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Original Research Article

Nebulized Dexmedetomidine Versus Nebulized Lignocaine for Attenuating Stress Response: A Narrative Review

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Abstract

Laparoscopic surgeries and airway manipulations trigger sympathetic surges, resulting in tachycardia, hypertension, and increased catecholamine release, which can compromise perioperative hemodynamics, especially in patients with cardiovascular comorbidities. Non-invasive premedication strategies, including nebulized dexmedetomidine and lignocaine, have been evaluated for their ability to suppress these responses. This review synthesizes evidence from randomized controlled trials (RCTs) assessing the efficacy, safety, and clinical utility of nebulized dexmedetomidine, lignocaine, and their combination. Evidence suggests that nebulized dexmedetomidine effectively attenuates heart rate and blood pressure elevations during airway manipulation and pneumoperitoneum, provides mild sedation without respiratory compromise, and reduces intraoperative anesthetic requirements. Lignocaine is effective as a topical anesthetic and moderately reduces sympathetic responses. Combination therapy enhances procedural comfort and hemodynamic stability. Nebulized dexmedetomidine, therefore, represents a safe and practical non-invasive strategy for perioperative stress response management.

Keywords: Dexmedetomidine, Lignocaine, Nebulization, Pneumoperitoneum, Hemodynamic Stress, Laryngoscopy, Fiber-optic Bronchoscopy.

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Introduction

Airway instrumentation, including laryngoscopy and endotracheal intubation, as well as pneumoperitoneum during laparoscopic surgery, activate the sympathetic nervous system [1]. The resulting catecholamine surge increases heart rate, blood pressure, myocardial oxygen consumption, and systemic vascular resistance [1]. While healthy patients tolerate these transient changes, those with cardiovascular comorbidities are at increased risk of perioperative complications, including arrhythmias, myocardial ischemia, and heart failure exacerbations[14,17].

Traditional approaches to attenuating these responses involve intravenous opioids, β-blockers, α_2-agonists, and local anesthetic infiltration [4]. Intravenous medications are not as useful in certain population due to its risks of hypotension, respiratory depression, and excessive sedation [21,9]. Topical administration of local anesthetics has been shown to blunt airway reflexes but does not consistently address systemic sympathetic activation[3,5].

Rationale for Nebulization: Nebulization provides a needle-free, non-invasive method for drug delivery through the respiratory mucosa.

Advantages include:

- Rapid absorption through alveolar-capillary networks [21]
- Reduced systemic side effects due to slower peak plasma levels[13]
- Patient-friendly administration, especially for pediatrics or needle-phobic adults

Simultaneous local airway anesthesia and systemic effect(in the case of dexmedetomidine)[24,25]

Given these advantages, nebulized dexmedetomidine and lignocaine have gained interest as premedication strategies to attenuate perioperative hemodynamic surges.

Pharmacology Overview

Dexmedetomidine:

Class: Highly selective α_2-adrenergic agonist[2]

Mechanism of action: Stimulates central $\alpha_2$receptors in the locus coeruleus, inhibiting norepinephrine release → sedation, anxiolysis, and sympatholysis[2]

Clinical effects: Sedation without respiratory depression, analgesia, hemodynamic stabilization[4]

Dosing (nebulized): 1–2 µg/kg

Advantages: Non-invasive, minimal respiratory depression, opioid-sparing, favorable recovery profile.

Lignocaine (Lidocaine)

Class: Amide local anesthetic[2]

Mechanism of action: Sodium channel blockade inhibits sensory nerve conduction → reduced airway reflexes[3]

Clinical effects: Blunts cough, gag reflex, and minor pressor response1

Dosing (nebulized): 2–4% solution, 3–5 ml

Advantages: Widely available, inexpensive, safe, effective for airway topicalization

Methods of Literature Synthesis: A literature search was conducted across PubMed, Scopus, Embase, and Google Scholar for studies published from 2010 to 2025.

The search strategy included the following keywords and Medical Subject Headings (MeSH) terms:"dexmedetomidine", "lignocaine", "lidocaine", "nebulization", "laryngoscopy", "endotracheal intubation", "pneumoperitoneum", and "hemodynamic response". These terms were combined using Boolean operators (AND, OR) to optimize sensitivity and specificity of the search. Reference lists of relevant articles were also manually screened to identify additional eligible studies.

Study Selection

Inclusion criteria

- RCTs, observational studies
- Adult and pediatric populations undergoing airway manipulation or laparoscopic surgery
- Interventions using nebulized dexmedetomidine, lignocaine, or their combination

Outcomes included heart rate (HR), blood pressure (SBP, DBP, MAP), sedation, procedural comfort, anesthetic requirements, recovery profile, and adverse events.

Exclusion criteria

- Non-English publications
- Case reports, editorials, or animal studies

Risk of Bias Assessment: The risk of bias of included studies was assessed qualitatively based on study design, sample size, randomization methods, allocation concealment, blinding, and completeness of outcome reporting.

Randomized controlled trials were considered to have a lower risk of bias compared to observational studies. Any potential sources of bias were carefully considered during data interpretation.

Data Extraction and Outcomes: Relevant data extracted from included studies

- Study characteristics (author, year, population)
- Intervention details (drug, dose, route)
- Outcome

The primary outcomes assessed were:

Hemodynamic parameters: heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP)

Secondary outcomes included:

- Sedation levels, Procedural comfort
- Anaesthetic requirements
- Recovery profile
- Adverse events

Comparative Evidence: Sumayya[6] E and colleagues (2025) conducted a study to compare the effectiveness of preoperative dexmedetomidine nebulization versus lignocaine nebulization in attenuating the stress response associated with direct laryngoscopy and endotracheal intubation in adult patients undergoing elective surgeries under general anesthesia. A total of 60 adult ASA I and II patients scheduled for elective surgery under general anesthesia were enrolled and randomly assigned into two equal groups.

