Original Article

The Effect of Inhaled Ipratropium Bromide as a Premedication For Bronchoscopy on Dyspnea, Cough, and Tracheobronchial Secretion

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Abstract

Background: Bronchoscopy is a minimally invasive procedure used for diagnostic examination and intervention of the airways. Patient comfort and cooperation during bronchoscopy are very important because they affect the success and outcome. The sympathetic anticholinergic effect of ipratropium bromide can improve procedure tolerance and airway visualization. This study was conducted to analyze the effect of inhaled ipratropium bromide as a bronchoscopy premedication for the assessment of dyspnea, cough, and tracheobronchial secretion.

Methods: This was a clinical study with a quasi-experimental pretest-posttest control group design in pulmonary patients who underwent bronchoscopy at Dr. Moewardi General Hospital Surakarta in October 2021 using consecutive sampling. The subjects of the study were divided into an intervention group with inhaled ipratropium bromide and a control group without inhaled ipratropium bromide. The Borg scale of dyspnea and the visual analog scale (VAS) score of cough were assessed before and after bronchoscopy in both groups. The grading of tracheobronchial secretion was assessed during bronchoscopy.

Results: Thirty-six pulmonary patients who underwent bronchoscopy were included in this study. The intervention group showed a lower Borg scale (0.28±0.57) and VAS score (3.22±8.54), lower tracheobronchial secretion grading, and there was a significant difference compared to the control ($P \leq 0.05$).

Conclusion: There was a significant difference in the Borg scale of dyspnea, VAS score of cough, and the grading of tracheobronchial secretion in patients undergoing bronchoscopy as an effect of ipratropium bromide inhalation.

Keywords: Borg scale of dyspnea, bronchoscopy, grading of tracheobronchial secretion, inhaled ipratropium bromide, VAS score of cough

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INTRODUCTION

Bronchoscopy is a minimally invasive procedure used for diagnostic and interventional examination of the airways. Bronchoscopy is generally performed using light sedation and intravenous (IV) premedication. Bronchoscopy can be performed without sedation or under general anesthesia if needed.[1,2] The invasive procedure of bronchoscopy causes discomfort for the patient. Complications of bronchoscopy include anxiety, dyspnea, coughing, and pain. Complications of bronchoscopy increase patient discomfort.[1–3]

Patient comfort and cooperation during bronchoscopy are very important because they affect the success and outcome. A good doctor-patient relationship, informed consent, and the use of premedication are expected to reduce anxiety and minimize complications experienced by patients.[2] In 2011, the American College of Chest Physicians stated that optimal procedure conditions are achieved when the patient is comfortable, the doctor can perform the procedure, and the risk is minimal.[4]

Premedication with anticholinergics during bronchoscopy procedures is used to reduce excessive secretion caused by general anesthetics. Anticholinergic drugs are still being used as premedication in health centers.[1,4] The main rationale for using anticholinergic agents during bronchoscopy is to improve visualization of the tracheobronchial tree by their antisecretory effect, prevent the bronchoconstriction reflex, and prevent vasovagal phenomena.[4] Anticholinergic drugs such as atropine, glycopyrrolate, and ipratropium bromide are used in bronchoscopy because of their sympathetic effect in

preventing vasovagal reactions such as bradycardia, coughing, and airway secretion. Anticholinergic sympathetic effects may increase procedure tolerance and airway visualization.[4,5]

Premedication with atropine has been commonly used in bronchoscopy procedures. Ipratropium bromide is an anticholinergic agent with a low systemic effect. Ipratropium bromide is a synthetic quaternary ammonium congener of atropine with atropine bronchodilator properties but minimal systemic absorption.[1,5]

Dyspnea can be assessed using the Borg scale, baseline dyspnea index (BDI), or transition dyspnea index (TDI). The Borg scale was modified from its original form to a 10-point scale with verbal expressions of severity associated with a specific number.[6,7] The modified Borg scale has good reproducibility in healthy individuals and can be applied to patients with cardiopulmonary disease as well as to statistical parameters.[7]

Cough control is very important for quality bronchoscopy because it makes visualization of the bronchi easier and helps obtain good samples. Cough severity can be assessed with subjective or objective tools.[8,9] A subjective evaluation of cough severity was assessed by a questionnaire. Methods that can be used to assess cough are the visual analog scale (VAS), cough symptoms score (CSS), simplified cough score (SCS), and cough severity diary (CSD).[8–12]

Hypersecretion of airway mucus makes visualization difficult during bronchoscopy. Williams et al assessed tracheobronchial secretion using a scale of 1 to 3 based on the presence or absence of the tracheobronchial secretion and the amount of saline solution used for washing. Reduced tracheobronchial secretion will facilitate bronchoscopy procedures and increase patient comfort.[13,14]

