

Comparison of Bricanyl[®] Turbuhaler[®] and Berotec[®] dry powder inhaler

L. B. RIBEIRO¹ & J. E. WIRÉN²

¹University Paediatric Clinic, Santa Maria Hospital, Lisbon, Portugal, and ²Medical Department, AB Draco, Lund, Sweden

Terbutaline (Bricanyl[®]) 0.5 mg t.i.d. administered via Turbuhaler[®] was compared with fenoterol (Berotec[®]) 0.2 mg t.i.d. administered via Inhalator Ingelheim[®] in 36 asthmatic children aged 7–12 years. The study was of an open crossover design with two randomly allocated treatment periods, each lasting 2 weeks. Forced expiratory volume in 1 s (FEV₁) and forced vital capacity (FVC) were measured at clinic visits before study start and at the end of each treatment period. The patients recorded peak expiratory flow (PEF) before and after inhaler use, morning and evening. They also recorded asthma symptoms and number of extra inhalations. At the end of the study, children and parents were asked for inhaler preference. No differences between the treatments were found concerning the results of the lung function measurements at the clinic or at the PEF measurements at home. No differences were found between the treatments as regards asthma symptoms or number of extra inhalations. Two patients experienced mild side effects during fenoterol treatment, none during terbutaline treatment. Treatment with terbutaline in Turbuhaler was preferred by a majority of children and parents. In conclusion, in this group of asthmatic children, treatment with terbutaline administered via Turbuhaler was as efficacious as treatment with fenoterol administered via Inhalator Ingelheim. There was a clear preference in favour of the Turbuhaler.

Key words: asthma; children; fenoterol, lung function; powder inhaler; preference; terbutaline, Turbuhaler[®].

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CLINICAL ASPECTS

Terbutaline (Bricanyl[®]) 0.5 mg t.i.d. administered via Turbuhaler[®] was compared with fenoterol (Berotec[®]) 0.2 mg t.i.d. administered via Inhalator Ingelheim[®] in 36 asthmatic children aged 7–12 years. Each treatment period lasted 2 weeks. Both treatments resulted in an increase in peak expiratory flow of 14–19% (mean values). Treatment with Turbuhaler was preferred by a majority of patients and parents. No other statistically significant differences were found between the two treatments. Thus, treatment with Bricanyl Turbuhaler as well as treatment with Berotec Inhalator Ingelheim seem to be of value in the treatment of asthma in children of the studied age group.

Many patients with obstructive airways disease do not obtain maximum benefit from inhaled bronchodilators because of inability to use pressurized metered dose inhalers (MDI) efficiently (4). The most common problems encountered involve the need to co-ordinate inhaler actuation with inspiration (1) and for this reason

breath actuated inhalers have been developed. Two such inhalers are the Berotec[®] dry powder inhaler (Inhalator Ingelheim[®]) and Bricanyl[®] dry powder inhaler (Turbuhaler[®]), used to disperse fenoterol and terbutaline, respectively.

Bricanyl Turbuhaler (7) is a multiple dose powder inhaler which dispenses 0.5 mg of ter-

Table 1
Clinic visits. Mean values (SD) *n* = 36

	FEV ₁ (l)		
	Before	15' after inhaler use	30' after inhaler use
Before start of study	1.25 (0.35)	1.47 (0.36)	1.53 (0.34)
After 2 weeks with Berotec powder inhaler	1.34 (0.33)	1.59 (0.32)	1.64 (0.32)
After 2 weeks with Bricanyl Turbuhaler	1.38 (0.36)	1.63 (0.32)	1.71 (0.33)
	FVC (l)		
	Before	15' after inhaler use	30' after inhaler use
Before start of study	1.61 (0.39)	1.79 (0.39)	1.86 (0.36)
After 2 weeks with Berotec powder inhaler	1.76 (0.39)	1.93 (0.40)	1.97 (0.39)
After 2 weeks with Bricanyl Turbuhaler	1.83 (0.40)	1.99 (0.39)	2.04 (0.39)

butaline sulphate without any carrier powder. It is preloaded with 200 doses. It is primed for use by rotating a turning grip at the base of the inhaler.

The Berotec dry powder inhaler requires each drug dose to be loaded separately in the form of a gelatine capsule containing 4.8 mg of glucose powder and 0.2 mg of fenoterol hydrobromide. Rotation of the inhaler then punctures the capsule, rendering its contents available for inhalation. When used in MDI, 0.2 mg fenoterol has been shown to be equipotent to 0.5 mg of terbutaline (2).

The aim of this study was to compare efficacy, safety and acceptability of Bricanyl Turbuhaler and Berotec Inhalator Ingelheim when used in children with asthma.

PATIENTS AND METHODS

The study was of an open crossover design and consisted of two randomly allocated treatment periods each lasting 2 weeks. Terbutaline sulphate 0.5 mg was administered three times daily via Turbuhaler during one treatment period and was compared with 0.2 mg fenoterol hydro-

bromide administered three times daily via Inhalator Ingelheim in the other treatment period. Extra inhalations were permitted and these were recorded. Forty children entered the study. Two children did not revisit the clinic. One of these children dropped out during the terbutaline period, the other during the fenoterol period. Two children dropped out due to deterioration of their asthma, both of these during the terbutaline period. Thirty-six children (25 boys and 11 girls) completed the study. Their age was between 7 and 12 years (mean 9 years). They fulfilled all of the following inclusion criteria: chronic stable asthma, reversibility > 15 % after inhalation of 0.5 mg terbutaline or equivalent from an MDI. None of the children had pulmonary disease other than asthma, significant cardiac disease, hyperthyroidism, insulin-dependent diabetes or any ongoing infection. None of the children had any previous experience of either of the two study inhalers. Children/parents were instructed not to use any inhaled bronchodilator other than trial medication during the study. Doses of inhaled or oral corticosteroids, disodium cromoglycate and oral bronchodilators were to be kept constant during the study.

