

A multiple dose powder inhaler (Turbuhaler®) compared with a conventional aerosol

An acceptance study in asthmatics

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Nineteen patients with asthma completed an open, randomized, crossover study in which 0.5 mg terbutaline sulphate was administered either via Turbuhaler® or via the metered dose inhaler (MDI) for 2-week periods. The clinical effect of the two treatment forms was comparable; both provided adequate bronchodilator therapy. Patients also considered Turbuhaler and MDI equally effective, with a small preference for the MDI. Turbuhaler seems to be a valuable alternative to bronchodilator MDI therapy.

CLINICAL ASPECTS

This study showed equipotent bronchodilatory efficacy from terbutaline sulphate when administered via Turbuhaler® and via MDI. Additional advantages of Turbuhaler, such as absence of coordination problems and additives, make it an attractive alternative in the daily treatment of asthma.

Key words: acceptance; asthma; powder inhalation; terbutaline.

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The administration of a β_2 -agonist by inhalation is advantageous in the treatment of asthma and other obstructive lung diseases. The drug is delivered directly to the affected area, the onset of action is rapid and efficacy is obtained with a low dose, thereby reducing unwanted side effects. Many patients, however, do not obtain maximum benefit from such therapy because they are unable to use their metered dose inhaler (MDI) efficiently. The problems mostly encountered arise from the need to synchronize inhaler actuation with inspiration (2, 3).

The MDI also requires additives, such as propellants and lubricants which may cause irritation and even bronchoconstriction (1, 4). Powder inhalers currently used present no coor-

dination problems, but carriers such as lactose are added to the active compounds and they are inconvenient to handle since they must be loaded before use.

The new powder inhaler used in this study, Turbuhaler®, is a multiple dose powder inhaler. Turbuhaler is loaded with 200 doses of pure terbutaline sulphate, and by a single manoeuvre, each dose is ready to inhale.

The technical construction of Turbuhaler has been described by Wetterlin (5). Turbuhaler is always ready for instant use and easy to handle. A metered dose is prepared by twisting the turning grip at the bottom of the inhaler (Fig. 1).

The aim of this study was to compare Turbuhaler with an MDI, both devices containing terbutaline sulphate, with regard to clinical effects as well as patient opinion on ease of use.

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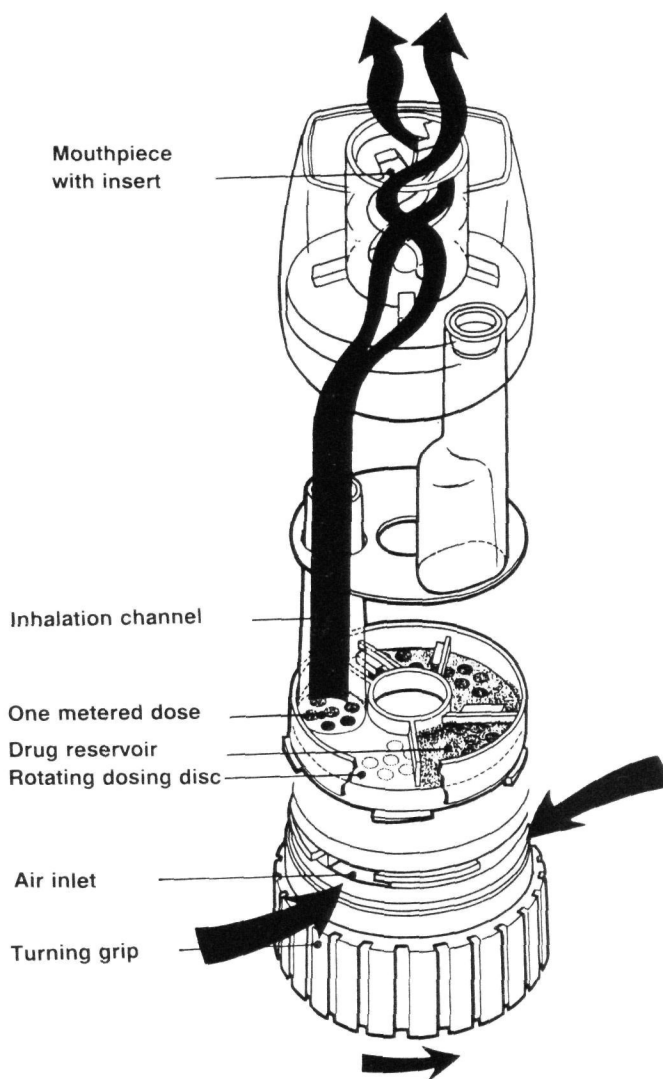


