Original Article

Efficacy Of Preoperative Dexmedetomidine Nebulization On Blunting The Hemodynamic Response To Laryngoscopy And Intubation

Dr. Chhaya Suryawanshi[1], *Dr. Dheeraj Gopal Ravindran[2], Dr. Pati Sathvika[3], Dr. Reema Jawale[4]

1. Professor & Head of Department, Department of Anaesthesiology, Dr. D. Y. Patil Medical College, Hospital & Research Centre, Dr. D. Y. Patil Vidyapeeth, Pimpri, Pune, Maharashtra, 411018, India
2. Junior Resident, Department of Anaesthesiology, Dr. D. Y. Patil Medical College, Hospital & Research Centre, Dr. D. Y. Patil Vidyapeeth, Pimpri, Pune, Maharashtra, 411018, India
3. Junior Resident, Department of Anaesthesiology, Dr. D. Y. Patil Medical College, Hospital & Research Centre, Dr. D. Y. Patil Vidyapeeth, Pimpri, Pune, Maharashtra, 411018, India
4. Junior Resident, Department of Anaesthesiology, Dr. D. Y. Patil Medical College, Hospital & Research Centre, Dr. D. Y. Patil Vidyapeeth, Pimpri, Pune, Maharashtra, 411018, India

***Corresponding Author:**
Dr. Dheeraj Gopal Ravindran, Junior Resident, Department of Anaesthesiology, Dr. D. Y. Patil Medical College, Hospital & Research Centre, Dr. D. Y. Patil Vidyapeeth, Pimpri, Pune, Maharashtra, 411018, India
DOI: 10.47750/pnr.2022.13.S06.555

Abstract

Background and aim - The efficacy of dexmedetomidine in decreasing the hemodynamic response to laryngoscopy and intubation has been studied through various routes. However, intravenous administration may cause bradycardia and hypotension, and intranasal administration may be associated with irritation. As drug deposition following nebulization takes place over nasal, buccal, and respiratory mucosa, nebulized dexmedetomidine may be a better alternative to both intravenous and intranasal routes of administration. This study aimed to study the effect of preoperative dexmedetomidine nebulization on the hemodynamic response to laryngoscopy and intubation. Method – A prospective, randomized, double-blinded study where a total of 60 ASA 1 & 2 adult patients of either gender undergoing elective surgeries under general anaesthesia were randomized and given either nebulized dexmedetomidine (1mcg/kg in 3-4 mL NS) or normal saline (4 ml) 30 mins before the induction of anaesthesia. Hemodynamic parameters including heart rate and non-invasive blood pressure were monitored for 10 minutes following laryngoscopy. Result – Following laryngoscopy and intubation, there was a marked and significant increase in heart rate, systolic blood pressure, and mean arterial pressure in the control group compared to the dexmedetomidine group. Conclusion – Preoperative dexmedetomidine nebulization effectively blunts the stress response to laryngoscopy and intubation with no adverse effects.

INTRODUCTION

Being painful stimuli, laryngoscopy, and intubation cause remarkably high sympathetic activity. the pressor response, which is characterised by a sudden increase in heart rate and blood pressure 30 seconds following laryngoscopy and intubation, gradually recovers to baseline levels usually lasts for 5-10 minutes. These hemodynamic responses harm patients with reactive airways, hypertension, coronary artery disease, myocardial insufficiency, and cerebrovascular diseases [1]. Reid and Brace were the first to provide the description of a hemodynamic reaction to laryngoscopy and intubation in 1940.[2]

A few of the prevalent factors responsible for the pressor response to laryngoscopy and intubation include light planes of anaesthesia, prolonged duration of procedure, the elevation of the vagally innervated posterior part of the epiglottis by a straight or Miller blade, anatomically difficult view, greater force used to displace the tongue, and more manipulations/attempts at these procedures.

Dexmedetomidine has sympatholytic, sedative, amnestic, and analgesic characteristics. It is a powerful and highly selective alpha-2 receptor agonist. Dexmedetomidine has been tested intravenously, intranasally, and intramuscularly for its ability to lessen the hemodynamic response to laryngoscopy and intubation [3].

Intranasal delivery, on one hand, may be accompanied by irritability, whereas intravenous injection on the other hand may result in bradycardia and hypotension. Nebulized dexmedetomidine may be a superior option than both intravenous and intranasal modes of administration since drug deposition after nebulization occurs over nasal, buccal, and respiratory mucosa. Additionally, the bioavailability of nebulized dexmedetomidine is 65% & 82% through the nasal & the buccal mucosa respectively. Nebulized drug delivery is preferred over intranasal drug administration due to the absence of temporary nasal discomfort, coughing, vocal cord irritation, and laryngospasm [4].

