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ORIGINAL RESEARCH

A comparative evaluation of nebulised and IV dexmedetomidine on attenuation of haemodynamic response to laryngoscopy

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ABSTRACT

Background and aims: Laryngoscopy and tracheal intubation incite remarkable sympathetic activity and are associated with transient but significant hemodynamic pressor response. Dexmedetomidine is a highly selective alpha 2 agonist which attenuates the pressor response. Our study comparatively evaluated the efficacy of nebulized and intravenous dexmedetomidine on the attenuation of hemodynamic response to laryngoscopy. **Methods**: In this prospective, randomized, double-blinded study, sixty adults were divided into two groups of thirty each. Group A received nebulized dexmedetomidine 1 mcg/kg and Group B received Inj. dexmedetomidine 1mcg/kg IV infusion over 10 minutes, 30 min before intubation. The primary objective was to compare the mean arterial pressure (MAP) between the two groups following laryngoscopy and tracheal intubation for up to 10 minutes. The secondary objectives were to compare preoperative Ramsay sedation scores, mean dose of propofol required for induction of anesthesia, changes in heart rate (HR), and any side effects in both groups. RStudio Desktop Version 2023.03.0+386 was used for statistical analysis. **Results**: In both groups, there were no changes seen in the MAP ($p > 0.05$) or HR ($p > 0.05$) after laryngoscopy and intubation. Preoperative sedation scores were comparable in both groups. Statistically, no significant difference was noted. The mean propofol consumption was found to be higher in Group A compared to Group B ($p < 0.05$). **Conclusion:** We conclude that the MAP and HR response to laryngoscopy and tracheal intubation were equally attenuated in both nebulized and intravenous dexmedetomidine groups.

Keywords: Nebulized dexmedetomidine; intravenous dexmedetomidine; laryngoscopy; intubation; Ramsay sedation score; pressor response; propofol consumption.

INTRODUCTION

Induction of general anesthesia, laryngoscopy and tracheal intubation incite remarkable sympathetic activity and hemodynamic changes which are transient but significant. These hemodynamic changes are termed 'pressor responses' which arise within 30 seconds following direct laryngoscopy and endotracheal intubation and approaching baseline in 10 minutes. [1,2] This response may precipitate hypertensive episodes, cardiac arrhythmias/ischemia, or intracranial hypertension in susceptible individuals. Hence, these noxious responses need to be attenuated. Several pharmacological agents like local anesthetics, beta-adrenergic blockers, calcium channel antagonists, and opioids were used with varied success for the attenuation of intubation response. [3]

Dexmedetomidine is a highly selective alpha 2 adrenergic agonist with an alpha 2: alpha 1 selectivity ratio of 1620:1. Its action on postsynaptic alpha 2 receptors inhibits the release of catecholamines and decreases sympathetic activity. The pre-synaptic activation of alpha 2 receptors in locus coeruleus by dexmedetomidine causes sedation without respiratory depression and is hence used for premedication[3], anxiolysis, and sedation in ICU [4]. It decreases analgesic requirements by acting on dorsal horns. It is well absorbed systemically through the oral mucosa and hence buccal route can be used as an effective non-invasive route of drug administration. The

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bioavailability of the buccal route is 73-92 % and 100% with the intravenous (IV) route and its half-life is 1.9 ± 0.5 hours. [5] It also reduces the consumption of opioids and induction agents. [1-3]

In our study, we compared the efficacy of the inhalational (nebulization) route to the IV route of dexmedetomidine administration and hypothesized that dexmedetomidine, when used through the inhalational route, attenuates the intubation response with a better hemodynamic profile in comparison with IV dexmedetomidine with minimal adverse effects.

The primary objective of the study was to compare the mean arterial pressure (MAP) between the two groups following laryngoscopy and intubation. The secondary objectives were to assess the sedation scores preoperatively by Ramsay sedation scores (RSS), to determine the dose-sparing effect of induction dose of propofol, to compare the heart rate response following laryngoscopy and intubation and to assess for side effects if any.

