

Treatment of Acute Bronchoconstriction in Children with Use of a Tube Spacer Aerosol and a Dry Powder Inhaler

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In a double blind cross-over study 24 children suffering from acute bronchoconstriction were treated with either placebo, or terbutaline delivered by a pressurized aerosol with a tube spacer (TS), or salbutamol from a dry powder inhaler (Rotahaler = RO). Both active treatments resulted in a significant increase in FEV₁ as compared with placebo ($P < 0.001$). Furthermore, TS treatment resulted in significantly greater improvement in FEV₁ than treatment with the RO ($P < 0.05$). Under the conditions of marked airways obstruction problems with correct handling of the RO (loading and breaking the capsule) were prevalent and many children were unable to empty the RO capsule. These difficulties seemed to account for the smaller bronchodilation after RO treatment and were not seen under quiet circumstances. It is recommended that inhalation therapy in children is supervised by an adult during periods of marked airways disease.

Key words: acute bronchoconstriction; asthma; children; dry powder inhaler; tube spacer aerosol.

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Inhalation of therapeutic agents is a safe, effective way of drug administration which for many reasons is preferable to the oral route. However, patients often fail to benefit sufficiently from inhalation therapy because they cannot use their aerosols correctly (2, 5). Therefore, measures have been taken to make inhalation therapy more simple, and as a result two new inhalers have been designed:

A powder inhaler with cartridges (Rotahaler = RO)

A pressurized aerosol with a tube spacer (TS).

Both these devices may partially reduce the coordination problems which are experienced by many asthmatics when using pressurized aerosols, and studies have indicated that patients find them easy to use (1, 7, 8). However, conclusions from studies performed in patients under quiet circumstances may not be valid in children who are in acute distress because of an

asthma attack without any adults to help with the treatment (7). It is our experience that testing the inhaler under such circumstances may often reveal otherwise unnoticed problems that are important in the normal day-to-day treatment.

Therefore the present study was designed to assess if a) one inhaler was preferable to the other in the treatment of acute bronchoconstriction in children, and b) to reveal the problems inherent in their use.

PATIENTS AND METHODS

Sixteen boys and eight girls between the age of 7 and 14 years (mean 9.6) were studied. All suffered from exercise-induced asthma. They were studied while participating in a 4-month programme of physical training. Prior to the study informed consent was obtained from the children and their parents.

On a regular basis nine children were treated with beclomethasone and 11 with disodium-cromoglycate. In addition, all regularly inhaled β_2 -agonists. No children had taken β_2 -agonists for 4 h before exercise on the days of study, and exercise was always carried out at the same time of day (3–4.30 p.m.). Before, and throughout the training period three children used a RO, two a TS, and 19 a pressurized aerosol without a tube spacer, when they took their regular medications.

Before the training period all children had been given thorough instruction in the use of both TS and RO inhalers so that they were able to demonstrate a correct inhaler use. The children had been taught to close the nose during the inhalation and to hold their breath for 10 sec after the inspiration.

We used pressurized terbutaline aerosols with a 10×3.2 cm tube spacer and the dry powder inhalers named Rotahaler. The TS delivered 0.25 mg terbutaline/placebo per activation and the RO capsules contained 0.20 mg salbutamol/placebo powder per capsule.

Three alternative treatment regimens were randomly allocated and administered in a double-blind, double-dummy design during three different days of training:

- a) Terbutaline in TS and placebo in RO
- b) Placebo in TS and salbutamol in RO
- c) Placebo in both inhalers.

The children themselves administered all the treatments. Help from an adult was given only when a child was unable to insert the capsule into the RO. Forced expiratory volume in 1 sec (FEV_1) was measured before and at the end of each training session. If a child had acute bronchoconstriction during the exercise (measured as a fall in $FEV_1 > 25\%$ from the baseline value obtained before the training session) treatment was administered as a single puff from the TS aerosol, followed immediately by an RO treatment. The treatments were repeated in reverse order 5 min later.

FEV_1 was measured during the acute attack (pretreatment FEV_1) as well as 5 and 10 min after the first puff from the TS aerosol. If at

that point FEV_1 had reached a value corresponding to at least 90% of that measured before the training session the child resumed exercise; otherwise treatment with a rectal enema of an aminophylline solution was given and the child waited to resume the exercise until FEV_1 was normalized.

FEV_1 was measured on a dry wedge spirometer (Vitalograph®). The best of three recordings was chosen for study. Before the trial all children were familiar with pulmonary function measurements.

The following criteria had to be met before the results from a patient were evaluated: 1) the child should participate on 3 different study days, and 2) the variation in FEV_1 before exercise and the variation in pretreatment FEV_1 during all 3 test days had to be less than 15%. If a child was treated on more than three occasions the results from the first 3 treatment days that fulfilled this criterion were chosen for study.

