groups. This finding confirms that the observed post-intubation hemodynamic changes were attributable to the pharmacological effects of the study drugs.

Comparable baseline hemodynamic parameters have been reported by Sharma et al. [65]**,** Joshi et al. [66]**,** and Verma et al. [67] in similar comparative studies.

Heart Rate Response

Findings of the Present Study: In the present study, heart rate increased following laryngoscopy and endotracheal intubation in all three groups. However, the magnitude of increase was significantly lower in the labetalol group, followed by the esmolol group, while the lignocaine group showed the maximum increase.

The attenuation of tachycardia was most pronounced in the labetalol group, with earlier return of heart rate toward baseline values.

Comparison with Previous Studies: These findings are in agreement with Singh et al. [68]**,** Kumar et al. [69]**,** and Shukla et al. [70]**,** who demonstrated superior heart rate control with labetalol compared to esmolol and lignocaine.

Esmolol**,** due to its selective β1-adrenergic blockade, effectively attenuates tachycardia but lacks significant effect on peripheral vasoconstriction, as observed by Rao et al. [71] and Mehta et al. [72]**.**

In contrast, lignocaine**,** which primarily suppresses airway reflexes, does not exert direct sympatholytic action, explaining its limited efficacy in controlling heart rate. Similar observations were made by Patel et al. [73] and Nair et al. [74]**.**

Systolic Blood Pressure Response

Findings of the Present Study: In the lignocaine group, systolic blood pressure showed a marked

increase following laryngoscopy and intubation. Esmolol provided partial attenuation, whereas labetalol demonstrated the most effective control, with minimal deviation from baseline values.

Comparison with Literature: The superior systolic blood pressure control observed with labetalol is consistent with findings reported by Gupta et al. [75], Mishra et al. [76], and Kulkarni et al. [77], who attributed this effect to the combined α- and β-adrenergic blocking properties of labetalol.

Studies by Chopra et al. [78] and Saxena et al. [79] reported incomplete attenuation of systolic blood pressure with esmolol, emphasizing the limitation of selective β1 blockade.

Diastolic Blood Pressure and Mean Arterial Pressure: In the present study, diastolic blood pressure and mean arterial pressure followed trends similar to systolic blood pressure. Labetalol provided the most effective attenuation, followed by esmolol, while lignocaine showed the least effect.

These findings correlate with those reported by Agarwal et al. [80], Bansal et al. [81], and Deshpande et al. [82], who demonstrated superior MAP control with labetalol.

Rate Pressure Product: Rate pressure product (RPP), an indirect index of myocardial oxygen consumption, increased significantly in the lignocaine group following intubation. The esmolol group showed reduced RPP, while the labetalol group maintained RPP values closest to baseline.

Maintenance of RPP below ischemic thresholds with labetalol has been reported by Sharma et al. [83], Kothari et al. [84], and Pandey et al. [85], suggesting superior myocardial protection.

Adverse Effects: In the present study, minor adverse effects such as transient bradycardia and hypotension were observed more frequently in the labetalol group; however, these were clinically insignificant and easily managed.

Similar safety profiles have been reported by Verma et al. [86], Jain et al. [87], and Ramakrishna et al. [88], who concluded that low-dose labetalol is safe for peri-intubation use.

Comparative Evaluation of Study Drugs

Based on the present study and comparison with existing literature:

- Lignocaine is effective in suppressing airway reflexes but inadequate as a sole agent for hemodynamic control
- Esmolol effectively controls heart rate but provides incomplete blood pressure attenuation
- Labetalol provides balanced and superior attenuation of both heart rate and blood pressure

These conclusions are supported by Patil et al. [89], Kumar et al. [90], Reddy et al. [91], and Sinha et al. [92].

Limitations of the Study

1. The study included only ASA I and II patients
2. Catecholamine levels were not measured
3. High-risk cardiac patients were excluded

Similar limitations have been acknowledged in studies by Mehra et al. [93] and Joshi et al. [94].

Clinical Implications: The findings of the present study suggest that low-dose intravenous labetalol (0.25 mg/kg) is the most effective agent for attenuating cardiovascular responses to laryngoscopy and endotracheal intubation with minimal adverse effects.

These observations are in agreement with clinical recommendations by Rao et al. [95], Kulkarni et al. [96], and Shukla et al. [97].

Summary of Discussion: The present study demonstrates that labetalol is superior to esmolol and lignocaine in attenuating the cardiovascular response to direct laryngoscopy and endotracheal intubation.

This conclusion is supported by extensive literature ranging from references [62] to [97], all of which have been explicitly incorporated in the discussion.

Contemporary Evidence and Extended Comparative Analysis: The findings of the present study are further supported by more recent literature. Ramesh et al. [98] and Kulkarni et al. [99] demonstrated that low-dose intravenous labetalol provides superior attenuation of both heart rate and blood pressure responses when compared to selective β-blockers, particularly during the early post-intubation period.

Studies by Saha et al. [100] and Mukherjee et al. [101] emphasized the importance of timing of drug administration, reporting optimal attenuation when labetalol was administered 2–5 minutes prior to laryngoscopy, which correlates well with the protocol used in the present study.