METHODOLOGY

After obtaining approval from the Institutional Ethics Committee (IEC: 321), the study was registered with the Clinical Trial Registry of India (CTRI/2023/05/052183). A prospective, comparative study was conducted at our tertiary care hospital from May 2023 to October 2023. The study was conducted as per the guidelines of the 'declaration of Helsinki, 2013'. Sixty patients aged between 18 to 60 years, with American Society of Anesthesiologists' Physical Status (ASA-PS) I and II who were scheduled to undergo elective surgery under general anesthesia with laryngoscopy and endotracheal intubation were selected. Patients with BMI > 30kg/$m^{2.}$, anticipated difficult airway, pregnancy and lactation, history of hypertension, ischemic heart disease, and smokers were excluded from the study.

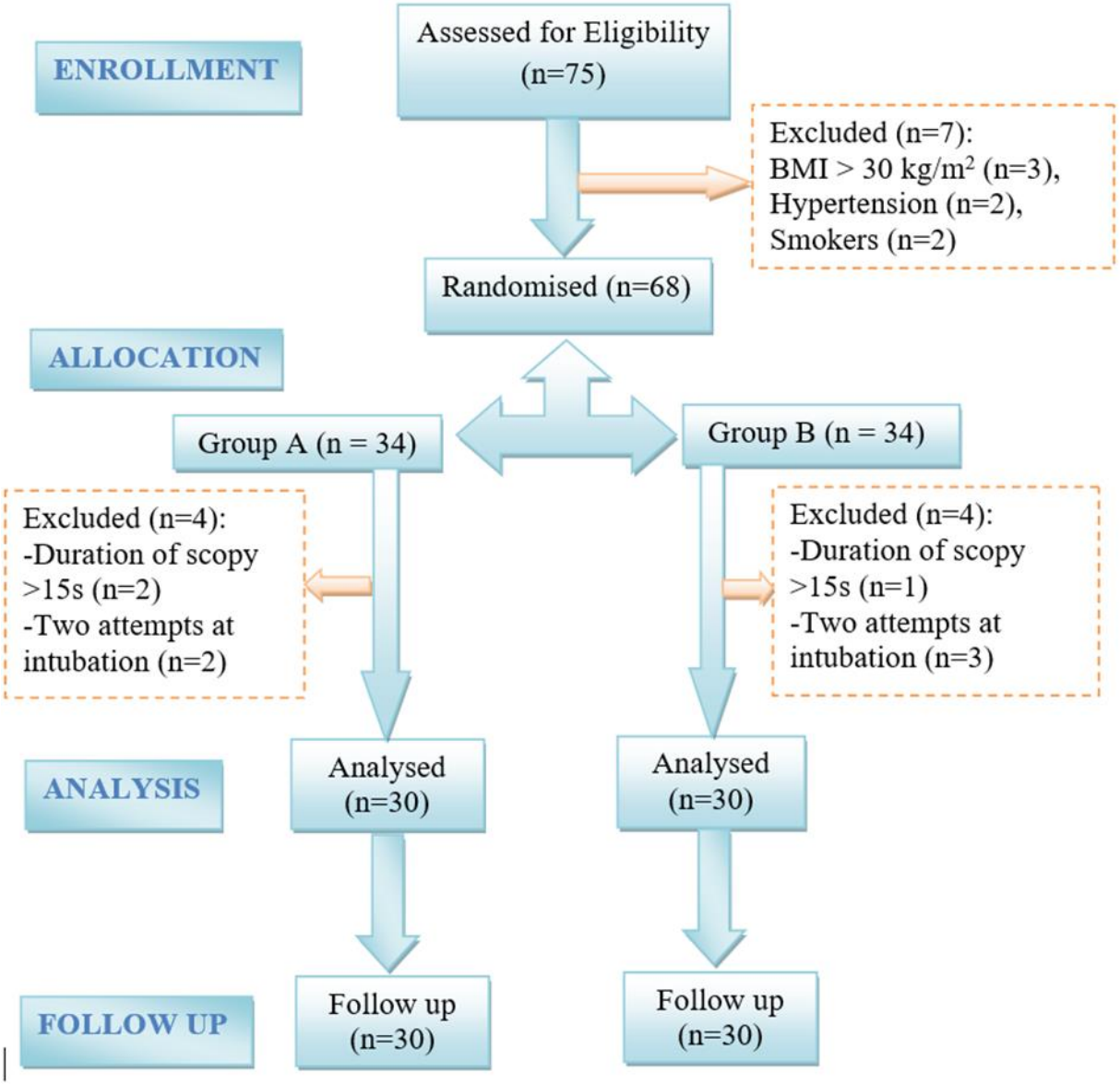

Figure 1: Consort flow chart

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A thorough pre-anesthetic evaluation was done a day before the surgery and the patients were explained about the study protocol and written informed consent was taken. During this visit, all patients were examined for any nasal pathology which was recorded in the pre-anesthetic evaluation sheet. Patients were given IV pantoprazole 40 mg the previous night and IV ondansetron 4 mg on the day of surgery. Based on computer-generated random numbers, patients were divided into two groups of 30 each. Allocation concealment was done using sealed opaque envelopes and was handed to the anesthesiologist on the day of surgery. All the patients were examined in the preoperative room and nil per oral status was confirmed. Standard ASA monitors such as an electrocardiogram (ECG), non-invasive blood pressure (NIBP), and pulse-oximeter were connected, and baseline vitals like heart rate (HR), systolic (SBP), diastolic (DBP), mean arterial pressure (MAP), oxygen saturation (SpO_2), respiratory rate (RR) were recorded. IV Ringer lactate was started at a maintenance rate of 10 ml/kg/hr through an 18G peripheral venous cannula. All the patients were given both nebulization and intravenous drugs 30 minutes before induction to ensure blinding.

