

Nebulized lignocaine for topical anaesthesia in no-sedation bronchoscopy (NEBULA): A randomized, double blind, placebo-controlled trial

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ABSTRACT

Background: The role of nebulized lignocaine administration for flexible bronchoscopy is unclear. **Methods:** In this randomized, double-blind, placebo-controlled trial, subjects undergoing diagnostic flexible bronchoscopy were randomized to receive either nebulized lignocaine (2.5 ml of 4% lignocaine) or nebulized (2.5 ml of 0.9%) saline (placebo). All received 10% lignocaine pharyngeal spray (4 sprays) and 5-ml nasal 2% lignocaine gel. 1% lignocaine solution was used for spray-as-you-go administration in all. Co-primary outcomes were Operator-rated overall procedure satisfaction and Operator-rated cough scores on Visual Analog Scale (VAS). Secondary objectives were cumulative lignocaine dose, proportion of subjects receiving >8.2-mg/kg lignocaine, and complications between the groups. **Results:** Two hundred and twenty subjects were randomized and 217 (109 – nebulized lignocaine and 108 – placebo) received the intervention. Baseline characteristics were comparable. Operator-rated overall procedure satisfaction scores on VAS (7.30 ± 1.54 nebulized lignocaine and 7.50 ± 1.31 placebo group, $P = 0.85$) and Operator-rated cough scores on VAS (3 [2–5] nebulized lignocaine and 3 [2–4] placebo group, $P = 0.18$) were similar. Cumulative lignocaine dose was significantly greater in nebulized lignocaine group (331.46 ± 9.41 mg vs. 232.22 ± 12.77 mg, $P < 0.001$), and a significantly greater number of subjects in this group received lignocaine dose >8.2 mg/kg. Minor complications occurred in 6 and 9 subjects in nebulized lignocaine and placebo groups, respectively, $P = 0.41$. **Conclusion:** Administration of nebulized lignocaine in addition to pharyngeal lignocaine spray, during no-sedation bronchoscopy, increases the cumulative lignocaine dose without improved procedural comfort. Additional nebulized lignocaine during bronchoscopy is not recommended.

KEY WORDS: Bronchoscopy, cough, lignocaine, nebulization

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INTRODUCTION

Optimization of patient comfort is important during bronchoscopy. Inadequate topical anesthesia and poor cough control may be associated with operator dissatisfaction and suboptimal procedure. Strategies to

improve patient comfort include sedation and topical anesthesia. Unlike majority of centers in North America and Europe, “no-sedation” bronchoscopy is the most common practice in certain regions including Japan and India.^[1]

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Adequate topical anesthesia is paramount in bronchoscopy performed without sedation. Lignocaine is the most commonly used drug for topical anesthesia. Although uncommon, toxicity related to topical administration of lignocaine has been reported; therefore, minimization of lignocaine dose during bronchoscopy is important.^[2]

Lignocaine is usually administered to the nasal cavity, the pharynx, and the vocal cords – tracheobronchial tree during bronchoscopy. The role of nebulized lignocaine during bronchoscopy is controversial, and the British Thoracic Society Bronchoscopy Guidelines do not favor its use.^[3] A recent study (the lignocaine in flexible bronchoscopy (LIFE) randomized trial, 500 participants, 92% procedures performed without sedation) demonstrated the feasibility of performing flexible bronchoscopy without the administration of nebulized lignocaine though the primary objective of the study was to compare two different lignocaine concentrations.^[4] In the setting of bronchoscopy performed with combined sedation, no benefit in procedural comfort or cough and higher cumulative lignocaine exposure with nebulized lignocaine administration was observed.^[5] A recent small-sample randomized controlled trial (RCT) (30 participants) reported lower lignocaine and fentanyl requirements with nebulized lignocaine and no differences between patient tolerance and safety. Other studies have demonstrated benefits such as faster procedure, greater patient preference, reduced additional lignocaine requirements, and lower serum lignocaine levels with administration of nebulized lignocaine during bronchoscopy. There are concerns that nebulized lignocaine administration might increase the cumulative lignocaine dose received without any improvement in patient comfort. There is a correlation between total lignocaine dose administered during bronchoscopy and plasma lignocaine levels; therefore, minimization of lignocaine exposure during bronchoscopy is important.^[6] We hypothesized that nebulized lignocaine administration to subjects undergoing bronchoscopy without sedation is not associated with greater procedural comfort as evaluated by operator-rated assessments of overall procedure satisfaction and cough during the procedure.

