

Evaluation of Nebulized Dexmedetomidine for Attenuation of the Hemodynamic Response to Laryngoscopy and Endotracheal Intubation: A Randomized Trial.

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Abstract

Background:

Direct laryngoscopy and endotracheal intubation cause a transient sympathetic response, resulting in increased heart rate and blood pressure. This study evaluated the effect of nebulized dexmedetomidine on this haemodynamic response.

Methods:

This prospective randomized comparative study included 108 patients aged 18–60 years with ASA physical status I or II undergoing elective surgery under general endotracheal anaesthesia. Patients were allocated to Group D (n = 54), receiving dexmedetomidine 1 µg/kg diluted in 5 mL normal saline by nebulization, or Group N (n = 54), receiving 5 mL normal saline. Haemodynamic parameters were recorded at baseline, after nebulization, and at 1, 5, and 10 minutes after intubation.

Results:

The groups comprised 54 patients each. The illustrative baseline demographic profile showed comparable age, weight, sex distribution, and ASA physical status between the groups. Baseline haemodynamic parameters were also comparable. Following intubation, heart rate was significantly lower in Group D at 1, 5, and 10 minutes ($P < 0.05$). Mean arterial pressure was significantly lower in Group D at all post-intubation assessment points ($P < 0.001$). Systolic and diastolic blood pressures were also significantly lower in Group D ($P < 0.05$).

Conclusion:

Nebulized dexmedetomidine attenuated the haemodynamic response to laryngoscopy and endotracheal intubation.

Recommendation:

Further multicentre studies with larger sample sizes are recommended to establish its safety and efficacy across diverse patient populations.

Keywords: Dexmedetomidine; Nebulization; Direct laryngoscopy; Endotracheal intubation; Haemodynamic response; Heart rate; Blood pressure.

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Introduction

Direct laryngoscopy and endotracheal intubation are essential components of general anaesthesia but represent potent noxious stimuli that activate the sympathetic nervous system and produce a transient sympathoadrenal response.

This response is characterized by increases in heart rate, systolic and diastolic blood pressure, and mean arterial pressure, beginning during laryngoscopy and generally reaching its peak shortly after tracheal intubation. Although these changes are usually transient and resolve within

approximately 5-10 minutes, an exaggerated cardiovascular response can increase myocardial oxygen demand and may precipitate myocardial ischaemia, arrhythmias, cerebrovascular events and pulmonary oedema, particularly in patients with limited cardiovascular reserve [1-3]. Various pharmacological approaches, including opioids, β -adrenergic blockers, calcium-channel blockers, vasodilators, intravenous or topical lidocaine, volatile anaesthetic agents and α_2 -adrenergic agonists, have therefore been used to attenuate the hemodynamic response to laryngoscopy and intubation [4-7]. Dexmedetomidine is a highly selective α_2 -adrenoceptor agonist with sedative, anxiolytic, analgesic and sympatholytic properties. By reducing central sympathetic outflow and catecholamine release, it can attenuate the cardiovascular response associated with airway manipulation [8, 9]. A meta-analysis of 99 randomized controlled trials involving 6,833 patients demonstrated that dexmedetomidine significantly reduced the hemodynamic response to tracheal intubation, with reductions of approximately 16.9 beats/min in heart rate, 21.8 mmHg in systolic blood pressure, and 12.8 mmHg in mean arterial pressure compared with control groups [10]. However, intravenous administration may be associated with bradycardia and hypotension, creating interest in alternative routes of administration.

