Indian Journal of Clinical Anaesthesia 2023;10(4):358–364

Content available at: https://www.ipinnovative.com/open-access-journals

Indian Journal of Clinical Anaesthesia

Journal homepage: www.ijca.in

Original Research Article

A randomized double blind study to evaluate the effect of nebulized dexmedetomidine on the haemodynamic response to laryngoscopy – Intubation and intubation conditions

Neenu Susan Paul[1]*, **Valsamma Abraham**[1], **Dootika Liddle**[1]

[1]*Dept. of Anaesthesia, JDH Christian Medical College, Ludhiana, Punjab, India*

ARTICLE INFO

Article history:
Received 09-10-2023
Accepted 09-11-2023
Available online 28-11-2023

Keywords:
Dexmedetomidine
Haemodynamic response
Intubation
Intubation conditions
Laryngoscopy
Nebulization
Side effects

ABSTRACT

Background and Aims: A cardiovascular stress response is frequently brought on by direct laryngoscopy and intubation. It is widely known that the sympathetic adrenal stimulation elicited by mechanical stimulation to the upper respiratory tract is what causes the haemodynamic response during laryngoscopy and intubation. The study's goal was to assess the impact of preoperative dexmedetomidine nebulization on the patient's hemodynamic response to laryngoscopy- intubation and the intubation conditions.

Materials and Methods: The American Society of Anaesthesiologists (ASA) I & II adult patients, of either gender, undergoing elective surgeries requiring tracheal intubation were randomized to receive nebulized dexmedetomidine (Group D) or 0.9% saline (Group P), 30 minutes prior to the induction of anesthesia. This study was conducted in the department of anesthesia and critical care at the Christian Medical College in Ludhiana. Following laryngoscopy, the patient's heart rate and non-invasive systolic and diastolic blood pressure will be monitored for 10 minutes. The intubation conditions were noted during laryngoscopy.

Results: Total 100 patients with 50 in each group were included. At the time of laryngoscopy and after the intubation 1 min, 3 min,5 min, 7min and 10 min there were significantly lower trend in increasing HR, SBP, DBP and RPP in dexmedetomidine group versus saline. The intubation score representing conditions for intubation was significantly better in the dexmedetomidine group (P=0.013) than the saline group. There was no significant side effect noted (p=1.000). There was significant reduction in intraoperative analgesic and sedative requirement observed in dexmedetomidine group

Conclusion: Our study concluded that the nebulized dexmedetomidine attenuated haemodynamic response to laryngoscopy- intubation and provided better intubation conditions without significant side effects. We advise using nebulized dexmedetomidine pre-operatively for a surgical procedure requiring general anesthesia in order to reduce the haemodynamic response to intubation and to facilitate intubation conditions without experiencing any severe adverse effects.

1. Introduction

Following the introduction of anaesthesia, direct laryngoscopy and tracheal intubation are linked to hemodynamic alterations brought on by increased sympatho-adrenal activity, which may cause hypertension and/or tachycardia. In the vulnerable group, the effects of laryngoscopy and intubation may lead to ischemia, arrhythmias, cerebrovascular stroke, pulmonary edema, and an increase in intracranial pressure.[1] Numerous medications, including as local anesthetics, beta-blockers, calcium channel blockers, and narcotic analgesics, have

* *Corresponding author*.
E-mail address: neenususan5nsp@gmail.com (N. S. Paul).

https://doi.org/10.18231/j.ijca.2023.075

been used with varying degrees of efficacy to reduce the laryngoscopy and intubation response.[1]

A selective alpha 2 adreno receptor agonist with short acting, sedative, hypnotic, anxiolytic, sympatholytic, analgesic, and antisialogogue effects is dexmedetomidine. It encourages neurological, respiratory, and cardiac stability. It has eight times more alpha 2 and less alpha 1 receptor selectivity. Its activity lasts less time than clonidine.[2] Additionally, it reduces the need for analgesics and anesthetics during surgery.[3] Theoretically, because of these qualities, it might be used as a component of an anesthetic regimen. Due to its pleiotropic properties, its use in the perioperative period is rising.[4]