METHODS

The NEBULized Lignocaine for Airway anaesthesia (NEBULA) study was an investigator-initiated, nonfunded, randomized, double-blind, placebo-controlled trial. The trial was prospectively registered with the clinicaltrials.gov registry (NCT03040193). Ethical approval was obtained from the Institute Ethics Committee (Ref. No. IEC-594/05.01.2017). Written informed consent was obtained from all the subjects before randomization. Consecutive subjects aged 18 years or older and planned for flexible bronchoscopy who were willing for participation and randomization were included in the study. The following were exclusion criteria: (a) pregnancy, (b)

hypoxemia (oxygen saturation [by pulse oximetry] <92% while breathing Oxygen at Fio₂ of ≥0.3), (c) bronchoscopy performed through endotracheal or tracheostomy tube, (d) refusal of consent, (e) subjects planned for administration of upfront sedation, and (f) subjects with documented hypersensitivity to lignocaine. Subjects willing for participation were randomized in a 1:1 ratio to receive nebulized lignocaine or normal saline (placebo) nebulization. Randomization sequence was computer generated in block size of 10. Group allocation was concealed in sealed envelopes.

Baseline demographic characteristics (age, gender, and weight) were recorded for all subjects. Before procedure initiation, blood pressure, oxygen saturation, respiratory rate, and heart rate were recorded for all and monitored continuously during the procedure. Subject preparation was similar in both the groups apart from the administration of either nebulized lignocaine or saline. Intravenous access was routinely secured and none of the subjects received anticholinergic premedication, dextromethorphan, or other premedication agents. All procedures were planned without administration of upfront sedation. However, sedation was allowed at bronchoscopist discretion during the procedure, and the details of the same were recorded. Baseline topical anesthesia regimen in all randomized subjects before bronchoscope introduction included 4 sprays (10 mg/spray) of 10% lignocaine applied on the pharynx along with intranasal administration of 5 ml of 2% lignocaine gel (equivalent to 100 mg of lignocaine). All subjects underwent nasal bronchoscopy, and any failure to negotiate bronchoscope nasally was noted. All subjects received low-flow supplemental oxygen using a thin nasopharyngeal catheter. 1% lignocaine solution was used for spray-as-you-go administration, and the total baseline spray aliquot volume was 9 ml (1.5-ml aliquots – 2 at the vocal cords, 1 – trachea and carina each, 1 – each in the right and left main bronchus). None of the subjects received transtracheal/transcricoid lignocaine injection. Procedures were performed by experienced operators (either faculty or fellows) with each having experience of a minimum of 200 nasal flexible bronchoscopy examinations.

Subjects were randomized to receive either nebulized lignocaine or nebulized saline. 2.5 cc of solution (either 4% lignocaine or normal saline) were used for nebulization. A dedicated assistant was assigned the responsibility of group allocation. A compressor jet nebulizer (OMRON Healthcare, India) with mouthpiece was used, and neither the assisting bronchoscopy nurse nor operator was aware of the group allocations. Nebulization was followed by administration of pharyngeal spray and nasal lignocaine gel administration. Separate nebulizer mouthpieces were used for each subject and were sterilized before use. Flexible bronchoscopy was performed using either the Olympus BF-TE2 fiber-optic bronchoscope or Olympus 1T180 video bronchoscope (Olympus Corporation, Japan) with insertion diameter of 5.9 mm. Administration of additional lignocaine aliquots (spray as you go) was

allowed at operator’s discretion, and the details of the same were documented. The hemodynamic parameters were monitored, and subjects were carefully monitored for any adverse effects. After completion of procedure, the bronchoscopist-rated overall procedure satisfaction and bronchoscopist-rated cough were recorded on a 10-point Visual Analog scale (VAS). The VAS for Operator-rated overall procedure satisfaction was anchored between “totally unsatisfactory (0)” to “very satisfactory (10).” Similarly, the VAS for Operator-rated cough was anchored between “no cough (0)” at one end and “worst cough (10)” at the other.