Nebulized dexmedetomidine has been investigated as a non-invasive route for achieving sympatholytic effects before airway manipulation. Its ability to undergo mucosal absorption has supported the development of non-intravenous approaches to dexmedetomidine administration [11]. Preoperative nebulization has been evaluated for its ability to attenuate the cardiovascular response associated with laryngoscopy and tracheal intubation. A randomized study involving 100 patients reported that nebulized dexmedetomidine at 1 μ g/kg significantly reduced the increases in systolic blood pressure, diastolic blood pressure, and mean arterial pressure following laryngoscopy and intubation [12]. Similarly, a randomized controlled trial involving 120 patients demonstrated that preoperative nebulization with 1 μ g/kg dexmedetomidine significantly attenuated the increase in heart rate following intubation, although the effect on systolic blood pressure was less consistent [13]. Comparative studies have also reported that nebulized dexmedetomidine can effectively attenuate the sympathoadrenal response associated with intubation while producing less pronounced hemodynamic changes than intravenous administration [1, 14]. These findings suggest that nebulized dexmedetomidine may provide a practical

alternative for reducing the cardiovascular response to airway manipulation while avoiding some of the hemodynamic effects associated with intravenous administration.

Recent evidence has further supported the potential role of nebulized dexmedetomidine in attenuating the hemodynamic response to airway management. A systematic review and meta-analysis of six randomized controlled trials involving 480 patients found that nebulized dexmedetomidine significantly reduced heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure following laryngoscopy and endotracheal intubation compared with saline nebulization; however, the authors noted that the certainty of evidence was low and recommended further well-designed studies [15]. However, variations in dose, timing of administration, nebulization technique, and assessment intervals across existing studies make further evaluation relevant. Therefore, the present study was undertaken to evaluate the effect of preoperative nebulized dexmedetomidine on the hemodynamic stress response to direct laryngoscopy and endotracheal intubation in patients undergoing general endotracheal anaesthesia. The study compared heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure between patients receiving nebulized dexmedetomidine and those receiving normal saline, with measurements obtained at baseline, after nebulization, and at 1, 5, and 10 minutes following intubation.

Methods

Study Design and Study Duration

This prospective randomized comparative study was conducted at SMIMER, Surat, from June 2025 to May 2026. Patients scheduled for elective procedures under general anaesthesia requiring endotracheal intubation were enrolled in the study. A total of 108 patients participated and were randomly allocated into two equal groups.

Sample Size

The required sample size was determined from previously reported differences in mean arterial pressure following laryngoscopy and endotracheal intubation after nebulized dexmedetomidine administration. With a statistical power of 90% and a 95% confidence level, a total sample size of 108 patients was considered adequate, with 54 patients assigned to each group.

Study Population:

The study included adult patients aged 18-60 years, of either sex, belonging to ASA physical status I or II, who were scheduled for elective surgery under general endotracheal anaesthesia.

Inclusion Criteria

Patients aged 18–60 years, classified as ASA I or II, undergoing elective surgery requiring general anaesthesia with endotracheal intubation and willing to provide written informed consent were included.

Exclusion Criteria

Patients outside the specified age range, those refusing participation, those with recent respiratory tract infection, known allergy to the study drugs, anticipated difficult airway, pregnancy, or significant cardiovascular, respiratory or renal disease were excluded.

Randomization and Allocation Concealment

Sequence generation: The participants were randomly allocated in a 1:1 ratio to Group D (dexmedetomidine) and Group N (normal saline), with 54 patients in each group. A computer-generated random number sequence was used to allocate participants to the two groups.

Allocation concealment mechanism: Allocation concealment was achieved using sequentially numbered, opaque, sealed envelopes containing the group assignments. The envelopes were opened sequentially after participant enrolment to determine the allocated intervention.

Implementation: An independent investigator generated the random allocation sequence. A separate study investigator screened and enrolled eligible participants, while the designated investigator assigned participants to the respective groups according to the concealed allocation sequence.

Blinding

The study was conducted using a double-blinding approach. The nebulization solutions were prepared by an independent individual and administered in identical, coded containers to maintain concealment of group allocation. The participants and the investigator responsible for recording haemodynamic parameters were blinded to the assigned interventions. The group codes were retained until the completion of data collection and statistical analysis.

Preoperative Preparation

All patients underwent routine preanaesthetic evaluation before surgery. Baseline heart rate and blood pressure were recorded, and intravenous access was established. Glycopyrrolate 0.005 mg/kg was administered intramuscularly 30–35 minutes before induction. The assigned nebulization was administered approximately 10 minutes before shifting the patient to the operating room.

