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Comparison of intravenous nalbuphine and dexmedetomidine in combination with lidocaine aerosol inhalation in awake direct laryngoscopy: a randomized, double-blind, placebo-controlled trial

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Abstract

Background The airway should be thoroughly and accurately evaluated before anesthesia induction and endotracheal intubation. Awake direct laryngoscopy (ADL) can provide rapid, accurate, and intuitive airway assessment, especially for suspected difficult airways, and sometimes eliminates the need for fiberoptic intubation in some suspicious difficult airway cases. However, an optimal regimen has not been determined.

Methods In this double-blind, controlled study, prior to ADL, 60 patients scheduled for general anesthesia were randomly allocated to receive 0.75 μg/kg of dexmedetomidine (Dex group, $n=20$), 0.15 mg/kg of nalbuphine (Nal group, $n=20$), or a placebo (control group, $n=20$) intravenously over 10 min. At the same time, all study subjects received nebulized lidocaine for 15 min. The primary outcome was patient tolerance as assessed by a 5-point ADL comfort score, while secondary outcomes included satisfaction, coughing, pain, nausea and vital signs.

Results Patients undergoing ADL in the Nal group had higher tolerance scores than those in the control and Dex groups [4 (3,4) vs. 3 (2,2.75), $P<0.017$, and 4 (3,4) vs. 2 (2,2,75), $P<0.001$, respectively] and higher satisfaction [7 (6,8) vs. 4 (3,5.75), $P<0.017$, and 7 (6,8) vs. 5.5 (5,6), $P<0.001$, respectively]. Additionally, the Nal group had significantly fewer adverse events, such as pain and nausea than the control and Dex groups. The sedation score and peripheral oxygen and saturation were significantly higher in the Nal group than in the Dex group, with no difference between the Nal and control groups ($P<0.001$, $P=0.159$, respectively).

Conclusions Intravenous nalbuphine in combination with lidocaine aerosol inhalation significantly improved patient tolerance and satisfaction while reducing nausea, coughing, pain, sedation, and SpO_2 levels during ADL.

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Highlights

- Awake direct laryngoscopy (ADL) allows rapid and accurate assessment of suspicious airways prior to the induction of anesthesia.
- The combination of nalbuphine and lidocaine resulted in higher tolerability, comfort, and satisfaction than dexmedetomidine combined with lidocaine or lidocaine alone during ADL.
- Nalbuphine combined with lidocaine could be safer than dexmedetomidine combined with lidocaine in terms of maintaining higher SpO_2 levels and reducing the risk of loss of consciousness during anesthesia.

Keywords Dexmedetomidine, Nalbuphine, Lidocaine, Awake direct laryngoscopy

Introduction

Difficult airway management is one of the most challenging tasks in anesthesia (Gómez-Ríos et al. 2024). Before anesthesia induction and endotracheal intubation, adequate and accurate airway assessment is required (Ahmad et al. 2020; Marchis et al. 2024). Awake direct laryngoscopy (ADL) allows for visualization of the larynx and provides valuable information about airway anatomy, which helps determines how the airway will be secured during airway establishment (Moorthy et al. 2005; Takaishi et al. 2021). For patients with suspected difficult airway, awake laryngoscopy can directly and accurately assess intubation conditions. The ability to safely assess a patient using awake direct laryngoscopy can eliminates the need for fiberoptic intubation in some suspicious difficult airway cases and provides valuable information about the ability to visualize the larynx through simple direct laryngoscopy during airway establishment (Johnson et al. 2002). ADL can be performed using topical anesthesia, nerve block anesthesia, or intravenous anesthesia. However, topical and nerve block anesthesia require longer procedure times and may not effectively suppress unpleasant reactions (Takaishi et al. 2021; Sitzman et al. 1997), while intravenous anesthesia carries the risk of excessive sedation and respiratory depression (Peterson et al. 2023). Therefore, it is necessary to establish a simpler, more rapid, and more comfortable procedure for laryngoscopy in awake patients.

Laryngoscopy and tracheal intubation are both intensively stimulating but usually brief procedures. Successful awake laryngoscopy in a patient with a potentially difficult airway necessitates both the blunting of airway reflexes and the maintenance of oxygenation and ventilation (Gómez-Ríos et al. 2024). Traditional lidocaine spray was initially used as a topical anesthetic for ADL, but it is prone to causing discomfort and hemodynamic disturbances (Sitzman et al. 1997). In 2002, Ken et al. used intravenous anesthetics, such as midazolam and remifentanil, for ADL.