Statistical analysis

The study had two co-primary outcomes: Operator-rated overall procedure satisfaction and Operator-rated cough scores on VAS between the groups. The secondary outcomes included cumulative lignocaine dose, number of subjects receiving lignocaine dose >8.2-mg/kg body weight, and complications between the groups. The sample size was calculated based on an expected VAS score for procedure satisfaction 7.2 in the control group with standard deviation (SD) of 2.0. With alpha 0.05 and power 90%, 103 subjects were required in each arm. Data were presented as mean ± SD or median (interquartile range) for continuous variables and proportions for categorical variables. Categorical variables were compared using the Chi-square or Fisher’s exact tests while continuous

variables were compared using the *t*-test or Wilcoxon rank-sum test. *P* < 0.05 was considered statistically significant. Statistical analyses were performed using STATA statistical analysis software V.9.0 (StataCorp, College Station, Texas, USA).

RESULTS

Two hundred and twenty-nine subjects were screened for randomization, and after exclusion of 9 subjects who failed to meet the inclusion criteria, 220 subjects were randomized. Three subjects were excluded after randomization (2 subjects – one in each group had elevated blood pressures before nebulization leading to procedure cancellation and one patient in the saline placebo group refused to undergo nasal bronchoscope insertion). Two hundred and seventeen randomized subjects (109 – nebulized lignocaine and 108 – nebulized saline) underwent bronchoscopy according to the planned protocol. The flow of subjects in the study is depicted in the CONSORT diagram [Figure 1].

Baseline characteristics between the groups were comparable [Table 1]. Majority of the subjects were male and mean age was 48 years. Baseline hemodynamic parameters were similar between the groups. Although a greater number of subjects underwent transbronchial lung biopsy in the nebulized lignocaine group (11 vs. 3 participants,

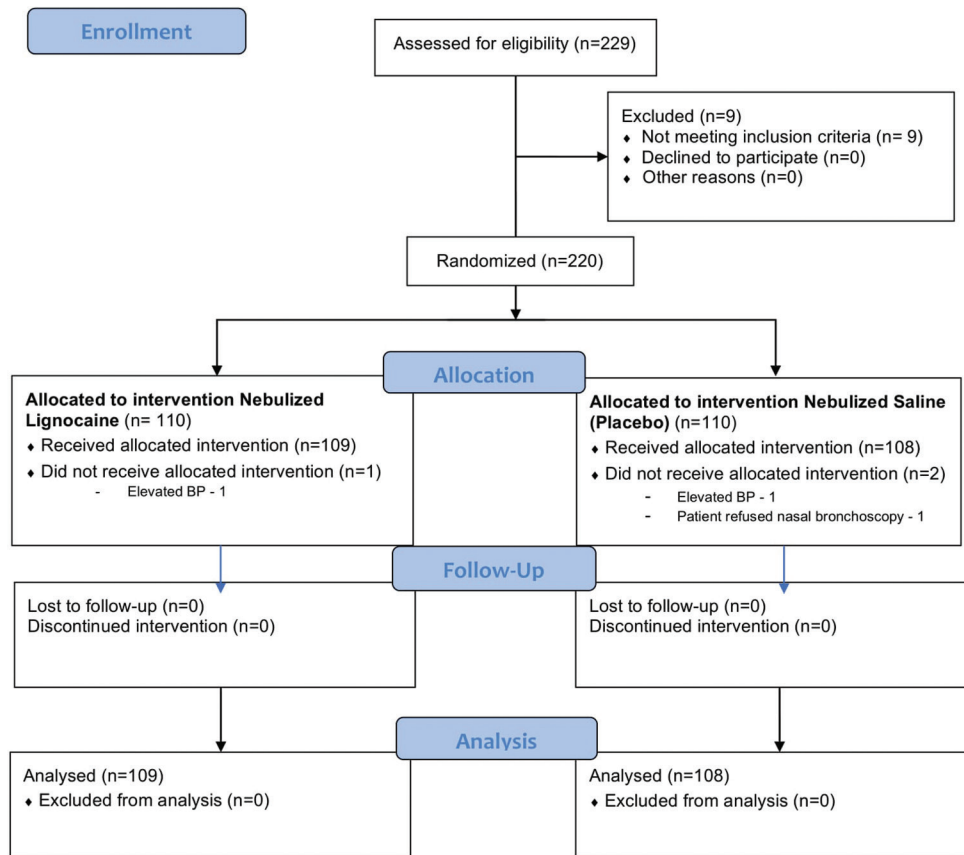


Figure 1: CONSORT diagram showing the flow of participants in the Nebulized Lignocaine for Airway Anesthesia study

