

1 **Two different methods of lidocaine inhalation before diagnostic flexible**
2 **bronchoscopy: effects on post-bronchoscopy respiratory symptoms**

3 **Abstract**

4 **Background/aim:** Use of topical anesthesia before flexible bronchoscopy for the
5 evaluation of the upper airways prevents cough and stridor during and after the procedure
6 while reducing the need for sedation. In practice, lidocaine is the medication of choice
7 before bronchoscopy. There various types of nebulizers used for inhalation treatments. In
8 this study, we compared the respiratory tract symptoms after flexible bronchoscopy
9 between children who received pre-procedure topical lidocaine with mesh or jet
10 nebulizers.

11 **Materials and methods:** We enrolled 4-18 years old subjects that underwent flexible
12 bronchoscopy due to treatment-resistant asthma in this retrospective case-control study.
13 Twenty subjects received topical lidocaine with jet nebulizers while 20 received it with
14 mesh nebulizers. Age, sex, duration of bronchoscopy, duration of anesthesia, time to
15 awaken, and time to recovery were recorded as well as cough and laryngospasm scores
16 after flexible bronchoscopy.

17 **Results:** Severe cough after flexible bronchoscopy was not encountered in the mesh
18 nebulizers group but was seen in 10% of the jet nebulizers group ($p = 0.027$). On the other
19 hand, Age, sex, duration of bronchoscopy, duration of anesthesia, time to awaken, and
20 time to recovery were not significantly different between the mesh and jet nebulizer
21 groups ($p = 0.44, 0.34, 0.51, 0.88, 0.88, 0.22$, respectively).). Moreover, croup and
22 laryngospasm scores between the two groups were similar ($p = 0.62, 0.50$ respectively).
23 Cough score was significantly worse jet nebulizers group ($p=0.03$).

24 **Conclusion:** Topical lidocaine application with mesh nebulizers decreases the most
25 common complication, cough, after flexible bronchoscopy in children more effectively
26 compare to jet nebulizers. Thus, mesh nebulizers may be a faster way of nebulization
27 before flexible bronchoscopy as an alternative to jet nebulizers.

28 **Key Words:** Flexible bronchoscopy, mesh nebulizer, jet nebulizer, lidocaine

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42 **1. Introduction**

43 Use of topical anesthesia prior to flexible bronchoscopy (FB), performed to
44 evaluate the upper airways and tracheobronchial tree, prevents cough and stridor during
45 and after the procedure while reducing the need for sedation [1,2]. In clinical practice,
46 lidocaine is the medication of choice for topical anesthesia before FB, due to its short
47 half-life and wide safety range [3]. Lidocaine nebulization before FB was found to be
48 well tolerated with better oxygenation and fewer side effects compared to systemic
49 administration [4,5].

50 Effective delivery of aerosol drugs with a nebulizer depends on age, physical-
51 cognitive development, and patient-device compatibility [6,7]. In addition, airway
52 caliber, breathing rate, inspiratory flow rate, and breathing pattern determine the efficacy
53 of aerosol delivery [8,9]. There are various types of nebulizers; one is a jet nebulizer (JN),
54 which produces aerosol drug particles of various diameters and requires a flow rate of 5
55 - 6 L / min and pressure of 2 bars to transmit these particles to the airway [10]. Noise
56 generation between 65-100 dB is a disadvantage for JN use in children [11]. The other
57 type of nebulizer is the mesh nebulizer (MN) that used a micro-pump technology for
58 aerosol generation without making noise [10]. MNs aerosolize the medication in liquid
59 form by passing it through the multiple micro-holes in a vibrating plate [10]. They are
60 small, portable devices with high output efficiency and minimal residual volume, that
61 work on battery or electricity. Advantages of MNs are the efficiency of aerosol
62 generation, constant aerosol size, the dominantly small aerosol fraction that is suitable to
63 reach the peripheral airways, and nebulization of low drug volume [10]. MNs have

64 minimal residual drug volume (0.1-0.3 ml) compared to JNs and ultrasonic nebulizers
65 (UN) (0.8-1.5 ml) and are more efficient in drug distribution than JNs [12,13].

