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## A prospective comparative study of intranasal dexmedetomidine and clonidine on sedation and hemodynamic response during laryngoscopy in adult patients

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### Abstract

In general anesthesia, hemodynamic changes during endotracheal intubation are major concerns. Sedative premedications like Dexmedetomidine and Clonidine, when used intranasally are effective options for reduction of preoperative anxiety and preventing untoward hemodynamic responses at the time of induction. Thirty eight patients of ASA 1 and 2 aged 18-70 years were randomly allocated in 2 groups of 19 patients: Group C received inj. Clonidine 3 mcg/kg and Group D received inj. Dexmedetomidine 1 mcg/kg intranasally 45 min before induction. All patients were monitored after premeditation and throughout the surgery. We observed sedation, HR, SBP, DBP, MAP and SPO<sub>2</sub> at various intervals. Intranasal Dexmedetomidine was found to be more effective in producing perioperative sedation and more stable hemodynamics at the time of induction. Dexmedetomidine via intranasal route can be considered as a useful alternative of conventional medications to produce sedation and to blunt hemodynamic response during laryngoscopy.

**Keywords:** Hemodynamic response, intranasal, dexmedetomidine, clonidine

### 1. Introduction

Induction of anaesthesia is a stressful and anxiety provoking experience. The fear and anxiety at the time of induction of anesthesia lead to increase in catecholamine levels. Laryngoscopy and endotracheal intubation are also associated with sympathetic stimulation which lead to tachycardia and hypertension<sup>[1]</sup>. Haemodynamic changes occurring during laryngoscopy and endotracheal intubation were first described by Reid and Brace. All these effects can be detrimental in patients with cardiovascular and cerebrovascular diseases<sup>[2]</sup>.

Several techniques have been used to eliminate or suppress the stress response including deepening of anesthesia, intravenous and local lignocaine spray, intravenous nitroglycerine, hydralazine, beta blocker, calcium channel blockers, opioids, etc. The proper use of appropriate premedication may actually decrease anaesthetic and analgesic drug requirements as well as some side effects, such as postoperative emesis and untoward hemodynamic responses at the time of induction.

Clonidine is a centrally acting sympatholytic drug with predominant alpha-2 agonistic action. Commonly, it has been used as an antihypertensive agent, with additional sedative, anxiolytic, and analgesic properties<sup>[3]</sup>.

Dexmedetomidine is a highly selective, short-acting, alpha 2-adrenoreceptor agonist. It provides sedative, analgesic, and anxiolytic effects with minimal respiratory depression, which makes it a preferable choice among anaesthesiologist for use as an adjuvant for anaesthesia, as well as pre-medication for relieving anxiety or producing sedation before anaesthesia. The intranasal route is a convenient and effective method of administration with high rate of patient acceptance. It has been suggested that a smaller dose or routes other than rapid intravenous delivery may help to minimize the hemodynamic complications of Dexmedetomidine like hypotension, bradycardia even cardiac arrest<sup>[2]</sup>.

The aim of the present study was to compare the efficacy of intranasal Dexmedetomidine and intranasal Clonidine as a premedication for producing satisfactory levels of sedation as well as blunting of hemodynamic responses due to laryngoscopy in adult patients undergoing surgery under general anaesthesia.

**2. Materials and Methods**

After obtaining approval from ethical committee of our institute a written and informed consent was obtained from the patients. The study was conducted in prospective randomized manner using a computer generated random number program and allocation concealment was done using serially numbered opaque sealed envelope technique where patients with even numbers were given intranasal Clonidine and patients with odd numbers were given intranasal Dexmedetomidine as premedication.

This study included 38 patients of either sex between age group of 18-70 years of American Society of Anaesthesiologists (ASA) grade 1 and 2 posted for elective surgical procedure under general anaesthesia.

Exclusion criteria included-patient refusal, patients with history of drug abuse, patients with pre-existing neurological or psychological disease, BMI >30, anticipated difficult airway, cardiac or respiratory system disease, hemodynamically unstable, previous history of allergy to the study drugs.

