

A comparison between a combination of ipratropium bromide plus fenoterol in a single metered dose inhaler (Duovent) and salbutamol in asthma

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Summary

The efficacy of a single metered dose inhaler containing a combination of fenoterol (100 µg/puff) and ipratropium bromide (40 µg/puff) has been assessed in 12 asthmatics. We conclude that the bronchodilator effect of 2 puffs of the combination inhaler was significantly greater than that achieved by 2 puffs of salbutamol (100 µg/puff).

KEY WORDS: fenoterol, ipratropium bromide, salbutamol, asthma.

Introduction

Both salbutamol and fenoterol are selective β_2 adrenergic agonists which produce effective bronchodilatation in asthma. Ipratropium bromide is a synthetic anti-cholinergic bronchodilator which has been assessed in both asthma and bronchitis (Poppius and Salorinne, 1973; Petrie and Palmer, 1975). In severe chronic bronchitis and emphysema, it has been shown to be at least as effective as salbutamol, the most commonly used β_2 adrenergic agonist with bronchodilator properties (Douglas *et al.*, 1979).

The combination of fenoterol and ipratropium bromide has been shown to produce a greater bronchodilator response than that achieved by either agent alone both in asthma (Martin, Berend and Harrison, 1979) and chronic bronchitis (Addis, Barclay and Chang, 1979; Anderson, Jariwalla and Turnbull, 1980). This combination has recently become available in a single metered dose inhaler.

In a double-blind, crossover study we have compared the onset of action, peak effect and side effects of this combination with salbutamol similarly administered.

Methods

Twelve chronic stable asthmatics (5 male, mean

age 52 years, range 24-75 years, mean duration of disease 15.5 years) were assessed at the same time on 2 consecutive days having taken no bronchodilator for at least 12 hr. Five patients were on inhaled β_2 adrenergic agonists only, 5 were on inhaled and 2 were on oral corticosteroids. All were non-smokers.

After 5 min rest, baseline measurement of pulse, blood pressure, forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC) were recorded. FEV_1 and FVC were taken as the best of 3 recordings. After inhalation of 2 puffs of salbutamol (200 µg) or 2 puffs of Duovent (the combination of 200 µg of fenoterol plus 80 µg of ipratropium bromide [2 puffs]) from identical inhalers, pulse rate, FEV_1 and FVC were recorded every 10 min for 0.5 hr, then every 15 min for a further 90 min. Blood pressure was recorded at 1 and 2 hr.

Results

Baseline values for FEV_1 were similar on both treatment days (combination mean 1.4 litres \pm 0.23 s.e.m. and salbutamol 1.34 litres \pm 0.22). The bronchodilator effect of the combination was significantly greater than that of salbutamol from 20 to 120 min inclusive ($P < 0.05$ at 20, 30 and 45 min, $P < 0.01$ at 60, 75, 90, 105 and 120 min). Peak values obtained were 1.88 litres \pm 0.26 at 45 min for salbutamol, and 1.98 litres \pm 0.35 at 60 min for the combination.

Significant differences were observed for posttreatment FVC in favour of the combination from 30 to 105 min inclusive ($P < 0.05$ at 60 and 105 min, $P < 0.01$ at 30, 45, 75 and 90 min). Peak values were obtained with salbutamol at 1 hr (3.25 litres \pm 0.38) and with the combination at 45 min (3.39 litres \pm 0.38). When percentage increases rather than absolute values were considered significant differences for percentage increase in FEV_1 from 75 to 120

min inclusive ($P < 0.05$ for 105 min, and $P < 0.01$ at 75, 90 and 120 min). However, there were no significant differences observed between the treatments for percentage increase in FVC. There was no significant difference between salbutamol and the combination with respect to pulse rate and blood pressure before and after treatment and no difference related to the order of treatments.

Tremor was a common side effect (5 out of 12) but was equally common with salbutamol and the combination. Two patients complained of the taste of the combination. One patient felt nauseated with the combination.

Discussion

The different sites of action of β_2 adrenergic agonists and anti-cholinergic agents has led to their use in combination in patients with chronic airways obstruction. The combination of fenoterol with ipratropium bromide has been shown to produce additional bronchodilatation (Martin, Berend and Harrison, 1979) and in a single metered dose inhaler, to provide optimal bronchodilatation with few side effects (Ulmer, 1979). This combination inhaler is now widely available in the U.K. and may increase compliance in those patients shown to respond to both agents. There is, as yet however, no published information on the efficacy of this combination in asthma.

We conclude that, at conventional doses (2 puffs of

the metered dose inhaler, Duovent [the combination of fenoterol (100 $\mu\text{g}/\text{puff}$) and ipratropium bromide (40 $\mu\text{g}/\text{puff}$)] produced significantly greater bronchodilator effect than salbutamol (100 $\mu\text{g}/\text{puff}$).

We have not examined dose response relationships and it is possible that this advantage may be lost at other doses.

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