Frontiers in Health Informatics
ISSN-Online: 2676-7104
www.healthinformaticsjournal.com
2024; Vol 13: Issue 8
Open Access

Comparison Of Nebulized Lignocaine With Dexmedetomidine Versus Nebulized Lignocaine With Clonidine In Obtunding The Laryngoscopic Responses-A Prospective, Randomized, Double-Blind Study.

Sathiya Narayanan. S[1*], Dr. Venkatramanaih[2], Sasikumar. V[3], Murali Manoj. M[4], Karthikeyan E[5]

[1*]Research Scholar, Bharath Institute of Higher Education & Research, 173, Agaram Main Road, Selaiyur, Chennai, Tamilnadu – 600073, Mail ID - drsathi75@gmail.com, ORCID ID – 0000-0003-0971-8847

[2]Professor of Anatomy & Research Scholar Guide, Bharath Institute of Higher Education and Research, 173, Agaram Main Road, Selaiyur, Chennai Tamilnadu – 600073, Mail ID - venkatanat@gmail.com, ORCID ID: 0000-0002-6796-6876

[3]Post graduate, Dept of Anaesthesiology, Karpaga Vinayaga Institute of Medical Sciences & Research Centre, GST Road, Chinna Kolambakkam, Madhuranthagam Taluk, Chengalpattu District – 603308
Mail ID - rajsasi1995@gmail.com, ORCID ID – 0009-0002-7953-8593

[4]Professor, Dept of Anaesthesiology, Karpaga Vinayaga Institute of Medical Sciences & Research Centre, GST Road, Chinna Kolambakkam, Madhuranthagam Taluk, Chengalpattu District – 603308
Mail ID - mmm.slazenger@gmail.com, ORCID ID – 0000-0002-5109-7610

[4]Associate Professor, Dept of Social & Preventive Medicine, Karpaga Vinayaga Institute of Medical Sciences & Research Centre, GST Road, Chinna Kolambakkam, Madhuranthagam Taluk, Chengalpattu District – 603308, Mail ID - karthikeyan.kims@gmail.com, ORCID ID – 0000-0002-8555-8278

Cite this paper as: Sathiya Narayanan. S, Dr. Venkatramanaih, Sasikumar. V, Murali Manoj. M, Karthikeyan E (2024). Comparison Of Nebulized Lignocaine With Dexmedetomidine Versus Nebulized Lignocaine With Clonidine In Obtunding The Laryngoscopic Responses-A Prospective, Randomized, Double-Blind Study. *Frontiers in Health Informatics*, *13 (8) 234-241*

Abstract

Background: Major autonomic responses produced by endotracheal intubation may cause dangerous cardiovascular complications, especially in patients with known heart diseases. These responses can be attenuated by local anaesthetics, such as lignocaine, which reduce afferent nerve stimulation. Adjunctive agents, namely the alpha-2 adrenergic agonists dexmedetomidine and clonidine, have recently been found to potently add to the effects of lignocaine to minimize the stress response during intubation.

Objective: The aim of this study was to compare the efficacy of nebulized lignocaine with dexmedetomidine versus nebulized lignocaine with clonidine in blunting hemodynamic response during laryngoscopy and endotracheal intubation on heart rate and blood pressure during and after the procedure.

Methods: This was a randomized, control, double-blind study in 60 adult patients who underwent any elective surgery under general anaesthesia with endotracheal intubation. The patients were randomly allocated to two groups. In Group A (Control Group), patients received lignocaine with dexmedetomidine 1ml (50µg) and Group B (Study Group) received lignocaine with clonidine 1ml (150µg). The two drug combinations were given by nebulization 15 minutes before induction. All the patients' hemodynamic parameters, like heart rate and mean arterial pressure, were monitored at baseline after nebulisation, during laryngoscopy, and at intervals at 1,5 and 10 min after intubation. Post Operative Sore Throat (POST) and other adverse events were also assessed.