Dexmedetomidine has been tested to reduce the haemodynamic response to laryngoscopy and intubation via intravenous,[5] intranasal,[6] and oral[7] routes. Inhaling dexmedetomidine may be a novel, non-invasive approach that shows promise. Following nebulization, the bioavailability of dexmedetomidine is 65% and 85% across the nasal and buccal mucosa, respectively.[7] Since the drug is deposited after nebulization over the nasal, buccal, and respiratory mucosa, nebulized dexmedetomidine may present an alluring option to both intravenous and intranasal modes of administration.[8]

2. Materials and Methods

This prospective, randomized, placebo-controlled, double-blind study was conducted, following approval from the Institutional Research Committee and Ethics Committee. The study spanned from December 1, 2020, to September 30, 2022, and involved ASA I and II adult patients aged 18 to 60, of either gender, scheduled for elective surgeries requiring tracheal intubation and general anesthesia. Prior to participation, all individuals provided informed consent and were subsequently divided into two groups, with 50 participants in each group. Group P received a nebulization of 0.9% saline (4 ml) 30 minutes before the induction of anesthesia, while Group D received a nebulization of 1 ug/kg of dexmedetomidine diluted in 0.9% saline, also 30 minutes before anesthesia induction.

Inclusion criteria encompassed patients with ASA I & II, either gender, adults between 18 and 60 years, and Mallampati Score (MPS) I & II. Exclusion criteria included patients undergoing emergency surgeries, those with a body mass index exceeding 30 kg/m^2, individuals with known or unanticipated difficult intubation, requiring more than 30 seconds or two attempts at laryngoscopy by a senior anesthesiologist, patients with rhythms other than sinus, those on anti-hypertensive medications or beta blockers, individuals with a known allergy to dexmedetomidine, and those on preoperative drugs that could potentially confound the study (clonidine, gabapentin, pregabalin, steroids). Cardiac surgeries were also excluded from the study. Preoperative preparations included pre-anaesthetic checkup, obtaining informed consent, fasting for at least 6 hours, and administration of medication as prescribed.

During the surgery, patients were monitored and received nebulization as per their assigned group. After pre-oxygenation, anesthesia was induced, and intubation was performed. Intubation conditions were assessed using the Helbo-Hansen score (Steyn's modifications), and patients were monitored for any adverse events or complications. Post-surgery, patients were extubated and monitored in the postoperative care unit before being transferred to the ward upon meeting discharge criteria.

3. Result

A total of 100 patients posted for elective surgeries requiring general anaesthesia and tracheal intubation were divided into two different groups- Group D and Group P (based on randomization 1:1), each group including 50 patients. Data was described in terms of range; mean ±standard deviation (± SD), frequencies (number of cases) and relative frequencies (percentages) as appropriate. Comparison of quantitative variables between the groups were done using Student t-test and Mann Whitney test for parametric and non-parametric respectively. For comparing categorical data, Chi square ($\chi 2$) test was performed and exact test is used when the expected frequency is less than 5. A probability value (p value) less than 0.05 was considered statistically significant. All statistical calculations were done using (Statistical Package for the Social Science) SPSS 21version (SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Windows.

3.1. Demographic variables

In terms of demographic variables, a total of 100 patients were included in the study. The mean age of patients in Group D and Group P was 36.68 ± 11.83 years and 39.64 ± 14.01 years, respectively. The mean weight of patients in Group D and Group P was 65.94 ± 8.92 kg and 66.04 ± 8.96 kg, while the mean height of patients in both groups was 1.65 ± 0.07 meters. The mean BMI for patients in Group D and Group P was 24.23 ± 2.04 kg/m^2 and 24.27 ± 2.07 kg/m^2.(Table 1)

Out of the 100 patients, 80 patients were classified as ASA 1 status, and 20 patients were ASA 2 status. Specifically, in Group D, 82.0% of the patients were ASA 1, while 18.0% were ASA 2. In Group P, 78.0% of the patients had ASA 1 status, and 22.0% had ASA 2 status.