$P = 0.03$), overall a similar number of participants underwent any bronchoscopic biopsy in the two groups (27 in nebulized lignocaine group vs. 28 in the saline group, $P = 0.84$). Procedure duration was similar between the groups.

There was no significant difference between the co-primary outcomes: Operator-rated overall procedure satisfaction and Operator-rated cough scores on VAS between the two groups [Table 2]. Mean (SD) Operator-rated overall procedure satisfaction scores on VAS were 7.30 (1.54) in the nebulized lignocaine group and 7.50 (1.31) in the nebulized saline group, $P = 0.85$. Median (interquartile) range Operator-rated cough scores on VAS were 3 (2–5) in the nebulized lignocaine group and 3 (2–4) in the nebulized saline group, $P = 0.18$. On analysis of secondary outcomes, the overall cumulative lignocaine dose received in the nebulized lignocaine group was significantly greater (331.46 ± 9.41 mg vs. 232.22 ± 12.77 mg, $P < 0.001$), and a significantly greater number of subjects received cumulative lignocaine doses >6 mg/kg (64 vs.

10, $P < 0.001$) and >8.2 mg/kg (8 vs. 0, $P < 0.01$) in the nebulized lignocaine group. More participants required intraprocedural sedation in the nebulized lignocaine arm (10 in nebulized lignocaine vs. 3 in the saline arm) ($P = 0.047$). Procedure duration and subject willingness to return for a repeat procedure were similar between the two groups. Minor complications occurred in 6 (5.5%) and 9 (8.3%) subjects in the nebulized lignocaine and saline groups, respectively, $P = 0.41$.

DISCUSSION

The findings of NEBULA study demonstrate that additional nebulization with 4% lignocaine during flexible bronchoscopy is not associated with greater operator-rated procedure satisfaction or reduction in cough and is associated with higher cumulative lignocaine dose exposure in subjects undergoing no-sedation bronchoscopy. In addition, there are no advantages in terms of procedure duration and patient willingness to return for a repeat procedure. Furthermore, more subjects in the nebulized lignocaine arm required intraprocedural

Table 1: Baseline characteristics of the study participants

Parameter	Nebulized lignocaine group (n=109)	Nebulized saline group (placebo) (n=108)	P
Age (years); mean±SD	47.08±15.70	48.94±16.48	0.80
Males; n (%)	77 (70.6)	69 (63.9)	0.29
Weight (kg); mean±SD	55.09±10.27	52.78±9.83	0.05
Baseline heart rate (beats/min); mean±SD	98.39±12.87	99.34±12.45	0.71
Baseline oxygen saturation (%); mean±SD	96.92±3.14	97.57±6.59	0.82
Baseline systolic blood pressure (mmHg); mean±SD	129.55±17.61	131.28±17.86	0.76
Baseline diastolic blood pressure (mmHg); mean±SD	81.05±9.65	80.53±11.20	0.35
Intraprocedural sedation; n (%)	10 (9.17)	3 (2.78)	0.047*
Procedure duration (min)	10.60±4.63	10.63±4.73	0.52
Procedures performed			
Any biopsy: Either TBLB or EBB or both; n (%)	27	28	0.84
TBLB; n (%)	11	3	0.03*
EBB; n (%)	23	27	0.49
TBNA; n (%)	7	4	0.36
Airway inspection alone; n (%)	10	9	0.82
BAL/bronchial washings alone; n (%)	67	66	0.95

TBLB: Transbronchial lung biopsy, EBB: Endobronchial biopsy, TBNA: Transbronchial needle aspiration, BAL: Bronchoalveolar lavage

