Original Article

Lidocaine Nebulization Compared to Lidocaine Spray in Decreasing Pain, Cough and Breathless in Flexible Fiber Optic Bronchoscopy

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Abstract

Background: Flexible optical fiber bronchoscopy (FFB) is a visual airway tract examination for diagnostic and therapeutic purposes. This procedure often causes discomfort for patients, such as cough, breathlessness and pain. Lidocaine is a topical anesthetic premedication used in bronchoscopy. This study compared the use of lidocaine nebulization and lidocaine spray in inhibiting pain, cough and breathlessness in complexity of flexible fiber optic bronchoscopy.
Methods: Pretest and posttest control group clinical study was conducted in patients prior to bronchoscopy at RSUD Dr. Moewardi from February to March 2020. The samples were taken by consecutive sampling technique, then randomly assigned into either lidocaine spray or nebulization. Cough and pain were assessed with VAS score while breathlessness was assessed with Borg score. The data were analyzed statically by using Chi-square test with $P<0.05$ was considered significant
Results: Cough scores were -17.78±11.66 for nebulization and -8.33±6.18 for spray ($P=0.005$). Pain score were -16.67±11.38 and -9.44±7.25 for nebulization and spray respectively ($P=0.045$). Borg score obtained the scores for nebulization and 0.06±0.42 for spray ($P=1.000$).
Conclusion: Both lidocaine nebulization and spray were effective in decreasing breathlessness during bronchoscopy. However, lidocaine nebulization was more effective in decreasing cough and pain.
Keywords: breathless, bronchoscopy, cough, lidocaine, pain

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INTRODUCTION

Flexible fiberoptic bronchoscopy (FFB) is a visual examination of the airways, also called airway endoscopy, that can visualize the tracheobronchial area. The FFB procedure is performed as a diagnostic tool to take airway and tissue mucus samples. Flexural fiberoptic bronchoscopy is the most commonly performed procedure for examining lung disease. Invasive measures for diagnosing and treating lung disease are quite developed along with advances in technology. Indications for this action are divided into diagnostic and therapeutic indications.[1,2]

Minimally invasive procedures in FFB often cause discomfort to the patient but can increase the value of diagnosis and result in more effective therapy. Minimizing contamination during invasive procedures is very important so that these actions do not cause secondary infections. This procedure is generally performed in patients using moderate sedation with intravenous premedication but may also be performed without sedation and general anesthesia. Patients with critical illnesses can also be treated with FFB to establish diagnosis and therapy. The patient considers the FFB procedure uncomfortable due to the side effects of the action taken. Discomfort and complications of this procedure include pain, coughing, and shortness of breath. The comfort and cooperation of the patient when it is carried out significantly affect the success of the action and affect the overall results to be achieved.[3–5]

Lidocaine is a topical anesthetic recommended as a premedication intervention in BSOL. Nebulized lidocaine as a premedication is expected to reduce pain, cough, and shortness of breath and eliminate unpleasant sensations during the procedure. The minimum effective dose should be used and should be used with caution in patients with advanced age, impaired liver function, or congestive heart failure. A well-established doctor-

patient relationship and *informed consent* are also expected to reduce discomfort in patients during FFB procedures. Research conducted by Sudarto et al. showed that administering anesthetic spray and nebulization comforts patients undergoing FFB procedures. Research by Dreher et al. showed that administration of lidocaine during nebulization was found to be well tolerated and safe compared to administration by injection. Bronchoscopy with general anesthesia is still an obstacle because it prolongs the duration of bronchoscopy, increases costs, and increases common complications, including hemodynamic disorders and respiratory depression.[4,5]

Research on the effect of nebulized lidocaine and spray on FFB premedication in reducing side effects of pain, cough, and shortness of breath has not been studied further. The results of this study are expected to show differences in the use of nebulized lidocaine and spray in reducing side effects in patients who will undergo FFB procedures at Doctor Moewardi Hospital Surakarta and can be applied to achieve better treatment results.