However, the procedure could not eliminate the risk of excessive sedation and hypoxemia (Johnson et al. 2002). Dexmedetomidine is now strongly recommended for awake tracheal intubation (Ahmad et al. 2020; Chen et al. 2024). It is an alpha 2-adrenoceptor agonist with sedative, anxiolytic, sympatholytic, and analgesic-sparing effects, with minimal respiratory function depression (Guo et al. 2023). It is currently strongly recommended for conscious endotracheal intubation (Ahmad et al. 2020). Additionally, nalbuphine, a synthetic opioid, is a non-controlled opioid analgesic commonly used to treat mild-to-severe pain. Nalbuphine effectively reduces the tachycardia, hypertension, and cardiac workload caused by laryngoscopy and endotracheal intubation (Shah and Sen 2024). Our team was the first report that nalbuphine could be used to reduce cough frequency and intensity (Wang et al. 2020). However, the use of dexmedetomidine and nalbuphine in awake laryngoscopy has not been reported. Considering all the above factors, we designed a double-blind, randomized, controlled study to compare intravenous nalbuphine and dexmedetomidine in combination with lidocaine aerosol inhalation during ADL with respect to tolerance, satisfaction and safety.

In this study, we hypothesize that the combination of lidocaine nebulization and intravenous nalbuphine is superior to dexmedetomidine and lidocaine alone for performing awake laryngeal endoscopy on patients. The patients were adults aged 18-65 years, classified as ASA I or II, undergoing elective surgery under general anesthesia. We designed a double-blind, randomized, controlled study to compare intravenous nalbuphine, dexmedetomidine and placebo in combination with lidocaine aerosol inhalation during ADL in adult patients undergoing elective surgery under general anesthesia. The primary outcome was patient tolerance during awake direct laryngoscopy and secondary outcomes included patient satisfaction, the incidence of coughing, pain, nausea, and changes in vital signs.

Methods

Study design

This randomized controlled, parallel-group study was conducted at the First Affiliated Hospital of Anhui Medical University, Hefei, China, from August 2022 to August 2023, and adheres to the applicable Consolidated Standards of Reporting Trials (CONSORT) guidelines for conducting and reporting clinical trials. Ethical approval was obtained from the Ethics Committee (PJ2022-06-56). This study was registered at the Chinese Clinical Registry Center (No. ChiCTR2200062116, https://www.chictr.org.cn/bin/project/edit?pid=168097, principal investigator: Yuanhai Li, date of registration: July 23, 2022) before the commencement of the study. All participants provided written informed consent. We informed patients that the study would not pose significant risks, though some discomfort could occur, and they were free to stop the procedure or not answer specific questions at any time. Patients were also made aware of their right to withdraw at any point without any impact on their medical care. Additionally, they were informed about alternative treatment options, including the choice of standard general anesthesia, which would not affect their overall medical treatment. We ensured clear communication to alleviate concerns and assured patients that they could pause the study at any time.

Inclusion criteria were as follows: patients between the ages of 18 and 65 years, with American Society of Anesthesiologists (ASA) physical status classes I and II, Mallampati-Samsoon upper airway classes 1 and 2, and scheduled for elective surgery under general anesthesia. Exclusion criteria were as follows: patients with severe cardiovascular and cerebrovascular diseases, suspected difficulty in mask ventilation, severe respiratory diseases, a history of related drug allergy, coagulation dysfunctions, a history of mental illness, self-reported nervousness and anxiety, or a history of susceptibility to nausea were excluded from this study.

Randomization and masking

A random allocation sequence was generated by a researcher. An anesthesiologist who was not involved in the study placed the patients' codes sequentially into sealed and opaque envelopes. A researcher who was not in charge of patient care opened each envelope at the time of randomization. Another anesthesiologist, who was not otherwise involved in patient care, prepared the study drugs. There was no visible difference (same color, transparency, and turbidity) between the syringes of nalbuphine, dexmedetomidine. The syringes were labeled "study drug" and hand-delivered to the anesthesia team by the clinical research nurse.