Table 2: Primary and secondary outcomes between the two study groups

Outcomes	Nebulized lignocaine group (n=109)	Nebulized saline group (placebo) (n=108)	P
Primary outcomes			
Operator-rated overall procedural satisfaction (VAS), mean±SD	7.30±1.54	7.50±1.31	0.85
Operator-rated cough (VAS), median (interquartile range)	3 (2–5)	3 (2–4)	0.18
Secondary outcomes			
Cumulative lignocaine dose (mg); mean±SD	331.46±9.41	232.22±12.77	<0.001
Patients receiving dose >8.2 mg/kg; n (%)	8 (7.3)	0	<0.01
Patients receiving dose >6 mg/kg; n (%)	64 (58.7)	10 (9.3)	<0.001
Complications; n (%)	6 (5.5)	9 (8.3)	0.41
Accelerated hypertension	1	4	
Bronchospasm	1	3	
Hypoxia	2	0	
Minor airway bleeding	0	2	
Excessive cough	2	0	
Additional lignocaine administration during procedure above the baseline dose; n (%)	3 (2.7)	3 (2.7)	0.99
Patient willingness to return for repeat procedure; n (%)	83 (76.2)	84 (77.8)	0.76

VAS: Visual analog scale, SD: Standard deviation

sedation. Therefore, additional nebulized lignocaine is not required during no-sedation bronchoscopy.

Nebulized administration of local anesthetics for bronchoscopy, especially lignocaine, has been actively studied over the past three decades. The summary of studies evaluating the role of nebulized local anesthetics during bronchoscopy is summarized in Table 3. Palva *et al.* demonstrated efficacy and better patient acceptability in subjects undergoing bronchoscopy with nebulized lignocaine administration, and since then, studies have evaluated the role of nebulized lignocaine in randomized designs.^[7] Palva *et al.* also demonstrated earlier attainment of peak serum levels with administration of nebulized lignocaine, and this may be relevant as delayed peak and toxicity can occur with spray administration (potentially when patient might have left the bronchoscopy room). Due to topical action, nebulized lignocaine was also described as a treatment option for intractable cough.^[8] The preliminary observations were contradicted by the first RCT comparing nebulized lignocaine administration with laryngotracheal spraying, (Korttila *et al.*, 1981) wherein the efficacy of local anesthesia and patient cooperation were superior with spray administration of lignocaine although the plasma lignocaine levels were lower with nebulized administration. However, the study included subjects undergoing rigid bronchoscopy and all received sedation with intravenous diazepam.^[9] With high-dose background sedation or topical anesthetics, it may be difficult to interpret the efficacy of individual components.^[10] Gove *et al.* reported similar acceptability of the procedure with nebulized lignocaine as compared with bolus administration and reported that the use of nebulized lignocaine also avoided additional nasal anesthetic administration to most participants and recommended routine use of nebulized lignocaine. However, a high dose of lignocaine (approximately 400 mg) was used for nebulization.^[11] Lack of patient cooperation to comply with nebulized lignocaine inhalation technique was mentioned as the reason of inadequate anesthesia in five participants receiving nebulized lignocaine. Shorter procedural duration was reported as an advantage with using nebulized lignocaine, and authors also mentioned possible advantages of no-sedation bronchoscopy with use of topical (nebulized) lignocaine alone without concomitant diazepam administration because of risks of fall in arterial oxygenation with use of parenteral diazepam.^[11] Keane *et al.* demonstrated similar efficacy of nebulized lignocaine and sprayed lignocaine for pharyngeal anesthesia (similar cough frequency objectively recorded) and advocated the nebulized route as participants found the spray unpleasant. This trial reported the equivalent efficacy of pharyngeal spray with nebulized lignocaine in the setting of flexible bronchoscopy performed with sedation as all participants received intravenous diazepam.^[12] This finding is important as most participants indeed complaint of a stinging unpleasant sensation on administration of 10% lignocaine spray in clinical practice. In contrast to the study by Keane and McNicholas, the NEBULA trial