METHODS

This study was clinical research with the pretest-posttest control group design. The target population was patients who underwent BSOL procedures at Dr. Moewardi Hospital Surakarta in February-March 2020 until the sample was met. The method of selecting the research sample is determined by consecutive sampling. Each patient who met the study criteria on consecutive sampling was included in the study for a certain time until the required number of patients was met. Determination of the control group is the order of patients with odd numbers, and the treatment group is the order of patients with even numbers. There were 36 participants included and assigned into two groups, 18 participants for each group.

The inclusion criteria in this study were patients who would undergo bronchoscopy at Dr. Moewardi Hospital Surakarta in medical treatment, willing to take part in the study by signing informed consent, age ≥18 years, the patient was aware and was not diagnosed with mental disorder, able to see, read, write, and communicate verbally well, was cooperative and met the requirements for FFB procedure. The exclusion criteria in this study were patients who had allergies or intolerances to lidocaine, refused the study, could not see, read, write, and communicate well verbally, patients with heart disorders and severe risk measures, a severe lung disease with severe risk measures, poor general condition, hypoxia, coagulopathy or a hemorrhagic diathesis.

The patient presented to Dr. Moewardi Surakarta to take FFB action. Patients, as research subjects, were initially explained about the aims and objectives of study. All study subjects were explained about standard education on bronchoscopy. Research subjects willing to participate in the study were asked to sign an informed consent form. Subjects who met the inclusion criteria were given education. The research subjects were assigned into two groups by consecutive sampling, treatment and control groups. Participants who had been explained about standard education on bronchoscopy implementation and education were asked to fill out questionnaires. The first treatment group was given nebulized lidocaine 2% 5cc for premedication before the FFB procedure. The second treatment group was given 10% lidocaine spray 3 actuations in the oropharynx before the FFB procedure. The assessment of pain, cough, and shortness scores was carried out before and after the FFB action was completed, and then a statistical analysis of the results was carried out.

Data analysis was carried out using SPSS version 19 for Windows and data presentation using Microsoft Office 2010. All research data were tested for normality, and research data used the Shapiro-Wilk normality test since the sample was <50 subjects. This study used an unpaired sample so that the research data was tested with independent T-test if the data was normally distributed and Mann-Whitney test if the data was not normally distributed. In contrast, the paired group sample test used paired T-test if the data distribution was normal. Wilcoxon test is used for both normal and abnormal data

distribution.

RESULTS

This study was conducted on 36 participants who were equally assigned into two groups. Each group consisted of 18 participants, namely the nebulized lidocaine group and the lidocaine spray group. Research subjects who had been explained about standard education in implementing FFB were given an initial assessment. Initial assessment of pain using the VAS of pain, cough with the VAS of cough, and shortness of breath with the modified Borg scale. The initial assessment was carried out in the bronchoscopy room before the procedure.

The first group was given 10% 5cc nebulized lidocaine for premedication, while the second group was given 10% lidocaine spray three times actuation in the oropharynx for premedication before FFB. A second-stage assessment of pain, cough, and shortness was performed after the FFB was completed. The characteristics of the research subjects in this study were age, gender, occupation, education, Brigman's index, and comorbidities. The characteristics of the subjects of this study were categorical data presented in the form of frequency and percentage distributions.

Characteristics of research subjects were based on several components. The average age of patients undergoing bronchoscopy in the Nebulization group was 50.06±12.72 years, and the average age in the spray group was 60.61±12.45 years. Statistical test results obtained *P*=0.017, which indicated that there was a significant difference in patient characteristics based on age between patients in the nebulized and spray group.

