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Research Article

EFFECT OF NEBULIZED DEXMEDETOMIDINE ON HEMODYNAMIC RESPONSE TO INTUBATION

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ABSTRACT

Objective: The aim of the study was to determine the role of nebulized dexmedetomidine in attenuating the stress response to laryngoscopy and intubation and to observe any adverse effects of the drug such as cough, bradycardia, hypotension, and dose-sparing result of propofol.

Methods: A prospective and observational study was conducted in a tertiary care teaching hospital for 12 months. A total of 62 patients (ASA 1 and 2) in the age group of 18–65 years scheduled for elective surgery under general anesthesia received either nebulized dexmedetomidine 10 min before intubation (Group A) or Inj. Lignocaine 90 s before intubation (Group B). Post-intubation hemodynamic parameters were compared in both groups. Data collected remained analyzed using SPSS version 16.

Results: Both groups were comparable with respect to demographic variables. Nebulization with Inj. Dexmedetomidine showed statistically significant blunting of hemodynamic response in the 1st min following intubation, in Group A. This was seen in the variables such as heart rate, diastolic blood pressure, and mean arterial blood pressure. There was no significant difference in the systolic blood pressure at all points of time. Furthermore, there was no significant change in the variables at 5 and 10 min following intubation. There was a significant decrease in the dose of propofol required for induction in Group A compared to Group B.

Conclusion: Nebulization with dexmedetomidine before laryngoscopy and intubation significantly reduced the hemodynamic response to intubation, immediately after intubation.

Keywords: Stress response, Nebulized dexmedetomidine, Laryngoscopy, Intubation.

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INTRODUCTION

Laryngoscopic manipulation and endotracheal intubation are painful stimuli that can produce a stress response resulting in tachycardia, hypertension, and arrhythmias It can be detrimental especially in patients with cardiovascular and cerebrovascular diseases. Many drugs as well as techniques have been tried to attenuate this response. This includes $\alpha 2$ agonist dexmedetomidine also. Lignocaine is the most commonly used drug to attenuate the stress response.

Dexmedetomidine is an $\alpha 2$ agonist with 8 times more affinity to $\alpha 2$ receptors compared to clonidine. It provides sedation, sympatholysis, analgesia, opioid, and anesthetic sparing effect and cardiovascular stability while avoiding respiratory depression. Thus, it has been found by many authors to be a great choice for blunting stress response to laryngoscopy and intubation. Its effect has been studied through intravenous, intranasal, and intramuscular routes. Nebulized dexmedetomidine has the advantage of depositing the drug over nasal, buccal, as well as respiratory mucosa. We hypothesized that effect of nebulized dexmedetomidine in blunting the hemodynamic response to laryngoscopy and intubation is more when compared to intravenous lignocaine, in patients undergoing elective surgery under general anesthesia. The objective of this study was to understand the role of nebulized dexmedetomidine in attenuating the stress response to laryngoscopy and intubation in patients undergoing elective surgery under general anesthesia as compared to intravenous lignocaine.

METHODS

This was a prospective and observational study done over a period of 1 year in a teaching hospital. Sixty-two American Society of Anaesthesiologists (ASA) I, ASA II patients of either sex, aged 18–65 years undergoing an elective operation under general anesthesia with endotracheal intubation were allocated into two groups of 31 patients each using simple randomization. The study was started after getting ethical clearance from Institutional Review Board of our institute. Informed written consent was taken from all patients included in the study.

Inclusion criteria

Patients with 18–65 years, ASA I and II, patients undergoing general anesthesia with endotracheal intubation for elective surgeries, and patients with normal airway were included in the study.

Exclusion criteria

Patients who were not consenting for the study, predicted airway difficulty, pregnancy, renal failure, uncontrolled hypertension, seizure disorders, patient on anti-depressants/anti-psychotics, and patients with a deprived cardiopulmonary reserve and body mass index >30 kg/m^2 were excluded from the study.