The primary aim of this study was to study the effect of preoperative dexmedetomidine nebulization on the hemodynamic response to laryngoscopy and intubation and any adverse effects from preoperative dexmedetomidine nebulization such as bradycardia and hypotension.

Aim: To study the effect of preoperative dexmedetomidine nebulization on blunting the hemodynamic response to laryngoscopy and intubation.

Objectives:

1. To evaluate the effects of dexmedetomidine nebulization in blunting the stress response to laryngoscopy and intubation.
2. To study any adverse effects from preoperative dexmedetomidine nebulization.

MATERIALS AND METHODS

Following institutional ethical committee approval and written informed consent, a prospective double blinded study was conducted with 60 patients of either gender, aged between 18 and 60 years of age belonging to ASA 1 or ASA 2 undergoing elective surgeries under general anaesthesia.

Exclusion Criteria:

1. Patients who are not willing to participate in the study.
2. Patients with ASA grade III and above physical status.
3. Patients who are aged less than 18 and more than 60 years of age.
4. Patients who are posted for emergency procedures.
5. Patients with known allergy to the study drugs.
6. Patients with difficult intubation.
7. Patients who are obese.
8. Patients who have psychiatric, neuromuscular, or cardiovascular disease or impairment of hepatic or renal function.

A computer-generated lottery method was used to randomly allocate the 60 patients into two groups,

- GROUP A (STUDY GROUP) patients were given 1 μg/kg dexmedetomidine nebulization diluted in 3–4 ml of 0.9% saline, 30 min before induction of anesthesia
- GROUP B (CONTROL GROUP): patients were given 0.9% saline nebulization (3– 4 ml), 30 min before induction of anesthesia

The drugs for nebulization (saline or dexmedetomidine) were prepared and administered by an independent investigator in the preoperative holding area. Hemodynamic parameters such as HR, SBP, DBP and MAP was recorded before nebulization. Nebulization was carried out with an electrical compressor nebulizer, capable of creating a fine mist until the entire volume is dispersed–usually within 15–20 min. The investigator oversaw the entire nebulization procedure and while taking no further part in the study was authorized to intervene if a patient developed bradycardia or experienced increased sedation or decreases in peripheral oxygen saturation. All patients were premedicated with Inj. Glycopyrrolate 0.004 mg/kg IV, Inj. Midazolam 0.02 mg/kg IV and Inj. Fentanyl 1-2 μg/kg IV. Pre-oxygenation was done with 100% O2 for 3 minutes. Hemodynamic parameters such as HR, SBP, DBP, MAP and Spo2 were recorded before induction of general anesthesia. Induction was done with Inj. Propofol 2mg/kg and loss of verbal response was considered to be the endpoint of induction. This was followed by administering Inj. Succinylcholine 2mg/kg IV to facilitate laryngoscopy and intubation with appropriate-size endotracheal tube. Hemodynamic parameters were then recorded every 1 minute till 10 minutes after laryngoscopy. Intubation was confirmed by EtCO2 and bilaterally equal air entry and then connected to a ventilator for intermittent positive pressure ventilation until completion of surgery. Maintenance of anaesthesia was done with 40% oxygen + 60% nitrous oxide and isoflurane (0.6-1%) and intermittent positive pressure ventilation. Maintenance of muscle relaxation was achieved with Inj. Vecuronium 0.1mg/kg. The response to skin incision was noted and recorded as a binary yes/no response (no, if < 20% changes in HR and/or SBP; yes, if > 20% changes in HR and/or SBP). Following surgery, neuromuscular blockade was reversed with Inj. neostigmine (0.05 mg/kg) and inj. glycopyrrolate (0.02 mg/kg). The patients were extubated once they were able to follow verbal commands. Patients were kept in the postoperative care unit for an additional 2 hours and discharged to the ward once they met the criteria for discharge. The presence of postoperative sore throat was noted as present or absent.

STATISTICAL ANALYSIS

The data was entered in Microsoft Excel and analyzed using the statistical software SPSS version 16. Continuous variables like Age, Height, Weight, Heart Rate, systolic, diastolic, mean arterial pressure and SPO_2 are expressed as Mean ± Standard Deviation and compared across the 2 groups using unpaired t test. Categorical variables like number of with Adverse Effects are expressed as Number of patients and percentage of patients and compared across the 2 groups using Pearson's Chi Square test for Independence of Attributes. Paired t test is used to compare the two means. An alpha level of 5% has been taken, i.e., if any p value is less than 0.05 it has been considered as significant.