Table 1. Characteristics of Research Subjects

Characteristics	Group		*P*
	Nebulization	Spray	
Age[a]	50.06±12.72	60.61±12.45	0.017
Gender[b]			
Male	14 (77.8%)	13 (72.2%)	1.000
Female	4 (22.2%)	5 (27.8%)	
Occupation[b]			
Laborer	2 (11.1%)	1 (5.6%)	
Housewife	2 (11.1%)	0 (0.0%)	
Pension	0 (0.0%)	1 (0.0%)	
Farmer	3 (16.7%)	9 (50.0%)	0.152
Civil Servant	2 (11.1%)	0 (0.0%)	
Self-employed	8 (44.4%)	7 (38.9%)	
Unemployed	1 (5.6%)	0 (0.0%)	
Education[c]			
Elementary School	4 (22.2%)	8 (44.4%)	
Junior High School	8 (44.4%)	3 (16.7%)	0.487
Senior High School	4 (22.2%)	6 (33.3%)	
College	2 (11.1%)	1 (5.6%)	
Index Brinkman[c]			
Non smoker	7 (38.9%)	7 (38.9%)	
Mild	4 (22.2%)	0 (0.0%)	0.852
Moderate	4 (22.2%)	11 (61.1%)	
Severe	3 (16.7%)	0 (0.0%)	
Contagious disease			
Plural effusion	3 (16.7%)	0 (0.0%)	
Hemoptysis	1 (5.6%)	0 (0.0%)	
Hydropneumothorax	1 (5.6%)	0 (0.0%)	
Hypertension	2 (11.1%)	0 (0.0%)	0.050
Pneumonia	5 (27.8%)	3 (16.7%)	
Chronic Obstructive Pulmonary Diseases	1 (5.6%)	1 (5.6%)	
Super Vein Cava Syndrome	1 (5.6%)	0 (0.0%)	
Others	4 (22.2%)	14 77.8%)	

Note=Numerical data is normally distributed, independent sample t test; [b] nominal categorical data; frequency (%), chi square/fisher exact test; declared significant if the test results in *P*<0.05.[c] Coordinal category: f (%) Mann Whitney test

Fourteen patients (77.8%) in the nebulization group were male and 13 participants (72.2%) in the spray group was male. Statistical test results obtained *P*=1.000 meaning there was no significant difference in patient characteristics based on gender in the nebulized and spray groups.

Based on the occupation of patients, 8 patients (44.4%) in the nebulization group were self-employed while in the spray group patients, 9 patients (50.0%) worked as farmers. The statistical test result obtained *P*=0.152, implying there was no significant difference in patient characteristics based on occupation between patients in the nebulized group and spray group.

Based on the education, eight patients (44.4%) in the nebulization group were junior high school graduate, while eight participants (44.4%) in the spray group were elementary school graduate. The statistical test results obtained *P*=0.487, meaning there was no significant difference in patient characteristics based on education between patients in the nebulized group and the spray group.

Based on IB, there were 7 patients (38.9%) in the nebulized group patients who did not smoke, while in the spray group, most of them were moderate smokers, amounting to 11 patients (61.1%). The statistical test results obtained *P*=0.852, implying there was no significant difference in patient characteristics based on IB between patients in the nebulized group and spray group.

Based on comorbidities, five patients (27.8%) in the nebulized group were diagnosed with pneumonia while majority of patients in the spray group had no comorbidities, 14 patients (77.8%). Statistical test obtained *P*=0.050, indicating that there was no significant difference in patient characteristics based on comorbidities between patients in the nebulized group and spray group. The characteristics of the research subjects can be seen in Table 1.

The difference and decrease in pre-post pain scores with nebulized lidocaine and spray are described in Table 2. Based on Table 2, the average pretest pain score in the nebulized group was 27.22±21.91, and the post-test pain score averaged 10.56±12.59. The difference in post-pre-nebulization pain score changes decreased by an average of 16.67±11.38. The pre-test pain score in the spray group had average score of 25.56±9.22, and the post-test pain scores an average of 16.11±7.78. The difference in changes in post-pre pain score in the spray group was revealed to have average decrease of -9.44±7.25.

Table 2. Test of Differences in Pain Scores Between the Nebulized Group and the Lidocaine Spray Group

Group	Painful			
	Pre	Post	*P*	Post – Pre
Nebulization	27.22±21.91	10.56±12.59	0.0001	-16.67±11.38
Spray	25.56±9.22	16.11±7.78	0.001	-9.44±7.25
P	0.135	0.043		0.045

Note=The results of the observations are described with mean SD, the unpaired group difference test did not pass the normality requirement (mann whitney); Buji different groups in pairs did not pass the requirements for normality (Wilcoxon rank test). Changes are declared significant if the test results in *P*< 0.05.

