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EFFECTS OF NEBULIZED AND INTRAVENOUS DEXMEDETOMIDINE IN ATTENUATING THE POST-EXTUBATION HEMODYNAMIC RESPONSE IN PATIENTS UNDERGOING ELECTIVE SURGERIES UNDER GENERAL ANAESTHESIA.

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Abstract

Background: Studies comparing the effects of nebulized and intravenous dexmedetomidine in attenuation of haemodynamic stress response, and emergence cough during endotracheal extubation are scarce. Hence, we aimed to compare the efficacy of nebulized and intravenous dexmedetomidine for attenuating the haemodynamic response during emergence from general anaesthesia. This is a prospective randomized comparative study conducted with total of 60 patients undergoing elective surgeries under general anaesthesia. Patients were randomly allocated to two groups viz. Group ND (n=30) and Group IVD (n=30). Group ND received Dexmedetomidine through nebulization route; while Group IVD received through intravenous. Effects on hemodynamic responses viz. mean arterial pressure (MAP), systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR) along with emergence cough at extubation and adverse event encountered were assessed. The demographic and baseline characteristics of patients such as age ($p = 0.68$), gender ($p = 0.79$), BMI ($p = 0.71$), ASA physical status ($p = 0.79$), and Mallampati class ($p = 0.80$) were comparable between the study groups. The hemodynamic responses viz. MAP, SBP, DBP, and HR were significantly ($p<0.01$) lower at all the time intervals recorded after drug administration and after extubation, indicated that nebulized dexmedetomidine significantly better attenuated post-extubation hemodynamic response compared to intravenous dexmedetomidine. In conclusion, administration of nebulized dexmedetomidine 10 minutes prior to extubation effectively attenuated the hemodynamic response without producing significant adverse effects. Therefore, nebulized dexmedetomidine may serve as a promising alternative to intravenous administration in patients undergoing elective surgeries under general anesthesia.

Keywords: Dexmedetomidine, Intravenous, Nebulized, Hemodynamic response, MAP, Cough.

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INTRODUCTION

The advent of general anesthesia has profoundly transformed surgical practice by producing a reversible state of unconsciousness in which patients remain insensible to pain and unaware of intraoperative events. This state is generally accomplished using a combination of induction agents, intravenous sedatives, analgesics, and maintenance with inhalational anesthetics.1,2 In the context of laparoscopic procedures performed under general anesthesia, extubation defined as the removal of the endotracheal tube represents one of the most uncomfortable phases. Endotracheal extubation is frequently associated with several undesirable effects, including respiratory and hemodynamic disturbances.3

When extubation occurs at lighter planes of anesthesia, it can provoke sympathetic reflex activity leading to alterations in hemodynamic parameters.4,5 These changes, which are often transient and unpredictable, typically present as elevations in heart rate and arterial blood pressure. Individuals with comorbidities such as systemic hypertension, cardiovascular disorders, cerebral aneurysms, or cerebrovascular disease are particularly vulnerable. Even short-lived increases in heart rate and blood pressure may result in serious complications, including cerebral hemorrhage, arrhythmias, myocardial ischemia, left ventricular failure, pulmonary edema, and rupture of intracranial aneurysms. In patients with respiratory conditions like bronchial asthma and chronic obstructive pulmonary disease, airway hyperreactivity during extubation may precipitate bronchospasm, laryngospasm, and coughing, thereby increasing morbidity.6

Various pharmacological agents and techniques have been explored to mitigate airway irritation and stress responses associated with endotracheal extubation.7 Dexmedetomidine, a selective α2-adrenoreceptor agonist with a distribution half-life of approximately six minutes, has demonstrated effectiveness in blunting the stress response to laryngoscopy.8,9 Additionally, it is widely used for sedation in mechanically ventilated patients in intensive care settings and for procedural sedation in non-intubated individuals undergoing surgical or diagnostic interventions.10

Although the intravenous route remains the most commonly employed method for administering dexmedetomidine, it is associated with adverse effects such as bradycardia and hypotension.11 Alternative routes, including intramuscular,12 and intranasal administration,13 have also been investigated. Nebulized dexmedetomidine offers a noninvasive approach characterized by favorable bioavailability and rapid systemic absorption.14 Recent research has proposed nebulization as an innovative method for administrating dexmedetomidine.15

Existing literature indicates that nebulized dexmedetomidine has been evaluated in several studies for attenuating the stress response to intubation. However, comparatively fewer investigations have assessed and contrasted the effects of intravenous and nebulized dexmedetomidine in reducing hemodynamic stress responses and emergence-related cough during endotracheal extubation. In view of this gap, the present comparative study was undertaken to evaluate and compare the effectiveness of intravenous and nebulized dexmedetomidine in attenuating the hemodynamic stress response during recovery from general anesthesia.