Ipratropium bromide works by blocking the muscarinic (M) receptors. Muscarinic antagonists reduce mucus secretion, increase the ability of the lungs to clear airway secretion, and reduce airway constriction due to activation of the parasympathetic nervous system.[4,5] Ipratropium bromide can also reduce dyspnea and coughing. The therapeutic effect of ipratropium bromide is in the form of an anticholinergic effect that inhibits the vagal reflex through an acetylcholine antagonist mechanism.[1,5] This study aims to determine the effect of inhaled ipratropium bromide as a bronchoscopy premedication for the assessment of dyspnea, cough, and tracheobronchial secretion. The results of this study are expected to strengthen the comfort level of the bronchoscopy procedure and increase the knowledge base in the fields of pulmonology and respiratory medicine.

METHODS

The study had a quasi-experimental pretest and posttest control group design for the assessment of dyspnea and cough. Posttest-only control group design for assessment of tracheobronchial secretion. The study population consisted of patients who underwent bronchoscopy procedure at the Dr. Moewardi General Hospital Surakarta in October 2021. The sampling technique was consecutive sampling. This study involved 36 patients. The subjects were grouped into the intervention and control groups.

The subjects were assessed for dyspnea with a modified Borg scale and cough with the VAS before bronchoscopy premedication. The intervention group was given inhaled ipratropium bromide (4 ml/1 mg) as a premedication for bronchoscopy. An inhaled solution of ipratropium bromide (4 ml) is given by nebulizer 20-40 minutes before bronchoscopy. The control group underwent standard bronchoscopy preparation. The assessment of tracheobronchial secretion grading is done during bronchoscopy. A second assessment of dyspnea and cough was performed after the bronchoscopy was completed.

The inclusion criteria for the study were pulmonary patients who were to undergo a bronchoscopy procedure at Dr. Moewardi General Hospital Surakarta, patients with lung tumors, mediastinal tumors, minimal pleural effusions, pneumothorax, age ≥18 years, and patients who could read and write. The exclusion criteria were

patients with allergies to ipratropium bromide, impaired consciousness, hemodynamic instability, cardiovascular disorders, hearing loss, cognitive or psychiatric disorders, asthma, and chronic obstructive pulmonary disease (COPD).

The study has been approved by the Ethics Committee of the Dr. Moewardi General Hospital Surakarta/Faculty of Medicine, Universitas Sebelas Maret Surakarta. Data analysis was carried out using SPSS version 19 for Windows, and data presentation was done using Microsoft Office 2010. All study data were tested for normality using the Shapiro-Wilk normality test because the sample size was <50 subjects. A value of *P*>0.05 means the subject in the study is homogeneous.

This study used a paired t-test for paired samples (pretest and posttest) and an independent t-test in the sample and intervention groups if the scale of numerical data and data distribution were normal. The study data was tested by the Mann-Whitney test to determine if the numerical scale of the data distribution was not normal. The Wilcoxon test was carried out if the two groups were paired and the data distribution was not normal. The unpaired group categorical data scale was tested using the Chi-Square test or Fisher's Exact test. The limit of significance is a value of *P*=0.05, which means it is statistically significant.

RESULTS

The demographic characteristics of the patients are presented in Table 1. The two groups of patients did not differ significantly in terms of age, sex, history of smoking, lung disease, or interventional procedures.

The modified Borg scale pretest in the intervention group had a mean value of 1.56±1.20. The mean of the modified Borg scale posttest increased to 1.83±1.42. The increase in the Borg scale was not statistically significant (*P*=0.059). The mean of the Borg scale at the pretest in the control group was 1.28±1.36. The mean Borg scale at the posttest in the control group increased to 2.44±1.95. The increase in the Borg scale was statistically significant, with *P*=0.004.

The changes between the two groups showed that in the intervention group patients, there was a mean increase of 0.28±0.57, and in the control group patients, it was 1.17±1.15. The difference in changes in the modified Borg scale (pretest-posttest) between the intervention and control groups was statistically significant, with *P*=0.014. The difference in the modified Borg scale between the treatment group and the control group can be seen in Table 2.

Table 1. Basic characteristics of research subjects.