Regarding the Mallampati Score (MPS), in Group D, 52.0% of the patients were classified as MPS class 1, and 48.0% as MPS class 2. In Group P, 58.0% of the patients were MPS class 1, while 42.0% were MPS class 2. These demographic variables provide important insights into the composition of the study groups and their characteristics

Table 1: Demographic variables

Variables	Group D (n=50) (nebulization with dexmedetomidine)	Group P (n=50) (nebulization with saline)
Age (years)	36.68±11.83	39.64±14.01
Weight (kg)	65.94 ±8.92	66.04 ±8.96
Height (m)	1.65± 0.07	1.65± 0.07
BMI (kg/m^2)	24.23±2.04	24.27±2.07

3.2. *Mean Heart rate at different intervals*

The mean heart rate (HR) was assessed in both Group D and Group P. The findings revealed a significant reduction in heart rate in Group D compared to Group P at various time points. Specifically, there was a significant attenuation of HR in Group D at the time of laryngoscopy (p=0.007), 1 minute after intubation (p=0.001), 3 minutes after intubation (p=0.001), 5 minutes after intubation (p=0.001), 7 minutes after intubation (p=0.004), and 10 minutes after intubation (p=0.004). These results indicate a notable impact of the intervention in Group D on heart rate compared to the control group, Group P, at various time intervals during the study. (Figure 1)

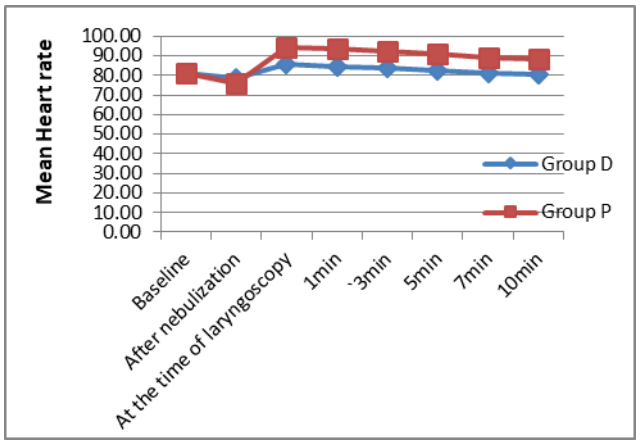

Figure 1: Mean Heart rate at different intervals

3.3. *Mean systolic BP at different intervals*

The study revealed a significant reduction in the mean systolic blood pressure (SBP) in Group D compared to Group P at various time points. Specifically, there was a significant attenuation of mean SBP in Group D at the time of laryngoscopy (p=0.001), 1 minute after intubation (p=0.001), 3 minutes after intubation (p=0.001), 5 minutes after intubation (p=0.001), 7 minutes after intubation (p=0.001), and 10 minutes after intubation (p=0.001). These findings indicate a substantial impact of the intervention in Group D on systolic blood pressure compared to the control group, Group P, at various time intervals during the study. (Figure 2)