Conduct of the study

Patients were randomly assigned to one of three ADL methods. The Dex group received a total dose of dexmedetomidine (0.75 μg/kg) infused for 10 min. The Nal group received nalbuphine (0.15 mg/kg) infused over 10 min. The control group received 0.9% saline solution infused over 10 min. At the same time, all patients in the three groups received airway anesthesia using nebulized lidocaine administered via a nebulizer with 10 ml of 2% lidocaine for 15 min and an oxygen flow of 5 L/min.

Upon arrival in the operating room, all patients' vital signs were continuously monitored and recorded. Patients were then treated with one of the three different drug administration methods described above. The study subjects underwent ADL five minutes after the intravenous infusion was completed, which was immediately after atomization inhalation was finished. The degree of glottis exposure was recorded by the same anesthesiologist The ADL procedures were performed by a single senior anesthesiologist with extensive clinical experience as an attending physician in anesthesia, in order to minimize variability and potential bias. This clinician used a UE visual laryngoscope, which is a direct non-flexible visual laryngoscope, to expose the glottis as much as possible. In addition, many indicators were recorded by another anesthesiologist, including tolerance, nausea, coughing, pain, and depth of sedation during laryngoscopy, and patient satisfaction after surgery. In the event of a loss of consciousness with poor oxygenation, emergency airway equipment, including a facemask and bag, a laryngeal mask airway, oral and nasopharyngeal airways, and a transtracheal jet ventilator, was immediately available. All procedures and assessments related to this study were completed prior to the surgery. After a brief period of rest, patients were transferred for the induction of general anesthesia and the subsequent surgical procedures.

General anesthesia was induced with midazolam (0.02 mg/kg, approximately), etomidate (0.3 mg/kg, approximately), sufentanil (0.4 ug/kg, approximately), and cisatracurium (0.2-0.4 mg/kg). Maintenance included propofol (4-6 mg/kg/h) and remifentanil (0.1-0.2 μg/kg/min), with cisatracurium administered every 40-60 min for muscle relaxation. Anesthetic depth was monitored using BIS, adjusting the propofol infusion to maintain a BIS value of 45-55. Remifentanil infusion was adjusted to maintain mean arterial pressure and heart rate within ± 20% of baseline. For postoperative pain, 0.2 μg/kg of sufentanil was given 30 min before surgery ended.

Assessment method

Tolerance assessment: patient tolerance was graded using a 5-point comfort score, with 5 indicating no reaction, 4 indicating slight grimacing, 3 indicating heavy grimacing,

2 indicating verbal objection, and 1 indicating defensive movement of the head or hands (Tsai et al. 2010).

Satisfaction assessment: patient satisfaction was assessed after ADL. The patients rated their ADL experience on a visual analogue scale of 0-10, with 0 representing 'extremely dissatisfied' and 10 representing 'extremely satisfied (Hanna et al. 2017; Sindhvananda et al. 2004).

Depth of sedation assessment: following medication, the patient's depth of sedation prior to laryngoscopy was graded using the Richmond Agitation-Sedation Scale (RASS), with 0 indicating alert and calm; −1 indicating drowsy, not fully alert but having sustained awakening for more than 10 s with eye contact to voice; −2 indicating light sedation, briefly awakens with eye contact to voice in less than 10 s; −3 indicating moderate sedation with any movement but no eye contact to voice; −4 indicating deep sedation with no response to voice but any movement in response to physical stimulation; and −5 indicating unarousable with no response to voice or physical stimulation (Otani et al. 2024).

Laryngoscopic exposure grading score: ADL glottis exposure was graded using the Cormack-Lehane (C-L) grading method as 1 for a full view of the glottis, 2 for a partial view of the glottis or arytenoids (glottis was observed with gentle pressure on the larynx), 3 for the only epiglottis being visible, and 4 for neither the glottis nor the epiglottis being visible (Won et al. 2024).

Cough severity scale: the severity of the patient's cough was graded as "no cough" (0 points), a mild cough (an intermittent cough of 1 to 3 sounds; 1 point), a moderate cough (an intermittent cough of 5 to 6 sounds; 2 points), and a severe cough (a more obvious cough of 7 to 8 sounds; 3 points).

Pain degree assessment: the visual analog pain scale (VAS) was used to grade patient pain, with 0 indicating "no pain" and 10 indicating "extreme pain."