RESULTS

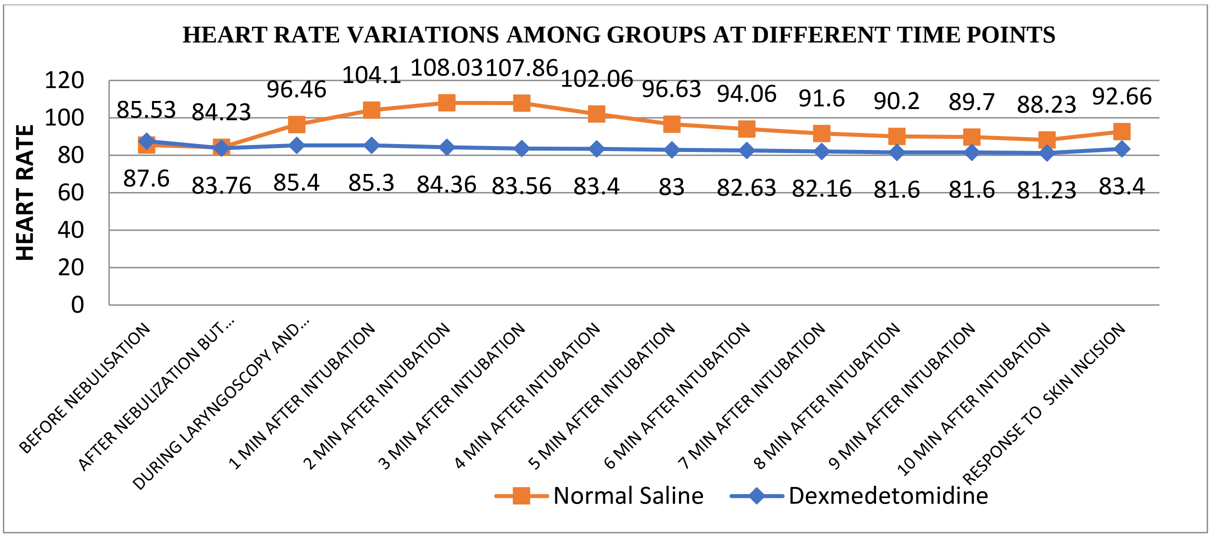
Both the study groups were comparable with regard to their demographic profile (Table 1).

<table>
<tr><td colspan="2" rowspan="2">VARIABLES</td><td colspan="2">GROUPS</td><td rowspan="3">p Value</td></tr>
<tr><td>GROUP A</td><td>GROUP B</td></tr>
<tr><td colspan="2">TOTAL NUMBER OF PATIENTS</td><td>30</td><td>30</td></tr>
<tr><td colspan="2">AGE (YRS)</td><td>45.06 ± 11.95</td><td>41.76 ± 14.47</td><td>0.308</td></tr>
<tr><td rowspan="2">Gender</td><td>Male</td><td>17(56.6%)</td><td>14(46.6%)</td><td rowspan="2">0.219</td></tr>
<tr><td>Female</td><td>13(43.4%)</td><td>16(53.4%)</td></tr>
<tr><td colspan="2">BODY WEIGHT (KG)</td><td>61.6 ± 9.9</td><td>56.38 ± 12.67</td><td>0.191</td></tr>
<tr><td colspan="2">ASA 1</td><td>13</td><td>18</td><td rowspan="2">0.198</td></tr>
<tr><td colspan="2">ASA 2</td><td>17</td><td>12</td></tr>
</table>

TABLE 1 - DEMOGRAPHY OF PATIENTS IN BOTH GROUPS

HEART RATE: The mean heart rates recorded at baseline and before induction were comparable in both groups ($p>0.05$). The mean heart rates during laryngoscopy and intubation at 1 minute, 2 minutes, 3 minutes, 4 minutes, 5 minutes, 6 minutes, 8 minutes, 9 minutes and 10 minutes after intubation were higher in Group B when compared to Group A and this difference was statistically significant with p value< 0.05 (Table 2 and Figure 1)

FIGURE 1



TIME PERIOD OF HEART RATE	GROUP A	GROUP B	p Value
BEFORE NEBULISATION	87.6±9.21	85.53±8.20	0.354
AFTER NEBULIZATION BUT BEFORE INDUCTION	83.76±9.89	84.23±8.18	0.841
DURING LARYNGOSCOPY AND INTUBATION	85.4±9.31	96.46±7.12	0.001
1 MIN AFTER INTUBATION	85.3±8.98	104.1±5.89	<0.001
2 MIN AFTER INTUBATION	84.36±8.67	108.03±6.72	<0.001
3 MIN AFTER INTUBATION	83.56±8.75	107.86±7.14	<0.001
4 MIN AFTER INTUBATION	83.4±8.59	102.06±7.27	<0.001
5 MIN AFTER INTUBATION	83±8.54	96.63±6.30	<0.001
6 MIN AFTER INTUBATION	82.63±8.40	94.06±6.83	0.001
7 MIN AFTER INTUBATION	82.16±8.39	91.6±7.34	0.001
8 MIN AFTER INTUBATION	81.6±8.74	90.2±7.71	0.001
9 MIN AFTER INTUBATION	81.6±8.75	89.7±7.73	0.002
10 MIN AFTER INTUBATION	81.23±8.82	88.23±8.11	0.003
RESPONSE TO SKIN INCISION	83.4±8.24	92.66±8.12	0.001