evaluated the role of nebulized lignocaine in addition to 40-mg pharyngeal spray versus 40-mg pharyngeal lignocaine spray alone. The NEBULA trial findings demonstrate that 40-mg pharyngeal (10% lignocaine spray) administration alone is adequate during no-sedation bronchoscopy, and when using the same, additional nebulized lignocaine or a higher 10% spray dose is not needed. Furthermore, it demonstrates that in this setting also, a lower concentration of lignocaine (1% lignocaine solution) administered by spray-as-you-go method can be used to perform flexible bronchoscopy. Foster and Hurewitz reported lesser requirements of additional lignocaine with nebulized lignocaine administration during “no-sedation” bronchoscopy. However, the limitation was that the comparator group was saline placebo without any upfront pharyngeal anesthesia.^[13] The study design of the NEBULA study was similar to the design by Stolz *et al.* (150 participants) evaluating the role of additional nebulized lignocaine over pharyngeal lignocaine spray administration. Authors demonstrated the lack of efficacy of additional nebulized lignocaine in operator- or patient-rated cough/comfort end points, and importantly, nebulized lignocaine use was not associated with reduction in total lignocaine dose administered. These findings are similar with our (NEBULA) study with the major difference being administration of combined sedation to all the participants in the study by Stolz *et al.*^[5] Other differences were two sprays of 10% lignocaine to the pharynx (Stolz *et al.*) versus four sprays (NEBULA study) and the use of nasal lignocaine gel in the NEBULA study instead of lignocaine spray used by Stolz *et al.* A RCT has previously demonstrated lignocaine gel as the preferred method for nasal anesthesia during bronchoscopy.^[14] Therefore, the findings of NEBULA study are more representative of the prevalent practice as lignocaine gel is the most commonly used method for nasal anesthesia during bronchoscopy at most centers.^[15] Charalampidou *et al.* also demonstrated lack of benefit of nebulized lignocaine in the setting of sedation bronchoscopy, but a limitation of this study was a high baseline lignocaine preparation regimen.^[16] All participants apart from sedation received transtracheal lignocaine, a high upfront (120 mg of 4% lignocaine) dose at the vocal cords, and underwent oral bronchoscope insertion. MacDougall *et al.* reported no benefit with use of nebulized lignocaine using a dedicated Enk device as compared with the conventional spray-as-you-go method.^[17] On the contrary, Dreher *et al.* demonstrated reduction in lignocaine and fentanyl doses during bronchoscopy with nebulized lignocaine using Enk device as compared with spray-as-you-go method. However, the study sample size was small (30 participants – 15 in each arm), and most of the participants received deep sedation limiting the generalizability of these observations.^[18] Furthermore, authors of this study highlighted the need for more studies in light sedation or no-sedation bronchoscopy.

The majority of available evidence does not support the use of nebulized lignocaine during sedation as well as

Table 3: Review of available studies comparing the utility of nebulized lignocaine/nebulized local anesthetic administration during bronchoscopy

