

Bricanyl® Turbuhaler® and Ventolin® Rotahaler® in exercise-induced asthma in children

J. M. LOPES DOS SANTOS¹, H. COSTA¹, E. STÅHL² & J. E. WIRÉN³

¹Serviço de Pediatria, Centro Hospitalar de Vila Nova de Gaia, Portugal, ²AB Draco, and ³AB Draco and Dept. of Anesthesiology, University Hospital, Lund, Sweden

Bricanyl® Turbuhaler® (0.5 mg terbutaline sulphate) and Ventolin® Rotahaler® (0.4 mg salbutamol) were compared in a randomized double-blind placebo controlled study on exercise-induced asthma in 19 children (14 boys) aged 7-14 years. The study was carried out on 3 separate days. Asthmatic attacks were provoked by free range running. Peak expiratory flow (PEF) was measured before and after exercise. If PEF decreased by > 20%, one inhalation from each of the inhalers was given under supervision of the investigator. Only one of the inhalers (none on the placebo day) delivered active drug. PEF was measured again 5 and 10 min after treatment. Already 5 min after treatment PEF had returned to baseline after active treatment. There was no statistically significant difference between the two active treatments. After placebo treatment, PEF did not return to baseline even at the 10 min post-exercise measurement. Ten children needed extra medication after the last PEF measurement on the placebo day, whereas no child needed extra medication after any of the active treatments. No adverse events were reported in this study. In conclusion, Bricanyl Turbuhaler (0.5 mg) and Ventolin Rotahaler (0.4 mg) were equally efficacious in the treatment of exercise-induced asthma in children.

Key words: exercise-induced asthma; Rotahaler; salbutamol; terbutaline; Turbuhaler.

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CLINICAL ASPECTS

In this study, exercise-induced asthma was used as a model to study the efficacy of Bricanyl Turbuhaler and Ventolin Rotahaler in acute asthma in children, aged 7-14 years. Treatment with either of the inhalers proved to be efficacious in the treatment of provoked bronchoconstriction. The effect was significantly better ($P < 0.001$) than that of placebo. Provided that the child can handle the devices, Bricanyl Turbuhaler and Ventolin Rotahaler can be used to treat moderate attacks of asthma in children.

Local administration of β_2 -agonists by means of pressurized metered dose inhalers (MDI) is widely used in the treatment of asthma. However, many children have problems in co-ordinating inhalation with inhaler actuation, especially during acute attacks of bronchoconstriction. Breath-actuated dry powder inhalers are easy to use. Ventolin Rotahaler is such a breath-actuated dry powder inhaler. Each dose

has to be loaded separately in the form of a gelatine capsule containing lactose powder and salbutamol (either 0.2 mg or 0.4 mg). Bricanyl Turbuhaler is also a breath-actuated dry powder inhaler (6). It is pre-loaded with 200 doses of 0.5 mg of pure terbutaline sulphate. The inhaler is primed for use simply by rotating the turning grip at the base of the inhaler.

The aim of this study was to compare Bricanyl Turbuhaler, Ventolin Rotahaler, and placebo in the treatment of exercise-induced asthma in children.

PATIENTS AND METHODS

The study was that of a single-dose randomized double-blind, double-dummy, crossover design. It was carried out on 3 separate days, at least a week apart, and comprised 19 children (14 boys) aged 7-14 years (mean 10 years). All the children were known to have exercise-induced asthma. After tuition, they all demonstrated satisfactory inhalation technique with both Turbuhaler and Rotahaler. None of the children had diabetes mellitus, significant cardiac disease, or hypersensitivity to sympathomimetics. Inhaled β_2 -agonists were withdrawn 6 h prior to the investigational events. No patients were taking oral β_2 -agonists or theophyllines. Concomitant prophylactic treatment with inhaled steroids was allowed and kept constant during the study period (10 pts). Concomitant treatment with sodium cromoglycate was not allowed.

On the study days, lung function (PEF; l/min) was measured with a Mini-Wright peak

flow meter. The first measurements (best of 3 attempts) were made before the start of the exercise test. The variation in the basal PEF was not allowed to be more than 25% between the 3 study days. The exercise test was carried out as free range running for 6 min indoors. PEF was measured again 2 min after exercise. If the variation between the 3 study days did not exceed 25% and if there was a decrease in PEF of at least 20% after exercise, inhalation of terbutaline 0.5 mg from Turbuhaler, salbutamol 0.4 mg from Rotahaler or placebo was given according to the following scheme (order between study days and within study days randomized):

Study day 1	Study day 2	Study day 3
Rotahaler active	Rotahaler placebo	Rotahaler placebo
Turbuhaler placebo	Turbuhaler active	Turbuhaler placebo

Five and 10 minutes after treatment new PEF measurements were carried out. If the child did not get a bronchoconstriction after the exercise test or if PEF variation exceeded 25% since the previous visit, the child returned on another day and repeated the exercise test.