Group A patients received nebulization with dexmedetomidine 1 mcg/kg in 2 mL of 0.9% normal saline (NS) along with an IV infusion of 10 mL of 0.9% normal saline over 10 minutes.

Group B patients received nebulization with 2 mL of 0.9% NS and dexmedetomidine 1mcg/kg in 10 mL of 0.9% NS administered as an infusion over 10 minutes.

The anesthesiologist performing the study and the patients were unaware of the group they were allocated to. Hemodynamic parameters such as HR, SBP, DBP, MAP, SpO_2, RR, and sedation scores using the Modified Ramsay Sedation Score (RSS) were noted every 5 minutes from the start of nebulization till induction of anesthesia. Any episodes of hypotension defined as a reduction of MAP > 20% from baseline, bradycardia (HR < 50bpm), and oxygen desaturation (SpO2 < 92%) were documented and treated accordingly.

After shifting the patient to the operation theatre, standard ASA monitoring was continued. All the patients were adequately pre-oxygenated with 100% oxygen. General anesthesia was induced with IV fentanyl (2 mcg/kg) and IV propofol 20 mg boluses titrated to loss of verbal response. The total dose of propofol required was noted. The patients were paralyzed with 0.1mg/kg of vecuronium. After adequate bag-mask ventilation, laryngoscopy and intubation were done using a Macintosh laryngoscope, and the trachea was intubated with an appropriate-sized endotracheal tube.

All hemodynamic parameters were recorded immediately after induction, every minute after intubation for the first 5 minutes, at the 10^{th} minute, and then every 5 minutes till the end of the surgery. Intravenous mephentermine 6 mg bolus was used to treat hypotension. Anesthesia was maintained with isoflurane with 50% Oxygen in Air. Intermittent doses of IV vecuronium 0.02 mg/kg were given to ensure adequate muscle paralysis to facilitate intermittent positive pressure ventilation and maintain EtCO2 around 32-35 mmHg.

