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Effect of dexmedetomidine by nebulizer for blunting stress response to direct laryngoscopy and intubation

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Abstract
Introduction: Direct laryngoscopy and intubation are noxious stimuli and are associated with transient, unpredictable and variable hemodynamic changes. Dexmedetomidine has the potential to produce bradycardia and hypotension when administered as a bolus; in a way to solve this problem, nebulization route chosen. Nebulized dexmedetomidine has a bioavailability of 65%. Nebulized drug preferred over intranasal administration to avoids adverse effects.
Aim and objectives: The aim of this study to evaluate the role of nebulized dexmedetomidine as a premedication in attenuating the stress response to laryngoscopy and intubation along with any adverse effects of drug.
Materials and methods: 50 patients of ASA grade I and II elective surgery undergoing general anesthesia were randomly divided in two groups N and D, who received nebulized normal saline(5ml) and nebulized dexmedetomidine (1ug/kg diluted in 5ml NS) respectively with a nebulizer face mask for 10 min before induction of anesthesia in sitting position.
Result: Following laryngoscopy and intubation, stress response markedly increased in the group N where stress response markedly decreases in group D.
Conclusions: Nebulized dexmedetomidine effectively blunts the stress response to laryngoscopy and intubation with no adverse effects.

Keywords: Dexmedetomidine, intubation, laryngoscopy, premedication, stress response

1. Introduction
Direct laryngoscopy and tracheal intubation are noxious stimuli and are associated with transient, unpredictable and variable hemodynamic changes due to increased sympathoadrenal activity. This response occurs after direct laryngoscopy and intubation and lasts less than 10 min. sometime they precipitate ischemia, arrhythmias, cerebrovascular stroke, pulmonary oedema, increase in intracranial pressure in the vulnerable group [1, 7].
Use of various drugs and various routes such as opioids, vasodilators, beta-blockers, calcium channel blockers, intravenous lignocaine, topical sprays, volatile agents, α2 agonist, intravenous, intranasal, nebulizer have been used for prevention of this stress response [1, 9].
Dexmedetomidine, a selective alpha2-adrenoceptor agonist, is short-acting and has sedative, hypnotic, anxiolytic, analgesic, anti-sialagogue, sympatholytic properties and promotes cardiac, respiratory and neurological stability [2].
Dexmedetomidine has the potential to produce bradycardia and hypotension, nebulization route was chosen for that. Nebulized dexmedetomidine has a bioavailability of 65% through the nasal mucosa and 82% through the buccal mucosa [1].
Nebulized drug administration may be preferred over intranasal administration, as it avoids transient nasal irritation, cough, vocal cord irritation or laryngospasm.
I have studied the effect of nebulized dexmedetomidine on hemodynamic stress response to direct laryngoscopy and intubation along with adverse effects if any, in patients undergoing general endotracheal anaesthesia.

2. Aims and Objectives
Evaluate the effect of dexmedetomidine by nebulizer for blunting stress response to direct laryngoscopy and intubation.
Aim of study is to evaluate following parameters by comparing two group:
Heart rate, Systolic blood pressure, Diastolic blood pressure, Mean arterial pressure, Pulse oximetry (SpO_2) at baseline (Tb), after nebulization (after neb), post-intubation at 1, 5 and 10 min (T1, T5 and T10).

Any other adverse effects of drug like bradycardia, hypotension, hypertension, cough, sedation etc.

3. Material and Methodology

After obtaining written and informed consent, we conducted a prospective observational study in 50 patients admitted in SMIMER, Surat. Patients were randomly divided in two groups with 25 patients in each group.

4.1 Inclusion Criteria

Age: 18-60 years
Sex: Male or Female
ASA (American society of anaesthesiology) grade I or II

4.2 Exclusion Criteria

Age below 18 years or above 60 years
Patient's refusal
History of recent upper respiratory tract infection
Allergy to any of study drug
Oral surgeries
body mass index (BMI) >30 kg/m2
predicted airway difficulty
pregnancy, renal failure, uncontrolled hypertension, seizure disorders, patient on anti-depressants/anti-psychotics, patients with a poor cardiopulmonary reserve

4.3 Preoperative Evaluation

Preanesthetic check-up was done in OPD and before the day of surgery in ward.
Written informed consent was taken.
NBM status of patient was noted.
Patient's heart rate, blood pressure and Spo_2 on room air were recorded pre-operatively. IV line was secured with 18/20-gauge iv cannula. Patients were premedicated 30-35 minutes prior to induction of anesthesia with
Inj. Glycopyrrolate 0.005mg/kg Intramuscularly.
Nebulization was given with one of study drug 10 minutes before shifting patient to operation theatre. Patients in group D (study group n-25) received nebulization with Inj. Dexmedetomidine 1mcg/kg with 5ml normal saline while group N (control group n-25) patients received nebulization with Inj. Normal saine 5ml.
Preoxygenation was done with 100% o_2 for 3 minutes. Induction was done with Injection Fentanyl 2 µg/kg and Propofol 2-2.5 mg/kg i.v. and neuromuscular blockade was achieved with Inj. Atracuriun 0.5mg/kg to facilitate intubated with appropriate size of endotracheal tube. Patient was maintained on O_2/N_2O 50%/50%, isoflurane and Inj. Atracurium 0.1mg/kg.