Characteristic	Groups		*P*
	Intervention (n=18)	Control (n=18)	
Age	61.61±7.11	55.89±12.17	0.096
Sex			
Male	14 (77.8%)	11 (61.1%)	0.278
Female	4 (22.2%)	7 (38.9%)	
History of smoking			
Positive	13 (72.2%)	8 (44.4%)	0.091
Negative	5 (27.8%)	10 (55.6%)	
Lung disease			
Pleural effusions	4 (22.2%)	2 (11.1%)	0.553
Pneumothorax	2 (11.1%)	3 (16.7%)	
Mediastinal tumors	4 (22.2%)	3 (16.7%)	
Lung tumors	8 (44.4%)	10 (55.6%)	
Interventional procedure			
Bronchial wash	11 (61.1%)	16 (88.9%)	0.101
Forceps biopsy and bronchial wash	3 (16.7%)	0 (0.0%)	
Bronchial brush dan bronchial wash	4 (22.2%)	2 (11.1%)	

Table 2. Differences in the modified Borg scale between the treatment group and the control group.

Groups	Pretest	Posttest	*P*	Difference
Intervention	1.56±1.20	1.83±1.42	0.059	0.28±0.57
Control	1.28±1.36	2.44±1.95	0.004	1.17±1.15
P	0.612	0.211	---	0.014

The mean VAS scores on the pretest in the intervention group were 12.61±13.26. The mean VAS scores on the post-test in the intervention group rose to 15.83±11.37. The increase in the VAS scores was not statistically significant (*P*=0.114). The mean VAS score on the pretest in the control group using standard bronchoscopy preparation was 15.33±16.66. The mean posttest VAS scores in the control group increased to 32.56±25.40. The increase in the VAS score was statistically significant, with *P*=0.001.

Table 3. Differences in the cough VAS scores between the intervention group and the control group.

Groups	Pretest	Posttest	*P*	Difference
Intervention	12.61±13.26	15.83±11.37	0.114	3.22±8.54
Control	15.33±16.66	32.56±25.40	0.001	17.22±17.32
P	0.742	0.015	---	0.009

The change between the two groups showed that the intervention group had a mean increase of 3.22±8.54 and the control group had 17.22±17.32. The difference in the change VAS scores (pretest-posttest) between the intervention and the control group was statistically significant with *P*=0.009. The difference in VAS scores between the intervention group and the control group can be seen in Table 3.

Table 4. Differences in the grading of tracheobronchial secretion between the treatment group and the control group.

Variable	Groups		*P*-value
	Intervention (n=18)	Control (n=18)	
Tracheobronchial Secretion Grading	12 (66.7%)	4 (22.2%)	0.012
Grade 1	5 (27.8%)	12 (66.7%)	
Grade 2	1 (5.6%)	2 (11.1%)	
Grade 3	12 (66.7%)	4 (22.2%)	

Assessment of tracheobronchial secretion was performed at the time of bronchoscopy. The grading of tracheobronchial secretion in the intervention group mostly tended to be grade 1, which was 12 patients (66.7%), while in the control group, it tended to be grade 2, which was 12 patients (66.7%). The difference in tracheobronchial secretion grading between the intervention and control groups was statistically significant with *P*=0.012. The difference in the grading of tracheobronchial secretion between the intervention and control groups can be seen in Table 4.

DISCUSSION

The number of male subjects in this study was 25 patients (69.44%). The American Cancer Society stated that patients with lung cancer in the United States in 2021 would be around 235,760 new cases of lung cancer (119,100 in men and 116,660 in women) and about 131,880 deaths from lung cancer (69,410 in men and 62,470 in women).[15,16] Lung cancer is the most common type of cancer in men in Indonesia, and the fifth most common of all types of cancer in women.[16,17]

The results of hospital-based research from 100 hospitals in Jakarta in 2017 showed that lung cancer was the most common case in men and the fourth most common in women, and was the leading cause of death in both men and women.[16] Data from the Global Burden of Cancer Study (Globocan) 2020 stated that the number of new cases of lung cancer patients in Indonesia in 2020 was 25,943 (14.1%) in men.[17]

The dominant risk factor for lung cancer is a history of smoking.[16,18] The group of patients with a high risk of developing lung cancer includes patients aged >40 years with a history of smoking ≥30 years and smoking cessation within ≥15 years before the examination, or patients ≥50 years with a history of smoking ≥20 years and the presence of at least one other risk factor. This study showed that 21 patients (58.3%) were smokers.[16]

The most common lung disease in this study was lung tumor. Lung tumor was experienced by 18 patients (50%). Patients who present with lung tumors will undergo diagnostic procedures. Bronchoscopy is the main procedure for diagnosing lung cancer. This procedure can be used to obtain tissue or specimens for cytologic and histopathological examination.[19] Setiadi et al reported that the most frequent indication for bronchoscopy

performed in the Dr. Moewardi General Hospital Surakarta was a lung tumor (45.66%).[20]