Methodology

Group A (study group n-31) received 1µ/kg of dexmedetomidine mixed with saline to a total of 5 mL,10 min before intubation and Group B (control group n-31) received 1.5 mg/kg 2% Inj. Lignocaine intravenously, 90 s before intubation. A day before the surgery, a preoperative visit included history taking and clinical examination of the patient was done. All patients were informed about the study protocol and consent was obtained for the same. Monitors were attached and baseline hemodynamic variables were noted. Dexmedetomidine at a dose of 1 µg/kg (mixed with saline to an entire volume of 5 mL) nebulization was administered to Group A (study group) with a nebulizer facemask and an incessant flow of 100% oxygen at 6 L/min for 10 min before induction of anesthesia in sitting position and the control Group B received 1.5 mg/kg IV 2% Inj. Lignocaine 90 s before intubation. Patients remained premedicated with injection glycopyrrolate (0.02 mg/kg), fentanyl 2 µg/kg, induced with propofol (1–2 mg/kg) titrated to the losing of verbal reply and the amount of drug administered was noted, and atracurium in the dose

of 0.5 mg/kg, to facilitate intubation. Direct laryngoscopy (appropriate size Macintosh blade) and intubation was done using an appropriate sized endotracheal tube by an experienced consultant anesthesiologist and connected to the ventilator. The patient remained undisturbed for a period of 10 min after intubation for noting the vital parameters such as heart rate (HR), blood pressure (systolic [SBP], diastolic [DBP] and mean arterial (MAP)], pulse oximetry (SpO_2), by an anesthesia resident doctor not involved in the study at the next time points: baseline (Tb), after nebulization (after neb), and post-intubation at 1, 5, and 10 min (T1, T5, and T10). All the patients were administered with inj. paracetamol 1-g IV intraoperatively. Once the surgical procedure was done, the reversal of neuromuscular blockade was done with Inj glycopyrrolate and neostigmine, the patient's trachea was extubated after meeting the extubation criteria and shifted to post-anaesthesia care unit.

Statistical analysis

Data collected for the study were compiled and entered into MS EXCEL software and analyzed using SPSS. The categorical data were analyzed with Chi-square test and quantitative data using the unpaired Student's t-test/Mann–Whitney test. For all observations analyzed, we chose a level of significance also called the alpha value as 0.005 and accepted it as significant and p<0.05 was considered as statistically significant.

RESULTS

The two groups were comparable in terms of age distribution since there was no statistically significant difference present. The p-value was 0.41(>0.05) (Table 1).

The two groups were comparable in terms of sex. There was no significant difference between the two groups with a p-value of 0.093(>0.05) (Table 2).

The two groups were comparable in terms of ASA PS grading. There was no significant difference between the two groups with a p-value of 0.437(>0.05) (Table 3).

The two groups were comparable in terms of weight. There was no important difference between the two groups with a p-value of 0.190(>0.05) (Table 4).

The heart rate was assessed at baseline level, at 1 min, 5 min, and 10 min post-intubation in both the groups and were compared. Heart rate at baseline, 5, and 10 min showed no significant difference between the two groups with p-values 0.584, 0.080, and 0.147, respectively. It was found that heart rate of Group A at 1 min showed a significant difference when compared to Group B. The p-value obtained was 0.001 and hence statistically significant (Table 5).

The SBP assessed at baseline, 1 min, 5 min, and 10 min post-intubation showed no significant difference between Group A and B. The p-value obtained were 0.355, 0.074, 0.137, and 0.463, respectively (Table 6).

DBP assessed at baseline, 5 min, and 10 min showed no significant difference with p-value >0.05. The DBP at 1 min showed significant difference between Group A and B with p-value 0.018(<0.05) (Table 7).

MAP at baseline, 5 min, and 10 min showed no significant difference with p-value being >0.05.The MAP at 1 min showed significant reduction in Group A compared to Group B with p-value 0.029(<0.05) (Table 8).