All patients were explained and counselled about the procedure one day before surgery. Patients were randomly allocated to one of the two groups for administration of study drug 45 minutes prior to surgery. Baseline heart rate, blood pressure and SpO<sub>2</sub> were recorded just before the administration of drug. Group C-received 3 mcg/kg intranasal Clonidine hydrochloride and Group D-received 1 mcg/kg intranasal Dexmedetomidine. The drugs were instilled in both nostrils using insulin syringe, with patient in recumbent position. We have used 0.5 ml per nostril as the maximum volume. The time of drug administration was noted, and the observer recorded SpO<sub>2</sub>, HR, SBP, DBP and MAP for 45 mins and sedation at 45 mins following drug administration. The sedation level was assessed by Ramsay Sedation Score.

Ramsay sedation scale:

1. Anxious, agitated or restless.
2. Co-operative, oriented and tranquil.
3. Responds to command.
4. Asleep with brisk response to the stimulus.
5. Asleep with sluggish response to the stimulus.
6. Asleep with no response.

All patients were given inj. Glycopyrrolate 0.2 mg, inj. Ondansetron 4 mg and inj. Pentazocine 30 mg and preoxygenated for 3 minutes with 100% oxygen. Patients were induced with 4-6 mg/kg Thiopentone sodium, 2 mg/kg Succinyl choline IV followed by direct laryngoscopy for tracheal intubation with appropriate sized cuffed endotracheal tube. HR, SBP, DBP, MAP and SpO<sub>2</sub> were noted at laryngoscopy, 1, 3, 5 and 10mins after laryngoscopy. Anesthesia was maintained on O<sub>2</sub>, N<sub>2</sub>O, isoflurane and vecuronium (loading dose-0.8-1 mg/kg; maintenance dose-0.01-0.02 mg/kg). After completion of surgery, neuromuscular block was reversed with appropriate dose of IV Neostigmine (0.05 mg/kg) and Glycopyrrolate (0.01 mg/kg). After adequate recovery, the patient was extubated.

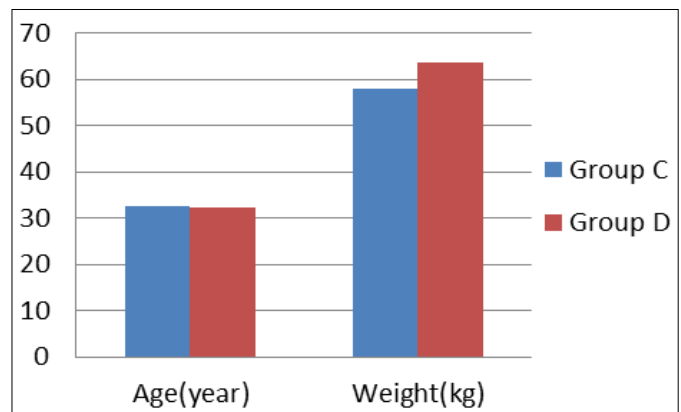
In the present study, data was presented as Mean ± SD and proportion. Statistical analysis was done using t-test where P value ≥0.05 was not significant, <0.05 was significant and <0.001 was highly significant.