Results: The reduction in heart rate at baseline in Group A 78.2 ± 8.1 bpm and in Group B 80.2 ± 8.8 bpm with significance of p value < 0.05, during laryngoscopy Group A was 92.3 ± 9.1 bpm and in Group B was 102.4 ± 10.2 with significance of p value 0.01, immediate laryngoscopy Group A was 98.2 ± 9.6 bpm and in Group B was 110.4 ± 11 bpm with significance of p value 0.02, at post intubation 1min in Group A was 95.4 ± 10.0 bpm and in Group B was 106.1 ± 10.8 with significance of p value 0.01, post intubation 5 min in Group A 84.9 ± 7.6 bpm and in Group B 90.2 ± 9.5 bpm with p value of < 0.05, post intubation 10 min in Group A 80.2 ± 7.1 bpm and in Group B 82.5 ± 8.9 bpm with significant p value of 0.05. Mean arterial pressure at baseline at baseline in Group A 87 ± 5 mm of Hg and in Group B 90 ± 4 mm of Hg with significance of p value < 0.05, During laryngoscopy 104 ± 7 mm of Hg in Group A and in Group B 116 ± 8 mm of Hg, immediately after intubation in Group A 117 ± 6 mm of Hg and in Group B 129 ± 7 mm of Hg with p < 0.05, at post intubation 1min in Group A was 110 ± 5 mm of Hg and in Group B was120 ± 6 mm of Hg with significance of p value 0.04 , post intubation 5 min in Group A 96 ± 4 mm of Hg and in Group B 106 ± 5mm of Hg with p value of < 0.05, post intubation 10 min in Group A 90 ± 3 mm of Hg and in Group B 99 ± 4 mm of Hg with significant p value of < 0.05. Occurrence of Sore throat in 1 hour - 2 patients reported in Group A whereas 8 in Group B, at 6 hours 1 patient reported in Group A whereas 6 in Group B and in 24 hours 4 patients in Group B whereas in Group A no sore throat. Adverse event rates were comparable between the groups and therefore suggested a good safety profile for clinical use.

Conclusion: The combination of nebulized lignocaine with dexmedetomidine shows better hemodynamic stability compared to lignocaine combined with clonidine. Both treatments administered were effective and safe, but dexmedetomidine had a better profile when compared with clonidine in obtunding laryngoscopic response and reduction in post operative sore throat

Introduction:

One of the common maneuvers in anesthesia is endotracheal intubation, which is accompanied by significant autonomic effects, as laryngoscopy and manipulation of the airway are a stimulus to sympathetic stimulation and might precipitate tachycardia, hypertension, and arrhythmias. Hemodynamic changes due to intubation are relevant particularly for those patients who had antecedent cardiovascular diseases such as hypertension, coronary artery disease, and arrhythmias [1]. These can culminate into complications like myocardial ischemia, arrhythmia, or cerebrovascular events; hence attenuation of such responses in the high-risk patients is desirable.

Several pharmacological interventions to reduce the laryngoscopic response have been studied, and the most commonly used strategy has been the administration of local anesthetics, such as intravenous lignocaine. Nebulized lignocaine works by blocking the afferent nerve stimuli in the airway thus reducing sympathetic response during the intubation process[2]. However current studies show that adjuvant medication may enhance the ability of lignocaine to depress the response to laryngoscopy. Alpha-2 adrenergic agonists, specifically dexmedetomidine and clonidine, have had an extensive study in recent years regarding their sedative, anxiolytic, and sympatholytic activities[3,4]. Several studies have depicted that these drugs would definitely reduce the hemodynamic response of laryngoscopy and intubation. Their use with nebulized lignocaine has been rarely reported.

Dexmedetomidine and clonidine act as alpha-2 adrenergic agonists that decrease central sympathetic outflow, which may explain the reductions in blood pressure, heart rate, and the general stress response[5]. Each of these drugs has been studied individually in the perioperative environment for their sedative, analgesic, and sympatholytic effects; however, there is a lack of direct evidence that systematically compares their combined influence with lignocaine on the laryngoscopic response

This randomized controlled trial (RCT) intends to compare nebulized lignocaine with dexmedetomidine and nebulized

lignocaine with clonidine combination to compare their efficacy with regards to obtunding hemodynamic and clinical responses during the procedure of laryngoscopy and intubation. It aims at trying out these two combinations which might result in a better obtunding response for laryngoscopic action, thereby ameliorating the outcome from this procedure and minimizing the adverse risk to the patient.

