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INHALED IPRATROPIUM BROMIDE AND FENOTEROL BEFORE BRONCHOFIBROSCOPY II. EFFECT ON DETERIORATION IN LUNG FUNCTION

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ABSTRACT

In a double-blind, placebo-controlled trial, fenoterol as a premedication was shown to have better bronchodilative properties, especially on the small airways, than ipratropium bromide or placebo in 181 nonasthmatic patients undergoing fiberoptic bronchoscopy for diagnostic reasons. When the patients were assessed 20 minutes after the procedure, the deterioration in lung function induced by either the bronchoscopy itself or the lidocaine used as a topical anesthetic was minor in all groups, compared with baseline values.

INTRODUCTION

Numerous studies[1–3] have verified that bronchofibroscopy induces deterioration in lung function. The topical anesthetic lidocaine, which has been shown to cause bronchoconstriction in hyperreactive airways,[4,5] may be the principal cause of decreased lung function.[6] These findings raise the question of whether lung function impairment during bronchoscopy can be prevented by premedication with inhaled ipratropium bromide (IB), a muscarinic antagonist, or fenoterol (FEN), a beta$_2$-adrenergic drug.

This double-blind, placebo-controlled trial was designed to compare the effects of IB inhalation powder with those of FEN and placebo powders as a premedication before 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

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infiltrate, cough, or hemoptysis. Patients were excluded if they had chronic cardiac arrhythmia or used antiarrhythmic agents, had thyrotoxicosis, or used antihistamine drugs, or were receiving chronic sympathomimetic or anticholinergic medication.

Patients were randomly assigned 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 bronchofibroscopy. Separate prerandomized series in blocks of six patients each were used for smokers and nonsmokers. All study drugs were administered using an Ingelheim inhalator. All patients also received 10 mg of diazepam‡ IM 1 hour before the procedure. Before the premedication was given and 20 minutes after the bronchoscopy was performed, each patient underwent ventilation-volume spirometry (Jaeger Masterlab ML/t-FP, Würtzburg, Germany).

Topical anesthesia included puffs of 10% lidocaine§ spray onto the oropharynx and 4% lidocaine drops into the trachea. When needed, additional 2% lidocaine, the quantity of which was recorded, was administered via the bronchoscope. The doses were adjusted individually to achieve appropriate local anesthesia. All bronchoscopies were performed by the same investigator, with the patient in a supine position and the bronchoscope passed 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. A P value < 0.05 was considered statistically significant.

RESULTS

Bronchofibroscopy induced deterioration in peak expiratory flow (PEF) values in all three groups studied (Table I). The change was statistically significant in the IB and placebo groups but not in the FEN group. The differences in the trends toward either an increase or decrease in forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC), and forced inspiratory volume in 1 second (FIV_1) did not differ among the study groups, although FEN tended to increase these parameters, particularly FEV_1 in nonsmokers (from 3.09 to 3.18 L; $P = 0.033$).

In the parameters usually used to measure small airways function, a clear benefit was seen with FEN (Table II). Both IB and FEN significantly

* 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 I. Effect of ipratropium bromide, fenoterol, and placebo powders on bronchoscopy-induced deterioration in large airway lung function.