Nausea rating scale:Patients were provided with a standardized diary to record severity of nausea using an 11-point numerical rating scale (with 0 = "no nausea" and 10 = "worst nausea imaginable") (Hyman et al. 2020). The nausea rating scale was assessed after ADL.

Statistical analysis

The sample size was estimated using PASS software, version 15. According to our preliminary experiment study, the tolerance scores for the control, Dex, and Nal groups were 2.1 ± 0.7, 2.7 ± 1, and 3.7 ± 1.5, respectively, with a sample size of 18 patients per group at a power of 80% and a two-tailed α-error of 5%. Given a 10% sample loss rate, the sample size of this study was increased to 20 patients in each group.

All data were collected using Excel software (Microsoft Corporation, USA) and analyzed using the Statistical Package for the Social Sciences, version 25.0 (IBM Corporation, USA). The Shapiro-Wilk test was used to determine the normality of the data distribution. When the test results indicated that the data were normally distributed, the data were described using the mean and standard deviation (mean ± SD) and analyzed using one-way analysis of variance (ANOVA) to compare groupwise differences in outcome parameters, such as age, body mass index (BMI), baseline mean arterial pressure (MAP), baseline heart rate (HR), and baseline peripheral oxygen saturation by pulse oximetry (SpO_2). Continuous data with a nonparametric dispersion were described using the median and interquartile range (IQR) and analyzed using the Kruskal-Wallis test to compare the groupwise differences in C-L scores. Repeated measures ANOVA was used to compare groupwise differences in MAP, HR, and SpO_2 at T0, T1, T2, and T3. For the tolerance, satisfaction, pain, nausea, coughing, and sedation scores, if the homogeneity of variance test was satisfied, one-way ANOVA was used for group comparisons, and the least significant difference test was used for pairwise comparisons. If the homogeneity of variance requirement was not met, the Welch test was used for group comparison, and the Games-Howell test was used for pairwise comparisons. The chi-square test was used to examine the relationship between qualitative variables and independent samples (ASA I/II). A P value less than 0.05 was considered statistically significant, except for pairwise between-group comparisons. For the multiple comparisons (each group versus each other group = 3 comparisons), a Bonferroni-corrected significance level of 0.05/3 = 0.017 was used.

Results

Sixty patients were enrolled in the study. Figure 1 depicts the Consolidated Standards of Reporting Trials (CONSORT) flow diagram showing patient progression through the study phases. There were no significant differences among the three groups in terms of demographic data and baseline vital signs (age, BMI, ASA, MAP, HR, etc.), duration of surgery, or duration of anesthesia (Table 1).

There was no significant difference in MAP among the three groups ($P = 0.578$).. However, HR and SpO_2 levels differed between the Nal, Dex and control groups, with the Dex group having a slower HR and lower SpO_2 levels than the control and Nal groups. There was no significant difference between the control and Nal groups ($P = 0.09$ and $P = 0.093$, respectively) (Fig. 2).

Tolerance scores after ADL increased significantly more in the Nal group than in the control and Dex groups [4 (3, 4) vs. 3 (2, 2.75), $P < 0.017$, and 4 (3, 4) vs. 2 (2, 2.75), $P < 0.001$, respectively] and significantly more in the Dex group than in the control group [3 (2, 2.75) vs. 2 (2, 2.75), $P < 0.017$]. Satisfaction scores also increased markedly in the Nal group

