

# Comparative evaluation of the effectiveness of nebulized dexmedetomidine V/S intravenous dexmedetomidine in blunting hemodynamic response to intubation – A prospective and randomized study



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## ABSTRACT

**Background:** Endotracheal intubation stimulates sympathetic system causing transient increase in heart rate and blood pressure which may be detrimental in patients with cardiovascular and cerebrovascular comorbidities. Intravenous dexmedetomidine given preoperatively prevents these unfavorable changes caused by endotracheal intubation. **Aims and Objectives:** The aims of this study were to compare effectiveness of nebulized dexmedetomidine and intravenous dexmedetomidine given preoperatively in blunting hemodynamic response (HR) to intubation. **Materials and Methods:** One hundred and twenty ASA I and II patients (either gender between 18 and 60 years) undergoing elective surgeries under general anesthesia were randomized into two equal groups in this prospective and comparative study. Thirty minutes before induction, Group IV received dexmedetomidine 0.50 µg/kg (diluted with normal saline [NS] to 50 mL) as slow IV infusion and nebulization with 5 mL NS, while Group N received nebulization with dexmedetomidine 1 µg/kg mixed with NS up to 5 mL along with 50 mL NS given as slow IV infusion. HR and mean arterial pressure (MAP) were noted at different intervals until extubation. Sedation score using Ramsay Sedation Scale (post-administration of drug) and adverse effects were noted. Comparison of HR and MAP was done using unpaired "t" test (P=0.05). **Results:** IV dexmedetomidine and nebulized dexmedetomidine given pre-induction were comparable in reducing stress response to intubation. The sedation score in both groups was comparable post-administration of drug. The incidence of hypotension was significantly more in IV group. **Conclusion:** Nebulized dexmedetomidine was equally efficacious in blunting HR to intubation as IV dexmedetomidine with fewer side effects making its administration safer for maintaining hemodynamic stability.

**Key words:** Dexmedetomidine; General anesthesia; Intubation

## INTRODUCTION

Direct laryngoscopy and tracheal intubation in patients with normal protective reflexes result in stimulation of sympathetic nervous system, leading to increase in heart rate, increase in systolic and diastolic blood pressure. These transient and unpredictable changes due to sympathetic stimulation can be detrimental to patients especially

in patients with cardiovascular and cerebrovascular comorbidities.

A variety of anesthetic drugs or techniques have been used to control hemodynamic response (HR) to laryngoscopy and intubation. Different drugs<sup>1</sup> such as midazolam, gabapentin, melatonin, esmolol, and others have been used in different forms or using different routes to

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decrease this effect. One such drug that can be used is dexmedetomidine – a potent  $\alpha$ -2 adrenergic agonist. It is short acting and has sedative, hypnotic, anxiolytic, analgesic, anti-sialagogue, and sympatholytic properties<sup>2</sup> and promotes cardiac, respiratory, and neurological stability.

Dexmedetomidine when given in intravenous form is an effective drug for suppressing HR to intubation but has been known to produce bradycardia and hypotension<sup>3</sup> to the patient. Nebulized dexmedetomidine – a modification of intranasal route, in which drug deposition takes place over nasal, buccal, as well as respiratory mucosa,<sup>4</sup> is suggested to have rapid onset and better bioavailability (~82%).<sup>5</sup>

The purpose of this study is to investigate the effectiveness of nebulized dexmedetomidine in blunting HR to intubation and if proven effective, it might be used as a non-invasive and an easier method for suppressing intubation response and might help in circumventing the side effects associated with intravenous route. Nebulized dexmedetomidine if proven effective may offer an attractive alternative to intravenous route of administration.

Our primary objective was to compare HR and mean arterial pressure (MAP) pre-administration of drug, post-administration of drug, at 1, 3, 5, and 10 min of intubation between the two groups. Our secondary objectives were to compare: intraoperative hemodynamic changes, sedation score using Ramsay Sedation Scale<sup>6</sup> (30 min post-administration of drug), and incidence of adverse effects (bradycardia, hypotension, nausea, and vomiting) between the two groups.

### Aims and objectives

The aim of this study is to compare the effectiveness of nebulized dexmedetomidine and intravenous dexmedetomidine given preoperatively in blunting hemodynamic response to intubation and laryngoscopy.