Author, year	Number of patients/type of study	Intervention	End points	Sedation/premedication	Outcome
Korttila K <i>et al.</i> , 1981	n=40, RCT	Laryngotracheal spraying (10% spray followed by 4% lignocaine solution) versus ultrasonic nebulizer administration of 4% lignocaine in patients undergoing rigid bronchoscopy	VAS for efficacy of anesthesia and VAS for cooperation of patients, plasma lignocaine levels	Intravenous diazepam and atropine premedication to all	Both modes produced adequate anesthesia. Efficacy of local anesthesia and cooperation of patients better after lignocaine spray. Amount of mucus, cumulative lignocaine dose, diazepam dose, and postbronchoscopy cough similar between two groups. Lower plasma lignocaine levels with nebulization
Gove RI <i>et al.</i> , 1985	n=52, RCT	Three arms Nebulized lignocaine versus nebulized lignocaine and diazepam versus bolus lignocaine and diazepam	Duration of procedure, lignocaine blood levels, patient acceptability, cardiac rhythm	Intravenous diazepam and atropine premedication to all	Duration of procedure shorter in both the arms with nebulized lignocaine, blood levels of lignocaine similar in three groups, patient acceptability similar in three groups
Keane D <i>et al.</i> , 1992	n=54, RCT	Nebulized (100 mg) 2.5-ml 4% lignocaine versus sprayed topical 10% (100 mg) lignocaine (+ 100 mg solution spray as you go in both groups) All received 100 mg lignocaine gel	Cough frequency on cassette tape	IV diazepam+atropine to all patients	No difference in overall cough frequency between groups, spray unpleasant
Foster WM <i>et al.</i> , 1992	n=38, RCT	Nebulized lignocaine (three different groups with varying formulations to deliver 50 mg lignocaine) versus saline nebulization (fourth group)	Additional lignocaine needed for upper airway and distal airway	Atropine+codeine to all patients	Significantly less additional lignocaine requirement with nebulized lignocaine predominantly due to lesser amounts required for anesthesia of pharynx and laryngotracheal regions
Salajka F <i>et al.</i> , 1999	n=80, RCT	1% trimecaine versus saline nebulization Followed by topical anesthesia using spray as you go and laryngeal syringe	Cough score, gagging episodes	NA	No statistically difference between outcomes
Stolz D <i>et al.</i> , 2005	n=150, RCT, double-blind, placebo-controlled	Lignocaine (4 ml of 4% lignocaine) versus saline nebulization In addition to 10% lignocaine nasal spray (4 times) and oropharynx (2 times), 1% lignocaine for spray-as-you-go administration	Supplemental lignocaine dose, operator- and patient-rated cough (VAS), patient-rated discomfort score, midazolam doses	Midazolam boluses a hydrocodone (5 mg iv initially)	No significant difference and any of the prespecified outcomes Higher lignocaine dose administered in nebulization arm (mean±SD - 318±41 versus 157±44 mg)
Charalampidou S <i>et al.</i> , 2006	n=83 RCT, blinded, placebo-controlled	Nebulized lignocaine (60 mg (24 patients), 120 mg (19 patients) versus placebo (40 patients) Transtracheal lignocaine (4%) 120 mg, 50 mg (5 sprays of 10% lignocaine) pharyngeal spray, 120 mg lignocaine spray to vocal cords, and IV diazepam to all, oral route for bronchoscopy	Ease of procedure and cough - VAS	Sublingual diazepam + IV midazolam±fentanyl	No difference in ease of procedure and cough VAS scores between the three groups

Contd...

Table 3: Contd...

Author, year	Number of patients/type of study	Intervention	End points	Sedation/premedication	Outcome
MacDougall M et al., 2011	n=50, RCT, nonblinded	Nebulized lignocaine through Enk device versus conventional injection through working channel	Duration of procedure, VAS for tolerability, ease of procedure, frequency of cough	Midazolam up to 0.1 mg/kg±alfentanil	No difference in any end point
Dreher M et al., 2016	n=30, RCT	Lignocaine through syringe through bronchoscope working channel or nebulized lignocaine	Lignocaine dose, sedative dose, patient tolerance by VAS, safety	1.5 mg midazolam and propofol in all, fentanyl if additionally required	Lower dose of fentanyl and lignocaine in nebulizer group, no difference in patient tolerance or safety

VAS: Visual analog scale, RCT: Randomized controlled trial

no-sedation bronchoscopy. Other practical issues with routine nebulization include additional infection control precautions to prevent transmission of infections related to nebulization, increase in the overall patient preparation time, and strain on available resources. In high-volume settings, the major disadvantage with administration of nebulized lignocaine is that it creates more strain on the resources required for performing flexible bronchoscopy, need for a dedicated nebulization area and personnel, infection control precautions, and requirement of separate mouthpieces for each patient. Furthermore, some authors have reported the unpleasant sensation experienced by participants with nebulized lignocaine administration.^[19] Adverse effects of nebulized lignocaine administration on airway conductance have also been reported.^[20] Most importantly, as nebulized lignocaine administration does not lead to improvement in clinically relevant outcomes, we do not recommend its use. Lignocaine spray is preferable for pharyngeal anesthesia during bronchoscopy, and when using it, the use of additional nebulized lignocaine is not required.

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Conflicts of interest
There are no conflicts of interest.