Group D received dexmedetomidine 1 µg/kg diluted to 4 mL with normal saline, and Group L received 4 mL of 4% lignocaine, both administered via ultrasonic nebulizer 15 minutes prior to induction. Standard induction and intubation protocols were followed, and hemodynamic parameters heart rate, systolic blood pressure, diastolic blood pressure, and MAP were recorded at baseline, during induction, immediately post-intubation, and at 1, 3, 5, and 10 minutes thereafter. The rise in HR and MAP was minimal in the dexmedetomidine group, returning to baseline more rapidly. Additionally, patients receiving dexmedetomidine exhibited mild sedation and reduced anxiety without significant bradycardia or hypotension, while the lignocaine group demonstrated effective airway topicalization but comparatively higher sympathetic stimulation. No adverse effects such as oxygen desaturation, arrhythmia, or delayed recovery were reported in

either group. The authors concluded that preoperative dexmedetomidine nebulization is a safe, simple, and effective non-invasive method to attenuate hemodynamic stress responses during laryngoscopy and intubation.

Paul NS [7], Abraham V, Liddle D (2023) performed a randomized, double-blind trial in 100 ASA I–II adults to evaluate nebulized dexmedetomidine (1 $\mu g.kg^{-1}$) administered 15 minutes pre-induction versus saline for blunting haemodynamic response to laryngoscopy and improving intubation conditions. The investigators recorded HR, SBP, DBP and MAP at baseline, during laryngoscopy/intubation and at 1, 3, 5 and 10 minutes post-intubation; sedation and intubation quality were also scored. The dexmedetomidine group demonstrated statistically significant attenuation of HR and BP excursions (mean HR rise <10% vs ~20–25% in controls; $p<0.001$), superior intubating conditions (better jaw relaxation, less coughing), and no clinically relevant bradycardia or hypotension, with a significant reduction in intraoperative analgesic and sedative requirements. Nebulized dexmedetomidine is an effective, safe non-invasive premedication to blunt post-intubation sympathetic surge without prolonging recovery.

Shrivastava[8] P, Kumar M, Verma S, et al. (2022) conducted a prospective, randomized, double-blind, placebo-controlled study to evaluate the efficacy of nebulized dexmedetomidine in attenuating haemodynamic responses to laryngoscopy and tracheal intubation. The trial included 90 ASA I–II adult patients aged 18–50 years, scheduled for elective surgeries under general anaesthesia. Participants were randomly assigned into two equal groups: Group D received dexmedetomidine 1 $\mu g \cdot kg^{-1}$ diluted in 5 mL of normal saline via ultrasonic nebulizer over 10 minutes, 15 minutes before induction; Group C received nebulized saline of equal volume. Anaesthetic induction was standardized with fentanyl, propofol, and vecuronium to ensure uniformity. Haemodynamic parameters heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) were recorded at baseline, after nebulization, post-induction, immediately after laryngoscopy, and at 1, 3, 5, and 10 minutes post-intubation. The mean increase in HR and MAP in Group D was less than 10% above baseline, whereas Group C demonstrated increases of 20–25%. The incidence of tachycardia and hypertension was notably lower in the dexmedetomidine group & no clinically significant bradycardia, hypotension, or sedation was observed, and recovery times were comparable between groups. The authors concluded that nebulized dexmedetomidine 1 $\mu g.kg^{-1}$ effectively blunts the sympathetic pressor response to laryngoscopy and intubation while maintaining haemodynamic stability and avoiding excessive sedation.

In 2022, Gandhi[9] et al did a prospective comparative study compare effectiveness of nebulized dexmedetomidine and intravenous dexmedetomidine given preoperatively in blunting hemodynamic response (HR) to intubation.120 ASA I and II patient between 18 – 60 years undergoing elective surgeries under general anesthesia were randomized into two equal groups. Thirty minutes before induction, Group I received slow IV infusion dexmedetomidine 0.50 µg/kg (diluted with normal saline to 50 mL) and nebulization with 5 mL NS, while Group II 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, mean arterial pressure (MAP) and ramsay sedation scoring were done at different intervals until extubation. Study concluded with both IV dexmedetomidine and nebulized dexmedetomidine were comparable in reducing stress response to intubation and sedation, but incidence of hypotension is more with IV dexmeditomidine.

Bhaskar [10] V, Shetty SR, Rajaram P, Varmudy MK (2021) conducted a prospective, randomized, double-blind, comparative study to evaluate the efficacy of nebulized lignocaine versus intravenous lignocaine in attenuating the haemodynamic pressor response to laryngoscopy and tracheal intubation. The study enrolled 60 ASA I–II adult patients, aged 18–50 years, undergoing elective surgeries under general anaesthesia. Participants were randomly allocated into two equal groups (n=30 each): Group N received nebulized lignocaine 4% (3 mL; approximately 120 mg) administered via ultrasonic nebulizer 15 minutes before induction, and Group I received intravenous lignocaine 1.5 $mg \cdot kg^{-1}$ administered three minutes before laryngoscopy. Anaesthetic induction was standardized with fentanyl 2 $\mu g \cdot kg^{-1}$, propofol 2 $mg \cdot kg^{-1}$, and vecuronium 0.1 $mg \cdot kg^{-1}$, followed by intubation using the same operator to minimize bias. Haemodynamic variables heart rate (HR), systolic (SBP), diastolic (DBP), and mean arterial pressure (MAP) were recorded at baseline, post-induction, immediately after laryngoscopy, and at 1, 3, and 5 minutes post-intubation. The results demonstrated that both routes of lignocaine administration effectively attenuated haemodynamic surges following laryngoscopy and intubation, but nebulized lignocaine provided smoother and more sustained control of HR and MAP with minimal fluctuations. Peak increases in HR and MAP were significantly lower in the nebulized group (average 10–12% rise from baseline) compared with the intravenous group (18–22% rise; $p<0.05$). HR and MAP returned to baseline by the third minute in Group N. The study hypothesized that nebulized lignocaine provides a dual mechanism of action:

direct topical anaesthesia of upper airway mucosa reducing afferent stimulation, and limited systemic absorption producing mild central sympatholysis. Nebulization also offered a needle-free, patient-friendly route, enhancing patient acceptance particularly relevant for day-care or short-duration procedures. The study concluded that nebulized lignocaine (4%) is an equally effective and potentially superior alternative to intravenous lignocaine.

In 2021, Varun[11] et Al did a study to evaluate if neb lignocaine can attenuate hemodynamic responses to intubation. 40 patients were enrolled for the study and randomly allocated into one of two groups, Group I (nebulised lignocaine) and Group II (IV lignocaine). Group I and Group II received nebulisation respectively with 5 mL of 2% lignocaine or 5 mL of normal saline 15 min before shifting the patient to the operation theatre. The patient was then shifted to the operation theatre and was monitored. After preoxygenation, anaesthesia was induced with IV fentanyl 2 µg/kg and IV propofol 2 mg/kg. After confirming adequate mask ventilation, patients were paralysed with vecuronium 0.1 mg/kg. After 90 s, patients in the group I received 5 mL of saline intravenously while patients in group II received 5 mL of 2% lignocaine intravenously. Intubation was performed after 90. Anaesthesia was maintained with isoflurane in a gas:oxygen mixture. No additional agent/drug was given for the first 10 min post intubation nor was surgery allowed to start. The study period ended after 10 min. There was a statistically significant rise in SBP ($P = 0.003$), DBP ($P = 0.004$) and MAP ($P = 0.004$) post intubation in the IV lignocaine group as compared to the nebulised lignocaine group. They concluded with significant attenuation of haemodynamic responses to intubation was observed with nebulised lignocaine group as compared to IV lignocaine group.

In 2020, Priya ganesan [12] et al conducted a prospective comparative study to compare the efficacy of nebulized 2% lidocaine versus intravenous (IV) lignocaine in suppressing the pressor response to laryngoscopy and intubation.100 patients around the age group of 18 - 65 years undergoing elective surgery under general anesthesia were randomized into two groups. group I intravenous lignocaine (IVL) ($n = 50$) and group II nebulized lignocaine (NL) ($n = 50$). Baseline values (HR 82+2,80+1; SBP 96+2, 94+3; in group I & II respectively) were noted. HR, saturation, BP, MAP, and arrhythmias were noted every minute from laryngoscopy up to 5 min post laryngoscopy and intubation. Immediately post intubation HR 90+3, 84+2; SBP 105+3, 99+2 in group I & II respectively. Within two minutes post-intubation, nebulized lignocaine significantly blunted the pressor response, and by four minutes, HR and BP values fell below baseline levels. study concluded suggesting neb lignocaine is more effective than iv lignocaine suppressing the pressor response to laryngoscopy and intubation.

Niyogi [13] *et al.* (2019) conducted a prospective, randomized, double-blind, comparative study including 90 ASA I–II adult patients, aged 18–60 years, randomly allocated into three groups of 30 each: Group IV-D received dexmedetomidine 1 $\mu g \cdot kg^{-1}$ intravenously over 10 minutes before induction, Group IN-D received dexmedetomidine 1 $\mu g \cdot kg^{-1}$ intranasally (using an atomizer) 40 minutes before induction, Group C received normal saline. All patients were premedicated uniformly, and anaesthesia was induced with fentanyl, propofol, and vecuronium, followed by tracheal intubation. Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) were recorded at baseline, post-study drug administration, after induction, and at 1, 3, 5, and 10 minutes following intubation. Results demonstrated that intranasal route produced a comparable attenuation to intravenous dosing, though with a slightly delayed onset due to slower absorption. In the IV group, the mean HR and MAP rose only 5–7% above baseline, whereas the intranasal group showed an 8–10% increase, both substantially lower than the 25–30% surges seen in controls. Additionally, patients receiving intranasal dexmedetomidine exhibited mild sedation and anxiolysis preoperatively without respiratory depression or excessive drowsiness. The incidence of bradycardia was slightly higher in the IV group but clinically insignificant. The authors concluded that intranasal dexmedetomidine (1 $\mu g \cdot kg^{-1}$) is a safe, non-invasive, and effective alternative to intravenous administration for attenuating sympathetic responses to airway instrumentation.

Gulabani [14] M et al. (2015) compared dexmedetomidine (0.5 $\mu g \cdot kg^{-1}$ and 1 $\mu g \cdot kg^{-1}$) against lignocaine 1.5 $mg \cdot kg^{-1}$ in attenuating haemodynamic responses to laryngoscopy and endotracheal intubation. This randomized study demonstrated a dose-response for dexmedetomidine: 1 $\mu g \cdot kg^{-1}$ dose produced the most consistent suppression of HR and MAP increases, outperforming both the lower dexmedetomidine dose and lignocaine. The authors found fewer excursions in SBP/DBP and HR with dexmedetomidine 1 $\mu g \cdot kg^{-1}$ (statistically significant differences), suggesting that systemic α_2-agonism provides a more robust sympatholytic effect than topical/local anesthetic alone. Strengths of the study include the multi-arm design that allowed direct intra-study dose comparison and facilitated objective evaluation against lignocaine as the standard control. However, limitations include its focus exclusively on airway-induced pressor responses rather than intra-abdominal stressors such

as CO_2 pneumoperitoneum, which involve additional neurohumoral pathways. Nonetheless, the study provides quantitative evidence that dexmedetomidine particularly at 1 μg·kg⁻¹ offers more robust hemodynamic stability than lignocaine by attenuating the catecholamine surge associated with laryngoscopy. These findings strengthen the rationale for choosing systemic α_2-agonists, including dexmedetomidine delivered intravenously or via mucosal absorption, when the primary clinical goal is tight control of peri-intubation hemodynamic fluctuations.