## MATERIALS AND METHODS

This prospective, randomized, controlled, and comparative study was conducted in Department of Anesthesiology, MGM Medical College and MY Hospital, Indore, Madhya Pradesh over a period of 12 months, from August 01, 2021, to July 31, 2022, after approval from the Institutional Ethics and Scientific Review Committee (EC/MGM/JUNE-21/28). The study included 120 patients who fulfilled the inclusion criteria. Inclusion criteria included patients with ASA Grades I and II, aged between 18 and 60 years, weighing 40–65 kg, either sex, with Mallampatti Classes I and II and with duration of intubation <20 s. Exclusion criteria included patient refusal, patients with predicted airway difficulty or

requiring >1 intubation attempts or first intubation attempt >20 s, patients with any intranasal pathology, pregnancy, uncontrolled hypertension, renal failure, seizure disorders, and patients on anti-depressants/anti-psychotics or with poor cardiopulmonary reserve. Randomization was done by closed envelope method using computer-generated randomized numbers in the pre-operative period. All patients underwent pre-anesthetic checkup including detailed history and general and systemic examination. Written informed consent was taken from all the patients included in the study. All patients were shifted to pre-operative room 30 min before induction where multipara monitors were attached and baseline hemodynamic parameters (HR and MAP) and sedation score (using Ramsay Sedation Scale) was recorded. IV Ringer's lactate was administered (20 mL/kg) as maintenance fluid. According to the group allotted, patients of Group IV received inj. dexmedetomidine 0.50  $\mu$ g/kg (diluted with normal saline (NS) to a volume of 50 mL) as slow IV infusion over 20 min and nebulization with 5 mL NS and patients of Group N received nebulization with inj. dexmedetomidine 1  $\mu$ g/kg mixed with NS up to volume of 5 mL along with 50 mL NS given as slow IV infusion over 20 min, 30 min before induction. Sedation score and hemodynamic parameters were noted again after drug administration. Then, the patients were shifted to operative room, where general anesthesia techniques were standardized for both groups. HR and MAP were noted at following points of time – post intubation at 1, 3, 5, and 10 min and intraoperatively at every 15 min until the end of surgery. Any side effects if encountered were noted and managed. The sample size was calculated using Statistical Software G Power 3.1.9.4. The sample size obtained at 95% confidence interval with an 80% power of the study is 51 per group (rounded off to 60 per group) where  $\alpha$  (type-I error rate) = 0.05 and  $\beta$  (power of the study) = 0.8. The data were recorded in the customized pro forma designed specifically for this study which was compiled in excel sheet and was subjected to statistical analysis with the advice of statistician. Comparison of mean HR and mean MAP at different time points was done using unpaired “t” test.  $P < 0.05$  was taken as statistically significant. Chi-square test was used for categorical data.  $P < 0.05$  was taken as statistically significant. The final data were presented in the form of tables.

## RESULTS

One hundred and twenty patients were divided into two groups equally. In Group IV, there were 22 females and 38 males. In Group N, there were 25 females and 35 males. Both the groups were independent of sex of the patients. ( $P=0.575$ ). The mean age in

Group IV was 38.92±14.368 years and in Group N, it was 36.25±14.460 years. The difference was found to be statistically not significant (P=0.318) showing a comparable mean age between the two groups.

The mean heart rate and MAP did not show any increase in response to intubation and remained stable throughout the surgery with both intravenous and nebulized dexmedetomidine.

The baseline mean HR in both the groups was comparable which decreased after drug administration, but no significant difference was seen. The mean HR was comparable at all time intervals, as shown in Table 1.

The baseline mean MAP in both the groups was comparable which decreased after drug administration, but no significant difference was seen. The mean MAP was comparable at all time intervals, as shown in Table 2.

After drug administration (pre-induction), most patients had sedation score 2 in both the groups. The difference of

sedation score after the drug administration was statistically not significant between the two groups (P>0.05). The sedation produced was satisfactory in both groups (Table 3).

The incidence of hypotension was more in intravenous group and was statistically significant as compared to nebulized group. Other side effects such as bradycardia, nausea, and vomiting noted were statistically insignificant in both the groups (Table 4).