**3. Result and Observation**

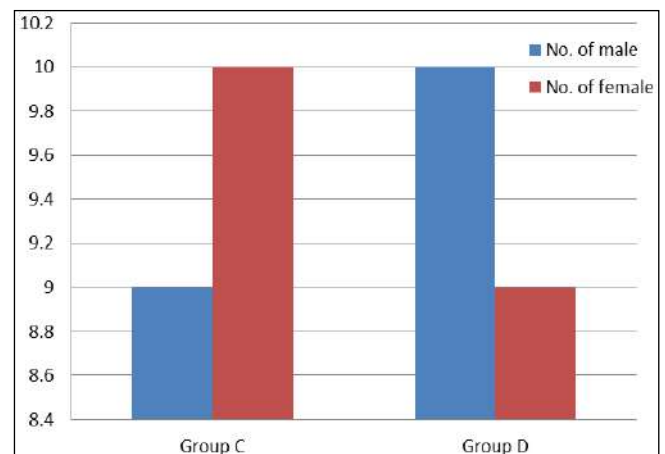
The demographic profile was comparable in both groups as shown in table-1. Sedation score was comparable in both groups before premedication. After 45mins of premedication, difference in sedation score between the two groups was significant (p< 0.05). As per table-3, mean heart rate of group D is significantly less as compared to group C at all-time intervals after 20mins of premedication (p< 0.05). Mean arterial pressure of group D is significantly low as compared to group C at 40mins after premedication, at laryngoscopy and intubation and at 1 min after intubation (p< 0.05). There was no incidence of significant bradycardia, tachycardia, hyper or hypotension in either group. None of the patients experienced nausea, vomiting or respiratory depression in the study period.

**Table 1:** Demographic profile

	<b>Group C (mean ± SD)</b>	<b>Group D (mean ± SD)</b>	<b>P Value</b>
Age (year)	32.53±9.66	32.23±10.07	>0.05
Duration of surgery	106.66±11.33	107±11.64	>0.05
Gender distribution (Male: female ratio)	9:10	10:9	>0.05



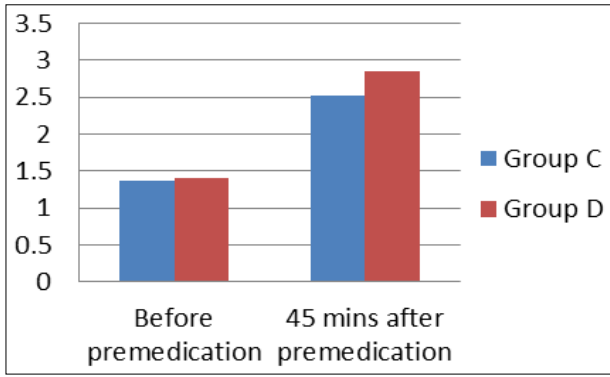
**Fig 1:** Demographic distribution



**Fig 2:** Gender distribution

**Table 2:** Ramsay Sedation Score

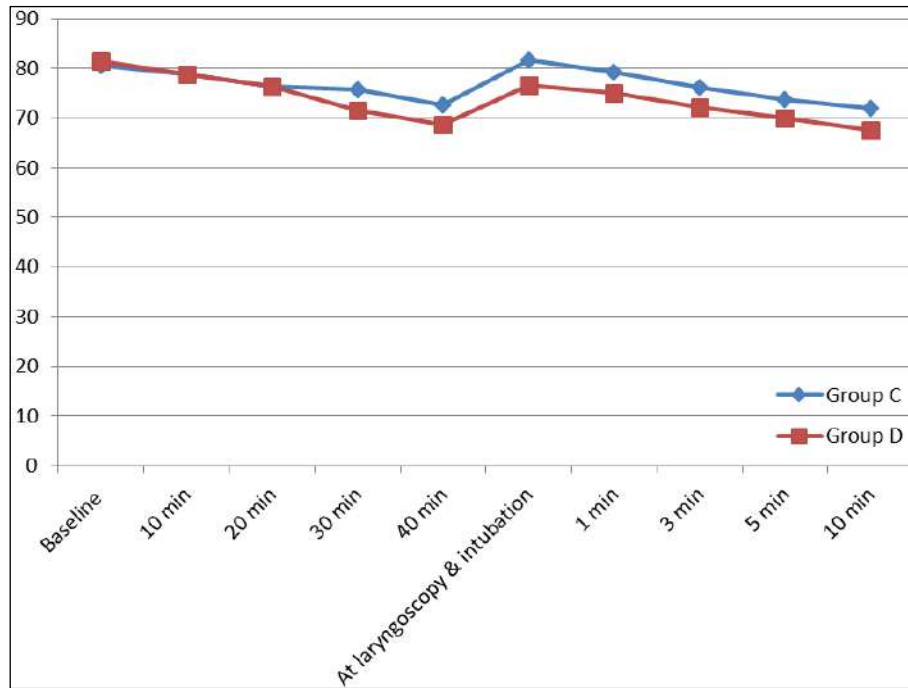
	<b>Group C (mean ± SD)</b>	<b>Group D (mean ± SD)</b>	<b>P value</b>
Before premedication	1.37±0.49	1.4±0.49	0.37
45mins after premedication	2.53±0.51	2.86±0.43	0.004