Need for extra medication, adverse effects, and presence of new bronchoconstriction within 10 min of study completion were also recorded.

The comparisons of the three treatments (Bricanyl Turbuhaler, Ventolin Rotahaler and placebo) were based on an ANOVA model with the following factors: patient, treatment and period. The period effect differences were tested by t-tests based on within-subject means or differences under suitable normality assumptions for the random effect.

The patients' and parents' informed consent was obtained. The study was approved by the Ethics Committee of the Portuguese Medical Association.

RESULTS

The results of the PEF measurements are presented in Fig. 1. There were no statistically significant differences between the three treatment groups regarding PEF before exercise and post exercise/pre-treatment PEF. At 5 and 10 min

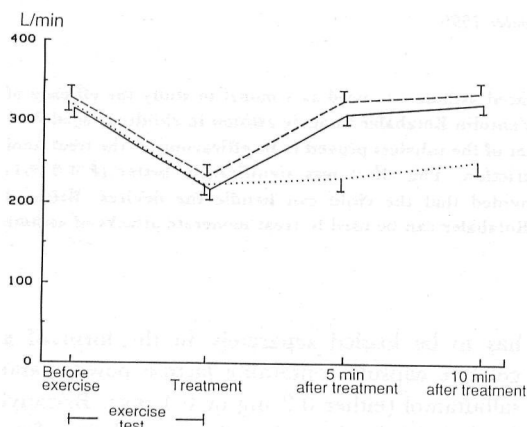


Fig. 1. Peak expiratory flow (l/min; mean $\pm$ SEM) before and after exercise, and 5 min and 10 min after treatment — Bricanyl Turbuhaler (0.5 mg terbutaline sulphate) - - - - - Ventolin Rotahaler (0.4 mg salbutamol) Placebo (n = 19)

after treatment there were significant differences ($P < 0.001$) between the two active treatments and placebo, but there was no statistically significant difference between Bricanyl Turbuhaler and Ventolin Rotahaler.

None of the children experienced another episode of bronchoconstriction after inhalation of either of the active drugs, whereas four children became obstructive within 10 min after placebo inhalation. On the placebo day, 10 children needed extra medication immediately after completion of the investigational measurements. No extra medication was needed on the days of active treatment.

No adverse effects were reported in this study.

DISCUSSION

This study was carried out to compare the efficacy of Bricanyl Turbuhaler and Ventolin Rotahaler in a situation of acute bronchoconstriction in children. Running exercise is a potent and reproducible stimulus for bronchoconstriction in many asthmatic subjects (1). Inhaled β_2 -agonists usually rapidly reverse exercise-induced asthma (2).

The study clearly showed that Bricanyl Turbuhaler (0.5 mg terbutaline sulphate) and Ventolin Rotahaler (0.4 mg salbutamol) were effective in the treatment of childhood exercise-induced asthma. No differences in efficacy could be found between treatments. This is not in accordance with the results of an earlier comparison between Ventolin Rotahaler and Bricanyl Turbuhaler (4). In that study, also performed in children with exercise-induced asthma, Turbuhaler was more efficacious than Rotahaler.

In the study by Pedersen (4), the recommended dose of salbutamol 0.2 mg, was used in connection with Rotahaler. In the present study the dose of salbutamol was doubled. This might be one explanation for the results achieved with Rotahaler in this study. Another explanation might be found in the study design. In the present study, the inhalers were loaded by the investigators, whereas in the study by Pedersen

the children had to load the inhalers themselves while they were bronchoconstricted. In that study, during Rotahaler treatment, seven of the 17 children had problems, such as failure to load the inhaler, failure to break the capsule, and failure to empty the capsule during inhalation, while only one child failed to use the Turbuhaler correctly.

The decrease in lung function in this study was moderate. When inspiratory flow rate is impaired, the efficacy of Rotahaler has been shown to decrease significantly (3). Turbuhaler has, however, been shown to work effectively even at very low flow rates (5).

In conclusion, this study has shown that Bricanyl Turbuhaler (0.5 mg) and Ventolin Rotahaler (0.4 mg) are both effective when studied under optimal conditions in children with moderate exercise-induced asthma.

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Address:

Jan Eric Wirén, M.D.

Dept. of Anesthesiology

University Hospital

S-221 85 Lund

Sweden

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