The nebulized group obtained *P*=0.0001, implying that the group experienced a significant change in pain scores. The spray group had value of *P*=0.001, which means that the spray group experienced a significant change in pain scores. The nebulization and spray treatments reduced the patient's pain scores. The subjects who were given the nebulization treatment experienced a decrease in pain scores more than the spray group and were statistically significant. This was evidenced in the unpaired difference test on the post-pre difference value (*P*=0.045). It can be concluded that lidocaine nebulization reduces pain scores more than spray.

Table 3. Differences in Cough Scores Between the Nebulized Group and the Lidocaine Spray Group

Group	Cough			
	Pre	Post	*P*	Post – Pre
Nebulization	25.00±15.43	7.22±8.26	<0,001	-17.78±11.66
Spray	25.56±11.49	17.22±8.95	0,001	-8.33±6.18
P	0.684	0.002		0.005

Note=The results of the observations are described by means of SD, the unpaired group difference test does not pass the normality requirement (mann whitney); The paired difference test did not pass the normality requirement (Wilcoxon rank test). Changes are declared significant if the test results in *P*<0.05.

The difference and decrease in pre-post cough scores with nebulized lidocaine and spray is outlined in Table 3. Based on Table 3, the pre-test cough scores in the nebulized group had an average score of 25.00±15.43 and the post-test cough scores

averaged 7.22±8.26. The difference in the post-pre nebulized cough score changes was decreased by an average of -17.78±11.66. Pre-test cough scores in the spray group had an average score of 25.56±11.49 and post-test cough scores averaged 17.22±8.95. The difference in post-pre cough score changes in the spray group was decreased by an average of -8.33±6.18.

The nebulized group had value of *P*<0.001, indicating that the group experienced a significant change in cough score. The spray group had value of *P*=0.001, suggesting that the spray group experienced a significant change in cough scores. The nebulization and spray treatments reduced the patient's cough scores, whereas the subjects who were given the nebulization experienced a greater reduction in cough scores than the spray group and were statistically significant. This was evidenced in the unpaired difference test on the post-pre difference value (*P*=0.005). It can be concluded that nebulization lowers cough scores more than spray.

Table 4. Test of Differences in Tightness Scores between the Nebulized Group and the Lidocaine Spray Group

Group	Congested			
	Pre	Post	*P*	Post – Pre
Nebulization	1.19±1.32	1.11±1.36	0.593	-0.08±0.55
Spray	1.94±0.73	1.89±0.58	0.564	-0.06±0.42
P	0.010	0.007		1.000

Note=The results of the observations are described by means of SD, the unpaired group difference test does not pass the normality requirement (mann whitney); b the paired difference test did not pass the normality requirement (Wilcoxon rank test). Changes are declared significant if the test results in *P*<0.05

The difference and decrease in pre-post shortness scores of nebulized lidocaine and spray are summarized in Table 4. Based on Table 4, the pretest score in nebulized group had an average of 1.19±1.32 and average post-test score of 1.11±1.36. The difference in the post-pre-nebulized dyspnea score in the nebulized group was reported to have an average decrease of -0.08±0.55. The score of pre-test tightness in the spray group had an average of 1.94±0.73 and an average post-test score of 1.89±0.58. The difference in score changes of post-pre breathlessness in the spray group had an average decrease of -0.06±0.42. The nebulized group had value of *P*=0.593 suggesting that the nebulized group experienced an insignificant change in the shortness score. The spray group had value of *P*=0.564, indicating means that the spray group also did not experience a significant change in the tightness score. Participants who had nebulization treatment experienced a decrease in shortness scores more than the spray group, although statistically insignificant (*P*=1.000).

DISCUSSION

This study aimed to determine the effectiveness of lidocaine using nebulization and spray techniques as a premedication for FFB by assessing shortness, cough, and pain scores. Lidocaine was proven to be effective in controlling cough and pain complaints by significantly decreasing VAS scores.

In contrast, lidocaine as a control of shortness of breath was shown to be less effective due to the decrease in the Borg scale score, which was not statistically significant. The basic characteristic and research variables were compared between the treatment group and control group by first testing the normality of data distribution as the basis for selecting statistical test to be used.