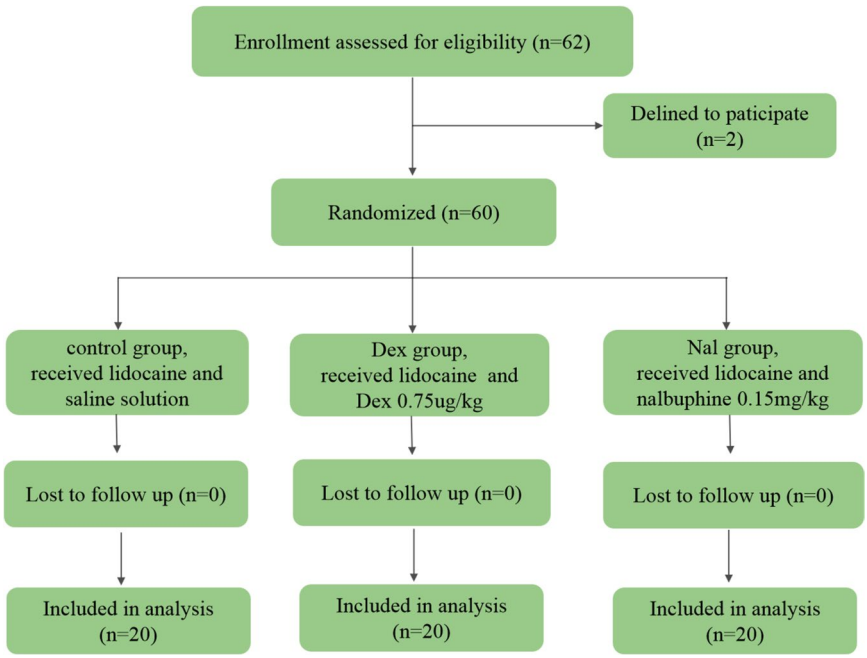

Fig. 1 CONSORT flow diagram of ADL patients

Table 1 Patients' baseline characteristics and intraoperative characteristics

Characteristics/ intraoperative variables	Control group ($n=20$)	Dex group ($n=20$)	Nal group ($n=20$)	*P* Value
Age (mean ± SD), yr	48 ± 13	43 ± 12	46 ± 11	0.525[a]
BMI (mean ± SD), kg/m^2	23.4 ± 3.9	23.7 ± 2.3	25.8 ± 3.8	0.068[a]
Sex, no. (%)				0.812[b]
Female	12 (60)	13 (65)	11 (55)	
Male	8 (40)	7 (35)	9 (45)	
ASA, no. (%)				0.889[d]
I	17 (85)	16 (80)	17 (85)	
II	3 (15)	4 (10)	3 (15)	
C-L	2 (2,2)	2 (2,2)	2 (2,2)	0.744[c]
Baseline MAP, mmHg	90 ± 12	92 ± 14	90 ± 13	0.843[a]
Baseline HR, beat/min	79 ± 11	71 ± 9	74 ± 11	0.086[a]
Baseline SpO_2, %	98 ± 1	98 ± 1	99 ± 1	0.974[a]

Abbreviations: *BMI* body mass index, *ASA* American Society of Anesthesiologists, *MAP* mean arterial pressure, *HR* heart rate, *SpO_2* peripheral oxygen saturation

[a] Analyzed using one-way ANOVA

[b] Analyzed using the χ^2 test

[c] Analyzed using the Kruskal-Wallis test

[d] Analyzed using continuity correction chi-square test

compared with the control and Dex groups [7 (6, 8) vs. 4 (3, 5.75), $P<0.017$ and 7 (6, 8) vs. 5.5 (5,6), $P<0.001$, respectively] and significantly more in the Dex group than in the control group [5.5 (5,6) vs. 4 (3, 5.75), $P<0.017$].

Furthermore, sedation scores were significantly higher in the Nal group compared to the Dex group, with no significant difference between the Nal group and the control group [0 (0, 0) vs. -3 (-3, -2), $P<0.001$, and 0 (0, 0) vs. 0 (0, 2.75), $P=0.159$, respectively] (Fig. 3).

The cough score did not differ significantly among the three groups. Nausea and VAS pain scores in the Nal group were significantly lower than those in the control and Dex groups, with no significant differences between the control and Dex groups (Fig. 4).

Discussion

Our findings indicated that lidocaine aerosol inhalation combined with intravenous nalbuphine provided the most effective and comfortable method for ADL. Nalbuphine resulted in higher SpO_2 levels and provided better patient alertness compared to dexmedetomidine. Additionally, the severity of nausea, and pain during laryngoscopy was significantly lower in the Nal group compared to both the control and Dex groups. The degree of sedation in the Nal group was also less pronounced than in the Dex group.