Dubey [15] *et al.* (2024), in a recent systematic review and network meta-analysis published in *BJA Anaesthesia*, synthesized randomized evidence assessing both intraperitoneal local anesthetic (IPLA) techniques and α_2-adrenergic agonist strategies for laparoscopic abdominal surgery demonstrating IPLA whether delivered as a bolus, nebulized intraperitoneally, or via continuous instillation consistently reduced postoperative pain and opioid consumption, with nebulized or continuous forms showing more pronounced benefits in early postoperative pain scores. However, when evaluating intraoperative hemodynamic stability, anesthetic sparing, and opioid-sparing effects, α_2-agonists such as dexmedetomidine (administered systemically or via mucosal routes, including nebulization) produced larger and more uniform effects across studies. The network meta-analytic framework allowed indirect comparisons across diverse regimens, revealing that α_2-agonists ranked highest for attenuation of pneumoperitoneum-related sympathetic surges. Clinically, the analysis reinforces that while IPLA is valuable for analgesia after laparoscopy, α_2-agonist strategies (including nebulized dexmedetomidine) are preferable when the research or clinical aim is robust intraoperative haemodynamic control.

In 2022, Kantharaju [16] Shankar et al conducted a prospective double-blind study to compare and evaluate efficacy of nebulized dexmedetomidine with intravenous dexmedetomidine and fentanyl in laparoscopic surgeries to provide hemodynamic stability following intubation and pneumoperitoneum. 90 patients who were ASA I & II aged between 18 – 65 years of either gender undergoing laparoscopic surgeries under general anesthesia were randomly separated into 3 groups with 30 patients in each. Group I received neb dexmedetomidine 1mcg/kg in 3ml of 0.9% saline for 15 mins before induction & 10ml intravenous 0.9% saline over 10 mins during induction, group II received 0.9% neb saline before induction & intravenous dexmedetomidine 1mcg/kg in 10ml 0.9% saline during induction, group III received 3ml 0.9% neb saline and iv fentanyl 2mcg/kg. Base line parameters noted HR 83.67 ± 8.58, 83.07 ± 9.02, 83.83 ± 8.69; SBP 125.97 ± 9.40, 126.37 ± 9.18, 127.73 ± 8.16 in group I, II & III respectively. They noticed significant drop in HR and SBP after administration of intravenous dexmedetomidine when compared to nebulized dexmedetomidine and intravenous fentanyl, post pneumoperitoneum HR 79.93+8.31, 64.30+5.06, 79.93+8.31; SBP 125.10 ± 8.16, 121.43 ± 10.00, 131.73 ± 6.55 in group I, II & III respectively. another drop in SBP after pneumoperitonium, group I (120.23 ± 12.83) group II (116.93 ± 12.20) group III (131.23 ± 7.95). The study showed hemodynamic response suppression with neb dexmedetomedine was better than iv fentanyl and iv dexmedetomedine. Using neb dexmedetomedine reduces opioid and propofol requirement than fentanyl group but not iv dexmedomedine.1 Total fentanyl used group I (58.00 ± 14.25) group II (13.33 ± 17.49) group III (123.27 ± 15.00), Propofol requirement group I (76.67 ± 14.46) group II (73.80 ± 9.18) group III (86.80 ± 10.49). The authors reported that nebulized dexmedetomidine achieved clinically meaningful attenuation of the pressor response to pneumoperitoneum while producing fewer episodes of bradycardia and hypotension than the IV route; opioid and propofol requirements were reduced in both groups but were slightly lower with IV administration.

Kataria [17] and colleagues (2016) conducted a prospective, randomized, double-blind, controlled study comparing the hemodynamic effects of dexmedetomidine and fentanyl in attenuating pressor responses to laryngoscopy, intubation, and pneumoperitoneum in patients undergoing laparoscopic cholecystectomy under general anesthesia. A total of 60 ASA I–II adult patients, aged 18–60 years, were randomly divided into two groups (n=30 each) - Group D (Dexmedetomidine group): received dexmedetomidine 1 μg·kg⁻¹ infused over 10 minutes before induction. Group F (Fentanyl group): received fentanyl 2 μg·kg⁻¹. Standardized general anesthesia was induced with thiopentone and vecuronium, followed by maintenance with isoflurane, nitrous oxide, and oxygen. Hemodynamic parameters heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) were recorded at baseline, during laryngoscopy and intubation, throughout pneumoperitoneum, and post-extubation. Results revealed that dexmedetomidine significantly blunted the pressor response at all stages during laryngoscopy, intubation, and throughout pneumoperitoneum compared with fentanyl ($p < 0.05$). In the dexmedetomidine group, HR and MAP remained within 10% of baseline, demonstrating effective attenuation of the sympathetic surge & provided better intraoperative hemodynamic stability, lower anesthetic and opioid requirements, and smoother emergence from anesthesia. Sedation scores were higher in the dexmedetomidine group, but without

clinically significant bradycardia or hypotension requiring intervention. The study concluded that intravenous dexmedetomidine is superior to fentanyl in controlling the pressor responses associated with laryngoscopy and pneumoperitoneum, offering stable intraoperative hemodynamics, reduced stress response, and opioid-sparing effects.