In this study, majority of the patients in the nebulization group were male, amounted to 14 patients (77.8%), and most of the patients in the spray group were male; 13 patients (72.2%). This is following research data reporting that men have a greater risk of lung cancer than women, so there were greater number of male patients who undergo bronchoscopy than women. Age is a risk factor for lung disease. Older age will affect the physiological condition, causing a decrease in the immune system. Diseases that can occur are shortness of breath and blood cough due to malignancy. The average age of patients who underwent bronchoscopy with nebulization was above 50 years and with spray was above 60 years.

Most participants in the nebulization group were self-employed, patients (44.4%), while the spray group patients mostly worked as farmers, with 9 patients (50.0%). Employment describes a person's socioeconomic history. Education can also affect the

incidence of lung diseases such as lung cancer. This relates to knowledge about using personal protective equipment at work and an unhealthy lifestyle.

In this study, majority of patients in nebulization group were junior high school graduates, 8 patients (44.4%). Most of the patients in the spray group were elementary school graduates, 8 patients (44.4%). The number and duration of smoking are the most significant risk factors for lung cancer. This can be seen through the Brinkman Index (IB). IB in the nebulization group participants who did not smoke, 7 patients (38.9%), while majority of the patients in the spray group were moderate smokers, 11 patients (61.1%).

Pain is a manifestation of unpleasant feelings which a person perceives, and its causes, in addition to nociceptive stimuli, are also psychological stimuli. Bronchoscopy may cause discomfort due to psychological stress and pain in patients' noses and throats (dysphagia). This perception is in the form of discomfort or unpleasant sensations and negative emotions interpreted as threats to the body. Lidocaine premedication plays a role in reducing the sensation of pain due to FFB.[6,7]

In this study, there was a decrease in pain through the VAS assessment. The use of nebulization and spray methods both reduce pain. However, the nebulization method was more effective in reducing pain than spray, following the results of this study which shows the difference in the average pain scores in the post-pre-nebulized group with spray, which has a significant value. It was revealed that post-pre-nebulization pain score had more significant decrease than the post-pre-spray pain score. Thus, it can be concluded that nebulization and spray can reduce the patient's pain score, but nebulization reduces pain scores more than lidocaine spray.[8,9]

The role of lidocaine in reducing pain through inhibition of transmission (one of a series of pain processes) of pain impulses through A-delta and unmyelinated C fibers from the periphery to the spinal cord. The action of lidocaine will block sodium channels which causes the electrical conduction process, which includes the inhibition of influx of Na-K ion pumps to prevent impulse conduction. Using a nebulizer, the administration of lidocaine is more effective since the nebulizer breaks down the active substance particles into tiny sizes of about 5 μm and enter the respiratory tract.[10–13]

The particle size of 5 μm has the potential to be deposited throughout the bronchial tree to the terminal bronchioles and alveoli by sedimentation. This deposition occurs due to the impaction of these particles in the upper respiratory tract due to air velocity and flows turbulence. Lidocaine diffuses through the membrane, which is a lipoprotein matrix consisting of 90% fat and 10% protein, into the axoplasm, then enters the sodium channel and interacts with receptors in it so that sodium channel blockade occurs and inhibits the depolarization process of nerve impulses so that pain stimuli can be inhibited.[10–13]

However, the study result does not support the research conducted by Sudarto et al., which reported no significant difference in pain reduction received by patients in the group using nebulization nor spray. This is possible because there were differences in number of samples and different characteristics in the research of Sudarto et al.[4,14]

Cough and hemodynamic turbulence at the time of bronchoscopy is an "emergence phenomenon" and is a daily clinical problem that is potentially dangerous because it may cause uncontrolled patient movement. Various techniques have been developed to help reduce cough, including administering intravenous opiates or administering intravenous or inhaled lidocaine as a premedication because systemic opiates and lidocaine have antitussive properties.[14,15]

In this study, there was a decrease in cough reflexes in patients assessed using the VAS scale for patients undergoing bronchoscopy with lidocaine premedication. Using nebulization and spray methods reduced the incidence of coughing, but the nebulization method was more effective than the spray. This follows the results of this study, where the difference in post-pre cough score changes in the nebulized group had a more significant decrease than in the spray group. Thus, both nebulization and spray

treatments reduced the patient's cough score, but the nebulization decreased the cough score more than the spray and was statistically significant.