An additional dose of fentanyl (1mcg/kg) was given as needed. Following the completion of the surgery, the residual neuromuscular blockade was antagonized with IV neostigmine 0.05mg/kg and glycopyrrolate 0.01 mg/kg. The patients were extubated once extubation criteria were met and all the patients were shifted to the recovery room and monitored for 30 minutes. After satisfactory recovery, they were shifted to wards and were observed for any side effects for up to 24 hours.

Sample size

Based on the study by Niyogi and others [6] MAP was 78.74 $\pm$ 6.41 after induction of anesthesia and it was 83.26 $\pm$ 5.61 after 10 minutes of intubation and for 95% confidence interval and 80% power, a sample size of 28 was obtained in each group. Considering the possible dropouts, 30 patients were allotted to each group.

Statistical Analysis

Continuous variables were represented as mean ± SD. An Independent t-test was used to compare the mean ± SD of continuous variables between the two groups. Mann-Whitney U test was used to compare the median for non-normally distributed continuous variables between two groups. Non-parametric Friedman test was used for the non-normally distributed data. For the pairwise comparison, Bonferroni post-hoc test was used. P value < 0.05 was considered statistically significant.

RESULTS

The patients in both groups had similar demographics and similar baseline hemodynamic parameters.

Table 1: Demographic characteristics of patients in both the groups

Parameters	Group A	Group B
AGE (years)	36.60 ± 8.63	38.07 ± 11.34
HEIGHT (cm)	161.60 ± 8.27	156.17 ± 7.21
WEIGHT (kg)	64.57 ± 9.58	62.70 ± 8.28
BMI (kg/m^2)	24.33 ± 1.64	25.15 ± 2.60
MALE / FEMALE	16 / 14	12 / 18
ASA I / II	17 / 13	19 / 11

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BASELINE MAP (mmHg)	91.1 ± 6.5	90.4 ± 7.57
BASELINE HR (bpm)	82.3 ± 14.36	79.07 ± 10.22

After the induction of anesthesia, laryngoscopy was done followed by tracheal intubation. It was observed that during 10 minutes of the study, the MAP decreased from the baseline in both groups and the difference between the two groups was not significant ($p > 0.05$).

Table 2: Mean Arterial Pressure (MAP) changes in patients of both the groups

TIME	Group A		Group B		p-value
	Mean	SD	Mean	SD	
BASELINE	91.1	6.5	90.4	7.57	0.702
LARYNGOSCOPY	83.37	8.08	81.43	7.58	0.343
1 MIN	81.53	7.99	79.93	7.45	0.426
2 MIN	78.6	8.06	77.2	7.22	0.481
3 MIN	77	10.15	74.73	8.17	0.345
4 MIN	73.87	10.01	72.87	7.6	0.665
5 MIN	72.6	9.82	71.37	7.75	0.591
10 MIN	70.97	8.74	70.33	7.72	0.767

It was observed that in both groups all the patients were well sedated and the median of RSS increased from baseline value.

