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Comparison of Dexmedetomidine and Labetalol for Attenuating Stress Response in Hypertensive Patients

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ABSTRACT

Laryngoscopy and tracheal intubation during general anesthesia provoke a sympathetic stress reaction that has significant hemodynamic changes. This can be risky, particularly in patients with controlled hypertension with compromised cardiovascular reserve. **Objective:** To compare the effect of dexmedetomidine and labetalol for attenuating stress response in hypertensive patients. **Methods:** A quasi-experimental study that involved 200 controlled hypertensive patients admitted to the elective surgery and placed under general anesthetic procedures. Patients received Intravenous dexmedetomidine (0.1 mcg/kg) or labetalol (0.1 mg/kg). It was observed that the mean heart rate and mean arterial blood pressure were measured at baseline and two minutes after endotracheal intubation. The statistics were performed using the independent sample t-test, which was used to compare the results observed between the two treatment groups. **Results:** The heart rate 2 minutes following intubation was much lower in Group D (78 ± 8.27 beats/minute) than in Group L (81 ± 5.30 beats/minute, p=0.0026). Further, the mean arterial blood pressure was declining remarkably in the dexmedetomidine group (98 ± 7.26 mmHg), compared to the labetalol group (101 ± 8.2 mmHg; p=0.0067). **Conclusions:** The present group of controlled hypertensive patients indicated that dexmedetomidine pre-induction, in comparison to labetalol, led to a significantly more significant reduction of hypertensive and tachycardic reaction to laryngoscopy and endotracheal intubation.

INTRODUCTION

Laryngoscopy and endotracheal intubation are obligatory parts of general anesthesia but are also known to be great triggering factors of substantial hemodynamic stress reactions. It is a sympathetic-mediated reflex that results in a short-lived but sharp increase in hemodynamic parameters [1, 2]. Though healthy individuals can withstand such changes, the reaction is risky in patients with cardiovascular comorbidities (especially hypertension). The acute rise in hemodynamic parameters in such individuals predisposes them to the onset of myocardial ischemia, cerebral vascular accidents, and perioperative arrhythmia [3]. This danger is also increased in hypertensive patients since chronic vascular remodeling, which reduces baroreceptor sensitivity in the process of buffering the sudden sympathetic stimulation [4]. There are many examples of pharmacologic agents:

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opioids, lidocaine, beta-blockers, and calcium channel blockers, which have been employed to reduce the intubation response [5]. Labetalol, an alpha-non-selective and beta-blocker, has proven to be the most popular in the perioperative units since it offers effective blood pressure regulation with no reflex tachycardia effect [6]. Research revealed that labetalol by the intravenous route has a greater effect in slowing the heart rate with a decrease in the elevation in blood pressure after laryngoscopy in hypertensive and cardiac-risk patients [7]. Dexmedetomidine is a very specific 2-adrenergic agonist that is very popular because it has strong sympatholytic, sedative, and analgesic but no respiratory depression properties [8]. Dexmedetomidine offers better hemodynamic stability during high-intensity noxious stimulation by decreasing the central sympathetic outflow. Different clinical trials indicated that dexmedetomidine pre-induction is very effective in blunting the hemodynamic effect of intubation and decreasing the amount of catecholamine release during peri-surgery [9, 10]. As much as the stress response around laryngoscopy has been proven to be reduced by both labetalol and dexmedetomidine separately, no head-to-head studies have been directly compared, especially in patients with well-managed hypertension. This group of individuals constitutes a special predicament, because continuous antihypertensive treatment might distort compensatory autonomic responses, and the choice of an agent is of paramount importance to prevent the occurrence of adverse cardiovascular events [11, 12]. It has been emphasized in recent literature that in hypertensive cohorts, special consideration should be directed towards the pharmacologic approach to assessment and evaluation since it has a disproportionately greater perioperative morbidity [13].

Enhancement of evidence in this field may make anesthetic practice safer in the perioperative management of a high-risk population. There is a lack of direct comparative evidence between intravenous dexmedetomidine and labetalol for attenuating the hemodynamic response to laryngoscopy and endotracheal intubation in patients with well-controlled hypertension. This study aimed to compare the effectiveness of intravenous dexmedetomidine and labetalol in the attenuation of hemodynamic stress response to laryngoscopy and endotracheal intubation in controlled hypertensive patients during elective surgery.