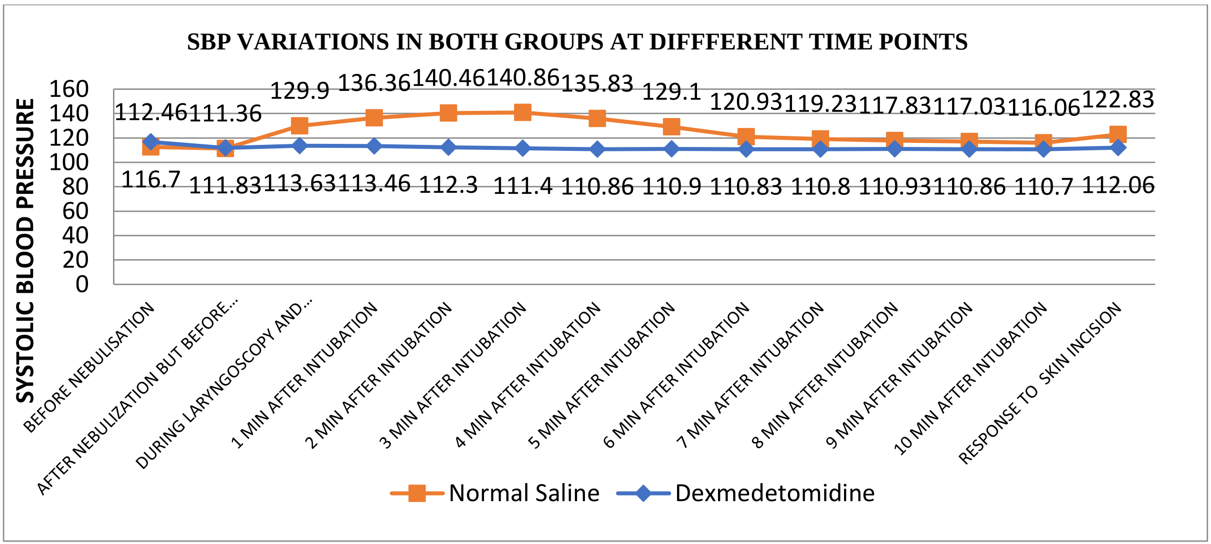
TABLE 2 – COMPARISON OF HEART RATE IN BOTH GROUPS.

SYSTOLIC BLOOD PRESSURE: The mean systolic blood pressures recorded at baseline and before induction were comparable in both groups (p>0.05). The mean systolic blood pressures during laryngoscopy and intubation at 1 minute, 2 minutes, 3 minutes, 4 minutes, 5 minutes, 6 minutes, 8 minutes, 9 minutes, and 10 minutes after intubation were higher in Group B when compared to Group A and this difference was statistically significant with p value< 0.05. (Table 3 and Figure 2)

TIME PERIOD OF SBP	GROUP A	GROUP B	p value
BEFORE NEBULISATION	116.7±10.63	112.46±9.06	0.101
AFTER NEBULIZATION BUT BEFORE INDUCTION	111.83±8.75	111.36±10.28	0.821
DURING LARYNGOSCOPY AND INTUBATION	113.63±8.59	129.9±8.05	<0.001
1 MIN AFTER INTUBATION	113.46±8.38	136.36±8.04	<0.001
2 MIN AFTER INTUBATION	112.3±8.66	140.46±7.73	<0.001
3 MIN AFTER INTUBATION	111.4±9.24	140.86±4.86	<0.001
4 MIN AFTER INTUBATION	110.86±8.83	135.83±5.49	<0.001
5 MIN AFTER INTUBATION	110.9±8.88	129.1±4.26	<0.001
6 MIN AFTER INTUBATION	110.83±8.89	120.93±5.27	<0.001
7 MIN AFTER INTUBATION	110.8±9.18	119.23±6.71	0.001
8 MIN AFTER INTUBATION	110.93±9.34	117.83±7.02	0.005
9 MIN AFTER INTUBATION	110.86±9.46	117.03±6.95	0.002
10 MIN AFTER INTUBATION	110.7±9.60	116.06±6.92	0.013
RESPONSE TO SKIN INCISION	112.06±9.76	122.83±5.87	<0.001