## DISCUSSION

In this study, we included 120 students undergoing elective surgery under general anesthesia (ASA grade I and II, aged 18–60 years of either gender) which were randomly divided into two groups. Group IV received inj. dexmedetomidine 0.50 µg/kg (diluted with NS to a volume of 50 mL – slow IV infusion over 20 min) and nebulized with 5 mL NS, while Group N received nebulization with inj. dexmedetomidine 1µg/kg mixed with NS up to 5 mL volume along with 50 mL NS given as slow IV infusion

**Table 1: Comparison of mean heart rate between the groups**

Heart rate	Group IV (Mean±SD)	Group n (Mean±SD)	“P”value
Pre-administration of drug (baseline)	90.03±8.952	88.05±11.475	0.293
Post-administration of drug (pre-induction)	87.38±9.891	86.55±10.365	0.653
1 min after intubation	88.33±9.333	88.10±11.565	0.903
3 min after intubation	87.67±9.610	88.53±10.336	0.635
5 min after intubation	87.67±9.552	87.93±10.742	0.886
10 min after intubation	87.58±10.442	88.27±11.378	0.732
15 min after intubation	87.48±9.921	87.85±10.295	0.843
30 min after intubation	86.72±10.041	87.33±9.625	0.732
45 min after intubation	86.70±8.615	86.37±9.469	0.841
60 min after intubation	86.20±8.657	86.30±9.261	0.951
75 min after intubation	86.77±10.063	86.60±9.046	0.924
90 min after intubation	85.40±13.426	86.53±8.179	0.578
105 min after intubation	85.35±13.189	86.53±9.677	0.576
120 min after intubation	84.81±14.043	85.60±16.312	0.794

SD: Standard deviation

**Table 2: Comparison of mean MAP**

Mean arterial pressure	Group IV (Mean±SD)	Group N (Mean±SD)	“P” value
Pre-administration of drug (baseline)	91.37±5.333	90.58±5.634	0.436
Post-administration of drug (pre-induction)	89.82±6.688	90.35±6.428	0.657
1 min after intubation	88.33±5.813	89.50±7.315	0.335
3 min after intubation	85.72±7.495	87.13±7.382	0.299
5 min after intubation	86.73±6.047	87.45±6.951	0.548
10 min after intubation	85.60±6.621	86.50±7.873	0.499
15 min after intubation	85.13±7.200	87.35±8.031	0.114
30 min after intubation	85.57±6.921	87.50±6.323	0.096
45 min after intubation	87.23±5.913	88.17±6.697	0.420
60 min after intubation	87.22±6.742	88.97±6.186	0.141
75 min after intubation	86.85±8.677	88.87±6.110	0.144
90 min after intubation	87.75±6.036	88.47±6.706	0.540
105 min after intubation	88.25±6.114	89.55±5.372	0.218
120 min after intubation	88.63±5.020	89.35±8.785	0.612

SD: Standard deviation

**Table 3: Comparison of sedation score between the groups 30 min after drug administration**

Sedation score	Group IV	Group N
Score 1	0	0
Score 2	55	58
Score 3	4	2
Score 4	1	0
Score 5	0	0
Score 6	0	0
Total	60	60

Pearson Chi-square test was used. Chi-square value=1.746, Df=1, P=0.575.

**Table 4: Comparison of side effects between the groups**

Side effect	Group IV (%)	Group N (%)
Hypotension	7 (11.7)	1 (1.7)
Bradycardia	4 (6.7)	3 (5)
Nausea/vomiting	3 (5)	2 (3.33)

Chi-square test was applied. Df=1, P=0.05

over 20 min, 30 min before induction. HR to intubation was compared between the two groups. Intraoperative hemodynamic parameters, sedation score (using Ramsay Sedation Scale<sup>6</sup>), and side effects were also compared.

Shankar et al.,<sup>7</sup> in their study, compared the efficacy of nebulized dexmedetomidine 1 µg/kg, intravenous dexmedetomidine 1 µg/kg, and intravenous fentanyl 2 µg/kg in blunting HR to intubation and pneumoperitoneum in laparoscopic surgeries under general anesthesia and found that mean HR and mean SBP in both intravenous dexmedetomidine and nebulized dexmedetomidine group post-intubation were comparable to each other and both were equally effective in preventing HR and BP increase in response to intubation. Misra et al.,<sup>1</sup> in their study, assessed the effect of pre-operative dexmedetomidine nebulization on the HR to laryngoscopy and intubation and found that nebulization with dexmedetomidine 1 µg/kg before induction significantly attenuated increase in heart rate and systolic blood pressure after intubation compared to nebulization with saline. Niyogi et al.,<sup>3</sup> compared the efficacy of intranasal dexmedetomidine 1 µg/kg and intravenous dexmedetomidine 0.5 µg/kg given 40 min before induction in attenuating the stress response of laryngoscopy and endotracheal intubation. There was no statistically significant difference in HR and MAP between two groups until 10 min after intubation.