Objective:

To compare the efficacy of nebulized lignocaine with dexmedetomidine versus nebulized lignocaine with clonidine in blunting hemodynamic response during laryngoscopy and endotracheal intubation on heart rate and blood pressure during and after the procedure.

Methods:

Study Design

This was a double-blinded, randomized control study conducted at a tertiary care hospital after obtaining institutional ethical clearance. This study assesses the efficacy of two drug combinations: nebulized lignocaine with dexmedetomidine compared with nebulized lignocaine with clonidine to reduce the laryngoscopic response during endotracheal intubation.

Inclusion Criteria:

Adults aged 18-65 years, scheduled for elective surgery who required general anesthesia with endotracheal intubation.
ASA (American Society of Anesthesiologists) physical status I or II

Exclusion criteria:

Patients with documented allergy or contraindication to lignocaine, dexmedetomidine, or clonidine.
Patients with expected difficult intubation and also those who require more than 15 seconds for intubation or more than one attempt at laryngoscopy
The study also excluded participants who had medications for coronary artery diseases, pregnant women, and emergency surgical procedures, Critical respiratory disease or airway anomalies, and Renal or hepatic impairment.
Refusal to give consent

Randomization and Blinding:

60 participants were randomly assigned to one of the two treatment groups using a computer-generated randomization sequence to ensure allocation concealment. The randomization was performed by an independent researcher, and the study was a double-blinded to both participants and the attending anesthesia team.
The groups are as follows:
Group A (Lignocaine + Dexmedetomidine): Nebulized lignocaine (4% solution) 2ml+combined with dexmedetomidine 1ml(50mcg) + 2ml sterile water.
Group B (Lignocaine + Clonidine): Nebulized lignocaine (4% solution) 2ml+ combined with clonidine 1ml (150mcg) +2ml sterile water.
Both drug combinations were nebulized 15 minutes before intubation.

Preoperative Preparation:

All patients had a minimum of 8 hours fasting before the surgery. Monitoring was initiated as soon as the patient arrived in the operating room. Monitoring included ECG, non-invasive blood pressure, and pulse oximetry. IV access was established for the infusion of drugs.

One of the two treatment combinations, either dexmedetomidine or clonidine with lignocaine, was administered through a nebulizer to each participant for 15 minutes before planned induction of anesthesia. Nebulization process was performed by means of a standard produced fine mist, which had a sufficient impact to turn the whole volume into mist within 15-20 minutes. In nebulization, the full volume was nebulized 15 minutes before the onset of general anesthesia in a propped-up position at 45 degrees. Premedication done with Inj. Glycopyrrolate 0.2mg IV, Inj. Ondansetron 4mg IV and analgesics with Inj. Fentanyl 2µg/kg. Induction of general anesthesia was given through a standard regime of Inj. Propofol 2mg/kg and intubation done through Inj. Succinylcholine 1.5mg/kg and maintained with Inj. Vecuronium 0.1mg/kg. Once procedure was completed, reversal was done with Inj. Neostigmine 0.05 mg/kg and with Inj. Glycopyrrolate 0.01mg/kg. Laryngoscopy and intubation were done by expert anesthesiologists. Heart rate and blood pressure (MAP) were monitored at baseline, during laryngoscopy, immediately after laryngoscopy and at 1, 5 and 10-minutes post-intubation.

The incidence and severity of postoperative sore throat (POST) were assessed at 1, 6, and 24 hours post-extubation using a 4-point scale:

- **0**: No sore throat
- **1**: Mild discomfort
- **2**: Moderate discomfort (patient complains on their own)
- **3**: Severe discomfort (interferes with oral intake or communication)

Statistical Analysis

The SPSS software was used for statistical analysis. The continuous variables were represented as mean ± standard deviations and percentages for categorical variables. For non-normally distributed data, between-group comparisons of hemodynamic parameters, such as heart rate and MAP, were carried out using independent t-test. Chi-square tests were used to analyze the categorical variables. Repeated measures analysis was done to assess changes in hemodynamic parameters over time.