MATERIALS AND METHODS

Study design and Patients

This is a prospective randomized comparative study conducted with total of 60 patients undergoing elective surgeries under general anesthesia (GA) with endotracheal intubation in the Department of Anaesthesiology at Kodagu Institute of Medical Sciences (KoIMS), Madikeri, Karnataka. A written informed consent was taken from all the patients participating in the study. Patients were randomly allocated to two groups viz. Group ND (n=30) and Group IVD (n=30). Group ND received Dexmedetomidine through nebulization route; while Group IVD received through intravenous route.

Inclusion criteria

1. Patients undergoing elective surgeries under GA
2. Age between 18 to 60 years
3. Patients belonged to American Society of Anesthesiologists Physical Status (ASA-PS) Grade 1 and 2
4. Mallampati class 1 and 2
5.

Exclusion criteria

1. Patients with anticipated difficult intubation
2. Patients having history of allergic reaction to dexmedetomidine
3. Patient taking medications that alters the heart rate such as beta-blockers and clonidine
4. Pregnant patients
5. Patients with COPD
6. Patients with BMI >40 kg/m2
7.

Randomization

Patients were recruited through consecutive sampling methods to reach the required sample size. Block randomisation technique was followed to allocate the participants into Group ND and Group IVD having the block sizes of 10. Sequentially Numbered, Opaque, Sealed Envelopes (SNOSE) technique was employed to ensure allocation concealment.

Preanesthetic Procedure

Patients included in the study were premedicated with Tab. Alprazolam 0.5mg and Tab. Pantoprazole 40mg orally on the night before surgery. Patients were kept nil orally 10 PM onwards on the previous night. All the patients underwent basic investigations required for the surgery. Pre-anesthetic checkup, fasting status, and informed written consent were checked.

After confirmation of identity, the patient was taken to the operation theatre. A peripheral IV line was secured with 18G cannula. The patients were connected to multi parameter monitor that records heart rate, non-invasive systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), end-tidal carbon dioxide, continuous electrocardiograph (ECG) monitoring and oxygen saturation. The baseline MAP, SBP, DBP, heart rate, and oxygen saturation were recorded. The heart rate and rhythm were monitored by lead II.

All the patients were premedicated intravenously prior to induction with inj. Midazolam 0.02mg/kg and inj. Fentanyl 2µg/kg. Preoxygenation with 100% oxygen for 3 minutes was done. Induction was done with titrated dose of inj. Propofol 1-2 mg/kg and the end point was marked by loss of verbal response and muscle relaxant inj. Vecuronium bromide 0.1mg/kg intravenously given. After adequate relaxation, intubation was done by an experienced anesthesiologist . Intubation was done with appropriately sized endotracheal tube using Macintosh laryngoscope and cuff pressure was maintained between 20-25 cm of water.

Anaesthesia was maintained with Isoflurane (0.8 -1% end-tidal concentration) and 66% Nitrous oxide in oxygen using mechanical ventilation. No additional opioid was given after induction. The patient was given intermittent bolus of Vecuronium 0.25 mg/kg iv.

Patients were allocated randomly to one of two groups in a double-blind manner. Ten minutes before the end of the surgery, patients in Group ND received nebulized dexmedetomidine at a dose of 1 µg/kg in 5 ml of isotonic solution, and in Group IVD received 0.5 µg/kg IV dexmedetomidine in 50 ml of isotonic solution, both given over 10 mins.

Isoflurane and nitrous oxide were stopped at the end of the operation and 0.05mg/kg iv neostigmine and 0.02 mg/kg iv glycopyrrolate was given for neuromuscular block reversal when extubation criteria was fulfilled. After tracheal extubation, 100% oxygen was given via a facemask for 5 min.

Data Collection

MAP, SBP, DBP and HR values were recorded at 1, 2, 3, 5 and 10 min after drug administration, and at 1, 2, 3, 5, and 10 min after extubation. Coughing after extubation was assessed with a four-point Minogue scale as follows:

- Grade I (None) - No coughing or muscle weakness
- Grade II (Mild) - Coughing once or twice or transient cough response to removal of tracheal tube that resolved with extubation
- Grade III (Moderate) - Less than or equal to 3 coughs lasting 1-2 s, or total duration of coughing last less than or equal to 5s
- Grade IV (Severe) - At least four coughs with each lasting >2 seconds, or total duration of coughing being more than 5s

Possible adverse effects during and after the administration of dexmedetomidine and during the postoperative period such as arrhythmia, bradycardia, tachycardia, hypotension, hypertension, vomiting and dry mouth were recorded.