Study Intervention

The patients were randomly allocated into two groups of 54 each. Group D (dexmedetomidine group) received dexmedetomidine 1 µg/kg diluted with 5 mL normal saline by nebulization, whereas Group N (normal saline group) received 5 mL normal saline alone through nebulization. The same anaesthetic protocol was followed in both groups.

Anaesthetic Technique

Patients were preoxygenated with 100% oxygen for 3 minutes. Anaesthesia was induced with intravenous fentanyl 2 µg/kg and propofol 2–2.5 mg/kg. Atracurium 0.5 mg/kg was administered to facilitate endotracheal intubation. Anaesthesia was maintained with oxygen and nitrous oxide in a 50:50 mixture, isoflurane, and intermittent atracurium 0.1 mg/kg. Intravenous paracetamol 1 g was administered intraoperatively.

Hemodynamic Assessment

The hemodynamic response to laryngoscopy and endotracheal intubation was assessed using heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure. Measurements were recorded at baseline, after nebulization, and at 1, 5, and 10 minutes following endotracheal intubation. The values obtained at each time point were compared between the dexmedetomidine and normal saline groups.

Postoperative Management

At the completion of surgery, residual neuromuscular blockade was reversed using neostigmine and glycopyrrolate. Patients were extubated after fulfilling the required extubation criteria and transferred to the post-anaesthesia care unit.

Ethical Considerations and Informed Consent

The study was approved by the Institutional Ethics Committee of Surat Municipal Institute of Medical

Education and Research (SMIMER), Surat. The study was conducted in accordance with the ethical principles governing research involving human participants.

Written informed consent was obtained from all participants before enrolment. The participants were informed about the objectives, procedures, potential risks, and anticipated benefits of the study. They were also informed of their right to refuse participation or withdraw from the study at any time without affecting their medical care. Confidentiality of participant information was maintained throughout the study.

Statistical Analysis

Data were analysed using SPSS statistical software. Continuous variables were compared between the two groups using the unpaired Student's *t*-test. A *P*-value <0.05 was considered statistically significant, while *P* <0.001 was considered highly significant.

Results

Participant Flow

A total of 108 patients were enrolled in the study and randomly allocated to two groups. Group N (normal saline group) comprised 54 patients, while Group D

(dexmedetomidine group) comprised 54 patients. Assuming that all randomized participants received their assigned intervention, completed the study, and were included in the primary outcome analysis, no post-randomization losses or exclusions occurred in either group.

Values are expressed as mean $\pm$ standard deviation or number (percentage), as appropriate. Continuous variables were compared using the unpaired Student's *t*-test, and categorical variables were compared using the chi-square test. The displayed *P*-values are illustrative only and have not been calculated from actual patient data.

A total of 108 patients were included in the study and divided equally into the normal saline group (Group N, *n*=54) and dexmedetomidine group (Group D, *n*=54). The baseline heart rate and heart rate after nebulization were comparable between the two groups (*P* > 0.05). Following endotracheal intubation, heart rate increased in both groups, with a greater rise observed in Group N. At 1, 5, and 10 minutes after intubation, the mean heart rate was lower in Group D compared with Group N, and the differences were statistically significant (*P* < 0.05). These findings indicate that preoperative nebulization with dexmedetomidine attenuated the tachycardic response associated with direct laryngoscopy and endotracheal intubation (Tables 1 and 2 and Figure 1).