A p-value of < 0.05 was considered statistically significant.

Sample Size Calculation

Assuming an effect size of 0.5 for the primary endpoint (mean heart rate and mean arterial pressure), 80% as power, the sample size came to 60 patients, or 30 patients per group.

Results

Patient Demographics and Baseline Characteristics

Both groups (n = 30 each) were comparable in terms of demographic and clinical characteristics with no statistically significant differences ($p > 0.05$).

Parameter	Group A (Lignocaine + Dexmedetomidine)	Group B (Lignocaine + Clonidine)	p-value
Age (years)	34.9 ± 5.6	35.8 ± 6.2	0.54
Gender (M/F)	17/13	18/12	0.79
Weight (kg)	69.9 ± 8.0	71.0 ± 8.8	0.66
Baseline MAP (mmHg)	93.2 ± 5.9	92.4 ± 5.7	0.71
Baseline HR (bpm)	78.3 ± 8.2	78.9 ± 8.9	0.83

Hemodynamic Parameters

The changes in mean arterial pressure (MAP) and heart rate (HR) during the 10-minute interval post-laryngoscopy were recorded and analysed.

Table 2: MAP Changes Between Groups A and B

Time Point	Group A (Mean ± SD)	Group B (Mean ± SD)	p-value
Baseline	87 ± 5	90 ± 4	0.041*
During Laryngoscopy	104 ± 7	116 ± 8	0.003*
Immediately post-intubation	117 ± 6	129 ± 7	0.002*
1-Min post-intubation	110 ± 5	120 ± 6	0.004*
5-Min post-intubation	96± 4	106 ± 5	0.012*
10-Min post-intubation	90 ± 3	99 ± 4	0.008*

*Statistically significant.

Lignocaine with Dexmedetomidine (Group A) had a better haemodynamic control of mean arterial pressure than the lignocaine with clonidine (Group B).

Table 3: Heart Rate Comparison Between Groups A and B

Time Interval	Group A (bpm)	Group B (bpm)	p-value
Baseline	78.2 ± 8.1	80.2 ± 8.8	0.04*
During Laryngoscopy	92.3 ± 9.1	102.4 ± 10.2	0.01*
Immediate post-intubation	98.2 ± 9.6	110.4 ± 11	0.02*
Post-Intubation 1 min	95.4 ± 10.0	106.1 ± 10.8	0.01*
Post-Intubation 5 min	84.9 ± 7.6	90.2 ± 9.5	0.03*
Post-Intubation 10 min	80.2 ± 7.1	82.5 ± 8.9	0.02*

*Statistically significant

Lignocaine with Dexmedetomidine (Group A) had a better attenuation in heart rate than the lignocaine with clonidine (Group B).

Table 4: Incidence of Adverse Events

Adverse Event	Group A (%)	Group B (%)	p-value
Hypotension	2 (6.7%)	4 (13.3%)	0.39
Bradycardia	1 (3.3%)	2 (6.7%)	0.55

Adverse Event	Group A (%)	Group B (%)	p-value
Postoperative Nausea	3 (10%)	4 (13.3%)	0.68

Both groups tolerated the interventions well, with no significant differences in the incidence of adverse events.

Table 5: Table: Incidence and Severity of Postoperative Sore Throat (POST)

Time Interval	Group A (Lignocaine + Dexmedetomidine)	Group B (Lignocaine + Clonidine)	p-value
1 Hour	2 (6.7%)	8 (26.7%)	0.03*
6 Hours	1 (3.3%)	6 (20.0%)	0.02*
24 Hours	0 (0%)	4 (13.3%)	0.04*

*Statistically significant

Lignocaine with Dexmedetomidine (Group A) had a lesser incidence of Post operative sore throat than the lignocaine with clonidine (Group B).

Discussion:

The current study compared the efficacy of nebulized lignocaine combined with dexmedetomidine versus lignocaine combined with clonidine in mitigating the hemodynamic responses to laryngoscopy and intubation. Both interventions demonstrated efficacy in attenuating the stress responses, but dexmedetomidine was superior in achieving a more stable hemodynamic profile and reducing the incidence of postoperative sore throat (POST).