Oxygen saturation at baseline, 1 min, 5 min, and 10 min showed no significant difference between the two groups with p-values >0.05. Hence, it was statistically insignificant (Table 9).

It was found that the amount of propofol used for induction was less in Group A compared to Group B with a mean of 92.26 in Group A and 113.17 in Group B. The p value obtained was 0.000(<0.05) and hence statistically significant (Table 10).

Table 1: Comparison of two groups according to mean age

Group	Age			Total	χ^2	p-value
	18–35	36–50	51–65			
Group A						
Count	7	19	5	31	1.826	0.401
%	22.6%	61.3%	16.1%	100.0%		
Group B						
Count	10	19	2	31		
%	33.3%	60.0%	6.7%	100.0%		
Total						
Count	17	38	7	62		
%	27.9%	60.7%	11.5%	100.0%		

Table 2: Comparison of two groups according to sex

Group	Sex		Total	χ^2	p-value
	Male	Female			
Group A					
Count	5	26	31	2.815	0.093
%	16.1	83.9	100.0		
Group B					
Count	2	29	31		
%	3.3	96.7	100.0		
Total					
Count	7	55	62		
%	9.8	90.2	100.0		

Table 3: Comparison of cases in both groups according to ASA PS grading

Group	ASA		Total	χ^2	p-value
	ASA 1	ASA 2			
Group A					
Count	21	10	31	0.604	0.437
%	67.7%	32.3%	100.0%		
Group B					
Count	24	7	31		
%	76.7%	23.3%	100.0%		
Total					
Count	45	17	62		
%	72.1%	27.9%	100.0%		

ASA: American Society of Anaesthesiologists

Table 4: Comparison of two groups according to mean weight

Group	Weight			Total	χ^2	p-value
	<50 kg	50 70 kg	>70 kg			
Group A						
Count	5	23	3	31	3.318	0.190
%	16.1	74.2	9.7	100.0		
Group B						
Count	7	23	0	30		
%	23.3	76.7	0.0	100.0		
Total						
Count	13	46	3	62		
%	19.7	75.4	4.9	100.0		

DISCUSSION

Laryngoscopy and intubation in general anesthesia is often accompanied by a stress response which are seen as hemodynamic fluctuations. Several drugs and techniques have been in use to blunt this response. Intravenous dexmedetomidine has been found to have a significant effect in blunting the stress associated with laryngoscopy and intubation [1-3]. It has the advantage of being a non-invasive

Table 5: Comparison of heart rate at baseline, 1 min, 5 min, and 10 min

Group	n	Mean	SD	t	p-value
HR (B)					
Group A	31	91.42	14.175	0.550	0.584
Group B	31	89.43	13.999		
HR (1')					
Group A	31	81.23	12.516	3.658	0.001
Group B	31	93.03	12.691		
HR (5')					
Group A	31	79.81	11.557	1.784	0.080
Group B	31	85.33	12.625		
HR (10')					
Group A	31	79.23	11.283	1.470	0.147
Group B	31	83.50	11.425		

HR (B): Heart rate-baseline, HR (1'): Heart rate at 1 min, HR (5'): Heart rate at 5 min, HR (10'): Heart rate at 10 min

Table 6: Comparison of SBP at baseline , 1 min , 5 min, and 10 min

Group	n	Mean	SD	t	p-value
SBP (B)					
Group A	31	138.71	15.210	0.932	0.355
Group B	31	134.63	18.808		
SBP (1')					
Group A	31	122.58	12.612	1.818	0.074
Group B	31	129.23	15.837		
SBP (5')					
Group A	31	118.03	10.081	1.508	0.137
Group B	31	122.77	14.161		
SBP (10')					
Group A	31	117.32	9.635	0.739	0.463
Group B	31	119.43	12.541		