66 The efficacy of topical lidocaine nebulization may influence the rate and severity
67 of post FB respiratory symptoms such as cough and laryngeal spasm. Aerosols generated
68 with different nebulizer types may influence the efficacy. Therefore, in this study, we
69 aimed to compare the respiratory tract symptoms after FB between children who received
70 pre-procedure topical lidocaine with MNs or JNs.

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82 2. Methods

83 2.1. Study Population and Ethics Committee Approval

84 We enrolled 4–18 years old subjects that underwent FB due to treatment resistant
85 asthma in Pediatric Pulmonology and Allergy Department between January 2015 and
86 April 2019 retrospectively in this study. Total number of FB procedures during this time
87 was 427 and 40 subjects fulfilled the inclusion criteria. Among these, 20 had received
88 topical lidocaine with JN while 20 with MN. Exclusion criteria were foreign body
89 aspiration, short term bronchodilator or systemic steroid use during the previous week,
90 congenital airway anomaly, cystic fibrosis, primary ciliary dyskinesia neurological
91 disease and cardiac disease. Moreover, subjects in which FB revealed any pathology
92 inconsistent with treatment resistant asthma were excluded.

93 This retrospective case-control study was approved by the Institutional Review
94 Board of Celal Bayar University, School of Medicine (Date of Approval: 07.10.2019,
95 Number of Approval: 48).

96 2.2. Data Collection

97 Age, sex, inhaler treatment used before FB, duration of bronchoscopy,
98 anesthetic and muscle relaxant medications used during FB, duration of anesthesia, time
99 to awaken and time to recovery were recorded from procedure files as well as croup,
100 cough and laryngospasm scores after FB.

101 After the bronchoscopy, the patients are routinely followed up by the
102 anesthesiologist until their vital signs are stable and spontaneous breathing starts and time
103 to awaken and time to recovery are recorded in their files. After the procedure, all cases
104 are followed up by pediatric pulmonology team and croup, laryngospasm and cough
105 scores are recorded in their files. Croup score is calculated as the sum of retraction,

106 airflow and cyanosis scores, each of which are graded from 0 to 2, increasing with
107 severity [14]. A total score of 1-3 is mild, 4-6 is moderate and ≥ 7 is severe croup.
108 Laryngospasm is scored from one to three; just stridor (grade 1), complete closure of
109 vocal cords (grade 2), complete closure of vocal cords and cyanosis (grade 3) [15]. Cough
110 is scored as mild (once), moderate (multiple coughs of short duration < 5 seconds) and
111 severe (continuous cough > 5 sec) [16]. Cough, laryngospasm and croup scores were
112 recorded from patient files.

113 **2.3. Nebulization and Anesthesia Prior to FB**

114 All patients received 4mg / kg of 2% lidocaine before FB either with JN
115 (Hospyneb Professional, 3A Healthcare, Italy) or MN (Aerogen Solo with Ultra, Aerogen
116 Ltd., Ireland) through an age appropriate mask. The decision to use JN or MN depended
117 on the time left before the procedure when the subject arrived the procedure room. Since
118 the JN takes a longer time to finish nebulization, the patients who arrive to the procedure
119 room early get their lidocaine through a JN which takes about ten minutes, but if the time
120 is shorter then they receive it with MN which takes about five minutes. The nebulization
121 was completed five minutes before the induction of anesthesia. Nebulization times and
122 nebulization types of patients were recorded from their files.

123 Anesthesia was induced by an Anesthesiologist in the operation room with
124 intravenous (IV) propofol for induction and sevoflurane inhalation for maintenance. Use
125 of neuromuscular blocker IV Rocuronium was recorded from the files. FB (Fujinon EB-
126 470S - Fujinon EB-470P, Fujifilm Corp., Saitama, Japan) was performed by a pediatric
127 pulmonologist using age and weight appropriate scopes. During the procedure, all cases
128 were monitored in terms of cardiac and respiratory parameters and the bronchoscopy
129 procedure is recorded in their files along with a video.