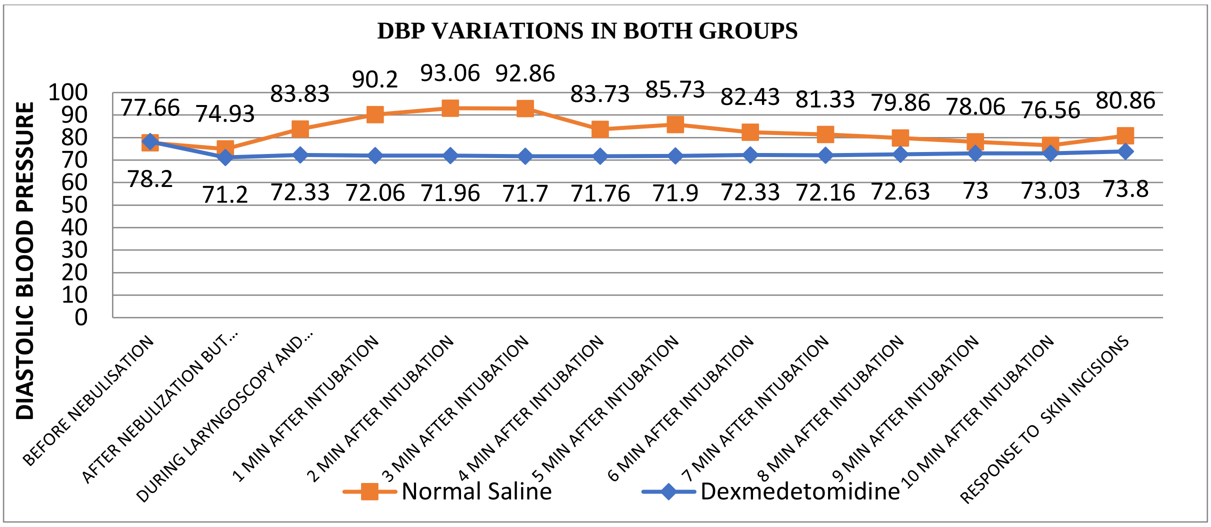
TABLE NO 3 - COMPARISION OF SYSTOLIC BLOOD PRESSURE IN BOTH THE GROUPS

FIGURE 2



DIASTOLIC BLOOD PRESSURE: The mean diastolic blood pressures recorded at baseline and before induction were comparable in both groups (p>0.05). The mean diastolic blood pressures during laryngoscopy and intubation at 1 minute, 2 minutes, 3 minutes, 4 minutes, 5 minutes, 6 minutes, 8 minutes, 9 minutes and 10 minutes after intubation were higher in Group B when compared to Group A and this difference was statistically significant with p value< 0.05. (Table 4 and Figure 3)

FIGURE 3



TIME PERIOD OF DBP	GROUP A	GROUP B	P value
BEFORE NEBULISATION	78.2±6.14	77.66±6.66	0.740
AFTER NEBULIZATION BUT BEFORE INDUCTION	71.2±5.37	74.93±7.04	0.077
DURING LARYNGOSCOPY AND INTUBATION	72.33±5.38	83.83±6.50	<0.001
1 MIN AFTER INTUBATION	72.06±5.15	90.2±6.74	<0.001
2 MIN AFTER INTUBATION	71.96±5.10	93.06±5.87	<0.001
3 MIN AFTER INTUBATION	71.7±5.23	92.86±6.78	<0.001
4 MIN AFTER INTUBATION	71.76±5.18	83.73±5.53	<0.001
5 MIN AFTER INTUBATION	71.9±5.54	85.73±4.82	<0.001
6 MIN AFTER INTUBATION	72.33±5.56	82.43±4.27	<0.001
7 MIN AFTER INTUBATION	72.16±6.24	81.33±4.50	<0.001
8 MIN AFTER INTUBATION	72.63±6.12	79.86±4.78	<0.001
9 MIN AFTER INTUBATION	73±6.45	78.06±5.28	0.007
10 MIN AFTER INTUBATION	73.03±6.86	77.56±4.94	0.007
RESPONSE TO SKIN INCISION	73.8±7.40	80.86±6.15	0.001