The patients visited the clinic at the beginning of the study and after each 2-week treatment period. At these visits the children were examined and inhaler technique was checked by the investigator and lung function (FEV₁ and FVC) measured. At the beginning of the study, lung function was measured before and after inhalation of 0.5 mg terbutaline or equivalent from an MDI. At visits after the treatment periods, lung function was measured before and after inhalation from the inhaler used in the preceding period. At the last visit the parents/children were asked for inhaler preference.

At home, the patients recorded asthma symptoms (score 0-3) and extra inhaler use in diary cards. Using a Mini-Wright peak flow meter they measured peak expiratory flow (PEF) (best of 3) before and after administration of the trial bronchodilator morning and evening.

Comparisons between treatments for measured variables were performed using Student's

t-test for paired variables. Scored variables were analysed using the sign rank test. Preferences for treatments were analysed using a binominal test. Parametric tests were corroborated by corresponding non-parametric methods.

The study was performed in accordance with the Helsinki declaration.

RESULTS

The results of the lung function measurements at the clinic are shown in Table 1. There were no statistically significant differences between treatments, either in baseline values or in increase from baseline values.

There was no statistically significant difference in asthma symptom scores between the two treatment periods. The mean values of asthma symptom scores for the last 10 days in the terbutaline period were 0.17 and 0.13 in day and night, respectively. In the fenoterol period the corresponding values were 0.23 and 0.22, respectively.

During the fenoterol period eight children needed 46 extra inhalations. During the terbutaline period three children needed 4 extra inhalations.

PEF measurements at home are shown in Table 2. The mean increase after inhaler use in the morning was 18% in the terbutaline period

and 19% in the fenoterol period. The corresponding evening values were 14% and 15%, respectively. There was no statistically significant difference between the two treatment periods.

Patient preference is illustrated in Fig.1. Twenty-four children preferred treatment with the Turbuhaler. Nine children preferred treatment with Inhalator Ingelheim. Three children had no preference. The difference in preference is statistically significant (*P* = 0.0135).

Twenty-three parents preferred Turbuhaler, six preferred Inhalator Ingelheim and seven gave no preference. Also this difference in preference was statistically significant (*P* = 0.0023).

Two children reported adverse events during the fenoterol period. Both children had tremblings during this treatment period. No adverse events were reported during the terbutaline period.

DISCUSSION

This study on asthmatic children, aged 7–12 years, was performed as an open study for practical reasons. The results of the study showed equal efficacy when recommended doses of fenoterol and terbutaline were delivered via dry powder inhalers (Inhalator Ingelheim and Turbuhaler, respectively). This statement was supported by the results of the lung function measurements at clinic visits. It was also supported by the results of the peak flow measurements at home, and by the asthma symptom scores recorded at home.

Table 2
PEF (l/min) at home. Mean values (SD) *n* = 36

	Bricanyl Turbuhaler	Berotec powder inhaler
Morning PEF		
before inhalation	261 (79)	267 (73)
Morning PEF		
after inhalation	307 (80)	317 (68)
Mean increase l/min	46 (25)	50 (28)
%	18	19
Evening PEF		
before inhalation	284 (73)	286 (69)
Evening PEF		
after inhalation	325 (74)	330 (66)
Mean increase l/min	41 (20)	44 (24)
%	14	15

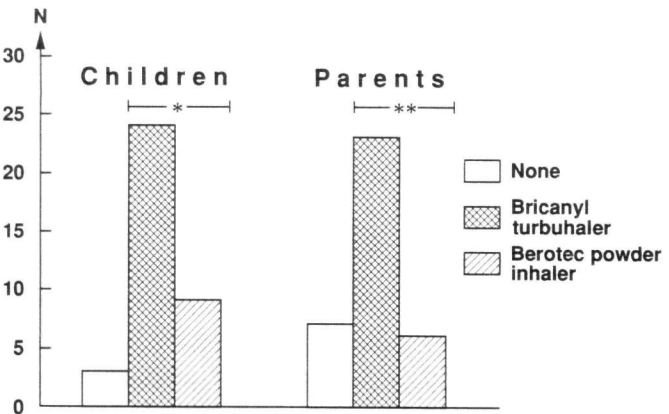


Fig.1. Inhaler preference among children and parents
* *P* = 0.0135. ** *P* = 0.0023.

In the present study, there was a statistically significant preference in favour of treatment with Turbuhaler both among children and parents. In earlier studies in children, there was also a preference in favour of Turbuhaler when it was compared with Ventolin® Rotahaler® (6), Bricanyl MDI (3) and Bricanyl MDI in connection with Nebuhaler® (5). Thus, it seems that Turbuhaler is a device that is well accepted among children.

Both treatments in this study seem safe in children of the studied age group.

In conclusion, this study in asthmatic children showed equal efficacy from terbutaline administered via Turbuhaler as from fenoterol administered via Inhalator Ingelheim, when recommended doses were used. There was clear preference in favour of the Turbuhaler.

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Address:

Jan Eric Wirén, M.D.

Dept. of Anesthesiology

University Hospital

S-221 85 Lund

Sweden

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