The present study also showed no significant difference between two groups when HR and MAP were compared in response to intubation. Our findings were similar to Shankar et al.,<sup>7</sup> Misra et al.,<sup>1</sup> and Niyogi et al.<sup>3</sup>

The heart rate and blood pressure lowering effect of dexmedetomidine may probably be attributed to its

sympatholytic actions mediated through postsynaptic α<sub>2</sub> receptors. It also inhibits noradrenaline release through presynaptic central α<sub>2</sub> receptors in the locus ceruleus.

In the study done in 76 patients by Silpa et al.,<sup>8</sup> compared, the efficacy of two different doses of dexmedetomidine (0.5 µg/kg and 1 µg/kg) given preoperatively in attenuating the HR to endotracheal intubation and assessed the sedative effect of both doses in patients undergoing elective cardiac surgery. They found that the mean sedation produced by two doses of dexmedetomidine 0.5 µg/kg and 1 µg/kg (assessed by Ramsay Sedation Scale<sup>6</sup>) after 15 min of infusion was comparable between two groups and produced satisfactory sedation. In the present study, the difference of sedation score after the drug administration was statistically not significant between the two groups (P>0.05). The sedation produced was satisfactory in both groups. Our findings were similar to Silpa et al.,<sup>8</sup> Niyogi et al.,<sup>3</sup> in their study, compared the sedative effect of intranasal dexmedetomidine 1 µg/kg and intravenous dexmedetomidine 0.5 µg/kg given 40 min before induction and found that sedation score was significantly higher in intravenous dexmedetomidine group (patients responded to commands only) than in intranasal dexmedetomidine (oriented, cooperative, and tranquil) group at 40 min interval after drug administration. Our findings were in contrast to the study done by Niyogi et al.<sup>3</sup>

Dexmedetomidine is known to produce conscious sedation in patients without causing any respiratory depression.<sup>9</sup> Our study demonstrated the similar action as the patients were awake, oriented, co-operative, and tranquil after the drug administration.

Seven patients in IV group and only one patient in nebulized group had an episode of hypotension and this difference was statistically significant. Other side effects such as bradycardia, nausea, and vomiting noted were statistically insignificant in both the groups in the present study. Our findings were comparable to the study conducted by Shankar et al.,<sup>7</sup> they found that incidence of hypotension immediately after the administration of dexmedetomidine was significantly lower with nebulized dexmedetomidine (Dexmedetomidine 1 µg/kg) than IV dexmedetomidine (Dexmedetomidine 1 µg/kg IV given over 10 min). Niyogi et al.,<sup>3</sup> in their study, compared the incidence of hypotension associated with intranasal dexmedetomidine 1 µg/kg and intravenous dexmedetomidine 0.5 µg/kg given before induction and found that there was no incidence of significant hypotension in either group which was contrary to the finding of our study.

Our findings were in contrast to the study done by Niyogi et al.<sup>3</sup>

A gradual onset of nebulized dexmedetomidine compared to earlier onset of intravenous dexmedetomidine might be the possible reason for lesser incidence of side effects associated with nebulized dexmedetomidine.

From our study, it can be said that both nebulized and intravenous dexmedetomidine when used preoperatively attenuated HR with almost same efficacy, however, nebulized dexmedetomidine proved to be safer than intravenous route. The fact that both forms attenuated the HR to intubation may be attributed to the fact that both intravenous and nebulized forms prevented central catecholamine surge.

### Limitations of study

This study only used one dose of intravenous dexmedetomidine and nebulized dexmedetomidine for comparison and thus effects of different doses cannot be commented. The plasma catecholamine levels were not measured.

## CONCLUSION

Nebulized dexmedetomidine given preoperatively was effective in blunting hemodynamic stress response to intubation as intravenous dexmedetomidine but with fewer side effects and provided stable hemodynamics throughout surgery. In addition, nebulized dexmedetomidine produced satisfactory sedation which was comparable to intravenous dexmedetomidine.

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**MG**- Concept and design of the study, prepared first draft of manuscript; **SS**- Interpreted the results; reviewed the literature and manuscript preparation; **AA**- Concept, coordination, statistical analysis and interpretation, preparation of manuscript and revision of the manuscript; **AKK**- Guidance.

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