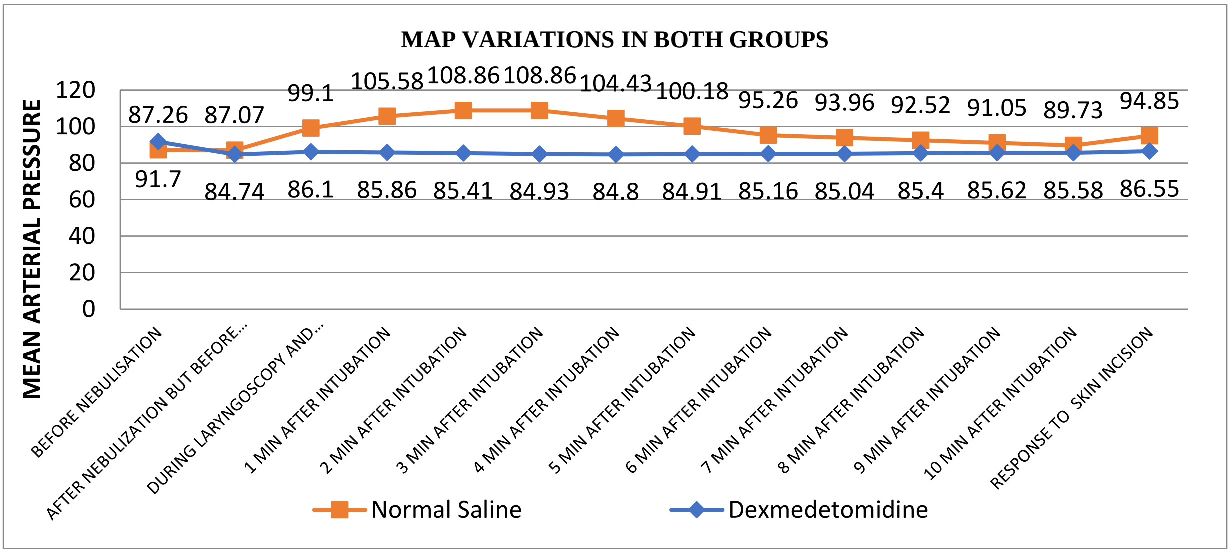
TABLE NO 4 - COMPARISON OF DIASTOLIC BLOOD PRESSURE IN BOTH THE GROUPS

MEAN ARTERIAL PRESSURE: The mean arterial pressures recorded at baseline and before induction were comparable in both groups (p>0.05). The mean arterial pressures during laryngoscopy and intubation at 1 minute, 2 minutes, 3 minutes, 4 minutes, 5 minutes, 6 minutes, 8 minutes, 9 minutes and 10 minutes after intubation were higher in Group B when compared to Group A and this difference was statistically significant with p value< 0.05. (Table 5 and Figure 4)

TIME PERIOD OF MAP	GROUP A	GROUP B	p Value
BEFORE NEBULISATION	91.7±6.15	87.26±7.07	0.490
AFTER NEBULIZATION BUT BEFORE INDUCTION	84.74 ±5.84	87.07±7.93	0.192
DURING LARYNGOSCOPY AND INTUBATION	86.1±5.91	99.1±6.27	<0.001
1 MIN AFTER INTUBATION	85.86±5.77	105.58±6.60	<0.001
2 MIN AFTER INTUBATION	85.41±5.73	108.86±5.83	<0.001
3 MIN AFTER INTUBATION	84.93±5.95	108.86±5.40	<0.001
4 MIN AFTER INTUBATION	84.8±5.83	104.43±4.92	<0.001
5 MIN AFTER INTUBATION	84.91±6.01	100.18±3.73	<0.001
6 MIN AFTER INTUBATION	85.16±6.14	95.26±3.72	<0.001
7 MIN AFTER INTUBATION	85.04±6.70	93.96±4.24	<0.001
8 MIN AFTER INTUBATION	85.4±6.73	92.52±4.64	<0.001
9 MIN AFTER INTUBATION	85.62±6.93	91.05±4.87	0.009
10 MIN AFTER INTUBATION	85.58±7.23	89.73±5.41	0.008
RESPONSE TO SKIN INCISION	86.55±7.59	94.85±5.15	<0.001