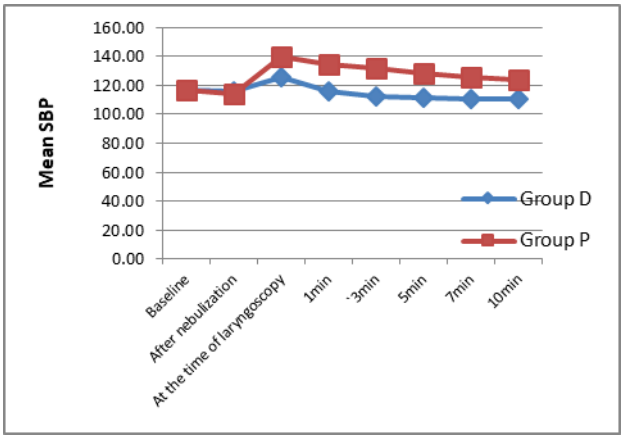

Figure 2: Mean systolic BP at different intervals

3.4. *Mean diastolic BP at different intervals*

The study demonstrated a significant reduction in the mean diastolic blood pressure (DBP) in Group D compared to Group P at various time points. Specifically, there was a significant decrease in mean DBP in Group D at the time of laryngoscopy (p=0.001), 1 minute after intubation (p=0.001), 3 minutes after intubation (p=0.001), 5 minutes after intubation (p=0.001), and 10 minutes after intubation (p=0.001). However, it's worth noting that there was a less significant reduction in mean DBP at 7 minutes after intubation (p=0.047) in Group D. These results indicate a substantial impact of the intervention in Group D on diastolic blood pressure compared to the control group, Group P, at various time intervals during the study, with the most pronounced effect observed in the earlier time points. (Figure 3)

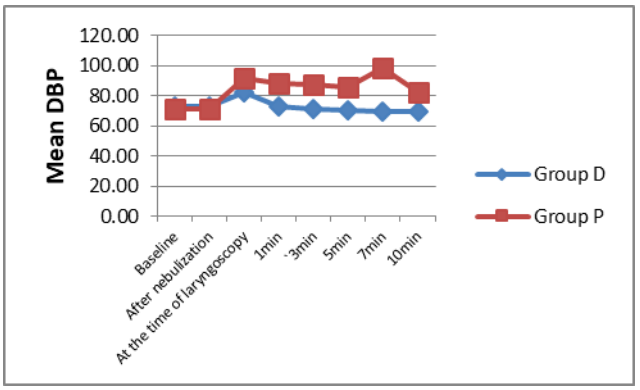

Figure 3: Mean diastolic BP at different intervals

3.5. *Mean arterial pressure at different intervals*

The study findings indicate that there were no statistically significant differences in the Mean Arterial Pressure (MAP) values measured at baseline (p=0.144) and after

nebulization (p=0.114) between Group D and Group P. However, it's important to note that the mean MAP was significantly lower in Group D compared to Group P at various time points, including at the time of laryngoscopy (p=0.001), 1 minute after intubation (p=0.001), 3 minutes after intubation (p=0.001), 5 minutes after intubation (p=0.001), 7 minutes after intubation (p=0.001), and 10 minutes after intubation (p=0.001). These results suggest that while there were no baseline or post-nebulization differences in MAP between the groups, the intervention in Group D had a significant impact on reducing MAP at different time intervals during the study when compared to Group P. (Figure 4)

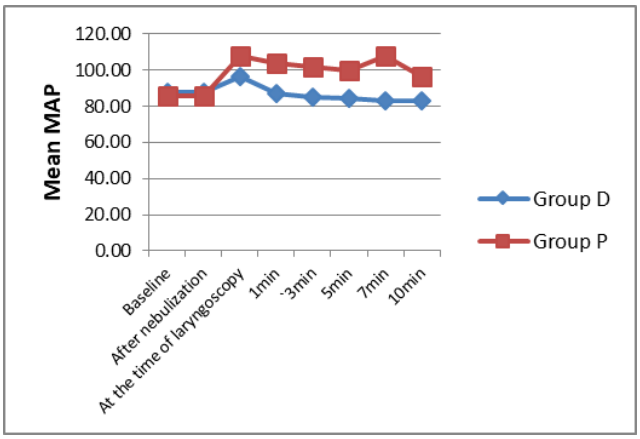

Figure 4: Mean arterial pessure at different intervals

3.6. Mean rate pressure product (RPP) at different intervals

The study results indicate that there were no statistically significant differences in the mean Rate Pressure Product (RPP) values measured at baseline (p=0.974) and after nebulization (p=0.111) between the Dexmedetomidine and Placebo groups. However, significant differences were observed at various time points during the study, including at the time of laryngoscopy (p=0.001), 1 minute after intubation (p=0.001), 3 minutes after intubation (p=0.001), 5 minutes after intubation (p=0.001), 7 minutes after intubation (p=0.001), and 10 minutes after intubation (p=0.001). These findings suggest that while there were no differences in RPP at baseline or after nebulization, significant variations were observed between the groups at different time intervals, particularly during and after intubation. (Figure 5)