SBP (B): Systolic blood pressure - baseline, SBP (1'): Systolic blood pressure at 1 min, SBP (5'): Systolic blood pressure at 5 min, SBP (10'): systolic blood pressure at 10 min

Table 7: Comparison of DBP at baseline, 1 min, 5 min, and 10 min

Group	n	Mean	SD	t	p-value
DBP (B)					
Group A	31	90.74	9.842	1.476	0.145
Group B	31	86.67	11.666		
DBP (1')					
Group A	31	76.35	9.998	2.423	0.018
Group B	31	83.00	11.393		
DBP (5')					
Group A	31	73.06	6.673	1.814	0.075
Group B	31	76.70	8.864		
DBP (10')					
Group A	31	73.23	7.356	0.163	0.871
Group B	31	73.53	7.417		

DBP (B): Diastolic blood pressure-baseline, DBP (1'): Diastolic blood pressure at 1 min, DBP (5'): Diastolic blood pressure at 5 min, DBP (10'): Diastolic blood pressure at 10 min

method with a rapid onset of action and good bioavailability through the large surface area of the respiratory mucosa. Our study aimed at studying the effect of nebulized dexmedetomidine in blunting this hemodynamic response to intubation during general anesthesia, to avoid the side effects of intravenous dexmedetomidine. Furthermore, the problems of transient nasal irritation, cough, vocal cord irritation, or laryngospasm associated with intranasal route [4] can be avoided. It was demonstrated that the use of nebulized dexmedetomidine as a component of general anesthesia has a significant role in blunting the hemodynamic stress response [5-7].

Kumar *et al*. [8] in 2020 conducted a prospective and randomized study on 100 ASA I and II patients. They divided this population into two

Table 8: Comparison of MAP at baseline, 1 min, 5 min, and 10 min

Group	n	Mean	SD	t	p-value
MAP (B)					
Group A	31	106.730	11.020	1.285	0.204
Group B	31	102.655	13.65		
MAP (1')					
Group A	31	91.763	10.457	2.245	0.029
Group B	31	98.4110	12.606		
MAP (5')					
Group A	31	88.053	7.226	1.746	0.087
Group B	31	92.055	10.343		
MAP (10')					
Group A	31	87.9240	7.679	0.429	0.670
Group B	31	88.833	8.8181		

MAP (B): Mean arterial pressure-baseline, MAP (1'): Mean arterial pressure at 1 min, MAP (5'): Mean arterial pressure at 5 min, MAP (10'): Mean arterial pressure at 10 min

Table 9: Comparison of SpO_2 at baseline, 1 min, 5 min, and 10 min

Group	n	Mean	SD	t	p-value
SpO2(B)					
Group A	31	99.13	0.846	1.628	0.109
Group B	31	98.70	1.179		
SpO2 (1')					
Group A	31	100.00	0.000		
Group B	31	100.00	0.000		
SpO2 (5')					
Group A	31	100.00	0.000[a]		
Group B	31	100.00	0.000[a]		
SpO (10')					
Group A	31	100.00	0.000[a]		
Group B	31	100.00	0.000[a]		

SpO2(B): Oxygen saturation-baseline, SpO2 (1'): Oxygen saturation at 1 min, SpO2 (5'): Oxygen saturation at 5 min, SpO2 (10'): Oxygen saturation at 10 min

Table 10: Comparison of amount of propofol used

Group	n	Mean	SD	t	p-value
PROPOFOL (mg)					
Group A	31	92.26	16.575	4.850	0.000
Group B	31	113.17	17.094		

groups: control Group C who received nebulization with normal saline and Group D who received 1 µg/kg of dexmedetomidine 5 ml 10 min before induction. They compared SBP, DBP, MAP, response entropy, and state entropy at baseline state and 1, 5, and 10 min of intubation. It was found that nebulized dexmedetomidine effectively blunts the stress to laryngoscopy and intubation, with no adverse effects.

