CURRENT
THERAPEUTIC
RESEARCH
VOL. 54, NO. 1, JULY 1993

INHALED IPRATROPIUM BROMIDE AND FENOTEROL BEFORE BRONCHOFIBROSCOPY I. EFFECT ON COUGH AND NEED FOR TOPICAL ANESTHESIA

A. PALOJOKI AND H. PUOLIJOKI

Departments of Diseases of the Chest and Clinical Allergology, University of Turku, Turku, Finland

ABSTRACT

Beta-adrenergic agonists, such as fenoterol, and anticholinergic agents, such as ipratropium bromide, have been shown to have antitussive effects. During bronchofibroscopy, coughing often is the most prominent discomfort and is only partially relieved by topical anesthesia. A double-blind, placebo-controlled trial was conducted to study the effects of ipratropium bromide (0.08 mg), fenoterol (0.4 mg), and placebo inhalation powders in preventing cough during bronchoscopy. Each study drug was administered as a premedication 1 hour before the procedure. No statistically significant differences were found in the mean number of coughs or the need for lidocaine among the three study groups, whether the values were calculated for all patients or separately for those who were smokers or nonsmokers. Our results confirmed the well-known clinical finding that smokers tend to cough more during bronchoscopy. Smokers also needed more topical lidocaine during the procedure.

INTRODUCTION

Beta-adrenergic agonists, such as fenoterol (FEN), and anticholinergic agents, such as ipratropium bromide (IB), are widely used as bronchodilators. Their antitussive effects have been verified in cough induced by distilled water and hypotonic saline inhalation.[1,2] In a 40-patient study, Vesco et al[3] showed that during fiberoptic bronchoscopy, FEN exhibited antitussive properties that reduced the need for additional lidocaine used as the topical anesthetic.

During bronchoscopy, coughing often is the most prominent discomfort and is only partially relieved by topical anesthesia. However, the value of administering anticholinergic medication in this situation is not known. Ipratropium bromide has been proven effective in blocking vagal activity,[4] which is mainly responsible for the afferent impulses of the

Address correspondence to: Hannu Puolijoki, M.D., Department of Internal Medicine, Etelä-Pohjanmaa Central Hospital, SF-60220 Seinäjoki, Finland.
Received for publication on April 27, 1993. Printed in the U.S.A.

0011-393X/93/$3.50

cough reflex.[5] Thus the aim of our double-blind, placebo-controlled trial was to study the effects of IB, FEN, and placebo inhalation powders in preventing cough during bronchofibroscopy.

PATIENTS AND METHODS

A total of 181 nonasthmatic patients (107 men and 74 women) participated in the study. The mean age was 53 years (range, 21 to 75 years). Ninety of the patients were smokers, of whom 68 were men. All patients underwent bronchofibroscopy for diagnostic reasons, primarily because of pulmonary infiltrate, cough, or hemoptysis. Patients were excluded if they had chronic cardiac arrhythmia or used antiarrhythmic agents, had thyrotoxicosis, or used antihistamine drugs or chronic sympathomimetic or anticholinergic medication.

Patients were randomly assigned in groups of six to receive either 0.08 mg of ipratropium bromide,* 0.4 mg of fenoterol hydrobromide,† or identical placebo (two capsules each) inhalation powder 1 hour before bronchoscopy. All study drugs were administered under supervision in a double-blind fashion using an Ingelheim inhalator. All patients also received 10 mg of diazepam‡ IM 1 hour before the procedure.

Topical anesthesia consisted of puffs of 10% lidocaine§ spray onto the oropharynx and 4% lidocaine drops into the trachea. The doses were adjusted individually to achieve appropriate local anesthesia. If cough occurred during the procedure and was judged troublesome, additional 2% lidocaine, the quantity of which was recorded, was administered via the bronchoscope.

All bronchoscopies were performed by the same investigator, who passed the bronchoscope transorally. Olympus BF types P20D, B3R, 10, and 20 and Pentax type FB19H bronchoscopes were used, all with a tip size of 6 mm. After the tip of the bronchoscope passed the vocal cords, cough sounds were continuously recorded for 5 minutes with a tape recorder attached to the patient's chest.

The protocol was accepted by the joint ethical committee of Turku University and Turku University Central Hospital, and the patients gave their informed consent. Student's t test and general linear models were used in the statistical analysis.[6] A P value < 0.05 was considered statistically significant.

* Trademark: Atrovent® (Boehringer Ingelheim International GMBH, Ingelheim am Rhein, Germany).
† Trademark: Berotec® (Boehringer Ingelheim International GMBH, Ingelheim am Rhein, Germany).
‡ Trademark: Diapam® (Orion, Espoo, Finland).
§ Trademark: Xylocaine® (Suomen Astra, Kirkkonummi, Finland).

RESULTS

Among the patients pretreated with IB or FEN, the number of coughs during bronchoscopy was statistically significantly higher in smokers than in nonsmokers (table). In the placebo group, the difference was not statistically significant, although the smokers coughed more. No statistically significant differences were found in the mean number of coughs among the three study drug groups, whether the values were calculated for all patients or separately for those who were smokers or nonsmokers.