3.7. Effect on intubation conditions

In the study, the assessment of intubation conditions revealed that 61% of the patients exhibited excellent intubation conditions, characterized by easy laryngoscopy,

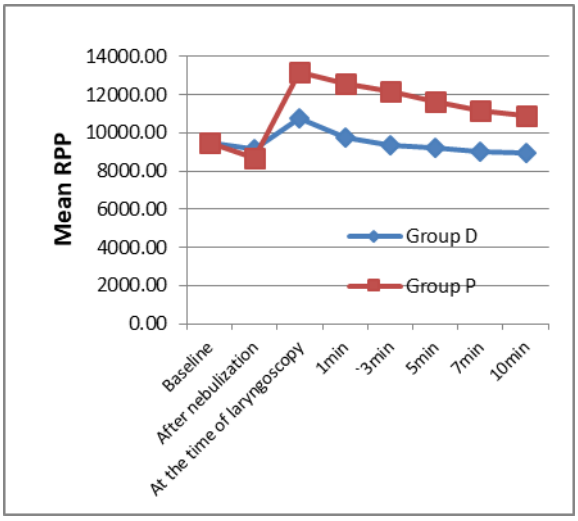

Figure 5: Mean RPP at different intervals

open vocal cords, absence of coughing, complete jaw relaxation, and no limb movements as per Steyn's modification of Helbo-Hansen score[9]. Additionally, 39% of the patients demonstrated good intubation conditions according to the same scoring system.

In Group D, 74.0% of the patients showed excellent intubation conditions, while 26% of them displayed good intubation conditions. In contrast, in Group P, 48% of the patients fell into the category of excellent intubation conditions, while 52% had good intubation conditions. The statistical analysis revealed a significant difference between the two groups, with a p-value of 0.013 and a chi-square value of 7.104. These findings suggest that the use of dexmedetomidine in Group D was associated with a higher proportion of patients exhibiting excellent intubation conditions compared to the control group, Group P. (Figure 6)

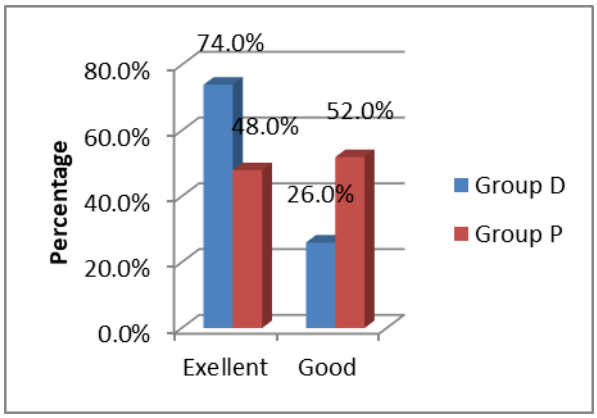

Figure 6: Distribution of patients according to intubation conditions

3.8. Incidence of side effects

Only 2% of the patients in each group experienced side effects, specifically sore throat. Notably, the vast majority of patients in both Group D and Group P, accounting for 98%, did not report any side effects, including symptoms like nausea, vomiting, dryness of the nose, headache, bradycardia, hypotension, or sore throat.