Statistical Analysis

Data were entered in Microsoft Excel 2021 and statistical analysis was done using IBM Statistical Software for Social Sciences (SPSS) version 20. Categorical variables were represented in the form of percentages, and frequencies. Continuous variables were presented as descriptive statistics (Mean and Standard deviation). Categorical variables were analysed using the Chi-square test. Comparison of continuous variables between the study groups was done using independent sample t-test. $p \leq 0.05$ was considered statistically significant.

RESULTS

The mean age of patients was 38.6 years and 39.8 years in Group ND and Group IVD without any statistically significant difference ($p = 0.68$). The other demographic and baseline characteristics of patients such as gender ($p = 0.79$), BMI ($p = 0.71$), ASA physical status ($p = 0.79$), and Mallampati class ($p = 0.80$) were comparable between the study groups.

Table 1. Demographic and baseline characteristics

Variable	Group ND (n = 30)	Group IVD (n = 30)	p-value
Age (years)	38.6 ± 10.4	39.8 ± 9.7	0.68
Gender, n (%)			0.79
Male	17 (56.7%)	16 (53.3%)	
Female	13 (43.3%)	14 (46.7%)	
BMI (kg/m²)	24.8 ± 3.2	25.1 ± 3.5	0.71
ASA Physical Status, n (%)			0.79
ASA I	18 (60.0%)	17 (56.7%)	
ASA II	12 (40.0%)	13 (43.3%)	
Mallampati Class, n (%)			0.80
Class I	19 (63.3%)	18 (60.0%)	
Class II	11 (36.7%)	12 (40.0%)	

Values were mean ± SD unless otherwise stated
BMI, Body mass index; ASA, American Society of Anesthesiologists

The results on comparison of MAP of patients between the study groups were represented in Table 2. Results depicted that the mean MAP significantly ($p<0.01$) lower at all the time intervals recorded after drug administration in Group ND.

After extubation, MAP was significantly ($p<0.01$) better maintained in Group ND compared to Group IVD indicated that nebulized dexmedetomidine significantly better attenuated post-extubation pressor response compared to intravenous dexmedetomidine.

Table 2. Comparison of MAP between study groups

Time Interval	Group ND	Group IVD	p-value
After drug administration			
1 min	86.4 ± 6.2	92.8 ± 7.1	0.001*
2 min	84.2 ± 5.8	91.5 ± 6.9	<0.001*
3 min	82.6 ± 5.4	89.9 ± 6.4	<0.001*
5 min	81.8 ± 5.2	88.7 ± 6.1	<0.001*
10 min	83.1 ± 5.7	89.2 ± 6.3	0.002*
After extubation			
1 min	90.2 ± 6.5	101.8 ± 8.4	<0.001*
2 min	88.4 ± 6.1	99.7 ± 7.9	<0.001*
3 min	87.6 ± 5.8	97.3 ± 7.5	<0.001*
5 min	85.9 ± 5.5	94.6 ± 6.8	<0.001*
10 min	84.7 ± 5.4	92.8 ± 6.4	0.001*

Values are expressed as mean ± SD; *Significant

The results on comparison of SBP of patients between the study groups were represented in Table 3. Results inferred that the mean SBP was significantly ($p<0.01$) lower at all the time intervals recorded after drug administration, and after extubation time intervals recorded in Group ND.

The nebulized dexmedetomidine significantly better attenuated post-extubation systolic blood pressure response compared to intravenous dexmedetomidine.

Table 3. Comparison of SBP between study groups

Time Interval	Group ND	Group IVD	p-value
After drug administration			
1 min	118.6 ± 8.4	126.8 ± 9.2	0.001*
2 min	116.4 ± 7.9	124.7 ± 8.8	<0.001*
3 min	114.2 ± 7.5	122.6 ± 8.4	<0.001*
5 min	112.8 ± 7.1	120.9 ± 8.1	<0.001*
10 min	114.1 ± 7.4	121.7 ± 8.3	0.002*
After extubation			
1 min	122.4 ± 8.6	138.9 ± 10.7	<0.001*
2 min	120.8 ± 8.2	136.2 ± 10.1	<0.001*
3 min	119.3 ± 7.9	133.6 ± 9.8	<0.001*
5 min	117.6 ± 7.5	130.4 ± 9.2	<0.001*
10 min	115.8 ± 7.3	127.8 ± 8.9	0.001*

Values are expressed as mean ± SD; *Significant

The results on comparison of DBP of patients between the study groups were represented in Table 4. Similar to SBP, mean DBP was significantly ($p<0.01$) lower in Group ND at all the time intervals recorded after drug administration, and after extubation time intervals recorded.