Kumar [18] S, Kushwaha B, Prakash B, Jafa S, Malik A (2014) conducted a prospective, randomized, double-blind, comparative clinical trial to evaluate and compare the effects of dexmedetomidine and clonidine premedication on perioperative haemodynamic stability and postoperative analgesia in patients undergoing laparoscopic cholecystectomy. The study enrolled 90 ASA I–II adult patients, aged 18–55 years, scheduled for elective laparoscopic cholecystectomy under general anaesthesia. Subjects were randomly assigned into three equal groups (n=30 each): Group D received dexmedetomidine 1 $\mu g \cdot kg^{-1}$ IV diluted in 10 mL of saline over 10 minutes before induction; Group C received clonidine 2 $\mu g \cdot kg^{-1}$ IV in 10 mL saline over the same duration; and Group N received normal saline as control. Anaesthetic induction was standardized using fentanyl, propofol, and vecuronium, followed by maintenance with oxygen, nitrous oxide, and isoflurane. Haemodynamic variables heart rate (HR), systolic (SBP), diastolic (DBP), and mean arterial pressure (MAP) were recorded at baseline, after study drug infusion, after induction, following laryngoscopy, and at intervals during pneumoperitoneum and recovery.

Postoperative pain was assessed using the visual analogue scale (VAS), and total rescue analgesic consumption in the first 24 hours was recorded. The results demonstrated that both dexmedetomidine and clonidine significantly attenuated the pressor and tachycardic responses to laryngoscopy, intubation, and pneumoperitoneum compared with placebo. However, dexmedetomidine produced a greater degree of haemodynamic stability, with smaller rises in HR and MAP during CO_2 insufflation (average <10% above baseline versus 15–20% with clonidine and >25% in controls) with reduced intraoperative isoflurane and fentanyl requirements and longer postoperative analgesia duration post-extubation. Mild intraoperative bradycardia was noted in a few patients but responded easily to atropine. No significant hypotension or delayed emergence occurred. The authors concluded that dexmedetomidine is superior to clonidine in providing perioperative haemodynamic stability, reducing anaesthetic and analgesic requirements, and prolonging postoperative pain relief in laparoscopic cholecystectomy.

Bhattacharjee [19] DP, Nayek SK, Dawn S, Bandopadhyay G, Gupta K (2010) performed prospective, randomized, double-blind trial assessing the effects of dexmedetomidine on perioperative haemodynamics in patients undergoing laparoscopic cholecystectomy. The study included 60 ASA I–II adult patients aged 20–50 years, randomly assigned into two groups of 30 each: Group D received dexmedetomidine 1 $\mu g \cdot kg^{-1}$ IV as a loading dose over 10 minutes before induction, followed by 0.5 $\mu g \cdot kg^{-1} \cdot h^{-1}$ infusion until 10 minutes after pneumoperitoneum, while Group C (control) received an equal volume of normal saline. Standardized anaesthetic technique was followed with fentanyl, propofol, and vecuronium for induction and maintenance with isoflurane in oxygen–nitrous oxide mixture. Haemodynamic variables heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) were continuously monitored at baseline, after drug infusion, post-induction, after intubation, during pneumoperitoneum (at 5, 10, and 20 minutes), and after desufflation. The study found that dexmedetomidine effectively blunted the sympathetic and pressor responses associated with both intubation and pneumoperitoneum. In the dexmedetomidine group, HR and MAP remained within 10% of baseline values, whereas in the control group, increases up to 25–30% were observed during CO_2 insufflation ($p < 0.001$). The dexmedetomidine group also showed reduced intraoperative isoflurane requirement and a smoother emergence profile with lower postoperative pain scores during the first 2 hours. Although mild bradycardia and hypotension occurred in a few patients, these were transient and easily managed without sequelae. The authors concluded that dexmedetomidine is highly effective in maintaining haemodynamic stability during laparoscopic cholecystectomy.

Priyadarshini [20], Anjali and colleagues (2025) did a randomized comparative study to evaluate efficacy and safety of combining nebulized dexmedetomidine with lignocaine versus lignocaine alone as premedication for flexible fiber-optic bronchoscopy (FOB) under sedation. The study included 60 adult patients (ASA I–II) scheduled for elective bronchoscopy under sedation. Participants were randomly assigned into two groups - Group DL: received nebulized dexmedetomidine (1 µg/kg) combined with 4 mL of 4% lignocaine, Group L: received 4 mL of 4% lignocaine nebulization alone. Nebulization was administered 15 minutes before the procedure. Standard premedication and sedation protocols were followed using midazolam and fentanyl, and topical lignocaine spray was applied during bronchoscope insertion. Hemodynamic parameters heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) were recorded at baseline, post-nebulization, at bronchoscope insertion, and

throughout the procedure. Patient tolerance, coughing, oxygen saturation, and procedural conditions were assessed using standardized scoring systems. Results demonstrated that Group DL (dexmedetomidine + lignocaine) had significantly attenuated increases in HR, SBP, and MAP during scope insertion and manipulation compared to Group L (lignocaine alone) ($p < 0.01$). Moreover, the combined group exhibited lower cough frequency, better patient comfort, and fewer procedural interruptions. Sedation was adequate but not excessive, and oxygen saturation remained stable in both groups. Importantly, no cases of bradycardia, hypotension, or desaturation requiring intervention were reported. Recovery time and discharge readiness were comparable across both groups. The authors concluded that nebulized dexmedetomidine with lignocaine provides superior attenuation of hemodynamic responses, enhances airway comfort, and improves procedural quality during flexible bronchoscopy without compromising safety or prolonging recovery.