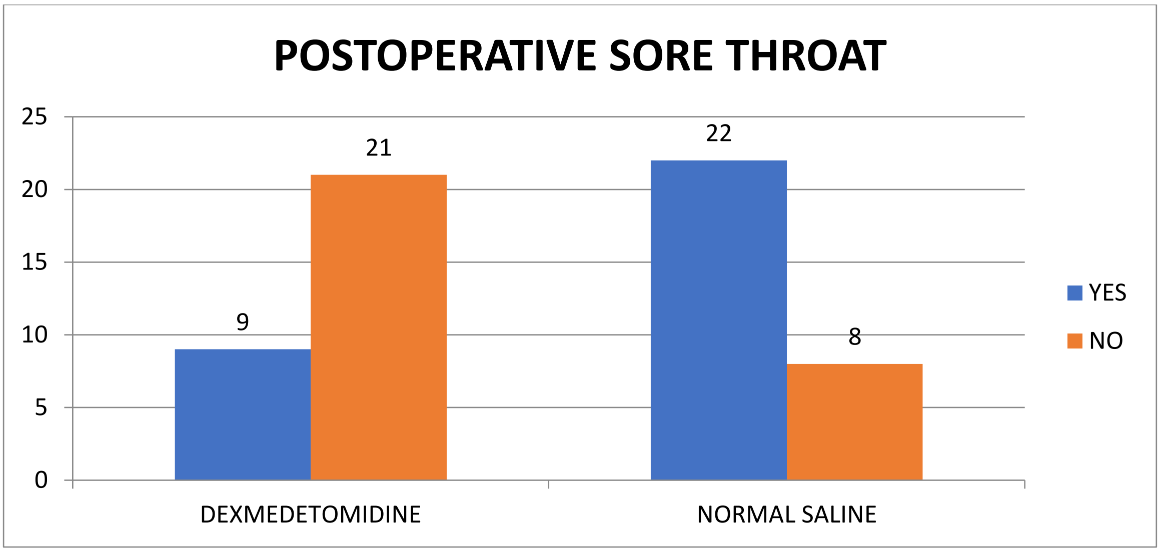
TABLE 5 SHOWING COMPARISON OF MEAN ARTERIAL PRESSURE IN BOTH GROUPS

FIGURE 4



<u>**POSTOPERATIVE SORE THROAT**</u>: Postoperative sore throat was observed in 30% of the patients in Group A and 73.5% of the patients in Group B. Group A had lesser incidence of post-operative sore throat and this difference was statistically significant with $p<0.05$. (Table 6 and Figure 5)

FIGURE 5



POST	GROUP A	GROUP B	P VALUE
YES	9(30%)	22(73.5%)	0.007
NO	21(70%)	8(26.5%)	
TOTAL	30(100%)	30(100%)	

TABLE NO 6 SHOWING NUMBER OF PATIENTS ACCORDING TO POST OPERATIVE SORE THROAT IN BOTH GROUPS

No side effects were observed in either group.

DISCUSSION

Laryngoscopy and tracheal intubation excite the sympathetic nervous system, resulting in various stress reactions such as tachycardia, hypertension, bronchospasm, higher intracranial pressure, and increased intraocular pressure [5].

Lignocaine, opioids, nitroglycerin, calcium channel blockers etc. are some of the few medications that have been shown to be helpful in reducing the laryngoscopy patient's painful reaction. One of the most recent additions to this list is dexmedetomidine. Presynaptic stimulation of α2A receptors in the locus caeruleus is the mechanism through which dexmedetomidine exerts its effects [6].

The effects of intravenous dexmedetomidine on the hemodynamic response to laryngoscopy and intubation have been the subject of several research. Although it has been discovered that dosages of 1-2 µg/kg are beneficial in reducing this hemodynamic response, they are also linked to serious side effects such bradycardia, hypotension, or respiratory depression.

The intra-nasal method of drug delivery is linked to brief nose discomfort and occasionally coughing. Nebulizing the medication as an atomized spray offered a superior solution to this drawback. As a result, there was greater clinical efficacy, higher patient acceptance, and maximal surface area coverage with a thin coating of medication with less effect on hemodynamics as compared to intravenous route.[7]

This study was done with the objective on finding the efficacy of nebulized dexmedetomidine (1µg/kg) on attenuating the hemodynamic responses following laryngoscopy and intubation.

From the results of our study there was significant effect of preoperative dexmedetomidine nebulization (1µg/kg on the attenuation of hemodynamic parameters following laryngoscopy and intubation. Similarly, there was a significantly lesser response to skin incision with dexmedetomidine group when compared to the saline group. It was also observed that there was a significant difference in the occurrence of post operative sore throat among both the groups with lesser incidence seen with preoperative dexmedetomidine nebulization. No adverse effects were observed in either group.

Misra, et al [8] concluded from their study that a single dose of nebulized dexmedetomidine at 1µg/kg, administered 30 min before induction of anesthesia, significantly attenuated the increase in HR but not SBP after laryngoscopy. In contrast, the results of our study also show a significant attenuation of SBP, DBP and MAP apart from the HR following laryngoscopy and intubation.

In their study on the effectiveness of nebulized dexmedetomidine at a dose of 1 g/kg in reducing the stress response to laryngoscopy and intubation, Kumar et al. [9] found that while SBP, DBP, and MAP significantly decreased after laryngoscopy and intubation, there was no significant difference in the HR. However, the results from our study show that nebulized dexmedetomidine helped in statistically significant attenuation of rise in heart rate following laryngoscopy and intubation apart from the attenuation of systolic and diastolic blood pressures and mean arterial pressures.

Silpa, et al [10] in their study compared the efficacy of dexmedetomidine given preoperatively at two different doses as intravenous infusions over 15 minutes in attenuating the hemodynamic response to endotracheal intubation in 70 patients undergoing elective cardiac surgeries. They concluded that Dexmedetomidine in a dose of 1 µg/kg is more effective than 0.5 µg/kg for attenuation of hemodynamic stress response to intubation in cardiac surgery. A more graded increase in the dose of dexmedetomidine may lead to an optimum dose in attenuating the hemodynamic response to intubation. The incidence of hypertension following intubation was significantly more in the low-dose group. Administration of 1 µg/kg dexmedetomidine was not accompanied by hypotension or bradycardia. Hypotension occurred in one patient in each group. There was no incidence of bradycardia or tachycardia in either group. Our study results show that preoperative dexmedetomidine nebulization (1 µg/kg) was effective in blunting the hemodynamic response to laryngoscopy and intubation without any side effects like bradycardia and hypotension.