Hence, the nebulized dexmedetomidine significantly better attenuated post-extubation diastolic blood pressure response also compared to intravenous dexmedetomidine.

Table 4. Comparison of DBP between study groups

Time Interval	Group ND	Group IVD	p-value
After drug administration			
1 min	72.8 ± 5.6	78.4 ± 6.3	0.001*
2 min	70.6 ± 5.2	76.9 ± 6.0	<0.001*
3 min	69.2 ± 5.0	75.4 ± 5.8	<0.001*
5 min	68.7 ± 4.8	74.6 ± 5.6	<0.001*
10 min	69.9 ± 5.1	75.8 ± 5.9	0.002*
After extubation			
1 min	76.4 ± 6.2	85.7 ± 7.6	<0.001*
2 min	74.8 ± 5.8	83.9 ± 7.2	<0.001*
3 min	73.6 ± 5.6	82.1 ± 6.9	<0.001*
5 min	72.4 ± 5.4	80.6 ± 6.5	<0.001*
10 min	71.8 ± 5.2	79.3 ± 6.2	0.001*

Values are expressed as mean ± SD; *Significant

The results on comparison of heart rate of patients between the study groups were represented in Table 5. The mean heart rate was significantly ($p<0.01$) lower after drug administration intervals and after extubation time intervals in Group ND when compared to Group IVD. These findings delineated that nebulized dexmedetomidine significantly better controlled the heart rate compared to intravenous dexmedetomidine

Table 5. Comparison of heart rate between study groups

Time Interval	Group ND	Group IVD	p-value
After drug administration			
1 min	74.6 ± 6.8	82.4 ± 7.5	0.001*
2 min	72.8 ± 6.4	80.6 ± 7.1	<0.001*
3 min	71.2 ± 6.1	79.3 ± 6.8	<0.001*
5 min	70.4 ± 5.9	77.8 ± 6.5	<0.001*
10 min	71.6 ± 6.2	78.6 ± 6.9	0.002*
After extubation			
1 min	78.8 ± 7.2	96.4 ± 9.3	<0.001*
2 min	76.9 ± 6.8	93.8 ± 8.9	<0.001*
3 min	75.6 ± 6.4	91.2 ± 8.4	<0.001*
5 min	74.2 ± 6.1	88.6 ± 7.9	<0.001*
10 min	73.4 ± 5.9	85.7 ± 7.5	0.001*

Values are expressed as mean ± SD; *Significant

The incidence and severity of emergence cough were significantly ($p<0.01$) lower in the ND group. Severe cough (Grade III/IV) was significantly higher with intravenous dexmedetomidine than nebulized dexmedetomidine (Table 6).

Table 6. Distribution of cough grading at extubation

Cough Grade	Group ND (n=30)	Group IVD (n=30)	p-value
Grade I	22 (73.3%)	12 (40.0%)	0.01*
Grade II	6 (20.0%)	10 (33.3%)	
Grade III	2 (6.7%)	6 (20.0%)	
Grade IV	0 (0%)	2 (6.7%)	

The incidences of adverse events were less frequent in the Group ND compared to the Group IVD. Furthermore, the incidences of tachycardia ($p = 0.04$), and hypertension ($p = 0.02$) were significantly less frequent with nebulized dexmedetomidine than intravenous dexmedetomidine (Table 7).