ADL is widely used in general anesthesia for patients with known or suspected difficult airways (Johnson et al. 2002), laryngeal tumors (Moorthy et al. 2005), and critically

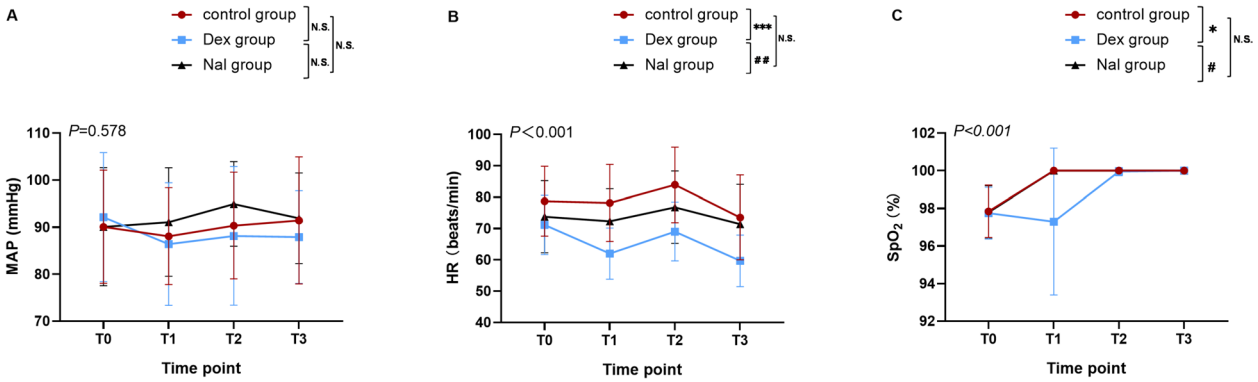

Fig. 2 Changes in MAP (**A**), HR (**B**) and SpO_2 (**C**) at different time points in the control group, Dex group and Nal group. *$P < 0.017$, **$P < 0.001$ vs. control group. #$P < 0.017$, ##$P < 0.001$ vs. Dex group. N.S.: no significant difference. MAP: mean arterial blood pressure; HR: heart rate; SpO_2: peripheral oxygen saturation. The time points indicated in Fig. 4 are described as follows: T0 (before anesthesia), T1 (after anesthesia before ADL), T2 (immediately after ADL), and T3 (5 min after ADL)

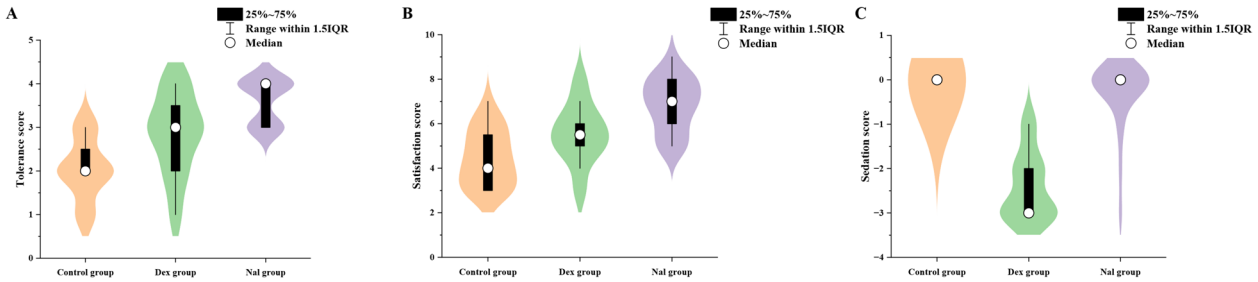

Fig. 3 Tolerance score (**A**), satisfaction score (**B**) and sedation score (**C**) in the control group (orange), Dex group (green), and Nal group (purple). Tolerance scores in the Nal group were significantly higher than control and Dex group ($P = 0.000$ and $P = 0.002$, respectively), Dex than control group ($P = 0.001$); Satisfaction scores at Nal group were significantly higher than control and Dex group ($P = 0.000$ and $P = 0.001$ respectively), Dex than control group ($P = 0.005$); Sedation scores at Dex group were significantly higher than control and Nal group ($P = 0.000$ and $P = 0.000$ respectively), no statistical difference between Nal and control group ($P = 0.159$); The box and dot plots represent the median (IQR) and outliers (defined as beyond 1.5 times the IQR) with the violin plot indicating the density distribution of data