Dhooria [21] S et al. (2020) undertook a large randomized trial comparing modes of delivering topical lignocaine for flexible bronchoscopy nebulized lignocaine, oropharyngeal spray, or combination enrolling over 1000 subjects across arms. Although carried out in the context of bronchoscopy rather than surgical pneumoperitoneum, this high-quality multicentre study provides strong evidence regarding the efficacy and limitations of nebulized lignocaine as an airway topicalizing modality.

The authors reported that nebulized lignocaine alone offered minimal incremental benefit over oropharyngeal spray in terms of cough suppression, procedural tolerance, and patient comfort but the study does not address hemodynamic modulation at abdominal insufflation. Study states that while nebulized lignocaine provides effective airway surface anesthesia, its ability to blunt systemic hemodynamic responses remains modest and inconsistent.

Kumar [22] and colleagues (2020) performed a prospective, randomized, double-blind, controlled study to compare the efficacy and safety of 4% versus 2% nebulized lignocaine for airway anesthesia during awake fiberoptic nasotracheal intubation in patients undergoing maxillofacial surgeries. A total of 60 adult patients (ASA I–II), aged between 20 and 50 years, were randomly allocated into two groups ($n = 30$ each) - Group A - 2% nebulized lignocaine, total dose 4 $mg \cdot kg^{-1}$. Group B - 4% nebulized lignocaine, total dose 4 $mg \cdot kg^{-1}$. Nebulization was administered for 10 minutes using a standard ultrasonic nebulizer. Sedation was achieved with dexmedetomidine infusion at 1 $\mu g \cdot kg^{-1}$ over 10 minutes, followed by maintenance at 0.2–0.5 $\mu g \cdot kg^{-1} \cdot h^{-1}$. The primary outcomes included quality of airway anesthesia (assessed by cough, gag, and comfort scores), ease of fiberoptic intubation, and patient tolerance. Secondary outcomes included hemodynamic stability (HR, MAP), oxygen saturation, and plasma lignocaine levels to assess safety. Both groups maintained stable hemodynamics throughout the procedure, though transient increases in heart rate and MAP occurred during intubation, which were less pronounced in the 4% group. serum lignocaine concentrations remained well below toxic thresholds in both groups, confirming the safety of the higher concentration. The study concluded that 4% nebulized lignocaine, when administered within safe dosing limits, produces superior airway anesthesia and greater patient cooperation than 2% lignocaine during awake fiberoptic intubation, without compromising hemodynamic stability or safety.

Gu W [23], Xu M, Lu H, Huang Q, Wu J. (2019) performed a randomized, parallel-group clinical trial to evaluate the safety and efficacy of nebulized dexmedetomidine combined with lidocaine as a premedication for flexible bronchoscopy. A total of 90 adult patients were enrolled and divided into three groups: Group DL received dexmedetomidine 1 $\mu g \cdot kg^{-1}$ plus 2% lidocaine 3 mL via nebulization; Group L received nebulized lidocaine alone; and Group S received nebulized saline as control. All patients underwent standardized topical airway anaesthesia and conscious sedation for diagnostic bronchoscopy. Primary outcomes included patient comfort, sedation scores (Ramsay Sedation Scale), and cough severity, while secondary outcomes assessed haemodynamic stability, oxygen saturation, and procedural tolerance. The combined dexmedetomidine–lidocaine nebulization produced a statistically significant reduction in HR and MAP during the procedure compared to lidocaine alone or control ($p < 0.01$), with fewer episodes of tachycardia and hypertension - higher comfort and lower cough scores. The study concluded that nebulized dexmedetomidine–lidocaine is a safe, effective, and non-invasive premedication that improves airway tolerance and haemodynamic control during airway instrumentation.

Abdel-Ghaffar [24] and colleagues (2018) performed a prospective, randomized, double-blind controlled trial assessing and comparing nebulized dexmedetomidine, ketamine, and midazolam as premedication agents in preschool children scheduled for painful bone marrow biopsy procedures. The trial recruited 90 ASA I–II children aged 3–7 years, randomized equally into three groups - Group D: nebulized dexmedetomidine 2 $\mu g \cdot kg^{-1}$, Group K: nebulized ketamine 2 $mg \cdot kg^{-1}$, Group M: nebulized midazolam 0.2 $mg \cdot kg^{-1}$. Premedication was administered 30 minutes before induction of anesthesia. Primary outcomes included sedation level (using the Modified Observer's

Assessment of Alertness/Sedation scale) and ease of parental separation. Secondary measures evaluated mask acceptance, hemodynamic changes, recovery profile, and adverse events such as bradycardia, desaturation, or agitation. Results showed that onset of sedation was slightly slower in dexmedetomidine than in ketamine, but the quality of sedation was more natural and calm, avoiding the dysphoric reactions occasionally seen with ketamine or paradoxical agitation with midazolam. Hemodynamic parameters (heart rate, systolic and diastolic blood pressure) remained remarkably stable in the dexmedetomidine group, demonstrating effective attenuation of sympathetic tone. In contrast, ketamine produced mild tachycardia and hypertension, while midazolam showed minimal cardiovascular impact but poorer sedation quality. Recovery times were comparable among the groups, and no clinically significant adverse events or oxygen desaturation episodes occurred. The authors concluded that nebulized dexmedetomidine (2 $\mu g \cdot kg^{-1}$) is a safe, non-invasive, and effective alternative to injectable sedatives for pediatric premedication, offering excellent sedation and anxiolysis with minimal hemodynamic fluctuation.