REFERENCES

- Asano F, Aoe M, Ohsaki Y, Okada Y, Sasada S, Sato S, et al. Bronchoscopic practice in Japan: A survey by the Japan Society for Respiratory Endoscopy in 2010. *Respirology* 2013;18:284-90.
- Mittal S, Mohan A, Madan K. Ventricular tachycardia and cardiovascular collapse following flexible bronchoscopy: Lidocaine cardiotoxicity. *J Bronchology Interv Pulmonol* 2018;25:e24-e26.
- Du Rand IA, Blaikley J, Booton R, Chaudhuri N, Gupta V, Khalid S, et al. British Thoracic Society guideline for diagnostic flexible bronchoscopy in adults: Accredited by NICE. *Thorax* 2013;68 Suppl 1:i1-44.
- Madan K, Biswal SK, Mittal S, Hadda V, Mohan A, Khilnani GC, et al. 1% versus 2% lignocaine for airway anesthesia in flexible bronchoscopy without lignocaine nebulization (LIFE): A randomized controlled trial. *J Bronchology Interv Pulmonol* 2018;25:103-10.
- Stolz D, Chhajed PN, Leuppi J, Pflimlin E, Tamm M. Nebulized lidocaine for flexible bronchoscopy: A randomized, double-blind, placebo-controlled trial. *Chest* 2005;128:1756-60.
- Milman N, Laub M, Munch EP, Angelo HR. Serum concentrations of lignocaine and its metabolite monoethylglycinexylidide during fibre-optic bronchoscopy in local anaesthesia. *Respir Med* 1998;92:40-3.
- Palva T, Jokinen K, Saloheimo M, Karvonen P. Ultrasonic nebulizer in local anesthesia for bronchoscopy. *ORL J Otorhinolaryngol Relat Spec* 1975;37:306-11.
- Howard P, Cayton RM, Brennan SR, Anderson PB. Lignocaine aerosol and persistent cough. *Br J Dis Chest* 1977;71:19-24.
- Korttila K, Tarkkanen J, Tarkkanen L. Comparison of laryngotracheal and ultrasonic nebulizer administration of lidocaine in local anaesthesia for bronchoscopy. *Acta Anaesthesiol Scand* 1981;25:161-5.
- Kumar A, Mittal S, Mohan A, Madan K. Comparison of sedation regimens during flexible bronchoscopy. *Clin Respir J* 2018;12:1775.
- Gove RI, Wiggins J, Stableforth DE. A study of the use of ultrasonically nebulized lignocaine for local anaesthesia during fibreoptic bronchoscopy. *Br J Dis Chest* 1985;79:49-59.
- Keane D, McNicholas WT. Comparison of nebulized and sprayed topical anaesthesia for fibreoptic bronchoscopy. *Eur Respir J* 1992;5:1123-5.
- Foster WM, Hurewitz AN. Aerosolized lidocaine reduces dose of topical anesthetic for bronchoscopy. *Am Rev Respir Dis* 1992;146:520-2.
- Randell T, Yli-Hankala A, Valli H, Lindgren L. Topical anaesthesia of the nasal mucosa for fibreoptic airway endoscopy. *Br J Anaesth* 1992;68:164-7.
- Madan K, Mohan A, Agarwal R, Hadda V, Khilnani GC, Guleria R, et al. A survey of flexible bronchoscopy practices in India: The Indian bronchoscopy survey (2017). *Lung India* 2018;35:98-107.
- Charalampidou S, Harris E, Chummun K, Hawksworth R, Cullen JP, Lane SJ, et al. Evaluation of the efficacy of nebulised lignocaine as adjunctive local anaesthesia for fibreoptic bronchoscopy: A randomised, placebo-controlled study. *Ir Med J* 2006;99:8-10.
- MacDougall M, Mohan A, Mills J, Munavvar M. Randomized comparison of 2 different methods of intrabronchial lidocaine delivery during flexible bronchoscopy: A pilot study. *J Bronchology Interv Pulmonol* 2011;18:144-8.
- Dreher M, Cornelissen CG, Reddemann MA, Müller A, Hübel C, Müller T, et al. Nebulized versus standard local application of lidocaine during flexible bronchoscopy: A randomized controlled trial. *Respiration* 2016;92:266-73.
- Kirkpatrick MB, Sanders RV, Bass JB Jr. Physiologic effects and serum lidocaine concentrations after inhalation of lidocaine from a compressed gas-powered jet nebulizer. *Am Rev Respir Dis* 1987;136:447-9.
- Miller WC, Awe R. Effect of nebulized lidocaine on reactive airways. *Am Rev Respir Dis* 1975;111:739-41.