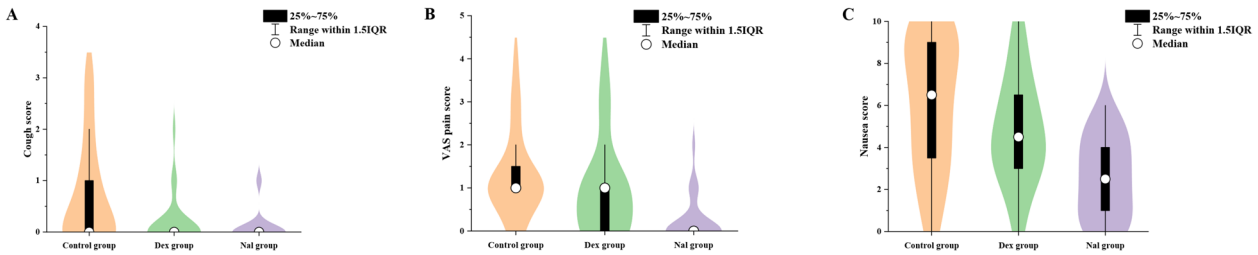

Fig. 4 Cough sedation score (**A**), VAS pain score (**B**) and nausea score (**C**) in the control group (orange), Dex group (green), and Nal group (purple). There was no statistical significance in the score of cough severity in three groups; VAS pain scores at Nal group were lower than control and Dex group ($P = 0.001$ and $P = 0.016$ respectively), Dex than control group ($P = 0.325$); Nausea scores at Nal group were significantly lower than control and Dex group ($P = 0.000$ and $P = 0.009$ respectively), no statistical difference between Dex and control group ($P = 0.261$). The box and dot plots were median (IQR) and outliers (defined as beyond 1.5 times IQR) with the violin plot indicating the density distribution of data

ill ICU patients (Zhang et al. 2022). While fiberoptic technology positively impacts awake tracheal intubation in these cases (Irwin 2022), it requires specialized equipment, operator expertise, and thorough airway anesthesia (Ahmad et al. 2020; Salem et al. 2023). Sitzman et al. first used lidocaine as a local anesthetic for ADL (Sitzman et al. 1997). For flexible laryngoscopy, topical lidocaine alone is usually sufficient (Joy et al. 2022), but it is often inadequate

for rigid laryngoscopy. There is no established gold standard for sedation in ADL (Gómez-Ríos et al. 2024). Johnson et al. used remifentanil and benzodiazepines, which are preferable to intravenous sedative-hypnotics (e.g., propofol) or potent inhaled anesthetics (e.g., sevoflurane). However, remifentanil can cause rigidity, respiratory depression, and loss of consciousness, and benzodiazepines can exacerbate these effects (Johnson et al. 2002).

When used for awake tracheal intubation (ATI), dexmedetomidine is associated with high patient satisfaction and a low risk of oversedation and airway obstruction (Johnston and Rai 2013). Nalbuphine, a potent mixed opioid analgesic, can reduce the pressure response of tracheal intubation and provide perioperative analgesia (Shah and Sen 2024; Jananimadi et al. 2024). Therefore, we decided to test and compare these two drugs in ADL. Given the characteristics of these intravenous drugs, analgesia alone might have been insufficient. Lidocaine nebulization not only improves airway passivation efficiency but also reduces drug dosage and side effects. Thus, in this study, we used a combination of local anesthetic (lidocaine) and intravenous drugs for laryngoscopy.

It is worth noting that dexmedetomidine's peak-dose hypertension, which refers to the significant blood pressure increase at peak concentration, can exacerbate bradycardia-related reductions in cardiac output, potentially limiting its clinical applications (Johnston and Rai 2013). Dexmedetomidine is typically administered as a slow bolus (0.5–1 μg/kg over 5 min), with an onset time of 1 to 2 min (Ahmad et al. 2020). In an early pre-experiment, we found that a 1.0 μg/kg loading dose over 10 min often caused drowsiness, so in this study, we used 0.75 μg/kg infused over 10 min. Nalbuphine, a synthetic opioid (μ-receptor antagonist and κ-receptor agonist), has a usual dose range of 0.2 to 0.3 mg/kg (Akheela and Chandra 2021), with an onset time of 2 to 3 min (Gupta and Gupta 2018). In our pre-experiment, 0.2 mg/kg nalbuphine typically caused nausea, so we used 0.15 mg/kg infused over 10 min. After 5 min of dexmedetomidine, nalbuphine, and placebo infusion, followed by lidocaine aerosol inhalation, the ADL procedure commenced.