Following vital parameters were noted:
Heart rate (HR)
Blood pressure (systolic (SBP), diastolic (DBP) and mean arterial pressure (MAP)
Pulse oximetry (SpO_2) at baseline (Tb), after nebulization (after neb), post-intubation at 1, 5 and 10 min (T1, T5 and T10).
All the patients were administered with inj. Paracetamol 1 gram IV intraoperatively. Once the surgical procedure was done, the residual neuromuscular blockade was reversed with inj. glycopyrrolate and neostigmine, the patients was extubated after meeting the extubating criteria and shifted to post anesthesia care unit.
Statistical analysis was done using open epi and SPSS statistical software. Interpretations of observations and results was done Using unpaired Student t- test. A P-value of <0.001 was Highly significant, <0.05 was significant and >0.05 considered not significant.
The sample size was calculated using open epi Software. In a study by Kumar NR *et al* [1], evaluation of nebulised dexmedetomidine in blunting hemodynamic response to intubation: A prospective randomised study. The effect size was calculated from this study taking into consideration the difference in the mean of mean arterial pressure at 1 min (99.68 ± 19.22) and 5 min after intubation (84.08 ± 13.66). With power of 90% and confidence interval 95% the sample size was calculated to be 50 (25 patients in each group) and a total of 50 patients were recruited for the study, but there were no dropouts in our study.

5. Observation and Results

- There was reduced incidence of systolic blood pressure, diastolic blood pressure, mean arterial pressure at 1min, 5min and 10min after direct laryngoscopy and intubation in patients who received preoperative nebulized dexmedetomidine compared to nebulized normal saline.

5.1 Patients Characteristics

Table 1: Patients characteristics

Characteristics	Group N (N=25)	Group D (N=25)
Age (Years)	29.60±7.63	28.40±7.40
Sex (M: F)%	M:14 (56%) F:11(44%)	M:13 (52%) F: 12(48%)
Weight (Kg)	58.09±6.36	56.73±5.19
Asa Grade	I: 23 (92%) II: 2 (8%)	I: 22 (88%) II: 3(12%)

In our study, no significant differences among both groups regarding age, body weight, gender or ASA grade.

5.2 Incidence of Heart Rate

Table 2: intraoperative heart rate

Intraoperative Hr	Group N		Group D		
	Mean	Sd	Mean	Sd	P Value
Baseline Hr	81.04	8.64	79.4	8.54	0.5
After Neb Hr	80.92	8.21	80.52	8.38	0.86
Post Intubation 1 Min Hr	105.68	7.78	106.8	6.31	0.25
Post Intubation 5 Min Hr	104.12	7.5	104.16	5.44	0.12
Post Intubation 10 Min Hr	101.96	6.59	101.52	5.45	0.36

Incidence of HR between the two groups at various time intervals following laryngoscopy and intubation was comparable but not statistically significant with 1min, 5min and 10 min after direct laryngoscopy and intubation (P value 0.25, 0.12, 0.35, respectively).

Chart 1: Heart rate

Table 3: intraoperative mean arterial pressure

Intraoperative Map	Group N		Group D		
	Mean	SD	Mean	SD	P Value
Baseline Map	85.68	4.41	89.62	7.63	0.05
After Neb Map	82.19	4.27	88.85	7.29	0.06
Post Intubation 1 Min Map	98.29	5.09	89.28	9.03	0.006
Post Intubation 5 Min Map	93.78	5.16	86.02	8.69	0.01
Post Intubation 10 Min Map	89.01	5.01	83.44	8.5	0.01

5.3 Incidence of Mean Arterial Pressure

Incidence of Mean blood pressure were significantly lower in nebulized dexmedetomidine group in a statistically highly significant at 1min, 5 min and 10 min after direct laryngoscopy and intubation compared to nebulized normal saline group (P value 0.0067, 0.013, 0.012, respectively).