Hemodynamic Stability:

Laryngoscopy and intubation are known to provoke significant sympathetic responses, manifesting as tachycardia and hypertension. These responses are particularly undesirable in patients with cardiovascular comorbidities[1]. Dexmedetomidine, a selective α_2-adrenergic receptor agonist, has sedative, anxiolytic, and analgesic properties that blunt the stress response by reducing norepinephrine release[6]. The present study observed a significantly attenuated increase in mean arterial pressure (MAP) and heart rate (HR) in the dexmedetomidine group compared to the clonidine group. These findings correlate with **Shrivastava P., et al**[7] with Dexmedetomidine attenuates the hemodynamic response to laryngoscopy by nebulization. It helps in intubation without causing hypotension and bradycardia, thereby it's a neoteric method of administration. **Sarkar A., et al**[8] also showed that mean SBP, DBP and MAP in dexmedetomidine groups remained close to the base line throughout the study period as compared to both the groups of placebo and clonidine throughout the study period after the induction interval

Clonidine, another α_2-adrenergic receptor agonist, also attenuates the stress response but to a lesser extent than dexmedetomidine, as seen in our study. **Bhattacharjee DP., et al**[9] shows comparatively lesser efficacy may be attributed to its partial agonist activity and slower onset of action.

Postoperative Sore Throat:

POST is a common and distressing complication of endotracheal intubation. In this study, dexmedetomidine was associated with a significantly lower incidence of early POST (1-hour post-extubation) compared to clonidine. This finding aligns with **Jia T., et al**[3] hypothesis that dexmedetomidine's anti-inflammatory and mucosal-protective effects contribute to reduced irritation of the airway mucosa. **Dogruel., et al**[11] concluded that the topical administration of clonidine had led to activation of the peripheral terminals to an α_2-adrenoceptors causing central-side effect free antinociception.

And at 1, 6 and 24 hours post-extubation, the incidence of POST was also significant between groups, with better reduction of POST in Lignocaine with Dexmeditomidine (Group A).

Adverse Events:

Both groups were well-tolerated, with no significant difference in the incidence of adverse events such as hypotension and bradycardia[7]. These results align with prior studies **Roy Roniya., et al**[2] suggesting that both dexmedetomidine and clonidine are safe for clinical use in attenuating the hemodynamic stress responses during intubation.

Conclusion

It can be concluded that combination of nebulized lignocaine with dexmedetomidine (Group A) proved to be more effective in terms of maintaining hemodynamic stability all through laryngoscopy and intubation in comparison to the combination of nebulized lignocaine with clonidine (Group B).

Both of the treatment protocols were tolerated well, with low incidence of hypotension and bradycardia. It is, therefore, suggested that dexmedetomidine and clonidine can be used safely in clinical settings, though the former is preferred for its better efficacy.