The use of lidocaine was studied in Iran in 2011, reporting that the administration of 2% lidocaine 1.5 mg/kg BW intravenously reduced the incidence of coughing during extubation. Lidocaine works by inhibiting the transmission of RAR impulses and C fibers from the vagus nerve afferent pathways to the medulla oblongata as the cough center so that the cough reflex can be suppressed. Cough reflex block by lidocaine may occur because it depresses brainstem function by blocking peripheral receptors in the trachea and hypopharynx. Lidocaine will also block sodium (Na+) channels in sensory neurons so that action potential formation and neuronal conduction do not occur, triggered by various stimulation of airway afferent fibers, thereby reducing the occurrence of reaction potentials in the event of the cough reflex.

However, this study's results do not follow the research conducted by Keane et al., which concluded that nebulization or spray anesthesia had the same efficacy in suppressing cough during flexible fiberoptic bronchoscopy. This is because, in Keane et al.'s study, the nebulized and spray patient group were given 100 mg of lignocaine before being nebulized 2.5 ml of 4% lignocaine and 100 mg of lignocaine spray. Hence, the results obtained in cough scores were not significantly different.[4,16]

Symptoms of shortness of breath due to bronchoscopy are possible. This situation occurs due to increased psychic stress due to bronchoscopy action, which stimulates parasympathetic nerve activation, which will result in the release of acetylcholine from the post ganglion vagus nerve, which in turn causes acetylcholine to bind to muscarinic receptors (M3) in bronchial smooth muscle and results in increased respiratory rate and bronchospasm. This process is bridged by action potentials that occur across the cell membrane. Some neurotransmitters also act as neuro-modulators as well as agonists, where neurotransmitters will affect the sensitivity of receptors to other neurotransmitters such as glycine.[17,18]

In this study, there was a decrease in the manifestation of dyspnea in patients undergoing bronchoscopy with lidocaine premedication by using the Borg scale. Both nebulization and spray methods can reduce the incidence of shortness of breath. This is following the results of the study where the difference in the post-pre-nebulized shortness score in the nebulized group had a more significant average decrease than the spray group although it was not statistically significant, so it can be concluded that nebulization and spray methods did not have a significantly different effect in reducing the incidence of dyspnea in post bronchoscopy patients.

Several possibilities cause the results of this study to be insignificant; including the patients who were not hypoxic, had no previous complaints of shortness of breath and from the results of lung function measurements had good lung function values, so that the assessment of pre and post breathlessness scores of lidocaine administration was nebulization and spray did not have a significant impact.

This study also proved that there were no bronchoconstriction side effects, so participants were unlikely to be short of breath, and it is safe to use. A study by Michelle et al. compared the effects of nebulized anesthesia with spray. The study suggested no significant difference in the output between the administration of anesthesia as a premedication using the nebulization and spray methods.[19,20]

LIMITATION

This study has only proved the hypothesis that the effect of lidocaine premedication given by nebulization and spray can reduce pain and cough complaints in bronchoscopy patients. In contrast, the effect of other pre-medications has not been studied. Further research is still needed to prove the hypothesis of the effect of premedication other than lidocaine used to reduce complaints of pain, cough, and shortness of breath on bronchoscopy.

CONCLUSION

Lidocaine nebulization and lidocaine spray reduced pain in FFB patients where the lidocaine nebulization reduction score was higher than the lidocaine spray score. Nebulized lidocaine and lidocaine spray reduced cough in FFB patients, where the score of decreasing cough in nebulized lidocaine was higher than lidocaine spray. Nebulized lidocaine and lidocaine spray did not reduce shortness of breath in FFB patients (there was no difference).

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CONFLICT OF INTEREST

None.

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REFFERENCES

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