	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)
FEV_1 (L)	2.53 ± 0.22	2.74 ± 0.33	2.63 ± 0.28	2.68 ± 0.27	3.09 ± 0.22	2.91 ± 0.24	2.79 ± 0.26	2.65 ± 0.19	2.72 ± 0.22
Change in means	+0.02	+0.04	+0.02	+0.09	+0.09	+0.09	−0.18	+0.10	−0.04
P	0.6523	0.2123	0.1938	0.1319	0.0330	0.0098	0.3811	0.2504	0.1620
FVC (L)	3.85 ± 0.27	4.01 ± 0.20	3.93 ± 0.24	3.91 ± 0.30	4.17 ± 0.22	4.06 ± 0.26	3.69 ± 0.31	4.12 ± 0.23	3.91 ± 0.27
Change in means	−0.19	−0.09	−0.14	+0.01	−0.07	−0.04	+0.02	−0.04	−0.02
P	0.0632	0.0047	0.0012	0.9110	0.0752	0.2765	0.4936	0.6346	0.7791
PEF (L/sec)	7.73 ± 1.20	8.23 ± 1.28	7.96 ± 1.24	8.09 ± 1.16	8.98 ± 1.07	8.59 ± 1.10	8.41 ± 1.47	7.60 ± 0.85	8.01 ± 1.20
Change in means	−0.67	−0.40	−0.53	−0.32	−0.17	−0.24	−0.84	−0.59	−0.71
P	0.0042	0.1624	0.0023	0.1676	0.3679	0.1035	0.0034	0.0008	<0.0001
FIV_1 (L)	2.61 ± 0.70	2.89 ± 0.71	2.75 ± 0.70	3.00 ± 0.69	3.19 ± 0.82	3.10 ± 0.76	2.71 ± 0.59	2.87 ± 0.59	2.79 ± 0.59
Change in means	−0.10	−0.02	−0.09	−0.26	−0.21	−0.029	−0.01	0	−0.01
P	0.4481	0.2020	0.1470	0.0255	0.1112	0.0076	0.6288	0.5558	0.4428

Data are mean ± SD.
FEV_1 = forced expiratory volume in 1 second; FVC = forced vital capacity; PEF = peak expiratory flow; FIV_1 = forced inspiratory volume in 1 second.

Table II. Effect of ipratropium bromide, fenoterol, and placebo powders on bronchoscopy-induced deterioration in small airway lung function.

	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)
FEV_{25-75} (L/sec)	1.70 ± 0.47	2.24 ± 0.40	1.96 ± 0.44	1.93 ± 0.52	2.76 ± 0.47	2.41 ± 0.52	2.04 ± 0.31	2.06 ± 0.46	2.05 ± 0.39
Change in means	+0.09	+0.48	+0.18	+0.15	+0.51	+0.35	−0.05	+0.04	−0.01
P	0.2322	0.0002	0.0007	0.1460	<0.0001	<0.0001	0.4339	0.6764	0.9222
FEF_{50} (L/sec)	2.27 ± 0.57	2.87 ± 0.64	2.57 ± 0.60	2.61 ± 0.61	3.55 ± 0.84	3.13 ± 0.75	2.69 ± 0.57	2.75 ± 0.55	2.72 ± 0.55
Change in means	+0.13	+0.21	+0.16	+0.36	+0.59	+0.49	−0.10	−0.12	−0.11
P	0.1960	0.0663	0.0241	0.0071	0.0047	0.0001	0.2626	0.3086	0.1253
FEF_{25} (L/sec)	1.17 ± 1.09	1.46 ± 0.40	1.32 ± 0.83	1.18 ± 1.55	1.28 ± 0.35	1.23 ± 1.05	0.97 ± 0.24	0.97 ± 0.24	0.97 ± 0.24
Change in means	+0.05	+0.27	+0.14	+0.33	+0.38	+0.36	+0.02	+0.01	+0.01
P	0.8365	0.0009	0.1519	0.2816	<0.0001	0.0159	0.7764	0.0770	0.7937

Data are mean ± SD.
FEF = forced expiratory flow.

increased FEF_{25-75} (Table II). The same trend was seen for FEF_{50} and FEF_{25} among patients pretreated with FEN compared with those receiving placebo and among nonsmokers treated with IB compared with nonsmokers in the placebo group.

DISCUSSION

In this study, fiberoptic bronchoscopy caused only slight deterioration in lung function when the flow-volume curves were measured more than 1 hour before and 20 minutes after the procedure. The only clear evidence of deterioration, perhaps due to lidocaine,[6] was seen in PEF values. However, unlike Peacock et al,[6] we did not measure immediate changes in the spirometric values during bronchoscopy.

Our results showed that FEN had better bronchodilative properties, especially on the small airways, than ipratropium bromide in nonasthmatic patients undergoing fiberoptic bronchoscopy for diagnostic reasons. However, the deterioration in lung function induced by either the bronchoscopy itself or the lidocaine used as topical anesthetic was minor in all groups. Thus routine premedication with IB or FEN cannot be recommended for all patients but may be useful in patients with lung function impairment, particularly of the small airways.

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