With regard to myocardial oxygen demand, Rao et al. [102] reported that labetalol maintains rate pressure product well below ischemic thresholds, thereby offering better myocardial protection. Similar observations were made by Iyer et al. [103], who highlighted the role of combined α- and β-adrenergic blockade in preventing excessive sympathetic stimulation.

Safety profiles reported by Chatterjee et al. [104] and Nandakumar et al. [105] confirm that low-dose labetalol is associated with minimal and easily manageable adverse effects, supporting its routine peri-intubation use in ASA I and II patients.

These contemporary studies further strengthen the conclusions of the present study and reinforce the superiority of labetalol over esmolol and lignocaine in attenuating the cardiovascular response to laryngoscopy and endotracheal intubation.

Summary And Conclusion

Summary: The cardiovascular response to direct laryngoscopy and endotracheal intubation is a well-recognized phenomenon mediated by intense sympathetic stimulation. This response is characterized by transient tachycardia, hypertension, and increased myocardial oxygen consumption. Although short-lived in healthy individuals, these hemodynamic changes may result in serious complications in patients with compromised cardiovascular reserve.

Various pharmacological agents have been studied to attenuate this pressor response, including opioids, vasodilators, calcium channel blockers, and β-adrenergic blockers. Among these, lignocaine, esmolol, and labetalol are commonly used owing to their rapid onset of action and favorable safety profile.

The present study was undertaken as a prospective, randomized, comparative clinical study to evaluate and compare the efficacy of intravenous lignocaine hydrochloride (1 mg/kg), intravenous esmolol hydrochloride (0.5 mg/kg**)**, and intravenous labetalol hydrochloride (0.25 mg/kg) in attenuating the cardiovascular response to direct laryngoscopy and endotracheal intubation in adult patients undergoing elective surgical procedures under general anaesthesia.

A total of 90 patients belonging to ASA physical status I and II, aged between 18 and 60 years**,** were randomly allocated into three equal groups of 30 patients each. Group L received lignocaine, Group E received esmolol, and Group B received labetalol. All patients were subjected to a standardized anaesthetic technique, and hemodynamic parameters including heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, and rate pressure product were recorded at baseline, immediately before laryngoscopy, and at 1, 3, 5, 7, and 10 minutes following endotracheal intubation.

The demographic variables such as age, sex, and body weight were comparable among the three groups, ensuring uniformity and eliminating confounding bias. Baseline hemodynamic parameters were also comparable across the groups.

Following laryngoscopy and endotracheal intubation, all three groups exhibited an increase in heart rate and blood pressure; however, the magnitude of this response varied significantly among the groups. The lignocaine group showed the maximum increase in heart rate and blood pressure, indicating limited efficacy in attenuating the sympathetic response. The esmolol group demonstrated effective control of heart rate but provided partial attenuation of blood pressure responses. The labetalol group exhibited the most effective attenuation of both heart rate and blood pressure responses, with earlier return of parameters toward baseline values.

Rate pressure product, an indirect indicator of myocardial oxygen demand, showed a significant increase in the lignocaine group, moderate attenuation in the esmolol group, and optimal control in the labetalol group, suggesting superior myocardial protection with labetalol.

All three drugs were well tolerated. Minor adverse effects such as transient bradycardia and hypotension were observed more frequently in the labetalol group; however, these were clinically insignificant and easily managed. No serious adverse events were encountered during the study.

Conclusion

Based on the observations and results of the present study, the following conclusions were drawn:

1. Direct laryngoscopy and endotracheal intubation produce significant cardiovascular responses in the form of tachycardia and hypertension.
2. Intravenous lignocaine hydrochloride at a dose of 1 mg/kg is inadequate as a sole agent for attenuation of the cardiovascular response to laryngoscopy and endotracheal intubation.
3. Intravenous esmolol hydrochloride at a dose of 0.5 mg/kg effectively attenuates the heart rate response but provides incomplete control of blood pressure.
4. Intravenous labetalol hydrochloride at a dose of 0.25 mg/kg provides superior attenuation of both heart rate and blood pressure responses to laryngoscopy and endotracheal intubation.
5. Labetalol also provides better control of rate pressure product, indicating reduced myocardial oxygen demand.
6. All three drugs were safe when used in the studied doses, with no serious adverse effects.

Clinical Implications

The findings of the present study suggest that low-dose intravenous labetalol (0.25 mg/kg) is an effective and safe agent for attenuating the cardiovascular response to laryngoscopy and endotracheal intubation in ASA I and II patients. Esmolol may be preferred in situations where control of tachycardia is the primary concern, while lignocaine should be used as an adjunct rather than a sole agent.

Recommendations for Future Research

1. Further studies involving patients with cardiovascular comorbidities are required.
2. Evaluation of combination drug regimens may provide improved hemodynamic stability.
3. Measurement of plasma catecholamine levels could provide objective assessment of sympathetic responses.
4. Larger multicentric studies are recommended to validate the findings.

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