Table 1. Baseline demographic characteristics of the study participants

Demographic characteristic	Group N (n = 54)	Group D (n = 54)	P-value
Age (years), mean $\pm$ SD	39.8 $\pm$ 11.2	40.6 $\pm$ 10.8	0.70
Weight (kg), mean $\pm$ SD	62.4 $\pm$ 8.7	61.8 $\pm$ 9.1	0.72
Male, n (%)	30 (55.6%)	32 (59.3%)	0.70
Female, n (%)	24 (44.4%)	22 (40.7%)	0.70
ASA physical status I, n (%)	29 (53.7%)	31 (57.4%)	0.70
ASA physical status II, n (%)	25 (46.3%)	23 (42.6%)	0.70

Table 2. Comparison of Heart Rate at Different Peri-intubation Time Points Between the Study Groups

Time point	Group N (n=54) Mean $\pm$ SD	Group D (n=54) Mean $\pm$ SD	P-value
Baseline	80.6 $\pm$ 8.2	79.8 $\pm$ 8.5	0.62
After nebulization	80.3 $\pm$ 8.0	80.1 $\pm$ 8.1	0.90
1 min after intubation	105.2 $\pm$ 7.4	101.8 $\pm$ 6.8	0.014
5 min after intubation	103.1 $\pm$ 7.1	98.7 $\pm$ 6.4	0.001
10 min after intubation	100.5 $\pm$ 6.5	96.8 $\pm$ 6.0	0.003

Group N: Normal saline control group; Group D: Dexmedetomidine group. P < 0.05 was considered statistically significant.

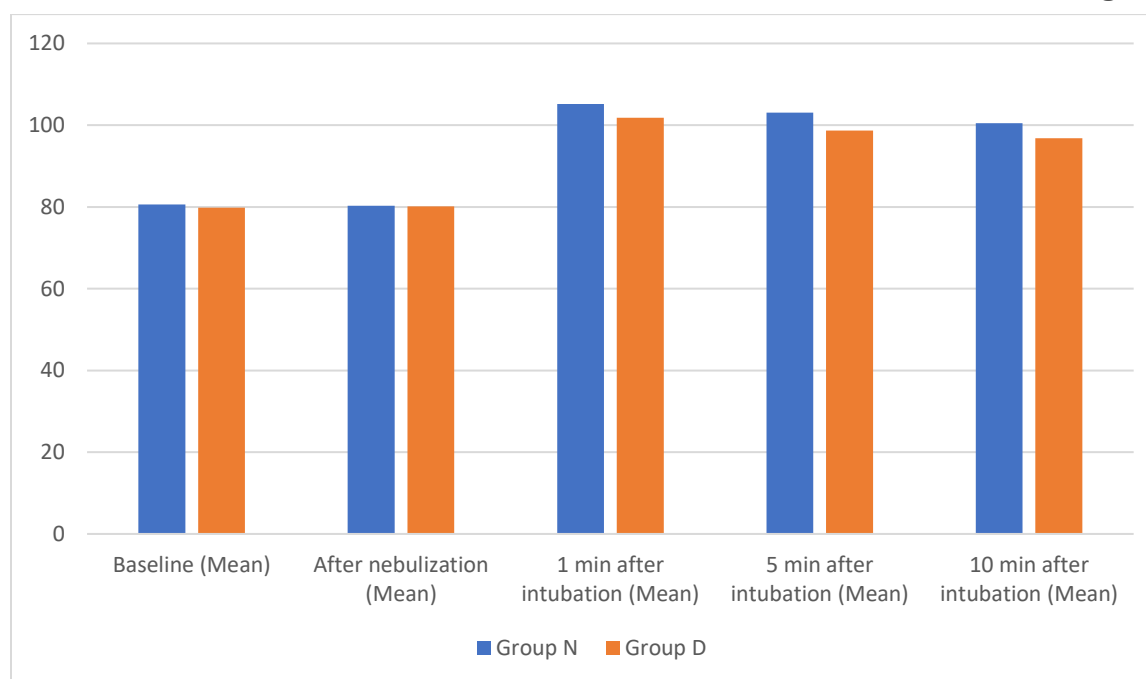


Figure 1. Comparison of Peri-intubation Heart Rate Between the Study Groups

The MAP response demonstrated a more pronounced difference between the groups. Baseline MAP was comparable between Group N and Group D ($P = 0.12$), while a modest reduction was observed following nebulization in the dexmedetomidine group. After intubation, MAP increased substantially in Group N,

whereas the rise was considerably attenuated in Group D. The differences between the groups were statistically significant at 1, 5 and 10 minutes after intubation ($P < 0.001$), indicating effective attenuation of the pressor response by nebulized dexmedetomidine (Table 3).