METHODS

A quasi-experimental study was conducted in the operating theaters of Mayo Hospital, Lahore, between March 20, 2019, and September 20, 2019, after getting permission from the ethics review committee (499/RC/KEMU). Two hundred potential patients were also identified and included in the ultimate analysis. The mean blood pressure in group D (70.50 ± 4.58) and group L (76.37 ± 5.52) was used to calculate the sample size by taking 80% power of the test, 5% margin of Error and 10% drop out rate is 136 (68 in each group) [14]. The inclusion criteria were: the presence of controlled hypertension (SBP less than 140 mmHg and DBP less than 90 mmHg on a single antihypertensive agent), both genders, and age between 18 and 70 years, and a scheduled elective surgery under general anesthesia. The patients predicted hard-to-manage airway (Mallampati class > 3), a laryngoscopy time longer than 30 seconds, or more than one attempt, pre-existing coagulation disorders (INR > 1.5), morbid obesity (BMI > 35kg/m2), uncontrolled hypertension, congestive heart failure, arrhythmias, acute bronchospasm, or initial hypotension were excluded from the study. After taking the informed and written consent, the patients were enrolled in the study. The treatment received was recorded by the researchers, and the patients were classified in the following way: Group D (Dexmedetomidine): Patients were treated with intravenous dexmedetomidine 0.1 mcg/kg before induction. Group L (Labetalol): Intravenous labetalol, 0.1mg/kg before induction. The study drugs were then ready prepared by the clinical team and were all diluted in normal saline to a billed volume of 10 mL and infused over 5 minutes before anesthesia induction. None of the observations were blinded; the study team was aware of the treatment administered. Upon arrival in the operating theatre, normal non-invasive monitoring was initiated: ECG, HR, NIBP, and peripheral oxygen saturation via a normal patient monitor. Once intravenous access had been achieved, nalbuphine 0.1 mg/kg was given to all the patients. Propofol 2mg/kg was administered intravenously to induce anesthesia. The Atracurium at 0.5mg per kilogram was administered after loss of consciousness to aid the endotracheal intubation. The anesthesia was maintained by isoflurane in 100% oxygen at 1.2MAC. An anesthetist who was senior carried out laryngoscopy and endotracheal intubation. With the help of hemodynamic parameters, the mean heart rate and the mean arterial pressure were measured at the induction (baseline) and at 2 minutes after intubation. Data analysis was conducted by SPSS version 25.0. The results of quantitative variables (age, BMI, heart rate, MAP) were in the form of mean standard deviation (SD). Frequencies and percentages were used to state qualitative variables (gender, ASA status). An independent sample t-test was utilized to compare the main outcome variables, mean heart rate and MAP, in the two non-randomized groups. A p-value of less than 0.05 was taken to be statistically significant.

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RESULTS

A total of 200 patients were enrolled and completed the study, with 100 patients receiving dexmedetomidine (Group D) and 100 receiving labetalol (Group L) based on the attending physician's standard clinical practice. The two groups were found to be comparable with respect to key baseline characteristics, including age, ASA physical status, and Body Mass Index. This finding suggests that major known confounders in these categories did not significantly differ between the observed groups (Table 1).

Table 1: Comparison of Demographic Characteristics of Both Groups

Characteristic	Group D, (n=100)	Group L, (n=100)	Total (n=200)
Age Group (Years)			
18-35	20 (20.0%)	21 (21.0%)	41 (20.5%)
36-50	50 (50.0%)	45 (45.0%)	95 (47.5%)
51-70	30 (30.0%)	34 (34.0%)	64 (32.0%)
ASA Physical Status			
ASA I	40 (40.0%)	45 (45.0%)	85 (42.5%)
ASA II	60 (60.0%)	55 (55.0%)	115 (57.5%)
Body Mass Index (kg/m^2)			
Normal (18-24.9)	41 (41.0%)	38 (38.0%)	79 (39.5%)
Overweight (25-29.9)	34 (34.0%)	39 (39.0%)	73 (36.5%)
Obese (30-35)	25 (25.0%)	23 (23.0%)	48 (24.0%)

Data are presented as n (%). ASA: American Society of Anesthesiologists

The primary findings of the study revealed a statistically significant difference in the observed hemodynamic response to intubation between the two treatment groups. At two minutes post-intubation, patients in Group D had a significantly lower mean heart rate and mean arterial pressure compared to patients in Group L (Table 2).

Table 2: Difference between the Hemodynamic Parameters 2 Minutes Post-Intubation

Parameters	Group D	Group L	p-value
Mean Heart Rate (beats/min)	78 ± 8.27	81 ± 5.30	0.006
Mean Arterial Pressure (mmHg)	98 ± 7.26	101 ± 8.20	0.007

Post-hoc stratification analysis was conducted to evaluate the outcomes across subgroups of age, ASA status, and BMI. The superior observed attenuating effect of dexmedetomidine was consistent across all subgroups. In every stratification for age, ASA status, and BMI, both mean heart rate and mean arterial pressure were significantly lower in the dexmedetomidine group compared to the labetalol group ($p<0.05$ for all comparisons). Table 3 presents a detailed stratification of the outcomes based on BMI (Table 3).

