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

INHALED IPRATROPIUM BROMIDE AND FENOTEROL BEFORE BRONCHOFIBROSCOPY III. EFFECT ON HEART RATE AND CARDIAC ARRHYTHMIAS

H. PUOLIJOKI AND A. PALOJOKI

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

ABSTRACT

The effects of premedication with inhaled ipratropium bromide and fenoterol powders on heart rate and cardiac arrhythmias in patients undergoing bronchofibroscopy were evaluated in a double-blind, placebo-controlled study. Bronchoscopy induced significant sinus tachycardia in all patient groups, including smokers and nonsmokers ($P < 0.0001$). The tachycardia was more pronounced in the patients treated with fenoterol compared with those receiving ipratropium bromide or placebo ($P < 0.05$). The difference was largely attributable to the results obtained in the smokers. No life-threatening or other severe adverse effects were noted in any patient. Both fenoterol and ipratropium bromide can be administered safely as a premedication before bronchofibroscopy.

INTRODUCTION

An early review[1] ascribed the majority of life-threatening complications and deaths from bronchofibroscopy to cardiac arrhythmias, most of which were clearly attributable to the premedication or topical or general anesthetic used in critically ill elderly patients. Sinus tachycardia has been noted to be the only new disturbance in rhythm during the procedure when a baseline cardiac rhythm is established before the bronchoscopy.[2] This finding agrees with those noted during bronchoscopy using the rigid technique.[3]

During bronchoscopy, coughing is often the most prominent discomfort. Fenoterol (FEN) has been shown to have antitussive properties that reduce the need for lidocaine during the procedure.[4] The value of administering anticholinergic medication, such as ipratropium bromide (IB), in this situation is not known. We administered inhaled IB, FEN, and placebo powders as premedication to patients undergoing bronchoscopy to determine the effect of each drug and that of the procedure itself on heart rate and cardiac arrhythmias.

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

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.

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.[5] A P value < 0.05 was considered statistically significant.

RESULTS

Bronchoscopy induced significant sinus tachycardia in all patient groups, including smokers and nonsmokers ($P < 0.0001$) (table). The tachycardia was more pronounced in the patients treated with FEN compared with those receiving IB or placebo ($P < 0.05$). The difference was largely attributable to the results obtained in the smokers, in whom FEN increased the

* 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).

Table. Effect of ipratropium bromide, fenoterol, and placebo powders on bronchofiberoscopy-induced increase in heart rate (beats/min) related to the location of the tip of the bronchoscope.

	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)
Baseline	74 ± 15	71 ± 14	73 ± 14	72 ± 12	70 ± 11	71 ± 11	75 ± 16	70 ± 11	72 ± 14
Mean increase versus tip at:									
Trachea	15 ± 20	21 ± 19	18 ± 20	28 ± 18	28 ± 21	28 ± 20	17 ± 18	23 ± 19	20 ± 19
Right side	16 ± 20	23 ± 21	19 ± 20	30 ± 20	28 ± 24	29 ± 22	23 ± 25	24 ± 21	23 ± 23
Left side	24 ± 21	33 ± 22	28 ± 22	39 ± 20	35 ± 23	37 ± 22	26 ± 23	28 ± 23	27 ± 23
Posttest	14 ± 13	22 ± 15	18 ± 15	33 ± 14	26 ± 17	29 ± 16	22 ± 19	24 ± 15	23 ± 17

Data are mean ± SD.

heart rate statistically more than did IB or placebo. Among nonsmokers, the differences between the three groups were not significant.

In all groups, the increase in heart rate was highest when the tip of the bronchoscope was located at the left side, but no statistically significant differences were noted among groups. Only 8 patients in the IB group, 10 in the FEN group, and 6 in the placebo group had heart rates > 130 beats/min at some phase of the study. Neither atrial fibrillation nor other abnormal tachyarrhythmias were noted.

Premature supraventricular beats (at least 1 in 20 normal beats) during some phase of the procedure were noted in 5 patients in the IB group, 3 in the FEN group, and 7 in the placebo group among those who had no premature beats at baseline. The number of premature ventricular beats (at least 1 in 20 normal beats) were 6, 4, and 3, in the IB, FEN, and placebo groups, respectively. The differences among groups were statistically insignificant. Left bundle branch block was noted in two patients in the placebo group. New ST depression of more than 1 mm in each of leads III, AVF, and V_2-V_4, which was indicative of ischemic heart disease, was found in one patient each in the IB and FEN groups. Altogether 6 patients treated with IB, 4 treated with FEN, and 3 receiving placebo had at least a 1-mm new ST depression in lead III at some phase of the study. None of the patients in this study reported chest pain.

DISCUSSION

In this study, cardiac abnormalities during or immediately after bronchofibroscopy were rare. This finding may be attributable to the overall good health of the study participants, since patients with chronic cardiac arrhythmias and those who used antiarrhythmic agents were excluded. Fiberoptic bronchoscopy usually is a well-tolerated procedure,[6,7] although cardiac arrhythmias, both supraventricular and ventricular, can occasionally occur. The arrhythmogenic potential of the procedure may be partially associated with its ability to produce hypoxemia.[8,9] We did not measure oxygen saturation during the procedure and therefore cannot draw conclusions about this relationship.

Our results showed that fenoterol, a $beta_2$-sympathomimetic drug, increased heart rate more than IB or placebo, although statistically significant increases were noted in all three groups. However, no life-threatening or other severe adverse effects were noted in any patient. Thus both FEN and IB can be administered safely as a premedication before bronchofibroscopy.

Acknowledgment

This study was supported by Boehringer Ingelheim, Finland.

References:

1. Suratt PM, Smiddy JF, Gruber B. Deaths and complications associated with fiberoptic bronchoscopy. *Chest* 1976; 69:747–751.
2. Luck JC, Messeder OH, Rubenstein MJ, et al. Arrhythmias from fiberoptic bronchoscopy. *Chest* 1978; 74:139–143.
3. Palojoki A, Kallio V, Tala E. Electrocardiographic changes during bronchoscopy. *Scand J Respir Dis* 1968; 49:32–34.
4. 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.
5. Freund RJ, Littell RC, Spector PC. SAS system for linear models, 1986 edition. Cary, NC: SAS Institute Inc., 1986.
6. Credle WF, Smiddy JF, Elliot RC. Complications of fiberoptic bronchoscopy. *Am Rev Respir Dis* 1974; 109:67–72.
7. Periera W, Kovnat DM, Snider GL. A prospective cooperative study of complications following flexible fiberoptic bronchoscopy. *Chest* 1978; 73:813–816.
8. Khan MA. Fiberoptic bronchoscopy revisited. *Chest* 1978; 74:119–120.
9. Katz AS, Michelson EL, Stawicki J, Holford FD. Cardiac arrhythmias. Frequency during fiberoptic bronchoscopy and correlation with hypoxemia. *Arch Intern Med* 1981; 141:603–606.