Table 7. Incidence of adverse events

Adverse Event	Group ND (n=30)	Group IVD (n=30)	p-value
Arrhythmia	0 (0%)	1 (3.3%)	0.31
Bradycardia	2 (6.7%)	4 (13.3%)	0.39
Tachycardia	1 (3.3%)	6 (20.0%)	0.04*
Hypotension	2 (6.7%)	5 (16.7%)	0.23
Hypertension	1 (3.3%)	7 (23.3%)	0.02*
Vomiting	1 (3.3%)	3 (10.0%)	0.30
Dry mouth	3 (10.0%)	8 (26.7%)	0.08

*Significant

DISCUSSION

General endotracheal anesthesia is widely practiced across the globe because it facilitates balanced anesthesia while maintaining effective airway protection.15 However, the process of extubation may be accompanied by complications such as coughing, respiratory disturbances, and hemodynamic fluctuations. Although these responses are generally brief and tolerated by most individuals, they can pose significant risks in vulnerable patient populations.10 Alpha-2 adrenergic agonists, including dexmedetomidine and clonidine, have demonstrated effectiveness not only in blunting the hemodynamic response to endotracheal intubation but also in providing sedation, anxiolysis, and analgesia. Rapid intravenous administration of these agents, however, is associated with adverse effects such as bradycardia, hypotension, and a biphasic cardiovascular response.16 Although an antidote that enhances central noradrenaline turnover has been suggested, its limited availability and higher cost restrict routine use.15,16 Consequently, alternative routes such as oral, intramuscular, intranasal, and more recently nebulized administration have been explored to minimize adverse effects. In this prospective randomized study, we therefore compared nebulized and intravenous dexmedetomidine for attenuation of the hemodynamic stress response during emergence from general anesthesia. The two study groups were comparable in terms of demographic and baseline parameters, including mean age ($p = 0.68$), gender distribution ($p = 0.79$), body mass index ($p = 0.71$), ASA physical status ($p = 0.79$), and Mallampati grading ($p = 0.80$). Our findings demonstrated that post-extubation MAP was significantly better controlled ($p < 0.01$) in patients receiving nebulized dexmedetomidine compared to those receiving through intravenous route, suggesting superior attenuation of the pressor response. A similar pattern was observed for SBP, DBP, and heart rate, indicating more effective modulation of post-extubation hemodynamic changes with nebulized administration.

Concurrently, supporting evidence in the literature indicates several benefits of nebulization, including cost-effectiveness, ease of administration, and suitability for resource-limited settings, as it does not require specialized equipment such as syringe pumps or intranasal atomization devices. Additionally, nebulization allows uniform drug deposition in the nasal and pharyngeal mucosa, may improve expiratory mechanics in patients with asthma or COPD when alpha-2 agonists are used, and has a potential role in sedation and attenuation of postoperative sore throat (POST). These features make the nebulized route a potentially comprehensive alternative.17.18 Furthermore, Hrishi et al. demonstrated that intranasal dexmedetomidine (1 μg/kg) provided improved surgical field conditions and reduced hemodynamic variability during transnasal transsphenoidal skull base procedures. Their study reported no significant differences in heart rate or blood pressure, along with reduced anesthetic requirements in the intranasal dexmedetomidine group. Furthermore, intranasal dexmedetomidine was effective in attenuating the rise in MAP associated with intubation.19 Similarly, Wang et al. found that intranasal dexmedetomidine (1 μg/kg) significantly mitigated the MAP increase during intubation, with concurrent stabilization of heart rate and Bispectral Index values, confirming effective suppression of intubation responses.20

In the present study, both the incidence and severity of emergence cough were significantly reduced in the nebulized dexmedetomidine group. Severe coughing episodes (Grade III/IV) were observed more frequently in patients who received intravenous dexmedetomidine. Additionally, adverse events such as arrhythmias, bradycardia, tachycardia, hypotension, hypertension, vomiting, and dry mouth occurred less often with nebulized administration compared to the intravenous route. Our study findings enhance the understanding of perioperative outcomes associated with different routes of dexmedetomidine administration and provide clinically relevant information for anesthesiologists when individualizing anesthesia strategies according to patient profile and procedural demands. While nebulized dexmedetomidine appears safe and effective in achieving stable hemodynamics with adequate sedation, further research across broader clinical contexts and larger patient populations is warranted. Future investigations should include multicenter trials with expanded sample sizes to validate and generalize these observations, as well as studies assessing its role in varied surgical settings. Like all clinical investigations, this study has certain limitations. Only a single dose of dexmedetomidine was evaluated; assessment of higher doses via both nebulized and intravenous routes would provide additional insight. Moreover, the relatively small sample size (n = 60) limits generalizability, underscoring the need for larger-scale studies.

CONCLUSION

Administration of nebulized dexmedetomidine 10 minutes prior to extubation effectively attenuated the hemodynamic response without producing significant adverse effects. Therefore, nebulized dexmedetomidine may serve as a promising alternative to intravenous administration in patients undergoing elective surgeries under general anesthesia.

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