

Breath-actuated inhalers in chronic asthma: comparison of Diskhaler and Turbohaler for delivery of beta-agonists

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ABSTRACT: An open, randomized, cross-over study was performed to compare the efficacy and acceptability of two breath-actuated inhalers, the Turbohaler® (T) and Diskhaler® (D), for delivery of beta-agonists.

Thirty six adults with chronic asthma requiring beta-agonists four times daily were treated with terbutaline 500 µg *via* T and salbutamol 400 µg *via* D four times daily, each period lasting four weeks. Additional bronchodilator *via* pressurized aerosol was permitted as required. Peak expiratory flow (PEF) was recorded in the morning (before and after beta-agonist) and in the evening.

The mean morning PEF was higher during the first two weeks using T (295 l·min⁻¹) than whilst using D (281 l·min⁻¹, *p*<0.01), but this difference did not persist during the second two weeks and there were no differences in post-bronchodilator PEF or rescue beta-agonist use. After four weeks, >90% of patients used both inhaler devices efficiently and they were equally acceptable in terms of ease of use and convenience to carry.

The Diskhaler and Turbohaler achieve similar clinical efficacy for delivery of beta-agonists.

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Many patients with asthma cannot use pressurized aerosols efficiently, the most common problem being failure to synchronize aerosol actuation with inspiration [1]. To overcome this problem, breath-actuated devices such as the Diskhaler® (D) and Turbohaler® (T), have been developed. When administered by pressurized aerosol, 200 µg salbutamol and 500 µg terbutaline are equipotent [2, 3]. T is at least as efficient as pressurized aerosol for delivery of terbutaline [4-6], but 400 µg salbutamol *via* D is equivalent to 200 µg *via* aerosol [7]. Recently, 400 µg salbutamol *via* the single-dose, breath-actuated Rotahaler device was shown to have similar bronchodilatory effects to 500 µg terbutaline *via* T [8].

This study assessed the efficacy and acceptability of D and T for delivery of salbutamol 400 µg and terbutaline 500 µg, respectively, to adults with chronic asthma.

Patients and methods

Patients selected for study were adults with stable, chronic asthma who needed to use beta-agonist inhalers at least four times daily, were able to use pressurized aerosols efficiently and who had not previously used a Diskhaler or Turbohaler. Those taking anticholinergic drugs were excluded but other asthma medication was permitted at constant dose.

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The study was of open, randomized, cross-over design with two treatment periods of four weeks and no wash-out period. During a two week run-in, patients inhaled their usual beta-agonist aerosol four times daily and recorded additional bronchodilator use. A mini-Wright peak flow meter was used to record peak expiratory flow (PEF) rates before and 15 min after the morning dose and before the evening dose. To be eligible for study, they had to show a minimum of 15% improvement in morning PEF following drug inhalation on two or more occasions.

During the treatment periods, patients inhaled salbutamol 400 µg four times daily *via* D or terbutaline 500 µg four times daily *via* T. Patients recorded PEF and additional beta-agonist use *via* pressurized aerosol. Every two weeks, forced expiratory volume in one second (FEV₁) and forced vital capacity (FVC) were measured at clinic visits, the time between beta-agonist inhalation and measurement being kept constant.

At the start of each treatment period, patients read the instruction leaflet for the inhaler they were to use. After two weeks, inhaler technique was assessed by experienced technicians and supplementary verbal instruction given, if necessary. After four weeks, inhaler technique was assessed again and a questionnaire concerning ease of use and adverse effects was completed. At the end of the study, patients were asked which inhaler they preferred.

Thirty six patients (19 female), aged 22–77 yrs (mean 50 yrs), were randomized into the two treatment groups. Their mean duration of asthma was 18 yrs and all but one were taking inhaled corticosteroids. Six patients were withdrawn because of deterioration of asthma and one because of non-compliance. Thirty patients completed at least two weeks of treatment with both inhaler devices and 29 completed the study. Written consent to participate was obtained from all patients and the study was approved by the local Ethics Committee.

Statistical analysis

The primary efficacy variable in the study was morning PEF. Assuming a standard deviation of 35–50 $l \cdot min^{-1}$, it was estimated that 30 patients would be required in order to have an 80% chance of showing a difference of 18–26 $l \cdot min^{-1}$ between treatment groups. Mean PEF values were compared by analysis of variance and frequency of extra bronchodilator use by Mann-Whitney tests. The ratio of correct/incorrect users of each inhaler was compared using McNemar's test. Questionnaire data regarding convenience for carrying, ease of use, inhaler-related cough and taste were analysed using Chi-squared tests.