130 2.4. Statistical Analysis

131 In this research; data analysis was performed using SPSS version 15 (IBM Corp,
132 Armonk, NY, US). Statistical analysis included descriptive statistics, Student-t test,
133 Pearson chi-square tests and Mann Whitney analysis. Group comparisons were performed
134 using Student t test for continuous variables and χ^2 test to compare categorical variables.
135 Categorical variables were reported as frequency and percentage. Mann Whitney U Test
136 was used to compare continuous variables not normally distributed between MN and JN
137 group. A p-value of 0.05 was considered statistically significant.

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148 3. Results

149 3.1. Sociodemographic Characteristics

150 Age was not significantly different among the two groups (8.3 ± 3.6 years in the
151 JN group vs 9.5 ± 4.6 years in the MN group, $p=0.44$) (Table 1).

152 3.2. Procedure and Anesthesia

153 Bronchoscopy duration was not significantly different between the two groups
154 (8.6 ± 2.9 vs 9.6 ± 5.4 minutes in the JN and MN groups respectively, $p=0.51$). Similarly,
155 anesthesia duration was similar (15.3 ± 6.2 and 15.9 ± 9.7 minutes in the JN and MN groups
156 respectively, $p=0.88$). Awakening and recovery times were not significantly different
157 between the two groups, either ($p=0.10$ and $p=0.22$ respectively) (Table 1) .

158 During bronchoscopy, 21 subjects received rocuronium as a neuromuscular
159 blocker; duration of bronchoscopy and anesthesia, time to awaken and recovery time were
160 not significantly different among the subjects who received rocuronium and who did not
161 ($p = 0.94$, $p=0.06$, $p=0.35$ and $p=0.80$ respectively). There was no difference in the croup,
162 laryngospasm and cough scores of the subjects that received rocuronium or not ($p = 0.73$,
163 $p=0.66$ and $p=0.66$, respectively).

164 3.3. Post-bronchoscopy Respiratory Symptoms

165 Most of the subjects enrolled had a mild croup score after the procedure (95% in
166 the MN and 90% in the JN groups, $p=0.62$). Similarly majority of the subjects did not
167 develop any degree of laryngospasm (80% in the MN and 90% of the JN groups, $p=0.50$).
168 On the other hand, cough was the most common post-FB respiratory symptom. 70% of

169 the MN group had mild and 30% had moderate cough scores but the JN group, 30% had
170 mild, 60% had moderate and 10% had severe cough score. On JN group; cough score was
171 significantly worse than the MN group ($p=0.03$) (Table2).

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186 **4. Discussion**

187 Flexible bronchoscopy is a method frequently used by pediatric pulmonologists
188 for the diagnosis of respiratory diseases and pre-operative topical anesthesia via
189 nebulization is applied commonly to decrease complications such as laryngospasm and
190 cough [17–19]. In this study, we compared the efficacy of two different nebulizer types
191 in decreasing the severity of post-procedure complications. There were no severe
192 complications in both JN and MN groups, but cough severity was lower in the MN group.

193 Cough is the most important and common complication in bronchoscopy with a
194 prevalence of 27% and it can lead to patient intolerance as well as physician
195 dissatisfaction [20,21]. Lidocaine with its rapid onset of action, short half-life and a good
196 safety profile is the most commonly used local anesthetic agent to reduce cough in the
197 bronchoscopy procedure [22]. Although, topical anesthetics carry the risk of side effects
198 upon rapid absorption through mucous membranes, lidocaine has a good safety profile
199 [23]. Thus, lidocaine nebulization either with JN or MN is used for topical anesthesia
200 before FB routinely in our clinic. We did not observe any side effects related to lidocaine
201 nebulization in our study.

