

Original Research Article

Effect of low dose versus high dose Ipratropium over Lung functions in chronic obstructive pulmonary disease patients

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Abstract: The objective is to determine the effect of changing anticholinergic therapy in patients with chronic obstructive pulmonary disease from low dose ipratropium to high dose ipratropium on pulmonary function. This study was conducted to evaluate single metered aerosol doses of 20 mcg, 40 mcg, and 80 mcg of ipratropium bromide; and placebo. 20 adult patients with partially reversible airway obstruction were included in the study. They were all tested for 6 hours with each dose range. Spirometric studies were performed 5, 30, 60, 120, 180, 240, 300 and 360 minutes after the dose was administered. The values for FEV1 and FVC were significantly increased within 5 minutes after all doses of ipratropium. The two lower doses ipratropium had significant effects for 3-4 hours, while the 80 mcg dose significantly increased both the FEV1 and FVC for 5 hours. Baseline mean FEV1 (litres) values for placebo, 20 mcg, 40 mcg, and 80 mcg of ipratropium bromide were 1.068, 1.078, 1.080, 1.089 litres respectively. Compared with placebo, each dose of ipratropium bromide produced a significant increase of the mean FEV1 ($P < 0.05$). When compared to baseline value, the FEV1 was significantly greater with 80 mcg than 40 mcg at 5 hours ($p < 0.05$). We concluded that ipratropium 80 mcg shows greater lung function improvement compared to lower doses in obstructive pulmonary diseases.

Keywords: Ipratropium, spirometry, forced vital capacity

INTRODUCTION

Ipratropium bromide is an anticholinergic agent, which inhibits vagally-mediated reflexes by antagonising the action of acetylcholine, the transmitter agent released from the vagus nerve [1]. For patients whose symptoms are not sufficiently controlled by maintenance monotherapy, combining bronchodilators of different classes, in particular an inhaled muscarinic antagonist (ipratropium bromide) and β_2 -agonist (levo salbutamol sulphate), seems a convenient way of delivering treatment and obtaining better results. Simultaneous administration of both an anticholinergic (ipratropium bromide) and a β_2 -sympathomimetic (levo salbutamol sulphate) is developed to benefit the patient by producing a greater bronchodilator effect than when either drug is utilised alone at its recommended dosage. This provides better lung function and improved symptoms [2].

A number of studies suggested ipratropium provides good bronchodilation, however, in all of these studies the investigator treated the patients with various doses of ipratropium ranging from 20 mcg to 80 mcg [3,4]. Hence this study was planned to determine the

effect of changing anticholinergic therapy in patients with chronic obstructive pulmonary disease from low dose ipratropium to high dose ipratropium on pulmonary function.

METHOD & MATERIALS

This study was conducted to evaluate single metered aerosol doses of 20 mcg, 40 mcg, and 80 mcg of ipratropium bromide; and placebo. 20 adult patients with partially reversible airway obstruction were included in the study. They were all tested for 6 hours with each dose range. Spirometric studies were performed 5, 30, 60, 120, 180, 240, 300 and 360 minutes after the dose was administered.

Pulmonary function testing:

Spirometry was performed by American Thoracic Society guidelines [5].

Statistical Analysis:

Differences between means were determined by T test. A P value less than 0.05 were considered significant.

RESULTS

Of the total 20 subjects, 10 patients had stage III, 3 subjects had stage IV and 7 subjects had stage II COPD as defined by GOLD. The average age for the 17 males was 58.98 years and that of 3 females was 62.87 years.

The values for FEV1 and forced vital capacity (FVC) were significantly increased within 5 minutes after all doses of the active compounds. The three lower doses ipratropium had significant effects for 3-4 hours, while the 80 mcg dose significantly increased both the

FEV1 and FVC for 5 hours. Baseline mean FEV1 (litres) values for placebo, 20 mcg, 40 mcg, and 80 mcg of ipratropium bromide were 1.068, 1.078, 1.080, 1.089 litres respectively. Compared with placebo, each dose of ipratropium bromide produced a significant increase of the mean FEV1 (P<0.05). When compared to baseline value, the FEV1 was significantly greater with 80 mcg than 40 mcg at 5 hours (p<0.05).

No side effects were reported by the patients in any group. Additionally, no significant alteration in pulse or blood pressure was observed.