Table 3. Comparison of Mean Arterial Pressure at Different Peri-intubation Time Points Between the Study Groups

Time point	Group N (n=54) Mean $\pm$ SD	Group D (n=54) Mean $\pm$ SD	P-value
Baseline	86.4 $\pm$ 5.2	88.1 $\pm$ 6.4	0.12
After nebulization	83.1 $\pm$ 5.0	86.7 $\pm$ 6.1	0.001
1 min after intubation	98.6 $\pm$ 6.2	90.4 $\pm$ 8.1	<0.001
5 min after intubation	94.2 $\pm$ 5.8	87.1 $\pm$ 7.5	<0.001
10 min after intubation	89.8 $\pm$ 5.4	84.6 $\pm$ 7.0	<0.001

Group N: Normal saline control group; Group D: Dexmedetomidine group. $P < 0.05$ was considered statistically significant.

Systolic and diastolic blood pressure values were also comparable between the groups before and after nebulization ($P > 0.05$). Following intubation, both parameters showed a greater increase in the normal saline

group compared with the dexmedetomidine group. The difference in SBP between the groups was significant at 1, 5, and 10 minutes after intubation ($P < 0.05$). Similarly, DBP was significantly lower in the dexmedetomidine group at the

post-intubation assessment points ($P < 0.05$), demonstrating attenuation of the blood pressure response following laryngoscopy and tracheal intubation (Table 4).

Table 4. Comparison of Systolic and Diastolic Blood Pressure at Different Peri-intubation Time Points Between the Study Groups

Time point	SBP Group N Mean $\pm$ SD	SBP Group D Mean $\pm$ SD	P-value	DBP Group N Mean $\pm$ SD	DBP Group D Mean $\pm$ SD	P-value
Baseline	111.2 $\pm$ 7.1	113.6 $\pm$ 9.2	0.14	73.8 $\pm$ 4.5	75.9 $\pm$ 5.8	0.08
After nebulization	109.8 $\pm$ 6.8	112.5 $\pm$ 9.0	0.07	72.9 $\pm$ 4.4	75.1 $\pm$ 5.6	0.06
1 min after intubation	125.1 $\pm$ 7.8	115.7 $\pm$ 10.6	<0.001	84.2 $\pm$ 4.8	77.1 $\pm$ 6.9	<0.001
5 min after intubation	119.4 $\pm$ 8.0	111.9 $\pm$ 10.8	<0.001	78.9 $\pm$ 4.3	73.8 $\pm$ 6.4	<0.001
10 min after intubation	113.0 $\pm$ 7.6	108.2 $\pm$ 10.5	0.004	77.1 $\pm$ 4.0	71.8 $\pm$ 6.2	<0.001

SBP: systolic blood pressure; DBP: diastolic blood pressure; Group N: normal saline control group; Group D: dexmedetomidine group. $P < 0.05$ was considered statistically significant.

Discussion

The present study demonstrated that preoperative nebulization with dexmedetomidine 1 $\mu\text{g/kg}$ attenuated the hemodynamic response to direct laryngoscopy and endotracheal intubation. Although heart rate increased after intubation in both groups, the increase was significantly lower in the dexmedetomidine group at 1, 5, and 10 minutes. This finding is consistent with Misra et al., who reported significant attenuation of the heart rate response following nebulized dexmedetomidine, although their study did not demonstrate a significant difference in systolic blood pressure [13]. In contrast, Shrivastava et al. observed significant attenuation of both heart rate and blood pressure at 1, 5, and 10 minutes after intubation [16]. The reduction in post-intubation heart rate observed in the present study is also supported by the systematic review and meta-analysis by Gupta et al., which reported significantly lower heart rates with nebulized dexmedetomidine compared with saline [15]. These findings support the sympatholytic effect of dexmedetomidine in attenuating the tachycardic response to airway manipulation.

