# Fenoterol + Ipratropium Bromide in Obstructive Lung Disorders

**Produces greater symptom improvement than salbutamol in chronic airways obstruction . . .**

20 patients with chronic obstructive lung disease received 2 puffs of either fenoterol + ipratropium bromide ('Duovent'), salbutamol or placebo for 1 week in a randomised crossover trial design.

$FEV_1$ and peak expiratory flow increased significantly (*vs* placebo) and specific airway resistance decreased significantly following both active treatments; the effect was more marked with the combination regimen, particularly 60 min postdose. The mean number of bronchospasms/day, number of additional puffs/day and the relative severity of symptoms decreased significantly following both active treatments; again, the effect was more marked (significant *vs* salbutamol) with the combination regimen.

Two patients on fenoterol + ipratropium bromide experienced transient tremor and palpitations initially.

Aquilina R, Bergero F, Noceti P, Mirabelli S, Luciani G. Respiration 50 (Suppl. 2): 240-244, 1986

**. . . is as effective as salbutamol in bronchopasm, with reduced dose frequency . . .**

In a double-blind randomised crossover trial, 15 patients with stabilised chronic bronchospasm received 2 puffs of a combination inhaler containing fenoterol 100μg + ipratropium bromide 40μg per puff tid and 2 puffs of salbutamol 100μg qid for 2 weeks each.

Good compliance and tolerability was obtained with both treatments; patients generally preferred the combination inhaler. Daytime and nocturnal dyspnoea were significantly more easily controlled with the combination treatment than with salbutamol. The number of additional puffs required was reduced with the combination inhaler, as was coughing. FVC and $FEV_1$ increased slightly with both treatments; fenoterol + ipratropium bromide raised and maintained $FEV_1$ at 30 min and 5 hours ($p < 0.05$) after administration.

Thus, although similar results were obtained with both treatments ***'. . . the results with Duovent [fenoterol + ipratropium bromide] were better in a number of parameters . . . and were obtained with administration of 3 daily doses instead of 4'.***

Macaluso S, Del Torre L. Respiration 50 (Suppl. 2): 222-225, 1986

**. . . and undesirable cardiovascular effects are minimised . . .**

In a multicentre double-blind trial, 16 asthmatic patients received, in randomised order over 3 days, 4 inhaled doses of fenoterol 100μg + ipratropium bromide 40μg in a single aerosol preparation, 2 doses of the preparation, or placebo.

No difference in spirometric parameters was found between the two dosage levels but VC, $FEV_1$, maximal middle expiratory flow (MMEF), and Vmax 75 were significantly increased over placebo. The alteration in these values observed suggests that dilatation of both central and peripheral airways may be involved.

Heart rate was found to increase significantly, though slightly. However, the combined preparation represents a halving of the fenoterol dosage normally used when it is administered alone, so that undesirable cardiovascular effects may be minimised, while efficacy is enhanced.

In conclusion, administration of this combined preparation ***'. . . in asthma may be recommended both in cases of prominent vagally mediated bronchoconstriction and in those of enhanced suscepibility to unwanted cardiovascular reaction to a beta stimulant'.***

Bonsignore G, Bellia V, Peralta G, Alessi N, Migliara G. Respiration 50 (Suppl. 2): 148-151, 1986

**. . . while there is a gradual improvement in basal lung function in elderly patients . . .**

12 patients > 60 years of age with chronic airways obstruction used 2 puffs from an aerosol, delivering fenoterol 100μg + ipratropium bromide 40μg per puff, 8 hourly for 12 weeks.

Gradual and constant improvements were seen between pre- and post-dose measurements of vital capacity, $FEV_1$ and residual volume on day 1 and every fourteenth day thereafter.

An increase in specific airway conductance also occurred after aerosol inhalation. All pre-dose lung function parameters gradually improved during the trial, compared with the initial baseline values. A mean increase in heart rate of 3.5 beats/min was seen at the first measurement; however, at 30 and 60 minutes the increases were not significant. Adverse effects included palpitations (4), tremors (1), and headache (2) with initial treatment, but they disappeared at later visits.

Thus, the combination of fenoterol + ipratropium bromide ***'. . . has a prolonged effective bronchodilator action which increases with duration of the treatment'*** and ***'. . . is on the whole well tolerated . . .'.***

Cecere L, Funaro G, De Cataldis G, Carnicelli P, Pinto R. Respiration 50 (Suppl. 2): 245-248, 1986


0156-2703/87/0314-0010/0$01.00/0 

**... and improvements in $FEV_1$ and FVC in those with chronic bronchitis and emphysema**

16 patients with chronic obstructive lung disease were randomly given fenoterol + ipratropium bromide, placebo and terbutaline by metered aerosol on 3 consecutive days with the placebo given on day 2.