Fig. 1. Technical description of Terbuhaler®

PATIENTS AND METHOD

Patients

Twenty-three patients with chronic stable asthma were entered into the study. Within the previous 12 months, all had shown an airways obstruction with a reversibility of at least 15% after inhalation of terbutaline sulphate (or equivalent medication). They had a basal forced expiratory volume in 1 s (FEV_1) of 1 l or more. All patients required regular bronchodilator inhalation and 15 patients used inhaled corticosteroids as additional therapy. Two patients withdrew from the study because of lack of time and one because of adverse effects. One patient was excluded because of an infection during one of the treatment periods. The

19 patients (4 male, 15 female) who completed the study had a mean age of 46 years (range 20–66 years). The mean duration of their asthma was 17 years (range 2–35).

The patients were informed verbally and in writing and their informed consent was obtained. The study was approved by the Ethics Committee of Stockholm and the National Board of Health and Welfare.

Study design

The study was performed at two lung clinics in Stockholm, and was of an open, randomized, crossover design consisting of two treatment periods each lasting 2 weeks.

The patients attended the hospital three times. On their first visit they were entered into the study, the first trial inhaler was demonstrated and it was confirmed that the patient's inhalation technique was adequate. The patients also received diary cards. Each treatment period lasted 2 weeks during which they inhaled 0.5 mg terbutaline sulphate four times daily from the trial inhaler. Extra inhalations from the trial inhaler were permitted, if required, and the patients were asked to note any such inhalations in the diary card.

On the second visit, the patients first demonstrated that their inhalation technique with the first inhaler was adequate and returned the inhaler. The second inhaler was then demonstrated and the adequacy of the patient's inhalation technique was confirmed by the investigator.

On the last visit, the patients once again demonstrated their inhalation technique and returned the second inhaler and the diary cards.

At home, the patients recorded their PEF before and 15 min after inhalation of the morning and evening doses. PEF was recorded with a mini-Wright peak flow meter and the best flow rate obtained from three trials on each occasion was noted in the diary cards. Questionnaires were completed by the patients at the end of each treatment period. Adverse events were recorded spontaneously by the patients.

Student's *t*-test for paired differences was used between treatments. Patient preference data was assessed using chi-square.

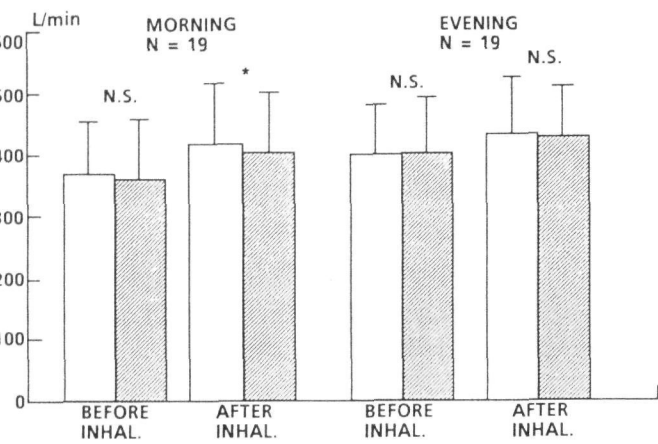


Fig. 2. Mean PEF values before and after inhalation of 0.5 mg terbutaline sulphate via Turbuhaler (□) or MDI (▨). **P* < 0.05, NS no significance.