Several studies have been made on the hemodynamic response to laryngoscopy and intubation after intravenous administration of dexmedetomidine. The effects of a single preoperative dosage of 2 g/kg dexmedetomidine on the need for isoflurane and peri-operative hemodynamic stability were investigated by Lawrence, et al [11]. According to their research, dexmedetomidine administration decreased both the intraoperative heart rate variability and the haemodynamic response to tracheal intubation and extubation. Dexmedetomidine administration also resulted in decreased postoperative analgesic and antiemetic needs as well as perioperative serum catecholamine concentrations. However, hypotension and bradycardia occurred more frequently after the use of dexmedetomidine. Similarly, Mahajan, et al [1] investigated the effects of intravenous dexmedetomidine vs magnesium sulphate on the pressor responses to laryngoscopy and endotracheal intubation. Both the dexmedetomidine and magnesium sulphate groups had considerably reduced HR and BP (P 0.001), but dexmedetomidine was responsible for much lower values in comparison due to its sympatholytic and vagomimetic effects. Instead of preserving stability, dexmedetomidine and MgSO4 cause a considerable drop in hemodynamics. MgSO4 turned out to be a more effective medication than either of the other two. Therefore, their study suggested that even though, intravenous dexmedetomidine was able to obtund the hemodynamic response to laryngoscopy, it didn’t help in maintaining the hemodynamic stability. In contrast, our study showed no occurrence of hypotension or bradycardia following the administration of nebulized dexmedetomidine but at the same time provided good hemodynamic stability by attenuating the pressor response to laryngoscopy and intubation

CONCLUSION

Dexmedetomidine nebulization at a dose of 1µg/kg given 30 minutes prior to induction of general anaesthesia is effective in attenuating the hemodynamic and stress response to laryngoscopy and intubation without any adverse effects. There was a significant difference in the skin incision response, with a more positive response to skin incision seen in the saline group. Dexmedetomidine nebulization was also effective in reducing the occurrence of post-operative sore throat.

REFERENCES

1. Mahajan L, Kaur M, Gupta R, Aujla KS, Singh A, Kaur A. Attenuation of the pressor responses to laryngoscopy and endotracheal intubation with intravenous dexmedetomidine versus magnesium sulphate under bispectral index-controlled anaesthesia: A placebo-controlled prospective randomised trial. Indian J Anaesth 2018;62:337-43.
2. Reid LC, Brace DE. Irritation of respiratory tract and its reflex effect on heart. Surg Gynecol Obstet 1940;70:157
3. Afonso J, Reis F. Dexmedetomidine: current role in anesthesia and intensive care. Rev Bras Anestesiol 2012; 62: 118-33.
4. Anttila M, Penttilä J, Helminen A, Vuorilehto L, Scheinin H. Bioavailability of dexmedetomidine after extravascular doses in healthy subjects. Br J Clin Pharmacol 2003;56:691- 3.
5. Shribman AJ, Smith G, Achola KJ. Cardiovascular and catecholamine responses to laryngoscopy with and without tracheal intubation. Br J Anaesth. 1987; 59:295-9.
6. Aantaa R, Scheinin M. Alpha-2-adrenergic agents in anesthesiology. Acta Anaesthesia! Scand. 1993; 37:433-48.
7. Mason KP, Lerman J. Dexmedetomidine in children: current knowledge and future applications. AnesthAnalg. 2011;113:1129-42.
8. Satyajeet Misra, Bikram Kishore Behera, Jayanta Kumar Mitra, Alok Kumar Sahoo, Sritam Swarup Jena, Anand Srinivasan Korean J Anesthesiol. 2021;74(2):150-157.
9. Kumar NR, Jonnavithula N, Padhy S, Sanapala V, Vasram Naik V. Evaluation of nebulised dexmedetomidine in blunting haemodynamic response to intubation: A prospective randomised study. Indian J Anaesth 2020;64:874-9.
10. Silpa AR, Koshy KA, Subramanian A, Pradeep KK. Comparison of the efficacy of two doses of dexmedetomidine in attenuating the hemodynamic response to intubation in patients undergoing elective cardiac surgery: A randomized double-blinded study. J Anaesthesiol Clin Pharmacol. 2020;36:83-7.
11. Lawrence CJ, De Lange S. Effects of a single pre-operative dexmedetomidine dose on isoflurane requirements and peri-operative haemodynamic stability. Anaesthesia 1997; 52: 736-44.