**Fig 3:** Sedation score

**Table 3:** Changes in Heart Rate

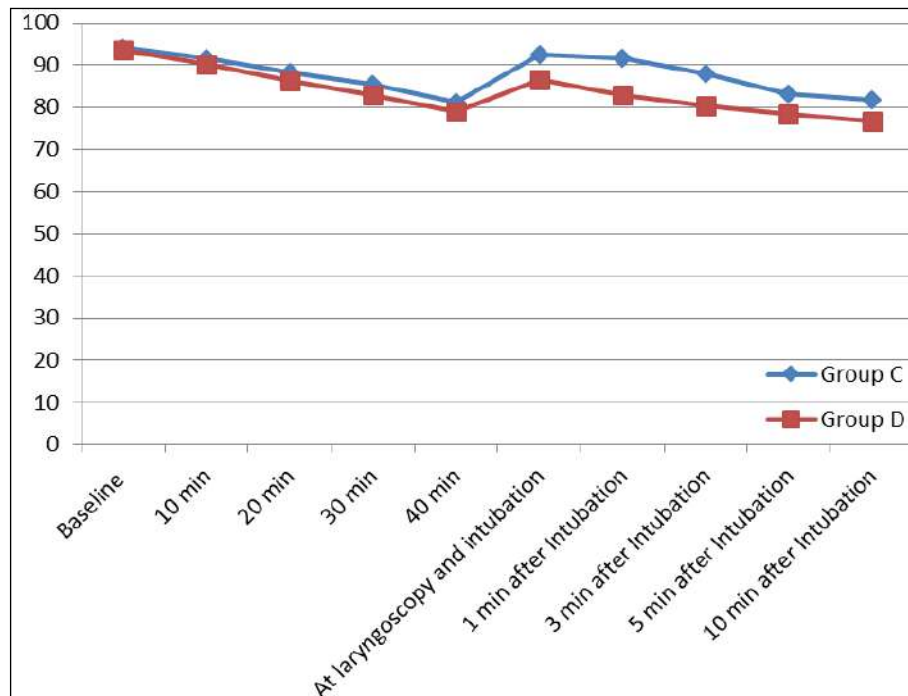
Time	Group C		Group D		P value
	Mean	sd	mean	sd	
Baseline	80.52	5.61	81.47	6.35	0.33
10 min	78.73	5.62	78.78	5.98	0.49
20 Min	76.31	5.60	76.31	6.28	0.50
30 min	75.63	6.26	71.57	6.38	0.04
40 min	72.57	5.77	68.68	6.58	0.04
At laryngoscopy and intubation	81.68	6.73	76.63	8.61	0.04
1 min after Intubation	79.26	6.18	75.10	6.31	0.02
3 min after Intubation	76.10	5.92	72.10	6.30	0.02
5 min after Intubation	73.78	5.05	70.05	6.07	0.01
10 min after Intubation	71.94	4.76	67.68	6.06	0.009



**Fig 4:** Show the group proportion

**Table 4:** Changes in Mean Arterial Pressure

Time	Group C		Group D		P value
	Mean	sd	mean	sd	
Baseline	94.00	4.51	93.67	4.18	0.75
10 min	91.67	4.23	90.23	5.28	0.35
20 min	88.34	4.88	86.30	4.34	0.62
30 min	85.32	4.12	83.00	5.28	0.30
40 min	81.33	4.07	79.03	6.56	0.04
At laryngoscopy and intubation	92.34	4.01	86.67	6.84	0.02
1 min after Intubation	91.65	4.24	83.01	6.98	0.04
3 min after Intubation	88.00	4.72	80.30	5.17	0.70
5 min after Intubation	83.30	4.06	78.28	4.86	0.45
10 min after Intubation	81.65	5.30	76.63	4.74	0.64