The statistical analysis demonstrated a chi-square value of 0.000, and the result was found to be statistically insignificant, with a p-value of 1.000. These results indicate that the occurrence of side effects, such as sore throat, was very low in both groups, and there were no statistically significant differences between the groups in terms of side effects. (Figure 7)

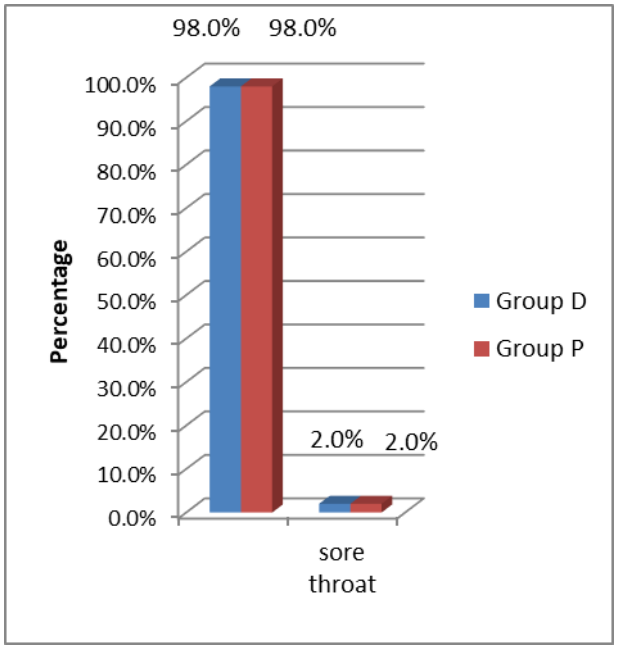

Figure 7: Distribution of patients according to side effects

4. Discussion

Endotracheal intubation and laryngoscopy are unpleasant stimuli that can cause a wide range of stress reactions, including tachycardia, hypertension, bronchospasm, laryngospasm, increased intracranial pressure, and increased intraocular pressure.[9] Patients with cardiovascular and cerebrovascular disorders may find increased cardiovascular reflexes to be harmful. During the administration of general anesthesia, avoiding the rise in sympathoadrenergic activity brought on by endotracheal intubation becomes crucial. Anaesthesiologists have experimented with a number of medications and innovative techniques to lessen patients' stress reactions during laryngoscopy and endotracheal intubation. The effectiveness of Dexmedetomidine at reducing the cardiovascular response to endotracheal intubation and providing better intubating conditions were to be assessed in the current study.

In our study, there was an increase in heart rate from baseline in both the groups after laryngoscopy and intubation, but the increase in heart rate was highly significant in group P (placebo) at the time of laryngoscopy, 1 min, 3 min, 5 min, 7 min and 10 minutes after intubation and was insignificant in group D(dexmedetomidine) at similar intervals. Similar to the study done by Misra S. et al,[10] who assessed the effects of preoperative dexmedetomidine nebulization on the hemodynamic response to laryngoscopy and intubation, we noticed a considerable reduction of the increase in heart rate in group D. Additionally, we noticed a decrease in perioperative opioid and anesthetic drug use.

In our study found that there was significant attenuation of SBP and DBP and MAP at 1 min, 5 min, and 10 min following intubation in the group of patients who received dexmedetomidine nebulization (1 μg/kg). Shrivastava P et al[11] observed there was a statistically significant difference in the SBP of the two groups (control and dexmedetomidine) recorded before laryngoscopy ($p = 0.019$), after intubation ($p = 0.007$), after one minute of intubation ($p < 0.001$), after five minutes ($p < 0.001$), and after 10 minutes ($p = 0.010$) of intubation which was similar to our study and the difference in mean DBP at time intervals before laryngoscopy ($p < 0.001$), after intubation ($p = 0.034$), after one minute ($p = 0.011$), after five minutes ($p < 0.005$), and after 10 minutes ($p = 0.009$) of intubation when compared between the control and study groups; however, at baseline, no significant difference was observed between the two groups ($p = 0.201$). The significant difference in the MAP at time intervals before laryngoscopy ($p < 0.047$), after intubation ($p = 0.042$), after one minute ($p = 0.001$), after five minutes ($p < 0.006$), and after 10minutes ($p = 0.018$) of intubation when compared between the control and study groups which was similar to our study.