We also recorded obvious errors in inhalation technique, the length of the breathholding pause, the number of acute attacks of bronchoconstriction during each training session, the necessity for other drugs, which inhaler the child preferred and whether the child had been helped with the treatment by an adult.

The results were analysed by parametric and non-parametric methods (paired t-test and Wilcoxon's rank sum test). However, as the results were similar only the results of the t-tests are given.

RESULTS

When the children demonstrated their inhaler use just prior to the training period (to ensure an efficient technique) all were able to use both inhalers correctly without help from an adult. At that time their demonstrations resulted in mean increases in FEV_1 of 25.2% (RO) and 19.7% (TS) respectively ($P < 0.01$).

The results of the pulmonary function measurements made during the 3 days of treatment are given in Fig. 1. There was no statistically significant difference between FEV_1 measured before the exercise or between pretreat-

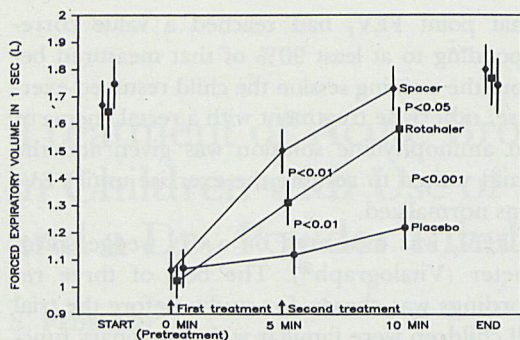


Fig. 1. Forced expiratory volume in 1 sec in 24 children with exercise-induced asthma treated with either placebo, terbutaline delivered by a pressurized aerosol with a tube spacer (TS), or salbutamol from a dry powder inhaler (rotahaler = RO). Values are expressed as mean $\pm$ SEM.

ment FEV₁ on the 3 days. The variation in pretreatment FEV₁ was from 21.6% to 62.7% (mean 45.2%) of the predicted normal.

Both active treatments resulted in a significant increase in FEV₁ as compared with placebo. Furthermore, both 5 and 10 min after the first treatment, FEV₁ was significantly higher after TS treatment than after RO treatment (Fig. 1). This difference between the active treatments was established by the first of the two treatments when the mean increase in FEV₁ was 40.4% (0.43 l) with TS and 28.3% (0.29 l) with RO ($P < 0.01$). After the second treatment with the two inhalers the mean improvement in FEV₁ was 15.5% (0.23 l) after TS and 21% (0.28 l) after RO treatment (n.s.).

Twenty-three children required treatment with aminophylline after placebo treatment, whereas such treatment was only needed on two occasions after TS treatment and on five occasions after RO treatment. One child experienced a second attack of bronchoconstriction later in the same training session after having resumed exercise following a RO treatment.

The breathholding periods varied from 5 to 10 sec (mean 8.7 sec) and there was no statistically significant difference between the three treatments.

Twelve children preferred the TS, five the RO and seven had no preference for either of the inhalers. The main objection against the RO was that most children found it inconvenient

when they had to load the inhaler with a new cartridge at every new treatment.

The following errors in inhalation technique were observed during TS treatments: forgetting to shake the canister before treatment ($n = 4$), neck flexed during inhalation ($n = 3$), fast inhalation ($n = 3$), submaximal inhalation ($n = 9$) and coordination problems (3 actuating during the middle third of inspiration).

When the RO was used the capsule did not break on six occasions (5 children discovered the mistake themselves and therefore were given a new capsule), seven children either did not tap the powder down into the clear portion of the capsule before loading, or turned the RO upside down after loading (but before breaking the capsule) so that some of the powder was in the opaque portion of the capsule at the time of inhalation, six patients held the mouthpiece of the RO downwards after breaking the capsule so that some powder had fallen out before the inhalation, 13 children did not empty the capsule, eight inhaled submaximally, three flexed the neck during inhalation and two exhaled through the RO before the inhalation. In addition two children (7–8 years old) were unable to load the capsule into the RO and had to be helped by an adult.

The powder in the RO was tolerated well and no side effects (particularly cough) were observed which could be ascribed to the inhalation therapy. Three children complained of nausea after aminophylline treatment.

DISCUSSION

The everyday life of many asthmatic children consists of recurrent episodes of acute attacks of bronchoconstriction. A rapid alleviation of these attacks is important because it may prevent, or at least reduce, inhaler abuse and unnecessary fear and anxiety in both the child and its parents. Therefore a child should also be able to use the inhaler efficiently under acute attacks of asthma.

The present study showed that under conditions of severe obstruction and dyspnea the majority of children obtained good benefit from the active treatments with both inhalers

tested. In addition the tube spacer was found to have some preference over the rotahaler.