In our study, we chose 62 patients of ASA I and II, in the age group 18–65 years scheduled for elective surgery under general anesthesia with endotracheal intubation. The sample size was calculated based on the study conducted by Sale *et al*. [9]. They were divided into two groups of 31 each. One group received nebulized dexmedetomidine 10 min before intubation and the other group received intravenous lignocaine 90 s before intubation. The hemodynamic variables HR, SBP, DBP, MAP, and SpO_2 were monitored at baseline level and at 1, 5, and 10 min of intubation.

The baseline characteristics of the population in terms of age, gender, weight, and ASA PS grading were analyzed and no significant differences were seen. Hence, both the groups were comparable. In this study, majority of patients in both groups belonged to ASA I group (Group A – 67.7% and Group B – 76.7%). In this study, the HR, DBP, and MAP were found to have a significant reduction at 1 min in dexmedetomidine group when compared with the control group.

However, SBP at all points of time and other variables at all other time points except at 1 min showed no statistically significant difference. This was consistent with the findings of Misra *et al.* [10]. They studied that 120 ASA I and II patients undergoing surgeries and requiring tracheal intubation were randomized to receive nebulized dexmedetomidine or saline. They monitored heart rate and non-invasive SBP for 10 min. They found that nebulized dexmedetomidine at 1 μg/kg attenuated the increase in heart rate but not SBP following laryngoscopy. This may be explained by our route of administration. The bioavailability of dexmedetomidine through inhalation is 65% through nasal mucosa and 82% through buccal mucosa [14]. This is comparable to 0.5 μkg of intravenous dose [15]. This will only have a modest effect on the hemodynamic parameters.

Sale *et al*. [9] in 2015 conducted a randomized comparative, and prospective study in 60 patients of either sex, of ASA I and II, aged between 20 and 60 years undergoing elective surgery. These patients were divided into two, Group L who received intravenous lignocaine and Group D who received intravenous dexmedetomidine. It was found that there was significant stress response associated with laryngoscopy and intubation in Group L, but this stress response was attenuated in Group D. They found significant attenuation of hemodynamic response in dexmedetomidine group, which was statistically better at 5 min of laryngoscopy and intubation than at 1 min.

In our study, the cumulative dose of propofol required for induction in Group A was decreased compared to Group B. The decrease in propofol dose was probably because of the sedative and analgesic properties of dexmedetomidine. This is consistent with the studies done by Walia *et al*. [11] which showed that pre-treatment with dexmedetomidine significantly reduced the dose of propofol. Furthermore, in a study conducted by Senapati *et al*. [12], it was demonstrated that dexmedetomidine as a pre-anesthetic medication significantly reduces intraoperative anesthetic requirement of thiopentone and propofol, with the dose requirement slightly less in case of propofol than thiopentone. Similar results were obtained by El-Shmaa *et al*. [13] in their study.

None of the patients in our study who received dexmedetomidine nebulization had any adverse effects such as bradycardia, hypotension or cough. This was consistent with the findings of study done by Kumar *et al*. [8]. In the study conducted by Sale *et al*. [9], no side effects were observed in the patients who received intravenous dexmedetomidine, except for an episode of bradycardia in a single patient in Group D.

Limitations

Cases with difficult airway were excluded from the study and the time required for laryngoscopy and intubation was also not considered. Furthermore, the results cannot be extrapolated to high-risk patients with comorbidities. We evaluated the effect of a single dose of nebulized dexmedetomidine and are thus unable to comment whether different doses will have different effects on hemodynamic parameters.

CONCLUSION

The use of nebulized dexmedetomidine before intubation and laryngoscopy significantly reduced the hemodynamic response in the 1st min following laryngoscopy and intubation, compared to intravenous lignocaine, without any adverse effects and also there was a reduction in the dose of intravenous propofol required for induction of anesthesia, in the dexmedetomidine group.

AUTHOR'S CONTRIBUTION

All the authors contributed to the preparation of the final manuscript.

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