Singh V13 et al. evaluated the effects of nebulized dexmedetomidine (1 g/kg in 3-4 ml of 0.9% saline) and intravenous (1 g/kg over 10 min) dexmedetomidine on attenuating the stress response to laryngoscopy and intubation. The rate-pressure product in their trial never reached the critical ischemia value of 12000 in either group, which is comparable to our findings and makes nebulized dexmedetomidine a feasible alternative for individuals who are poor candidates for hypo- or hypertension or Brady/tachycardia. In our study Group D showed better control on RPP than group P and it showed a better control of haemodynamics with nebulized dexmedetomidine. This showed cardioprotective effect of dexmedetomidine which leads to a reduction in perioperative myocardial ischemia episodes.

The study done by Gu W et al[12] observed the incidence and severity of coughing, condition of vocal cords, jaw relaxation and limb movements in patients for flexible bronchoscopy. They discovered that 15% of people receiving nebulized dexmedetomidine, 50% of people receiving intravenous dexmedetomidine, and 55% of people receiving nebulized lidocaine experienced moderate to severe coughing. In our study we used steyn's modification of Halbo-Hansen scoring[13] to evaluate the intubation conditions. We observed that the nebulized dexmedetomidine significantly facilitate the intubation conditions like easy laryngoscopy, open vocal cords, no coughing, complete jaw relaxation, and no limb movements and it showed a significant difference as compared to saline nebulization. Nebulized dexmedetomidine in their study shown a protective benefit for lowering coughing in comparison to intravenous dexmedetomidine, with the nebulized dexmedetomidine group having the lowest incidence of moderate to severe coughing (P=0.019). Nimmagadda et al.'s[14] evaluation of nebulized dexmedetomidine as a premedication to blunt hemodynamic response to laryngoscopy and tracheal intubation without bradycardia or hypotension was comparable to our study's findings that dexmedetomidine blunts stress response without any side effects. In our study we observed for perioperative hypotension, bradycardia and post-operative dryness of nose, nausea, vomiting, sore throat and headache. Only 2% patients showed side effects (sore throat) in each group. In both group D and group P 98% patients never showed any side effects. The chi square value was 0.000 and result was statistically insignificant (p value 1.000). Commonly seen haemodynamic instability associated with Dexmedetomidine was not seen in our study, this may be because of lower dose and nebulized route of administration.

Our study had some limitations. It was conducted in ASA 1 and ASA 2 status patients while the population who can most benefit from the study probably belong to ASA 3 and 4. It was decided not to include them in the study course due to ethical considerations.

5. Conclusion

In conclusion, our study demonstrated that nebulizing dexmedetomidine at a dose of 1 mcg/kg effectively reduces the hemodynamic response to laryngoscopy and intubation without elevating the risk of hypotension or bradycardia. Dexmedetomidine provided more stable heart rate and mean arterial pressure compared to the control group. Moreover, the intubation conditions were excellent following dexmedetomidine nebulization. This novel method of administration shows promise in mitigating the hemodynamic response to laryngoscopy and intubation.

Further research in this area is warranted, as preoperative nebulization of dexmedetomidine appears to be a potential intervention for minimizing the hemodynamic response to laryngoscopy and intubation while enhancing intubation conditions. Importantly, patients in both groups, whether receiving dexmedetomidine or a placebo, did not experience any adverse effects. Preoperative nebulization with dexmedetomidine may prove to be an effective strategy for reducing the hemodynamic response to intubation, improving intubation conditions, and reducing intraoperative anesthetic and analgesic requirements without causing significant adverse effects.

6. Source of Funding

Nil.

7. Conflicts of Interest

There are no conflicts of interest.