Results

Mean morning and evening PEF during each of the treatment periods were similar to the run-in values (fig. 1). The morning pre-bronchodilator PEF during the first two weeks using T was higher than during the corresponding period using D (295 vs 281 $l \cdot min^{-1}$; $p=0.003$). However, this difference did not persist during the second two weeks and there were no differences between T and D in morning post-bronchodilator and evening PEF throughout the study. Mean FEV_1 was 1.8 l and mean FVC 3.1 l during the run-in and neither changed significantly during the treatment periods.

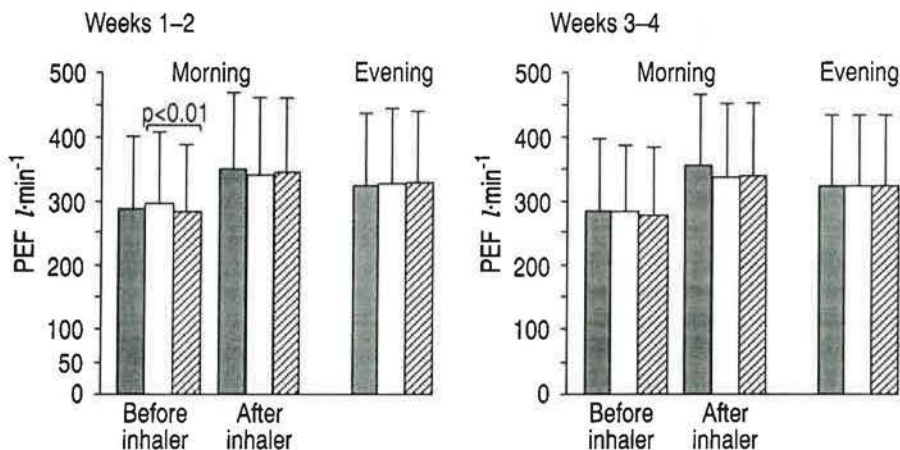


Fig. 1. — Morning and evening peak flow (mean±SD) in asthmatic adults inhaling beta-agonists four times daily. ■: Run in = salbutamol 200 μg via pressurized aerosol; ▨: Diskhaler = 400 μg salbutamol; □: Turbohaler = 500 μg terbutaline. PEF: peak expiratory flow.

During the run-in, the median number of extra puffs of bronchodilator was 0.2 during the day and 0.4 during the night. Rescue beta-agonist use did not change significantly during either treatment period.

Following written instruction alone, there was a trend towards more patients using D correctly (n=26 out of 30) than T (n=18 out of 30, $p=0.08$). The difference was due to T not being loaded in the upright ($\pm 45^\circ$) position. This was corrected by verbal instruction: after four weeks only one patient failed to use T correctly (exhaling through the device) and two failed to breath-hold after using D.

D and T were equally acceptable in terms of ease of use and portability. Two patients found the devices difficult to use and four thought them impractical to carry. Minor adverse effects occurred in a minority of patients: 10 (4 T, 6 D) admitted to cough after inhalation and 11 (6 T, 5 D) found the taste unpleasant. Twenty three patients expressed a preference for one device: 13 preferred T and 10 D (difference not significant).

Discussion

Terbutaline 500 μg four times daily *via* a Turbohaler and salbutamol 400 μg four times daily *via* a Diskhaler were equally effective in adults with chronic stable asthma who, despite inhaled corticosteroid therapy, needed to use beta-agonists four times daily. The devices were equally acceptable both in terms of ease of use and portability.

After written instruction alone, fewer patients tended to use T correctly. In nearly all, the error was a failure to load the device within 45° of the vertical position. However, this did not appear to compromise the efficacy of treatment during the first two weeks. It is possible that more patients used the device efficiently at home. Alternatively, failure to load the T in a near upright position may not be as important as previously thought. This loading error was easily corrected and after written and verbal instruction over 90% of patients used both devices efficiently.

During the first two weeks of terbutaline therapy,

the mean morning pre-bronchodilator PEF was significantly higher than during the first two weeks of salbutamol. This difference was still present when only those patients who used both inhalers correctly during this period were analysed. The reason for the difference is not clear but this has been observed in other studies comparing beta-agonists administered via a Turbohaler and pressurized aerosol [6, 8]. However, the magnitude of the difference in our study ($14 \text{ l}\cdot\text{min}^{-1}$, 95% confidence intervals 5–23 $\text{l}\cdot\text{min}^{-1}$) and its failure to persist during the second two weeks of Turbohaler use suggest that this finding is not clinically relevant.

Our finding that the Diskhaler and Turbohaler were equally acceptable to patients contrasts with a recent study with similar design and patient numbers in which the devices were compared for the administration of corticosteroids [9]. Patients in that study found the Turbohaler more convenient to carry and easier to use. However, the Diskhaler and Turbohaler were of similar clinical efficacy for steroid delivery and our study is complementary in that both devices achieve similar clinical efficacy with beta-agonists.

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