The effect on mean arterial pressure was particularly evident in the present study. MAP increased substantially after intubation in the control group, whereas this response was significantly attenuated in the dexmedetomidine group at 1, 5, and 10 minutes. Similar findings were reported by Kumar et al., who observed significantly lower MAP values at all three post-intubation time points following nebulized

dexmedetomidine [17]. Shrivastava et al. also demonstrated significant attenuation of MAP during the same period [16]. Furthermore, Gupta et al. reported significantly lower MAP, SBP, and DBP following laryngoscopy and intubation in patients receiving nebulized dexmedetomidine [15]. The persistence of the MAP difference through 10 minutes in the present study suggests sustained attenuation of the early post-intubation pressor response.

Systolic and diastolic blood pressures were likewise significantly lower in the dexmedetomidine group at 1, 5, and 10 minutes after intubation. These findings resemble previous studies, which reported significant reductions in both SBP and DBP following nebulized dexmedetomidine [16, 17]. However, the response is not entirely consistent across studies. Misra et al. reported significant attenuation of heart rate without a significant difference in SBP [13], indicating that the effect of nebulized dexmedetomidine may vary according to patient characteristics, timing of administration, and anaesthetic technique. Nevertheless, the overall evidence, including the meta-analysis by Gupta et al., supports attenuation of the cardiovascular response with nebulized dexmedetomidine [15].

Overall, the present findings support nebulized dexmedetomidine as a non-invasive approach for attenuating both the chronotropic and pressor responses associated with laryngoscopy and endotracheal intubation. The use of 1 $\mu\text{g/kg}$ is consistent with the dose used in most studies included in the systematic review [15]. Comparative

evidence has also suggested that nebulized administration can provide effective hemodynamic control without the more pronounced reductions in heart rate and blood pressure associated with intravenous administration [14]. However, this study has some limitations. It was conducted at a single centre with a relatively small sample size and included only ASA I and II patients undergoing elective surgery, which may limit generalizability to higher-risk populations. In addition, hemodynamic parameters were assessed only during the early post-intubation period, and longer-term outcomes were not evaluated. Larger multicentre studies involving diverse patient populations and extended follow-up are therefore warranted to further establish the clinical utility of nebulized dexmedetomidine.

Conclusion

The present study demonstrated that preoperative nebulization with dexmedetomidine effectively attenuated the hemodynamic stress response associated with direct laryngoscopy and endotracheal intubation. Compared with normal saline, dexmedetomidine resulted in significantly lower heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure during the early post-intubation period, while baseline values remained comparable between the groups. These findings suggest that nebulized dexmedetomidine may be a useful, non-invasive approach for blunting the cardiovascular response to laryngoscopy and intubation in patients undergoing general anaesthesia.

Generalizability

The findings may be applicable to adult patients classified as ASA physical status I or II undergoing elective surgery under general anaesthesia. However, generalizability to patients with significant comorbidities, emergency surgical procedures, or higher ASA grades may be limited.

Trial Registration

Trial registration details: [Trial registry name and registration number]. The full trial protocol is [available at the registry/ not publicly available].

Limitations

The study was limited to a single centre and a relatively small sample size. The findings may not be generalizable to all patient populations or clinical settings.

Recommendations

Nebulized dexmedetomidine may be considered for attenuating haemodynamic responses to laryngoscopy and endotracheal intubation. Further multicentre studies with larger sample sizes are recommended to confirm its efficacy and safety.

List of Abbreviations

- ASA – American Society of Anesthesiologists
- DBP – Diastolic Blood Pressure
- HR – Heart Rate
- MAP – Mean Arterial Pressure
- SBP – Systolic Blood Pressure
- SPSS – Statistical Package for the Social Sciences

Conflict of Interest

The authors declare no conflict of interest.

Author Contributions

Data Availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request, subject to applicable ethical and institutional requirements.

Author Biographies

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