The patient's tolerance and satisfaction, including objective acceptance and subjective feelings, are crucial for the smooth progression of awake laryngoscopy. Nausea, pain, and coughing not only disrupt the procedure but also cause hemodynamic fluctuations. Our study showed that using lidocaine with nalbuphine improved patient tolerance and satisfaction while causing minimal sedation. Nausea, and pain were lowest with this combination compared to lidocaine alone or lidocaine with dexmedetomidine. Although lidocaine with dexmedetomidine was superior to lidocaine alone, it caused transient lower SpO_2 levels, likely due to the higher sedation level, which may have reduced respiratory rate and tidal volume. Notably, all patients in our study were able to follow verbal instructions, indicating good compliance. While there was a statistically significant decrease in oxygen saturation levels, there was no evidence of hypoxemia in any of the patients.

Nalbuphine, while capable of causing nausea and vomiting (Shekhar et al. 2023), has also been reported to reduce these symptoms postoperatively (Jia et al. 2022). Similarly, dexmedetomidine has been shown to decrease postoperative nausea and vomiting (Gao et al. 2022). In this study, the observed effects on nausea may be due to the differing mechanisms between laryngoscopy-induced nausea and postoperative nausea. Additionally, lower doses of nalbuphine are less likely to cause nausea. Additionally, in response to the concern about using an agonist-antagonist opioid before a pure agonist, we chose to combine nalbuphine and sufentanil for its benefits in reducing the coughing reflex during anesthesia induction, without significantly compromising analgesic efficacy. Our observations indicate that small doses of nalbuphine do not affect sufentanil's effectiveness in minor surgeries such as cholecystectomy and appendectomy. However, further studies are needed to confirm these findings in larger, more diverse surgical cases.

Our study has several limitations: First, to ensure safety, we excluded patients with suspected difficult airways and selected only those with Mallampati-Samsoon class 1 or 2. Future research should evaluate the safety and efficacy of lidocaine combined with dexmedetomidine for ADL in patients with suspected difficult airways. Second, while dexmedetomidine can cause short-term hypotension and bradycardia (Guo et al. 2023), no significant blood pressure differences were observed among the three groups, possibly due to an insufficient sample size. Third, the atomizing machine used was relatively basic; an ultrasonic atomizer might have applied local anesthetics more effectively. Fourth, participants were not sampled consecutively but recruited during less busy times, potentially introducing selection bias, although this was necessary for study practicality. Finally, a larger study is needed to accurately assess the efficacy and safety of lidocaine combined with nalbuphine and dexmedetomidine in ADL patients. Additionally, we did not analyze patient compliance with different types of instructions during sedation in detail.

Conclusion

In conclusion, our findings indicate that nalbuphine could provide greater tolerance and satisfaction during ADL, with reduced levels of nausea, pain, and sedation compared to dexmedetomidine. The combination of nebulized lidocaine with intravenous nalbuphine appears to be an effective, comfortable, and safe strategy for ADL.

Abbreviations

ANOVA	Analysis of variance
ASA	American Society of Anesthesiologists
RASS	Richmond Agitation-Sedation Scale
BMI	Body mass index
BP	Blood pressure
CONSORT	Consolidated Standards of Reporting Trials
HR	Heart rate
IQR	Interquartile range
MAP	Mean arterial pressure
N.S.	No significant difference
SD	Standard deviation
SpO_2	Peripheral oxygen saturation

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Authors' contributions
Xingxing Li helped design the study, conduct the study, collect the data, analyze the data, prepare the manuscript, and made a significant contribution to the study, and approve the final version. Cuiyu Xie helped design the study, perform the collection of data, with statistical analysis, with revisions, create tables and figures, and approve the final version. Yang-yang Wu: Formal analysis. Weiwei Zhong helped with revisions, creating the tables and figures, and drafting the work; and made a significant contribution to the study. Yao Lu helped in the study conception and design, proposal writing, data analysis, data interpretation, as well as drafting and approving the final version of the manuscript. Yuanhai Li helped in the study conception and design, proposal writing, data analysis, data interpretation, as well as drafting and approving the final version of the manuscript. Final approval of the manuscript: All authors.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Ethics approvalof this study (No. PJ2022-06–56) was approved by the Ethics Committee of the First Affiliated Hospital ofAnhui Medical University, Hefei, China.Chairman of the ethics committee: Heng Wang. Written informed consent forms were signed by the patients or their guardians.

Consent for publication
Not applicable. The study did not contain any individual person's data in any form (including individual details, images or videos).

Competing interests
The authors declare no competing interests.

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