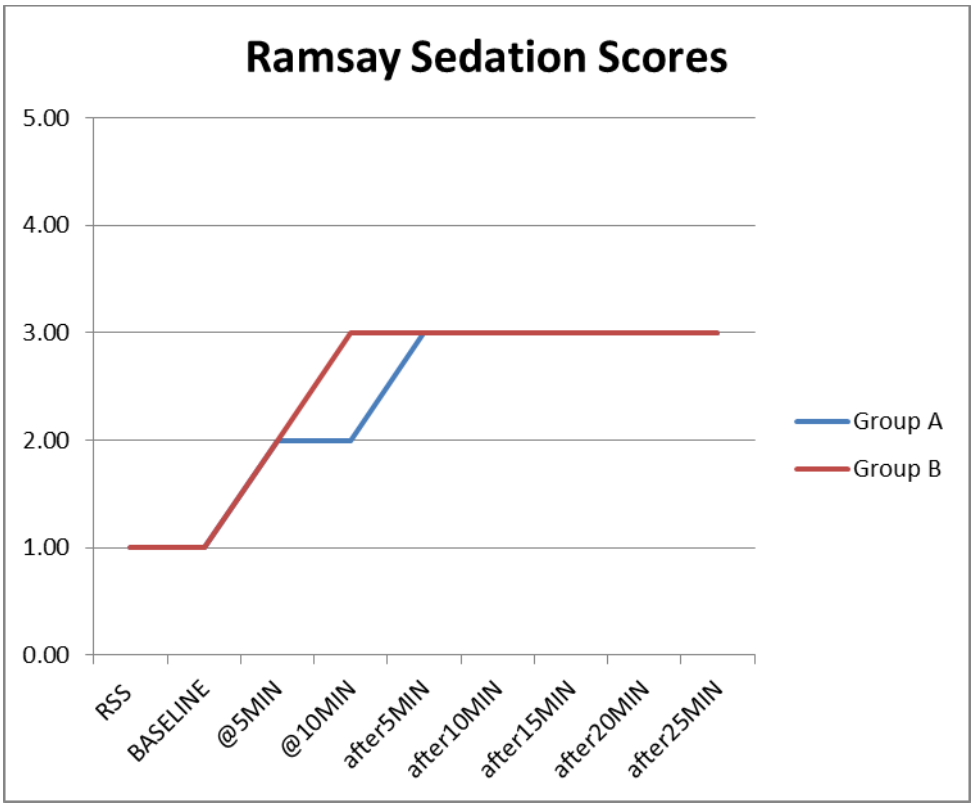

Figure 2: Modified Ramsay sedation scores (RSS) in patients of both the groups

There was a statistically significant difference in median RSS seen at different time points in Group B ($p < 0.05$).

Table 3: Modified Ramsay Sedation Scores (median [IQR]) in patients of both groups

TIME	Group A	Group B	p-value
BASELINE	1 [1, 1]	1 [1, 1]	1
DURING NEBULISATION			
5 MIN	1 [1, 1]	1 [1, 1]	1
10 MIN	2 [2, 2]	2 [2, 2]	0.021

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AFTER NEBULISATION			
5 MIN	2 [2, 2]	3 [2.8, 3.0]	< 0.001
10 MIN	3 [2.8, 3]	3 [3, 3]	0.339
15 MIN	3 [2.8, 3.0]	3 [3, 3]	0.023
20 MIN	3 [2.8, 3]	3 [3, 3]	0.023
25 MIN	3 [3, 3]	3 [3, 3]	1
30 MIN	3 [3, 3]	3 [3, 3]	0.317

The mean dose of propofol used in the nebulization group was 80 ± 10.43 mg compared to the IV group 73.53 ± 10.14 mg with a p-value of 0.018. None of the patients in either group had an increase in MAP or HR during the study. In both the groups, the HR decreased from the baseline value; there was a statistically significant difference ($p < 0.05$) in mean HR at different time points.

Table 4: 'Heart Rate' changes in patients of both the groups

TIME	Group A		Group B		
	Mean	SD	Mean	SD	p-value
BASELINE	82.3	14.36	79.07	10.22	0.319
LARYNGOSCOPY	72.23	9.75	72.9	10.63	0.801
1 MIN	70.6	9.48	71.23	10.49	0.807
2 MIN	69.03	8.7	69.57	8.59	0.812
3 MIN	68.23	8.5	68.9	8.44	0.762
4 MIN	67.47	8.4	67.57	7.42	0.961
5 MIN	67.6	8.61	67.53	8.18	0.976
10 MIN	67.43	8.22	68.27	8.99	0.709

DISCUSSION

Laryngoscopy and tracheal intubation is the technique through which general anaesthesia is administered to the patient. The pressor responses cause sympathetic activation which manifests within 30 seconds of laryngoscopy and returns to baseline within 10 minutes. [1,2] Hence, several pharmacological drugs are used to attenuate such pressor response. Dexmedetomidine, a centrally acting highly specific alpha 2 adrenergic agonist is one useful drug among them. It has many uses and has been used as pre-medication and for sedation in ICU. [3,4]