Table.1: Table showing change in FVC after 5 minutes and 5 hours following inhalation of ipratropium

	Ipratropium			
	Placebo	20 mcg	40 mcg	80 mcg
Baseline FVC (Litres)	1.441	1.559	1.546	1.588
5 Minutes	-17	+0.134	+0.161	+0.171
5 Hours	-0.106	+ 0.780	+0.117	+0.203

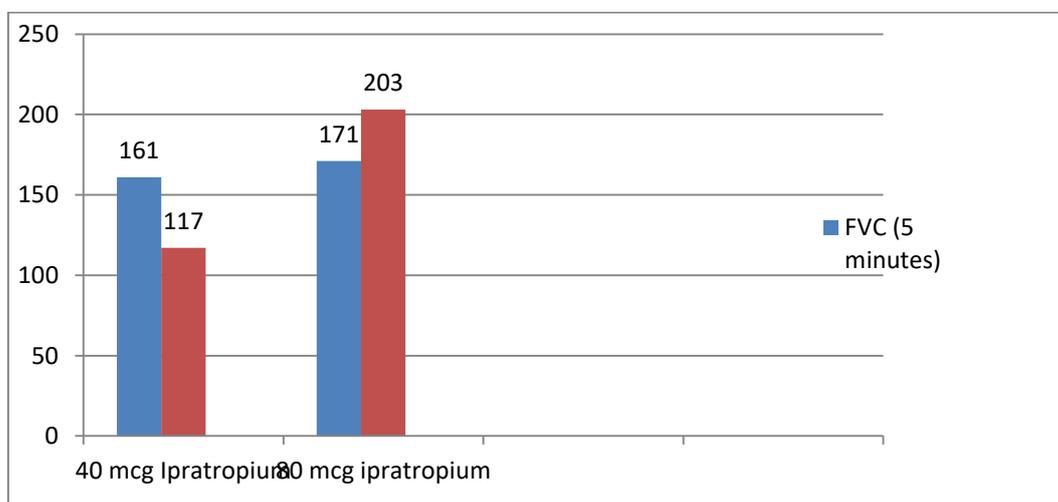


Fig 1: Mean change in FVC (ml) from baseline

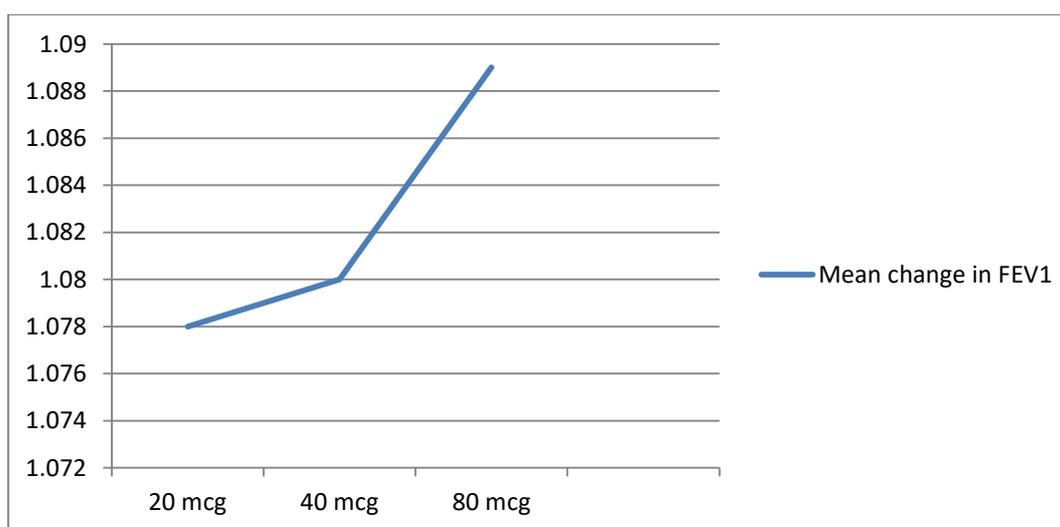


Fig 2: Mean change in FEV1 after various dose of ipratropium

DISCUSSION

Ipratropium bromide is an anticholinergic (para sympatholytic) agent, which appears to inhibit vagally-mediated reflexes by antagonizing the action of acetylcholine, the transmitter agent released from the vagus nerve. Anticholinergics prevent increase in the intracellular concentration of Ca⁺⁺, which are caused by the interaction of acetylcholine with the muscarinic receptors on bronchial smooth muscle.

Ipratropium bromide is a quaternary amine and hence, is not readily absorbed into the systemic circulation either from the surface of the lungs or from the gastrointestinal tract. Following inhalation, 10-30% of a dose is generally deposited in the lungs. The portion of the dose deposited in the lungs reaches the circulation rapidly (within minutes).

In a similar study by Ikeda *et al.*; increasing doses of ipratropium up to 240 µg had significant beneficial effects on FVC and FEV1 [6]. The dose of ipratropium used in our study was 80 µg, less than the optimal dose demonstrated in that study.

One published article reported a small excess number of tachyarrhythmias among patients with mild COPD who received ipratropium for several years[7]. However, an excess number of serious cardiac side-effects in patients receiving tiotropium has not been reported in any of the published trials. Barr *et al.*; found no significant difference in the incidence of chest pain, myocardial infarction, congestive heart failure, arrhythmias, or atrial fibrillation with tiotropium compared with controls in their meta-analysis [8].

CONCLUSION

We concluded that ipratropium 80 mcg shows greater lung function improvement compared to lower doses in obstructive pulmonary diseases.

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