202 Aerosol therapy with nebulizer is frequently used for the treatment of respiratory
203 symptoms and there are various nebulizer types depending on their operating principles.
204 Particle size and delivery rate are critical factors in determining the local and total lung
205 accumulation of inhaled aerosol drugs [24]. JNs, easy to operate and cheap, are frequently
206 used in daily life but have disadvantages of a large residual volume, electrical supply
207 requirement and noise [25]. MNs have gained popularity over the years lately due to its
208 low residual volume, completely silent operation, and easy use and cleaning [26]. MNs

209 are reported to be more efficient in delivery of aerosols to the peripheral airways
210 compared to JNs [27,28]. Therefore, we aimed to evaluate the efficacy of these two
211 nebulizers in terms of post-FB complications. The results of our study revealed that there
212 was no significant difference between JN and MN and lidocaine nebulization groups in
213 terms of croup score and laryngospasm score, whereas the cough score was significantly
214 higher in the group using JN compared to the group using MN.

215 Cough is one of the most important complication during and after bronchoscopy,
216 that impairs the quality and comfort of the FB procedure and impairs patient quality of
217 life and led to anxiety. In previous studies, the frequency of post-FB cough has been
218 reported to be 27% [21]. The frequency of moderate and severe cough was 30% in MN
219 group and 60% in the JN group in our study. This difference may be attributed to the
220 standard particle size and efficient distribution of these particles to the peripheral airways
221 with MNs compared to JNs. Moreover, shorter total duration of nebulization may increase
222 patient adherence to the technique.

223 The current study has a few limitations. Due to the limited number of mesh
224 nebulizers, the priority of jet nebulizer for routine lidocaine nebulization causes a limited
225 number of patients who receive lidocaine with mesh nebulizer. For this reason, the
226 number of patients who are applied lidocaine with a mesh nebulizer between the research
227 years and who meet the research criteria is limited. A prospective, double-blind study
228 with two groups with a higher number of subjects using JN or MN may add value to the
229 research.

230 In conclusion, MNs may be used as an alternative to JN for pre-FB local anesthetic
231 administration to decrease cough severity during and post-FB in children. Silent and short
232 duration of nebulization are the advantages of this technique.

233 **Conflict of interest**

234 The authors declare that the study has not received any funding and there are no conflicts
235 of interest

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247 **5. References**

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339 **6. Tables**

340 **Table 1. Sociodemographic and procedure characteristics of the study population**

341

	MN Group	JN Group	p=
	(n=20)	(n=20)	
Age (years) ****	9.5 (4.6)	8.3 (3.6)	0.44*
Sex (male) *****	12(60)	8 (40)	0.34****
Bronchoscopy duration (Minutes)*****	9.6 (5.4)	8.6 (2.9)	0.51**
Anesthesia duration (Minutes)*****	15.9 (9.7)	15.3 (6.2)	0.88**
Time to awaken (Minutes)*****	7.9 (9.0)	7.6 (3.0)	0.10**
Recovery time (Minutes)*****	4.8 (1.8)	5.9 (1.8)	0.22**

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343 *Student T Test

344 **Mann-Whitney U Test

345 *** Pearson Chi-Square

346 **** Expressed as mean (SD)

347 *****Expressed as n (%)

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353 **Table 2. Post FB croup, cough and laryngospasm scores of the groups**

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		MN Group	JN group	
		n=20	n=20	p=
Croup Score	Mild *	19 (95)	18 (90)	
	Moderate *	1 (5)	1 (5)	0.62 **
	Severe *	0 (0)	1 (5)	
Cough Score	Mild *	14 (70)	6 (30)	
	Moderate *	6 (30)	12 (60)	0.03 **
	Severe *	0 (0)	2 (10)	
Laryngospasm Score	No *	16 (80)	18 (90)	
	Grade 1 *	4 (20)	1 (5)	
	Grade 2 *	0 (0)	1 (5)	0.50 **
	Grade 3 *	0 (0)	0 (0)	

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356 *Values are expressed as n (%)

357 ** Pearson Chi-square