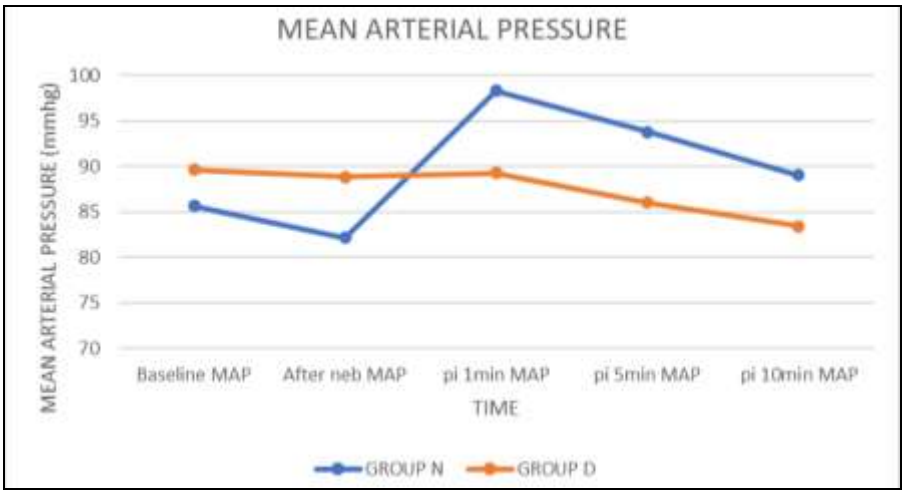

Chart 2: Mean arterial pressure

Table 4: intraoperative systolic blood pressure

Intraoperative SBP	Group N		Group D		
	mean	SD	Mean	SD	P Value
Baseline SBP	110.32	6.31	114.8	10.73	0.07
After Neb SBP	109.52	5.72	113.76	10.52	0.08
Post Intubation 1 Min SBP	124.96	7.41	114.88	12.65	0.011
Post Intubation 5 Min SBP	119.28	8.4	111.2	12.67	0.04
Post Intubation 10 Min SBP	112.48	8.23	107.76	12.69	0.038

5.4 Incidence of Systolic Blood Pressure

Incidence of Systolic blood pressure were significantly lower in the nebulized dexmedetomidine group in a statistically highly significant at 1min, 5 min and 10 min after direct laryngoscopy and intubation compared to nebulized normal saline group (P value 0.011, 0.04, 0.038, respectively).

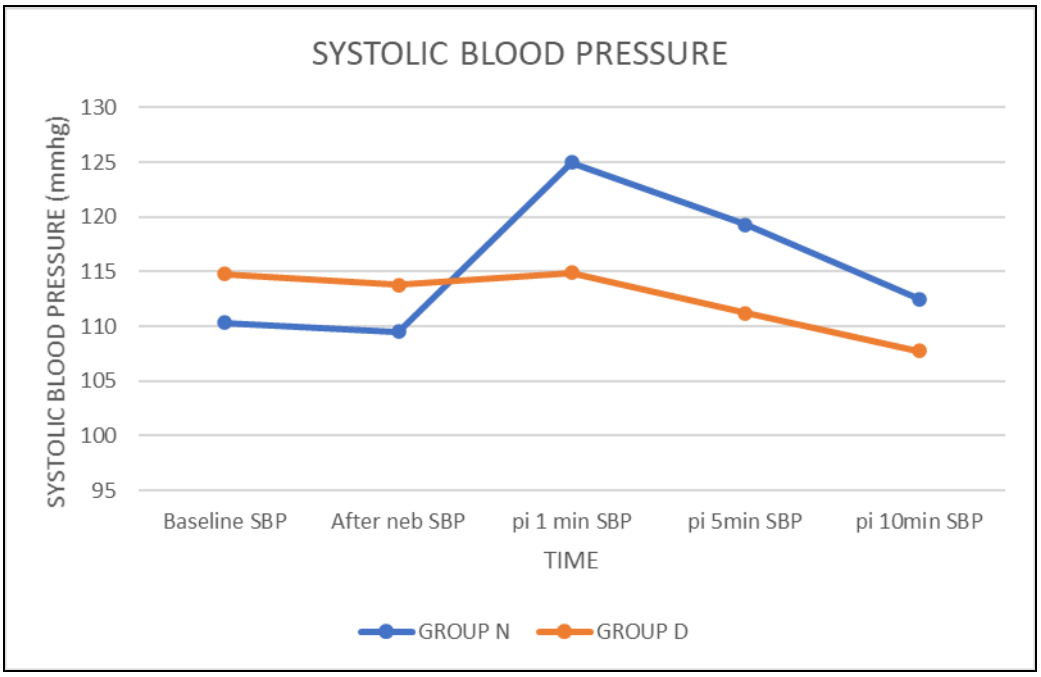

Chart 3: Systolic blood pressure

Table 5: intraoperative diastolic blood pressure

Intraoperative DBP	Group N		Group D		
	Mean	SD	Mean	SD	P Value
Baseline DBP	73.36	4.02	77.04	6.24	0.05
After Neb DBP	73.2	4	76.4	5.88	0.06
Post Intubation 1 Min DBP	84.96	4.24	76.48	7.48	0.007
Post Intubation 5 Min DBP	78.08	4.12	73.44	6.96	0.012
Post Intubation 10 Min DBP	77.28	3.69	71.28	6.68	0.051

5.5 Incidence of Diastolic Blood Pressure

Incidence of diastolic blood pressure were significantly lower in the nebilized dexmedetomidine group in a statistically highly significant at 1min, 5 min and 10 min after direct laryngoscopy and intubation compared to nebulized normal saline group (P value 0.0072, 0.012, 0.0051, respectively).