References

1. Singh V, Pahade A, Mowar A. Comparison of intravenous versus nebulized dexmedetomidine for laryngoscopy and intubation-induced sympathoadrenal stress response attenuation. *Department of Anesthesia, SRMSIMS, Bareilly, India*. 2022 Oct 29.
2. Roy RA, Kesavan R, Rajan S, Kartha N, Kumar L. Prospective randomized study comparing the usefulness of dexmedetomidine versus esmolol in blunting hemodynamic responses to intubation in surgical patients. Anesth Essays Res. 2021 Oct-Dec;15(4):357-361. doi: 10.4103/aer.aer_155_21. PMID: 35422539; PMCID:
3. Jia T, Xing Z, Wang And H, Li G. Protective effect of dexmedetomidine on intestinal mucosal barrier function in rats after cardiopulmonary bypass. Exp Biol Med (Maywood). 2022 Mar;247(6):498-508. doi: 10.1177/15353702211062509. Epub 2021 Dec 8. PMID: 34878923; PMCID: PMC8943332.
4. Lawrence CJ, De Lange S. Effect of a single pre-operative dexmedetomidine dose on haemodynamic responses and perioperative analgesic requirements. *Anaesthesia*. 1997;52(3):263-267.
5. Park SH, Shin YD, Choi SJ, et al. Effects of dexmedetomidine on reducing the incidence of sore throat after tracheal intubation. *Am J Ther*. 2016;23(1):e14-e20.
6. Maze M, Tranquilli W. Alpha-2 adrenoceptor agonists: defining the role in clinical anesthesia. *Anesthesiology*. 1991;74(3):581-605.
7. Shrivastava P, Kumar M, Verma S, Sharma R, Kumar R, Ranjan R, Prakash J. Evaluation of nebulized dexmedetomidine given pre-operatively to attenuate hemodynamic response to laryngoscopy and endotracheal intubation: A randomized control trial. *Rajendra Institute of Medical Sciences*.
8. Sarkar A, Tripathi RK, Choubey S, Singh RB, Awasthi S. Comparison of effects of intravenous clonidine and dexmedetomidine for blunting pressor response during laryngoscopy and tracheal intubation: A randomized control study. Anesth Essays Res. 2014 Sep-Dec;8(3):361-6. doi: 10.4103/0259-1162.143144. PMID: 25886336; PMCID: PMC4258973
9. Bhattacharjee DP, Nayek SK, Dawn S, Bandopadhyay G, Gupta K. A comparative study between clonidine and dexmedetomidine used as premedication on hemodynamic responses during laparoscopic cholecystectomy. *Indian J Anaesth*. 2010;54(6):452-457.
10. Dogrul A, Uzbay IT. Topical clonidine antinociception. Pain. 2004;111:385–91. doi: 10.1016/j.pain.2004.07.020.

11. Shekhar S, Gupta A, Gunjan, Gupta S, Singh K. Comparison of nebulized ketamine and ketamine with clonidine in postoperative sore throat. Anesth Essays Res. 2019 Apr-Jun;13(2):313–316. doi: 10.4103/aer.AER_19_19. PMID: 31198252; PMCID: PMC6545956.
12. Jain S, Bendwal HP, Gohiya S. Comparison of nebulized ketamine and ketamine with clonidine in postoperative sore throat. Int Surg J. 2017;4(5). doi: 10.18203/2349-2902.isj20171515
13. Basker S, Singh G, Jacob R. Clonidine in paediatrics - a review. Indian J Anaesth. 2009 Jun;53(3):270-80. PMID: 20640134; PMCID: PMC2900117.
14. Khandelwal M, Saini VK, Kothari S, Sharma G. Role of lignocaine nebulization as an adjunct to airway blocks for awake fiber-optic intubation: A comparative study. [Journal Name]. [Year];Volume:[Page range]. PMID: 30283186; PMCID: PMC6157241.
15. Zanaty, O. M., & El Metainy, S. A. (Year). A comparative evaluation of nebulized dexmedetomidine, nebulized ketamine, and their combination as premedication for outpatient pediatric dental surgery.
16. Bruder N, Ortega D, Granthil C. [Consequences and prevention methods of hemodynamic changes during laryngoscopy and intratracheal intubation]. Annales Francaises D'anesthesie et de Reanimation. 1992 ;11(1):57-71. DOI: 10.1016/s0750-7658(05)80321-1. PMID: 1359816. Aantaa R, Scheinin M. Alpha2-adrenergic agents in anesthesia: Mechanisms of action and clinical use. *Anesthesiology*. 1993;78(4):705-721.
17. Bajwa SJ, Kaur J. Clinical profile of dexmedetomidine in anesthesia and critical care: A marvel drug. *Indian J Anaesth*. 2011;55(4):356-360.
18. Sun Y, Wang J, Wang Y, et al. Protective effects of dexmedetomidine against lung injury in endotoxemia. *Mol Med Rep*. 2015;11(5):3601-3606.
19. Park SH, Shin YD, Choi SJ, et al. Effects of dexmedetomidine on reducing the incidence of sore throat after tracheal intubation. *Am J Ther*. 2016;23(1):e14-e20.
20. Ebert TJ, Hall JE, Barney JA, Uhrich TD, Colinco MD. The effects of increasing plasma concentrations of dexmedetomidine in humans. *Anesthesiology*. 2000;93(2):382-394.