References

1. Kutlesic MS, Kutlesic RM, Mostic-Ilic T. Attenuation of cardiovascular stress response to endotracheal intubation by the use of remifentanil in patients undergoing Cesarean delivery. *J Anesth*. 2016;30(2):274–83.
2. Grewal A. Dexmedetomidine : New avenues. *J Anaesthesiol Clin Pharmacol*. 2011;27(3):297–302.
3. Kumar S, Kushwaha B, Prakash B, Jafa S, Malik A. Comparative study of effects of dexmedetomidine and clonidine premedication in perioperative hemodynamic stability and postoperative analgesia laparoscopic cholecystectomy. *Internet J Anaesth*. 2014;33:1–8.
4. Bhattacharjee DP, Nayek SK, Dawn S, Bandopadhyay G, Gupta K. Effects of dexmedetomidine on hemodynamics in patients undergoing laparoscopic cholecystectomy– A comparative study. *J Anaesth Clin Pharmacol*. 2010;26:45–8.
5. Kumari K, Gombar S, Kapoor D, Sandhu HS. Clinical study to evaluate the role of preoperative dexmedetomidine in attenuation of hemodynamic response to direct laryngoscopy and tracheal intubation. *Acta Anaesthesiol Taiwan*. 2015;53(4):123–30.
6. Niyogi S, Biswas A, Chakraborty I, Chakraborty S, Acharjee A. Attenuation of haemodynamic responses to laryngoscopy and endotracheal intubation with dexmedetomidine: A comparison between intravenous and intranasal route. *Indian J Anaesth*. 2019;63(11):915–23.
7. Zanaty OM, ElMetainy SA. A comparative evaluation of nebulized dexmedetomidine, nebulized ketamine, and their combination as premedication for outpatient pediatric dental surgery. *Anesth Analg*. 2015;12(1):167–71.
8. Abdel-Ghaffar HS, Kamal SM, Sherif FE, Mohamed SA. Comparison of nebulized dexmedetomidine, ketamine, or midazolam for premedication in preschool children undergoing bone marrow biopsy. *Br J Anaesth*. 2018;121(2):445–52.
9. Mendonça FT, DeQueiroz L, Guimarães CC, Xavier AC. Effects of lidocaine and magnesium sulfate in attenuating hemodynamic response to tracheal intubation: single-center, prospective, double-blind, randomized study. *Rev Bras Anestesiol*. 2017;67(1):50–6.
10. Misra S, Behera B, Mitra J, Sahoo A, Jena S, Srinivasan A. The effect of preoperative dexmedetomidine nebulization on the hemodynamic response to laryngoscopy and intubation: a randomized control trial. *Korean J Anesthesiol*. 2021;74(2):150–7.
11. Shrivastava P, Kumar M, Verma S, Sharma R, Kumar R, Ranjan R, et al. Evaluation of Nebulised Dexmedetomidine Given Pre-operatively to Attenuate Hemodynamic Response to Laryngoscopy and Endotracheal Intubation: A Randomised Control Trial. *Cureus*. 2022;14(5):e25223.

12. Gu W, Xu M, Lu H, Huang Q, Wu J. Nebulized dexmedetomidine-lidocaine inhalation as a premedication for flexible bronchoscopy: a randomized trial. *J Thorac Dis*. 2019;11(11):4663–70.
13. Steyn MP, Quinn AM, Gillespie JA, Miller DC, Best CJ, Morton NS. Tracheal intubation without neuromuscular block in children. *Br J Anaesth*. 1994;72:403–6.
14. Kumar NRR, Jonnavithula N, Padhy S, Sanapala V, Naik VV. Evaluation of nebulised dexmedetomidine in blunting haemodynamic response to intubation: A prospective randomised study. *Indian J Anaesth*. 2020;64(10):874–9.

Author biography

Neenu Susan Paul, Senior Resident https://orcid.org/0009-0009-2749-7292

Valsamma Abraham, Professor

Dootika Liddle, Professor https://orcid.org/0000-0003-3897-6028

Cite this article: Paul NS, Abraham V, Liddle D. A randomized double blind study to evaluate the effect of nebulized dexmedetomidine on the haemodynamic response to laryngoscopy – Intubation and intubation conditions. *Indian J Clin Anaesth* 2023;10(4):358-364.