Zanaty [25] and El Metainy (2015) conducted a prospective, randomized, double-blind clinical trial including 90 healthy children (ASA I–II) aged 2–8 years randomly allocated into three equal groups (n=30 each): Group D: received nebulized dexmedetomidine 2 $\mu g \cdot kg^{-1}$, Group K: received nebulized ketamine 2 $mg \cdot kg^{-1}$, Group DK: received a combination of dexmedetomidine 1 $\mu g \cdot kg^{-1}$ + ketamine 1 $mg \cdot kg^{-1}$. Nebulization was administered for 10 minutes, 30 minutes before induction. The primary outcomes assessed were sedation level (using the Ramsay Sedation Scale), ease of parental separation, and mask acceptance score. Secondary outcomes included haemodynamic stability, time to recovery, and adverse effects such as bradycardia, desaturation, or excessive salivation. Results demonstrated that all groups achieved satisfactory sedation and cooperation, but the combination group (DK) provided the optimal balance of sedation, anxiolysis, and stable haemodynamics.

Dexmedetomidine alone resulted in smoother sedation with minimal tachycardia or hypertension, whereas ketamine alone produced higher HR and BP due to its sympathomimetic effects. Notably, nebulized dexmedetomidine (Group D) maintained HR and MAP within 10% of baseline values, indicating effective central sympatholysis without cardiovascular depression. Recovery was faster in the dexmedetomidine and combination groups, and no respiratory depression or significant adverse effects were reported. The study concluded with nebulized dexmedetomidine (2 $\mu g \cdot kg^{-1}$) is a safe, non-invasive, and effective premedicant providing sedation, anxiolysis, and haemodynamic stability in paediatric outpatients validating nebulization as an efficient route for dexmedetomidine delivery, achieving reliable absorption through the pulmonary mucosa.

Table 1: Hemodynamic Attenuation during Laryngoscopy and Intubation

Study	Population	Intervention	Dose & Route	Outcome	Key Findings
Sumayya et al [6] 2025	60 ASA I-II adults	Neb Dex vs Neb Lignocaine	Dex 1 µg/kg, Lig 4% 4ml	HR, MAP	Dex: minimal HR/MAP rise; faster return to baseline; mild sedation Lignocaine: effective airway topicalization but higher sympathetic response
Paul et al[7] 2023	100 ASA I-II adults	Neb Dex vs Neb saline	Dex 1µg/kg	HR, MAP, SBP, DBP	Dex significantly attenuated HR and BP excursions, improved intubation conditions
Shrivastava et al[8] 2022	90 ASA I-II adults	Neb Dex vs Neb saline	Dex 1µg/kg	HR, MAP	Mean HR/MAP rise <10% in Dex vs 20-25% in controls
Gandhi et al [9] 2022	120 ASA I-II adults	IV Dex vs Neb Dex	Dex 0.5 µg/kg IV vs Dex 1µg/kg neb	HR, MAP	Neb Dex attenuated pressor response with fewer bradycardia/ hypotension episodes
Bhaskar et al [10] 2021	60 ASA I-II adults	Neb Lignocaine vs IV Lignocaine	Neb 4% 3ml vs IV 1.5mg/kg	HR, MAP	Neb Ligno: smoother more sustained HR/MAP control

Varun et al [11] 2021	40 ASA I-II adults	Neb 2% Lignocaine vs IV Lignocaine	Neb 2% 5ml vs IV 2%5ml	SBP, DBP, MAP	Neb Ligno blunted pressor response significantly than IV
Priya Ganesan et al [12] 2020	100 adults	Neb 2% Lignocaine vs IV Lignocaine	Neb 2% 5ml vs IV 1.5mg/kg	HR, MAP, SBP	Neb Ligno blunted pressor response faster than IV
Niyogi et al[13] 2019	90 ASA I-II adults	IV Dex vs Intra nasal Dex via atomizer	Dex 1 µg/kg IV vs Dex 1µg/kg IN	HR, SBP, DBP, MAP	Intra Nasal Dexis safe & effective alternative to IV Dex
Gulabani M et al[14] 2015	90 ASA I-II adults	IV Dex vs IV Dex vs IV Ligno	Dex 0.5 µg/kg IV over 10 mins vs Dex 1µg/kg over 10 mins IV vs Ligno 1.5mg/kg IV	HR, SBP, DBP	Dex 1 µg/kg IV was more effective than Dex 0.5 µg/kg IV and Ligno 1.5mg/kg IV in attenuating pressor response

Data derived from respective cited studies

Table 2:

Study	Population	Intervention	Dose & Route	Outcome	Findings
Dubey et al [15] 2024	Laparoscopic abdominal surgery	α2 agonists vs IPLA	Dex 1µg/kg over 10 mins IV followed by 0.2-0.7 µg/kg/hrmaintenance vsintraperitoneal bupivacaine 0.25% 20-30 ml	HR, MAP	Dex superior in attenuating pneumoperitoneum induced sympathetic surge
Kantharaju Shankar et al [16] 2022	90 ASA I-II adults	Neb Dex vs IV Dex vs IV Fentanyl	Dex 1µg/kg neb vs Dex 1µg/kg over 10 mins IV vs Fent2 µg/kgIV bolus	HR, SBP post pneumoperitoneum	Neb Dex attenuated pressor response with fewer bradycardia/ hypotension episodes
Kataria et al [17] 2016	60 ASA I-II adults	IV Dex vs IV Fentanyl	Dex 1µg/kg over 10 mins IV vs Fent 2 µg/kg IV bolus	HR, SBP, DBP, MAP	IV Dex is superior to fentanyl in controlling pressor response
Kumar et al [18] 2014	90 ASA I-II adults	IV Dex vs IV Clonidine vs IV saline	Dex 1µg/kg over 10 mins IV vs Clonidine2 µg/kg over 10 mins IV vs saline IV	HR, SBP, DBP, MAP	Dex is superior to Clonidine in providing perioperative hemodynamic stability
Bhattacharje e et al [19] 2010	60 adults	IV Dex vs saline	Dex 1µg/kg over 10 mins IV followed by 0.2-0.7 µg/kg/hr maintenance	HR, MAP, SBP	Dex maintained HR/MAP within 10% of baseline and reduced anesthetic requirement