**Fig 5:** Show the baseline and intubation

#### 4. Discussion

Attenuation of laryngoscopic stress response is a major challenge for anaesthesiologist. The satisfactory role of preoperative Clonidine and Dexmedetomidine for attenuation of laryngoscopic stress responses is well established. Nowadays besides IV route, use of Intranasal as premedication is becoming popular, specially in pediatric population. In the present study, we compared the efficacy of intranasal Clonidine and Dexmedetomidine on the sedation and stress responses of laryngoscopy and intubation.

During general anaesthesia, pre-operative anxiety and fear as well as laryngoscopy and endotracheal intubation cause sympathetic stimulation with an increase in the circulating catecholamines levels which leads to significant increase in HR and MAP. The response is initiated within 5 seconds of laryngoscopy, peaks in 1-2 min and returns to normal levels by 5-10 min.

Both Clonidine and Dexmedetomidine are centrally acting  $\alpha_2$  agonists and have sedative, hypnotic, anxiolytic, analgesic, sympatholytic and analgesic properties. They stimulate  $\alpha_2$ -adrenergic inhibitory neurons in the medullary vasomotor center. Decreased central sympathetic outflow is manifested as peripheral vasodilatation and decrease in systemic blood pressure, HR and cardiac output. They have unique pharmacological property of conscious sedation and is devoid of any respiratory depression. Dexmedetomidine has a greater affinity for the  $\alpha_2$  receptor than  $\alpha_1$  receptor (1620:1) compared to Clonidine (220:1) [4]. The intranasal route is more convenient as it is relatively non-invasive, painless and easy to administer. Intranasal drug can penetrate the blood-brain barrier and reach the central nervous system directly. Due to the higher vascularity of the nasal mucosa, the drugs may access the systemic circulation rapidly, bypassing the first-pass metabolism of liver. The main disadvantages of IV premedication is that sedative action is more pronounced than analgesic effect with profound bradycardia and hypotension [2].

In present study, we observed that patients in group D achieved satisfactory sedation and better stress response to laryngoscopy as compared to group C.

Souhayl Dahmani *et al.* (2010) studied effects of Clonidine and benzodiazepines as premedication in children and concluded that Clonidine produces better sedation, decreases post-operative pain and emergent agitation [5].

Sukanya Mitra *et al.* (2013) conducted a study comparing intranasal Clonidine and Midazolam as premedication in children and concluded that intranasal Clonidine produces comparable level of sedation and effective anxiolysis as intranasal Midazolam with a better recovery in children [6].

Guang Han *et al.* (2014) observed that intranasal Dexmedetomidine is a new, safe and effective approach for patients undergoing gastroscopy with more stable respiratory and hemodynamic parameters than intravenous Dexmedetomidine [7].

Dharmendra Kumar Yadav *et al.* (2018) studied effect of intranasal Dexmedetomidine and Clonidine on hemodynamic response during laryngoscopy in hypertensive adult patients. They observed that intranasal Dexmedetomidine produced a comparable perioperative anxiolysis as Clonidine with higher sedation levels, more stable hemodynamics and improved patient satisfaction [1].

Saikat Niyogi *et al.* (2020) noticed that both intranasal and intravenous infusion of Dexmedetomidine are equally effective for attenuation of stress response and intranasal Dexmedetomidine can be used as a safer alternative premedication [2].

#### 5. Conclusion

From our study we concluded that both intranasal Clonidine and Dexmedetomidine effectively produced sedation when given 45mins before the surgery and blunted hemodynamic response during laryngoscopy in adult patients requiring general anesthesia although intranasal Dexmedetomidine is found to produce better sedation and blunted stress response as compared to intranasal Clonidine.

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