Table 3: Stratification of Hemodynamic Outcomes by Body Mass Index (BMI)

Parameters	BMI Category	Group D	Group L	p-value
Mean Heart Rate (beats/min)	Normal (18-24.9)	72.50 ± 3.40	76.35 ± 5.12	<0.001
Mean Heart Rate (beats/min)	Overweight (25-29.9)	75.00 ± 4.14	78.00 ± 3.77	0.001
Mean Heart Rate (beats/min)	Obese (30-35)	74.59 ±5.49	78.00 ± 2.40	0.008
Mean Arterial Pressure (mmHg)	Normal (18-24.9)	95.5 ± 2.5	97.0 ± 2.0	0.005
Mean Arterial Pressure (mmHg)	Overweight (25-29.9)	95.5 ± 3.6	97.8 ± 3.0	0.004
Mean Arterial Pressure (mmHg)	Obese (30-35)	97.6 ± 1.5	100.0 ± 2.71	0.002

DISCUSSION

The main observation of this observational study is that pre-induction dexmedetomidine was linked to a considerably superior decrease in the hemodynamic stress response. This implies that there is a possible efficacy benefit of dexmedetomidine compared to labetalol in clinical practice in the real world [15]. This noted excellent efficiency of dexmedetomidine is pharmacologically conceivable. Dexmedetomidine is a very selective 2-adrenergic CNS agonist; the stimulation of central nervous system presynaptic 2 receptors inhibit the release of norepinephrine, inhibiting sympathetic outflow and suppressing catecholamine response to noxious stimuli like intubation [16, 17]. Conversely, labetalol offers peripheral 2 and non-selective 3 adrenergic blockade, and this can be less efficient in managing the central sympathetic surge [16]. This process is in accordance with the earlier literature that indicated more hemodynamic stability in the presence of dexmedetomidine during airway control [18]. Further, the presence of uniform advantage in stratified subgroups (age, ASA status, BMI) confirms the clinical relevance of dexmedetomidine to represent a wide group of hypertensive patients [15, 19]. The effectiveness of the effect on such subgroups indicates that the hemodynamic benefits are not limited to a specific patient profile, but they might be extended to different demographic and physiologic backgrounds. A body of literature has substantiated these results. Recent controlled prospective, randomized, double-blind studies in hypertensive patients on intubation found that the single dose of dexmedetomidine showed significant lowering of HR and MAP at different time points after intubation, with no incidence of bradycardia or hypotension necessitating a response [17]. A meta-analysis of randomized trials also established the efficacy of dexmedetomidine in the attenuation of the hemodynamic reaction to tracheal intubation with decreased HR and MAP over placebo or none of dexmedetomidine [18]. Further, other controlled

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trials have continued to confirm dexmedetomidine's excellent profile during intubation stress response, such as decreased induction dosage and consistent hemodynamics [19, 20].

Our study should be limited by limitations. To begin with, causality cannot be well-established since it is observational research. Also, the two groups were well matched on measured variables (age, BMI, ASA), however, unmeasured confounders (e.g., clinician preference, baseline cardiovascular tone, frailty) could have contributed to the development of both drugs used and the final outcomes [15,22]. We did not test dose response relationships or other administration plans (e.g., continuous infusion), the effect of which may be different from our fixed single doses. With these constraints, future studies should incorporate multicenter randomized controlled trials between dexmedetomidine and labetalol, various dosing schedules (bolus vs infusion) as well as cardiovascular outcomes in the long run. These trials would aid in establishing causality and determining the most appropriate administration measures in hypertensive patients.

CONCLUSIONS

Pre-induction dexmedetomidine was associated with better attenuation of hemodynamic response to laryngoscopy and intubation in this group of patients with controlled hypertension than labetalol. These results clinically justify the use of dexmedetomidine to encourage improved perioperative hemodynamic stability in this predisposed group of patients. However, these observational relationships should be verified by randomized trials that have wider endpoints. This observation has direct clinical implications. It indicates that dexmedetomidine has the potential to be a better agent to use in the management of perioperative hemodynamic stability among vulnerable populations of patients, which may lessen the chances of cardiovascular complications associated with airway manipulation.

Authors Contribution

Conceptualization: RK
Methodology: RK, SN, ST
Formal analysis: FA, SS
Writing and Drafting: RK, SN, ST, SA, SS, RF
Review and Editing: RK, FA, SN, ST, SA, SS, RF

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

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