Dyspnea is one of the dependent variables assessed in this study. Dyspnea was assessed with a modified Borg scale. Based on the results of this study, it could be seen that the administration of inhaled ipratropium bromide before bronchoscopy was able to prevent an increase in dyspnea after bronchoscopy. Bronchoscopy is a minimally invasive procedure that can cause psychological stress or anxiety. Yildirim et al discovered that anxiety before bronchoscopy and the length of the bronchoscopy procedure were related to the level of patient discomfort.[3]

Psychological stress triggers the hypothalamus to activate the autonomic system (sympathetic and parasympathetic). Activated parasympathetic nerves cause the release of acetylcholine. Acetylcholine will bind to M3 receptors on bronchial smooth muscle. The binding of acetylcholine and M3 receptors will result in an increase in respiratory rate and bronchospasm, which can cause dyspnea.[1,3,21]

A study related to the effect of ipratropium bromide as premedication on the assessment of dyspnea has never been performed before. The study of inhaled ipratropium bromide's effect as a bronchoscopy premedication was conducted by Inoue et al. Inoue et al reported that ipratropium bromide significantly prevented a decrease in forced expiratory volume (FEV) and peak flow rates (PFR).[22]

Based on the results of this study, the administration of inhaled ipratropium bromide before bronchoscopy could prevent increased coughing after bronchoscopy. Yildirim et al stated that discomfort and cough were the main effects of bronchoscopy.[3] Bronchoscopy can cause mechanical and chemical stimuli that result in irritation of the cough receptors. Cough stimulation continues to efferent nerve fibers in the vagus nerve, trigeminal nerve, glossopharyngeal nerve, and phrenic nerve. Cough stimuli will be transmitted to the cough center in the medulla and then to the efferent nerve fibers, stimulating cough to the effector. The cough reflex occurs in the effectors.[23]

Administration of ipratropium bromide inhibits cholinergic transmission of cough impulses. Ipratropium bromide reduces the excitability of cough receptors so that cough impulses are transmitted to the cough center. The binding of acetylcholine and M3 receptors due to vagus nerve stimulation is inhibited by ipratropium bromide. Inhibition of acetylcholine binding and M3 receptors can reduce tracheobronchial secretion, which also affects cough control.[21]

This study has different results from the previous study. Rubins et al pointed out that the use of ipratropium bromide as a premedication in elderly patients during bronchoscopy did not produce clinical benefits such as coughing, wheezing, changes in pulse rate, blood pressure, or oxygen saturation. Rubins et al used inhalation of normal saline solution in the placebo group. Inhaling normal saline can induce mucus secretion. Excessive mucus secretion results in coughing.[24]

The grading of tracheobronchial secretion is as follows: grade 1 if there is almost no secretion; grade 2 if normal saline is required for rinsing; and grade 3 if the secretion is excessive and difficult to see even after rinsing. One aliquot contains 5 ml of normal saline solution. A statistical test proved that the grade of tracheobronchial secretion in the intervention group was lower than in the control group.

The result of tracheobronchial secretion grading in this study was similar to the study of Wang et al. The study of Wang et al proved that the inhalation of ipratropium bromide before the bronchoscopy procedure indicated a practical benefit on airway secretion (P=0.02).[14] Cowl et al had different results regarding the use of anticholinergics in bronchoscopy procedures. Cowl et al reported that tracheobronchial secretion was not statistically different in patients treated with anticholinergic drugs when compared with the placebo group. Cowl et al used atropine injection as a bronchoscopy premedication agent.[25]

The bronchoscopy procedure increases tracheobronchial secretion. Ipratropium bromide blocks cholinergic receptors and decreases the production of cyclic guanosine monophosphate

(cGMP). A decline in cGMP will decrease contraction of the smooth muscles. Ipratropium bromide dilates bronchial smooth muscle and inhibits salivary and mucous gland secretions. Inhalation of ipratropium bromide is a more potent antimuscarinic and smooth muscle bronchodilator than atropine.[14,26]

LIMITATION

The research subjects included in the study were patients with lung tumors and mediastinal tumors. The criteria for tumor size and location have not been explained in detail so all patients with lung tumors and mediastinal tumors can be included in this study. The large size of the tumor and pressing on the bronchi will cause more complaints of dyspnea, thus affecting the assessment of dyspnea. The research subjects' responses to the Borg scale for dyspnea and VAS score for cough were influenced by subjectivity and the subject's ability to understand the researcher's explanation.

CONCLUSION

Administration of inhaled ipratropium bromide affects the difference in the Borg scale of dyspnea, the VAS score of cough, and the grading of tracheobronchial secretion in patients undergoing bronchoscopy procedures.

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CONFLICT OF INTEREST

None.

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REFFERENCE

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