Hemodynamic Modulation during Pneumoperitoneum

Data derived from respective cited studies

Table 3:

Study	Population	Intervention	Dose & Route	Outcome	Findings
Priyadharshini et al [20] 2025	60 adults, fiberoptic bronchoscopy	Neb Dex+Ligno vs Neb Ligno	Dex 1 µg/kg +Lig 2-4% 3-4ml vs Lig 2-4% 3-4ml	HR, MAP, SBP, cough, patient comfort	Combination therapy attenuated HR/MAP rise, reduced cough and improved patient comfort
Dhooria et al [21] 2020	Over 1000 subjects	Neb Lignocaine vs oropharyngeal lignocaine spray vs Neb Lignocaine+ oropharyngeal lignocaine spray	Neb 2.5ml 4% vs 10 puffs of 10% oropharyngeal spray vs Neb 2.5ml 4% + 2 puffs of 10% oropharyngeal spray	cough, patient comfort, over all procedure satisfaction	Study states Neb Ligno provides effective airway anesthesia but its ability to blunt systemic hemodynamic response remains modest
Kumar et al [22] 2020	60 adults, fiberoptic intubation ASA I-II	Neb Lignocaine 2% vs Neb Lignocaine 4%	Neb 2% 4 mg/kg vs Neb 4% 4 mg/kg over 10 mins. Both groups sedated with Dex infusion 1µg/kg bolus followed by 0.2-0.5µg/kg maintenance IV	HR, MAP, SBP, cough, patient comfort, oxygen saturation, plasma lignocaine levels	4% lignocaine neb is superior to 2% neb when within safe dosing limits providing superior airway anesthesia and great patient cooperation
Gu et al [23] 2019	90 adults, bronchoscopy	Neb Dex+Ligno vs Neb Ligno vs saline	Dex 1 µg/kg +Lig 2% 3-5 ml vs Dex 1 µg/kg	HR, MAP, sedation	Dex+Ligno provided better hemodynamic stability and higher procedural comfort

Nebulized Dexmedetomidine for Procedural Sedation

Data derived from respective cited studies

Table 4:

Study	Population	Intervention	Dose & Route	Outcome	Findings
Abdel Ghaffar et al [24] 2018	90 children, bone marrow biopsy	Neb Dex vs Neb Ketamine vs Neb Midazolam	Dex 2 µg/kg vs Ketamine 2-3 mg/kg vs Midazolam 0.5 mg/kg	HR, MAP, sedation	Neb Dex provided effective sedation, anxiolysis and minimal hemodynamic changes
Zanaty & El Metainy et al [25] 2015	90 children	Neb Dex vs Neb Ketamine vs Neb Dex+Ketamine	Dex 2 µg/kg vs Ketamine 2 mg/kg vs Dex 1 µg/kg vs Ketamine 1 mg/kg	HR, MAP, sedation	Dex alone maintained HR/MAP within 10% of baseline, combination therapy optimal for sedation and hemodynamic stability

Pediatric Sedation and Safety: Data derived from respective cited studies

Discussion

Clinical Efficacy: Nebulized dexmedetomidine consistently attenuates HR, SBP, DBP, and MAP during airway instrumentation and pneumoperitoneum [6,7,8,15,16]. Its sedative, analgesic, and anxiolytic properties contribute to procedural comfort, reduce catecholamine release, and minimize myocardial oxygen consumption[4]. Nebulized lignocaine, while highly effective in suppressing airway reflexes and cough, provides only modest systemic hemodynamic control [5,10,12]. Combination therapy (Dex + Lign) has emerged as an optimal strategy for high-risk patients, producing additive benefits without significant adverse effects [20,23].

Safety Profile

1. Dexmedetomidine: Rare bradycardia or hypotension; minimal respiratory depression [2,4]
2. Lignocaine: Generally well-tolerated; risk of local anesthesia toxicity if dosing exceeds recommended limits [1,3]
3. Nebulization route: Slower systemic absorption reduces peak plasma concentrations and systemic adverse events [13]

Advantages over IV Administration

Nebulized delivery

- avoids IV access complications
- reduces peak plasma levels[13]
- provides concurrent airway topicalization[3,21]

This is particularly advantageous in pediatric, anxious, or needle-phobic patients.

Limitations of Current Evidence

- Heterogeneity in dosing, patient populations, and nebulization techniques
- Limited large-scale, multicenter RCTs directly comparing nebulized dexmedetomidine with IV α_2-agonists
- Short-term outcome measures; long-term postoperative outcomes are not well studied.

Conclusion

Nebulized dexmedetomidine offers superior attenuation of sympathetic responses during airway instrumentation and pneumoperitoneum compared with nebulized lignocaine. Its safety, non-invasive administration, and sedative-anxiolytic effects make it an attractive option for adult and pediatric populations. Nebulized lignocaine remains effective for airway topical anesthesia, and combination therapy may further optimize procedural tolerance and hemodynamic stability. These findings support its role as an effective non-invasive premedication strategy in modern anesthetic practice.

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