The excellent bronchodilation that was found after TS treatment was in agreement with the results of an earlier study (7). To our knowledge the RO has not previously been evaluated under double-blind conditions in severely obstructed children, whereas Linney (3) in an open study found the RO at least as effective as a pressurized aerosol in children not suffering from acute bronchoconstriction. In addition, Towns et al. (9) found a tendency for RO to give greater bronchodilation than TS when the inhalers were studied under basic laboratory conditions with an adult administering the treatments. This is in accordance with our findings when the children demonstrated their inhalers prior to the training period. Therefore, the lower increase in FEV_1 after RO treatment during the acute attacks must have been due to the many errors made by the children when using this inhaler under conditions of distress. The substantial difficulties with loading and breaking the capsule correctly resulted in a high frequency of spillage and consequently a reduced amount of medicine available for inhalation. Since the present study we have gained the experience that the handling difficulties are sometimes reduced if the child is using a pre-loaded RO. The child only has to tap the RO with the mouthpiece downwards and then twist it into the horizontal position. A disadvantage of this approach is that the capsules, if carried too long in a pre-loaded position, tend to bend or buckle instead of breaking into two halves when twisted (personal observation).

Another factor, which may have contributed to a reduced effect of the RO, was that even after correct loading many children had difficulties in emptying the capsules completely in one inhalation. The drug powder must be drawn out of the capsule by a turbulent air-stream to generate sufficiently small particles to be taken down into the lungs. The reduced inspiratory flow rates during the attacks of acute bronchoconstriction may have resulted in erratic emptying of the capsules and a greater oral deposition of the medicine. A low inhala-

tion rate does not reduce the efficacy when a tube spacer aerosol is used. On the contrary, bronchodilation after TS treatment has been shown to increase when the inspiratory flow rate is low (4).

The assumption that low inspiratory flow rates contributed to the reduced efficacy is consistent with the finding that incomplete emptying of the capsules was observed much more frequently after the first treatment when the children were more severely obstructed, and only after this treatment was there a significant difference in bronchodilation between the two inhalers.

The situation when the capsule buckled or bent instead of splitting into two halves delayed treatment and made the child nervous and anxious. This problem has also been reported by others (6, 8). The reason for this unfortunate characteristic is unknown, but in the study an incorrect insertion of the capsule sometimes seemed to cause this failure. In addition, too long handling of the capsule with wet, sweaty fingers may have softened the capsule somewhat and thus made it more liable to bend rather than split.

The inability of many children to maintain a perfect inhalation technique under conditions of marked airways obstruction is consistent with the results of an earlier study (4). This finding emphasizes that asthmatic children, during unstable periods of their disease, should not be responsible for their own treatment. Under such circumstances adult supervision or help is often needed or else the inhalation therapy may fail.

The low incidence of a second attack of bronchoconstriction after the children had resumed exercise confirmed the superior effectiveness of inhaled β_2 -stimulants in preventing exercise-induced asthma.

CONCLUSION

The majority of asthmatic children aged 7–14 years can be taught efficient use of a pressurized aerosol with a tube spacer and a Rotahaler. Under conditions of acute distress the tube spacer aerosol seemed to have some preference

over the rotahaler, mainly because the rotahaler was found less simple and convenient to operate by many children. The importance of a reduced inhaled flow rate for the efficacy of the rotahaler needs further investigation.

REFERENCES

1. Bloomfield, P., Crompton, G. K. & Winsey, N. J. P.: A tube spacer to improve inhalation of drugs from pressurized aerosols. *Br. Med. J.* 2, 1479, 1979.
2. Crompton, G. K.: Problems patients have using pressurized aerosol inhalers. *Eur. J. Respir. Dis.* 63, Suppl. 119, 101-104, 1982.
3. Lenney, W., Milner, A. D. & Hiller, E. J.: Use of salbutamol powder in childhood asthma. *Arch. Dis. Child.* 53, 958-961, 1978.
4. Newman, S. P., Pavia, D. & Clarke, S. W.: Simple instructions for using pressurized aerosol bronchodilators. *J. R. Soc. Med.* 73, 776-779, 1980.
5. Orehek, J., Gayrard, P., Grimaud, C. & Charpin, J.: Patient error in use of bronchodilator metered aerosols. *Br. Med. J.* 1, 76, 1976.
6. Pearson, M. W.: The Mk III Rotahaler: a short report. *Practitioner* 227, 1779-1780, 1983.
7. Pedersen, S.: Aerosol treatment of bronchoconstriction in children, with or without a tube spacer. *N. Engl. J. Med.* 308, 1328-1330, 1983.
8. Pover, G. M., Browning, A. K., Mullinger, B. M., Butler, A. G. & Dash, C. H.: A new dry powder inhaler. *Practitioner* 226, 565-567, 1982.
9. Towns, S. J., Sharota, E., Simpson, S. J. & Mellis, C. M.: Bronchodilator effects of salbutamol powder administered via Rotahaler and of terbutaline aerosol administered via Misthaler. *Med. J. Aust.* 1, 633-636, 1983.

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