Dexmedetomidine can be administered through nebulization and intranasal routes. The bioavailability of the drug administered through buccal, intranasal, and nebulization routes is 73 - 92%. [5] Studies have shown that preoperative administration of dexmedetomidine through nebulization can be used for attenuation of stress response of laryngoscopy and intubation. [3] Nebulized dexmedetomidine 1mcg/kg given 10 minutes before surgery showed attenuation of SBP, DBP, and MAP during the first 10 minutes of laryngoscopy when compared to nebulized saline. [7,8]

Nebulized dexmedetomidine in the dose of 2 mcg/kg in cardiac patients posted for non-cardiac surgery also showed better attenuation of hemodynamic responses when compared to IV lignocaine. [9] It is known to produce arousable conscious sedation when used both in nebulized and IV routes. [1,6] It was found to be very useful during IV cannulation [10] and procedural sedation [11-15] and helped in parental separation of the pediatric population. [16]

When compared with IV lignocaine, IV dexmedetomidine 1mcg/kg given 10 minutes before intubation effectively attenuated hemodynamic response. [17] In hypertensive patients, IV lignocaine was compared with IV dexmedetomidine for attenuation of pressor response and it was found that dexmedetomidine maintains hemodynamic stability. [18] When IV dexmedetomidine 0.5 mcg/kg and 1 mcg/kg were compared with lignocaine, the study concluded that 1mcg/kg of dexmedetomidine can attenuate HR, SBP, DBP, and MAP following laryngoscopy whereas 0.5 mcg/kg could attenuate only the heart rate and the study further observed that IV lignocaine in the dose of 1.5 mg/kg was found to be superior compared to 0.5 mcg/kg of dexmedetomidine in attenuating BP. [19]

Similar studies comparing 1mcg/kg of dexmedetomidine used by IV and nebulization routes 30 minutes before intubation concluded that nebulized dexmedetomidine attenuates the intubation response minimally compared to the IV group. [1,3] Another study using 0.5 mcg/kg IV and 1 mcg/kg intranasal dexmedetomidine also showed similar results. [6] Dexmedetomidine 1 mcg/kg in nebulization and IV, IV fentanyl 2 mcg/kg were compared in a study [2] and concluded that nebulized dexmedetomidine suppresses hemodynamic response when compared to IV dexmedetomidine along with dose sparing effect of the opioid. Dexmedetomidine also has a dose-sparing effect on propofol. [1-3,20-23] In a study comparing saline and 1mcg/kg dexmedetomidine nebulization, the propofol consumption was found to be reduced by 0.28 mg/kg in the dexmedetomidine group (1.17 mg/kg) when

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compared to the saline group (1.45mg/kg). [8] Preoperative administration of dexmedetomidine in the dose of 0.5 mcg/kg through nebulization and transtracheal route was compared with 1mcg/kg of dexmedetomidine through IV route for patients planned for elective awake fiberoptic intubation (AFOI). The nebulization and transtracheal route provided optimal conditions for AFOI with good patient tolerance in comparison with the intravenous route with a dose-sparing effect on the induction dose of propofol. [24]

In our study, dexmedetomidine was given preoperatively through nebulisation and IV routes for the attenuation of laryngoscopy and intubation response and we found that 1mcg/kg of dexmedetomidine when administered preoperatively through nebulization 30 minutes before intubation, the results were comparable with administration through IV route. Both the groups showed attenuation of laryngoscopy and intubation response, there was no significant increase in MAP seen in the first 10 minutes after intubation. Sedation scores were similar in both groups. The mean dose of propofol required for induction was found to be slightly higher in the nebulization group compared to the intravenous group. No significant increase in HR was seen in the first 10 minutes after intubation.

CONCLUSIONS

We conclude that both nebulized and IV infusion of dexmedetomidine (1mcg/kg) when administered 30 minutes before laryngoscopy and intubation are equally efficacious in attenuating the pressor response. Hence, dexmedetomidine nebulization can be used as an alternative to IV dexmedetomidine.

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