RESULTS

All 19 patients included in the analysis were judged to have an adequate inhalation technique with both Turbuhaler and MDI. Both inhalation methods produced an increase in PEF, the mean values being similar in both groups. The mean values of the morning PEF before and after inhalation were 370±80 l/min and 419±88 l/min, respectively, for the Turbuhaler group and 362±89 l/min and 406±87 l/min, respectively, for the MDI group. The mean increases in morning PEF were 13 % (49 l/min) and 12 % (44 l/min) for Turbuhaler and the MDI, respectively. The

mean values of the evening PEF before and after inhalation were 401±83 l/min and 433±87 l/min, respectively, for the Turbuhaler group and 42±88 l/min and 482±86 l/min, respectively, for the MDI group. The mean increases in evening PEF were 8 % (32 l/min) for Turbuhaler and 6 % (26 l/min) for MDI (Fig. 2).

When analysed statistically, there was a significant difference at the *P* < 0.05 level in the mean morning PEF values after inhalation, in favour of Turbuhaler.

On 123 occasions during Turbuhaler treatment and on 177 occasions during MDI treatment additional inhalations were required.

Two patients reported adverse experiences. One had tremor with the MDI but not with Turbuhaler. The second experienced tremor immediately after commencing treatment with Turbuhaler and withdrew from the study.

The majority of patients (*n* = 17) had been using an inhaler for more than 2 years. The questionnaire responses showed that Turbuhaler was easy to use (Table 1). Five patients showed an overall preference for Turbuhaler, eight preferred the MDI and six expressed no preference.

DISCUSSION

In this group of patients, terbutaline inhaled via Turbuhaler produced improvement in lung function equal to that observed following the

Table 1
Excerpt from the questionnaires

Question	Answer		
	No	Yes	Unimportant
1. "Was it difficult to remember to put the cover on the Turbuhaler?"	19	0	
2. "Was it difficult to load the Turbuhaler?"	18	1	
3. "Do you think the Turbuhaler should have an automatic return after dosing?"	1	2	16
4. "Was it troublesome that the Turbuhaler had to be loaded in an upright position?"	14	0	5
5. "Were the Turbuhaler instructions sufficient?"	0	19	
6. "Was it difficult to remember not to exhale through the Turbuhaler?"	18	1	

same dose of terbutaline inhaled via a conventional MDI. Thus, in the treatment of asthma, it seems that Turbuhaler could provide an alternative device for administration of terbutaline which is therapeutically equivalent to the well-established MDI. It should be noted that all patients in this study had good inhalation technique with the MDI. It is reasonable to believe that patients with inadequate ability to coordinate inhaler actuation and inhalation would benefit comparatively more from Turbuhaler treatment.

Turbuhaler and the MDI were also comparable with regard to patient opinion. The fact that many of the patients found Turbuhaler as easy to use as the MDI indicates that this new inhaler is a well-accepted device. All patients had been using an MDI for many years, and would thus be expected to prefer the conventional inhaler to a new device with respect to use and convenience.

In conclusion, this study showed that Turbuhaler provides an alternative to MDI for inhalation of terbutaline in the treatment of asthma.

REFERENCES

1. Bryant, D. H. & Pepys, J.: Bronchial reactions to aerosol inhalant vehicle. *Br. Med. J.* 1, 1319, 1976.
2. Crompton, G. K.: Problems patients have using pressurised aerosol inhalers. *Eur. J. Respir. Dis.* 63, Suppl. 119, 101-104, 1982.
3. Lindgren, S., Bake, B. & Larsson, S.: Clinical consequences of inadequate inhalation technique in asthma therapy. *Eur. J. Respir. Dis.* 70, 93-98, 1987.
4. Yarbrough, I., Mansfield, L. E. & Ting, S.: Metered dose inhaler-induced bronchospasm in asthmatic patients. A new concept in inhalation therapy. Medicom, The Netherlands, 1987. ISBN 905139004-1.
5. Wetterlin, K. I. L.: Design and function of Turbuhaler®. A new concept in inhalation therapy. Medicom, The Netherlands, 1987. ISBN 905139004-1.

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