Both fenoterol + ipratropium bromide and terbutaline at all times improved pulmonary function significantly over placebo for up to 6 hours. Effects peaked at 60 min and slowly declined thereafter. $FEV_1$ values were higher for fenoterol + ipratropium bromide but were not significantly greater than those seen with terbutaline. However, there was a significant difference in favour of fenoterol + ipratropium bromide for FVC values after 4 hours. There were no adverse effects reported or detected.

Longhini E, Bozzoni M, Mastropasqua B, Marazzini L. Respiration 50 (Suppl. 2): 169-172, 1986

**Four-hourly administration prevents exercise-induced asthma...**

12 patients with exercise-induced asthma randomly received either fenoterol 200 or 400μg, fenoterol 200μg plus ipratropium bromide 80μg, or placebo on separate days, in double-blind fashion.

Five hours after administration considerable bronchodilation was still evident, especially with fenoterol 400μg (12.2% increase in $FEV_1$ and 99.3% increase in specific airway conduction) and with fenoterol + ipratropium bromide (9.6% increase in $FEV_1$ and 55.4% increase in specific airway conduction). The bronchodilator effect of fenoterol alone was found to be dose-related. Inhibition of exercise-induced asthma by these drugs after this time was only partial. However, post-exercise values of respiratory function were still significantly higher than basal levels and hence advantageous to the patient. Fenoterol should be administered at least four-hourly to adequately control exercise-induced asthma.

Sanguinetti CM, De Luca S, Gasparini S, Massei V. Respiration 50 (Suppl. 2): 181-185, 1986

**... and asthmatic children require fewer additional inhalations...**

20 children, aged 5-14 years, with atopic asthma received inhaled fenoterol + ipratropium bromide 2 puffs tid and placebo for 1 week each in a double-blind crossover trial.

A significant reduction in dyspnoea and a marked reduction in cough were seen during active treatment. Basal peak flow rate improved throughout the treatment period and administration of fenoterol + ipratropium bromide caused further significant increases over baseline.

Patients required more additional sprays of medication ($p < 0.05$) when on placebo than when on active treatment. Only 2 patients required a dose increase while on fenoterol + ipratropium bromide to control symptoms.

Thus, fenoterol + ipratropium bromide induced clinical improvements and was well tolerated in this study group.

Pulejo R, Romano L, Noto M. Respiration 50 (Suppl. 2): 236-239, 1986

**... while improvements in respiratory function are better than those seen with reproterol...**

16 patients suffering from chronic reversible airway obstruction ($FEV_1$ 30-70% of predicted value), were randomly given on day 1 and day 3 of a 3-day trial either a combination of fenoterol 200μg and ipratropium bromide 80μg or reproterol 1mg. Two puffs of placebo were given on the second day.

Both treatments caused significant improvements in all measured variables, $FEV_1$, FVC, $FEF_{25-75}$, but the combination of ipratropium bromide and fenoterol resulted in significantly greater increases in FVC at 240 min, $FEV_1$ at 240-480 min and $FEF_{25-75}$ at 120-480 min.

Baronti A, Grieco A, Lelli M, Virgili G. Respiration 50 (Suppl. 2): 173-176, 1986

**... and better than those produced by salbutamol in patients with COLD**

In a 3-day trial, 16 patients with chronic obstructive lung disease (COLD) who showed reversible bronchospasm were given (at random) on day 1 and 3 either fenoterol 100μg plus ipratropium bromide 40μg or salbutamol 100μg. Day 2 was used to test for any placebo effect. A metered-dose inhaler was used to administer all treatments.

Fenoterol + ipratropium bromide caused a significant increase in $FEV_1$ in all measurements taken from 30 min after inhalation through to 420 min. However the initial effects seen with salbutamol were not evident at 360 and 420 min. Effects of both drugs were significantly superior to those of placebo. No patients had a significant increase in heart rate, and tremors, which cleared after 60 min, were seen in only 3 patients.

***'Duovent [fenoterol + ipratropium bromide] is an effective drug in the control of bronchospasm, with a lasting action and good tolerance...'.***

Marangio E, Pesci A, Mori A, Marchioni M, Bertorelli G. Respiration 50 (Suppl. 2): 165-168, 1986