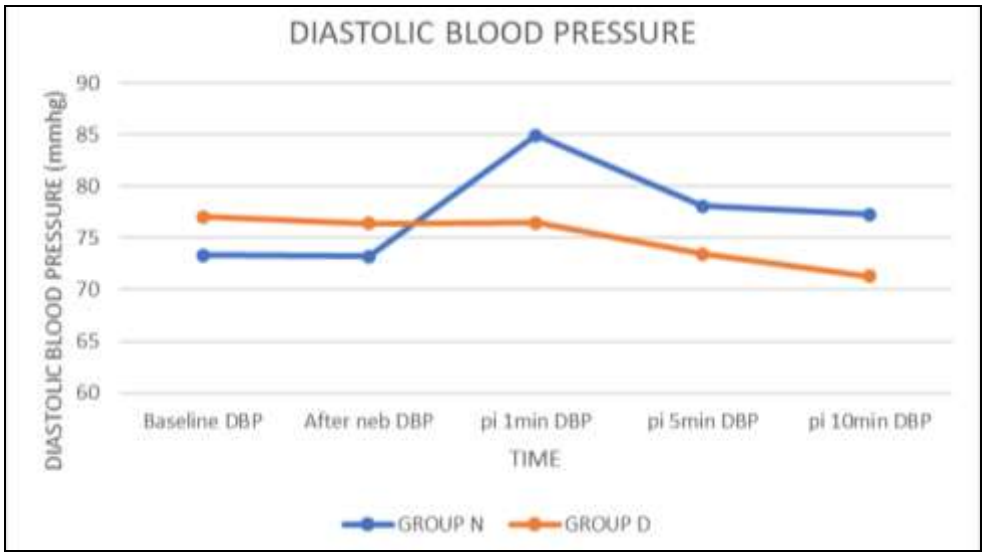

Chart 4: Diastolic blood pressure

6. Discussion

- Dexmedetomidine by nebulized route—a noninvasive method for blunting stress response to direct laryngoscopy and intubation by making use of its rapid onset and good bioavailability through the large surface area of the mucosa. Nebulized drug administration avoids transient nasal irritation, cough, vocal cord irritation or laryngospasm over intranasal administration and also transient adverse effects of bradycardia and hypotension by its intravenous route [1].
- Dexmedetomidine is a highly selective α2 agonist with sedative, analgesic and anesthetic sparing effects [1, 4]. Sedative action of dexmedetomidine in patient, without bradycardia and respiratory depression along with blunting of stress response to direct laryngoscopy and intubation is a newer response seen with the administration of dexmedetomidine by the nebulizer.
- Kumar NR *et al*. study nebulized dexmedetomidine and they found that nebulized dexmedetomidine effectively blunting hemodynamic response, significant change in response entropy and state entropy, significant reduction in propofol requirement.
- Various drugs have been tried through nebulization for sedation and blunting stress response such as lignocaine by Laurito *et al*., Zanaty and El Metainy compared nebulized dexmedetomidine, nebulized ketamine and their combination. They concluded that the combination resulted in better sedation, smoother induction and more rapid recovery.
- In several studies, dexmedetomidine given intravenously 10 min before induction was associated with adverse effects like bradycardia, hypotension, hypertension and respiratory depression [5, 8, 10]. In my study, nebulized dexmedetomidine did not produce a significant change in HR at any time point throughout the study period. The absence of bradycardia could probably be explained by the omission of the IV bolus dose of the drug. This finding suggests that nebulized dexmedetomidine may be safer than IV dexmedetomidine in patients receiving beta-blockers or with a low basal heart rate.
- In my study we found that nebulized dexmedetomidine was effective in blunting the stress response to direct laryngoscopy and intubation without any adverse effects. There was a statistically significant decrease in MAP, SBP, DBP at 1,5 and 10 min after intubation in group D because dexmedetomidine's highly selective α2 agonistic action that causes a decrease in sympathoadrenal activity thus leading to decrease in arterial blood pressure and perioperative morbidity and mortality.

7. Conclusion

- Pre-operative use of nebulized dexmedetomidine effectively reduces the incidence of stress response to direct laryngoscopy and intubation in patients undergoing GA with endotracheal intubation without any adverse effects.

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