The need for topical anesthesia did not differ among the study groups. The groups were similar in their need for lidocaine before the bronchoscopy, need for additional lidocaine during the procedure, and total amount of lidocaine needed (table). However, smokers in the IB and FEN groups needed statistically significantly ($P < 0.05$) more lidocaine than did nonsmokers. The difference was explained by the need for additional lidocaine during the bronchoscopy ($P < 0.05$). Although a similar trend was seen in the placebo group, the difference was not statistically significant. Between all smokers (n = 90) and nonsmokers (n = 91), the mean amounts of total lidocaine needed were 384.2 mg and 368.3 mg, respectively, and the mean amounts of additional lidocaine needed were 23.9 and 9 mg, respectively ($P < 0.01$).

DISCUSSION

Our results did not confirm the findings of Vesco et al,[3] who showed that inhaled fenoterol significantly attenuated the cough induced by fiberoptic bronchoscopy. In our study, bronchofibroscopy was performed according to standard techniques, including the use of premedication and topical anesthesia, although the oral route of passing the bronchoscope was used. All patients were examined by the same physician, which reduced the variability in this respect. However, the amounts of lidocaine used as premedication in our study were higher than those used by Vesco et al,[3] which may partly explain the lack of any additional advantage after inhaling IB or FEN.

Our results confirm the well-known clinical finding that smokers tend to cough more during bronchofibroscopy, and smoking was noted to be the best indicator for the number of coughs. Smokers also needed more topical lidocaine during the procedure. However, neither IB nor FEN could attenuate the frequency of cough or the amount of lidocaine needed by smokers or nonsmokers compared with those receiving placebo. According to our results, the routine use of a beta$_2$-adrenergic agonist or muscarinic antagonist as premedication for bronchofibroscopy, performed according to the methods described in our study, is not warranted. However, this type of

Table. Effect of ipratropium bromide, fenoterol, and placebo powders on bronchoscopy-induced cough and need for lidocaine.

	Ipratropium Bromide			Fenoterol			Placebo		
	Smokers (n = 31)	Nonsmokers (n = 30)	All (n = 61)	Smokers (n = 26)	Nonsmokers (n = 33)	All (n = 59)	Smokers (n = 31)	Nonsmokers (n = 30)	All (n = 61)
Number of coughs	37.6 ± 29.3*	21.5 ± 13.8	29.7 ± 24.2	41.6 ± 30.8*	25.2 ± 18.1	32.5 ± 25.7	37.6 ± 33.8	26.5 ± 24.1	32.1 ± 29.7
10% lidocaine spray onto oropharynx (mg)	155.5 ± 16.3	153.3 ± 19.9	154.4 ± 18.0	158.1 ± 16.7	154.6 ± 18.2	156.1 ± 17.5	155.2 ± 13.4	161.3 ± 25.4	158.2 ± 20.3
4% lidocaine drops into trachea (mg)	204.8 ± 20.8	205.3 ± 20.3	205.1 ± 20.4	200.4 ± 24.1	203.3 ± 19.8	202.0 ± 21.6	206.8 ± 21.5	200.0 ± 0	203.4 ± 15.6
Additional 2% lidocaine (mg)	21.9 ± 32.4*	8.0 ± 19.4	15.1 ± 27.5	26.9 ± 28.3*	7.3 ± 18.6	15.9 ± 25.1	23.3 ± 30.6	12.0 ± 21.4	17.7 ± 26.9
Total lidocaine (mg)	382.2 ± 41.2*	366.7 ± 49.1	374.6 ± 45.5	385.4 ± 40.1*	365.2 ± 34.2	374.0 ± 38.3	385.3 ± 39.0	373.3 ± 28.7	379.3 ± 34.5

* $P < 0.05$ between groups.
Data are mean ± SD.

pretreatment may be useful in asthmatic patients, who were not included in the trial.

Acknowledgment

This study was supported by Boehringer Ingelheim, Finland.

References:

1. Lowry R, Wood A, Johnson T, Higenbottam T. Antitussive properties of inhaled bronchodilators on induced cough. *Chest* 1988; 93:186–189.
2. Higenbottam TW. Anticholinergics and cough. *Postgrad Med J* 1987; 63(Suppl 1):75–78.
3. Vesco D, Kleisbauer J-P, Orehek J. Attenuation of bronchofiberscopy-induced cough by an inhaled beta$_2$-adrenergic agonist, fenoterol. *Am Rev Respir Dis* 1988; 138:805–806.
4. Lichterfeld A. Safety of Atrovent. *Scand J Respir Dis* 1979; 60(Suppl 103):143–144.
5. Fuller RW, Jackson DM. Physiology and treatment of cough. *Thorax* 1990; 45:425–430.
6. Freund RJ, Littell RC, Spector PC. SAS system for linear models, 1986 edition. Cary, NC: SAS Institute Inc., 1986.