

Optimal inhalation technique with terbutaline Turbuhaler

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ABSTRACT: The bronchodilator response after four different modes of inhalation of 0.25 mg terbutaline from a Turbuhaler was assessed, in a double-blind cross-over study, of 14 asthmatic children aged 8-14 yrs (mean 11.6 yrs). The children inhaled as fast as possible (mean peak inspiratory flow rate=53 lmin⁻¹), because fast inhalations have been found to be more efficient than slow inhalations when the Turbuhaler is used. Tilting the head back during inhalation and a breath-holding pause of 10 s after the inhalation had no significant effect upon bronchodilation. Furthermore, the response was the same whether the children inhaled from residual volume (RV) or functional residual capacity (FRC). These results suggest that this new inhaler can be used with a very simple inhalation technique without any loss of effect. A simple inhalation technique is likely to facilitate teaching and improve compliance.
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The majority of asthmatic patients do not benefit optimally from inhaled therapy with conventional pressurized aerosols, because they do not use these devices correctly. In consequence, various new inhalers have been developed to make inhaled therapy more convenient and effective. The Turbuhaler is one such device. It is a multiple dose, dry powder inhaler, which contains 200 doses of pure terbutaline sulphate, without any carrier substances or additives [1]. Studies have indicated that patients find this inhaler simple and convenient [2].

There is, at present, no information about the best inhalation technique with the Turbuhaler. Therefore, we conducted the present study with this inhaler in asthmatic children to elucidate the necessity of exhaling to residual volume before inhalation, and the importance of tilting the head back during inhalation and holding the breath afterwards - manoeuvres which complicate the use of this otherwise simple inhaler.

Patients and methods

Ten boys and four girls, aged 8-14 yrs (mean 11.6 yrs) participated in the study. All suffered from chronic or episodic wheeze, which showed at least 20% increase in forced expiratory volume in one second (FEV₁) after one puff of terbutaline. Thirteen received regular inhaled therapy with corticosteroids and all used inhaled beta₂-stimulants. The study was approved by the local Ethical Committee, and informed consent was obtained from all patients and their parents.

The study was a controlled double-blind, double-

dummy cross-over. Each child participated on four separate occasions, at the same time of the day. Before each visit, therapy with inhaled corticosteroids and beta₂-agonists was stopped for 48 h and 8 h, respectively.

Four different modes of inhalation were evaluated in randomized sequence:

1. A deep inhalation from residual volume (RV) with head tilted backwards, and breath-holding at total lung capacity (TLC) for 10 s.
2. As treatment 1, but with no breath-holding pause.
3. A deep inhalation from functional residual capacity (FRC) with head tilted backwards and 10 s breath-holding after inhalation.
4. A deep inhalation from FRC, with head not tilted backwards and no breath-holding pause.

On all four test days the children inhaled as fast as possible.

After baseline ventilatory function had been measured, the child inhaled 0.25 mg terbutaline from the Turbuhaler. Pulmonary functions were repeated 30, 60, 120 and 180 min after this inhalation. To evaluate whether maximum bronchodilation had been achieved after Turbuhaler treatment, the children inhaled 0.25 mg and then 0.75 mg terbutaline (separated by 20 min), from a conventional pressurized aerosol with a Nebuhaler attached, at the end of each study day (fig. 1). Ventilatory function measurements were repeated 20 min after each of these treatments.

To be included in the study FEV₁ measured before Turbuhaler treatment had to be $\leq 70\%$ of the predicted value and within 15% of its value on the first study day. If this was not the case, the child was asked to make a further visit on another day.

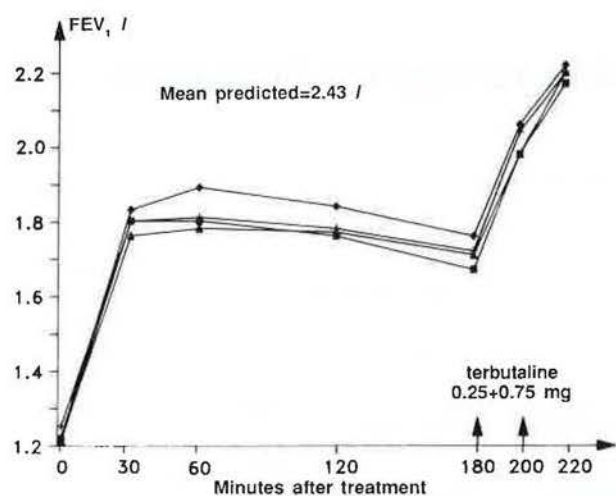


Fig. 1. — Mean forced expiratory volume in one second (FEV_1) after four different modes of inhaling 0.25 mg terbutaline from a Turbuhaler. ▲: from residual volume (RV), head tilted backwards, 10 s breath-holding; +: from RV head tilted backwards, no breath-holding; ◆: from functional residual capacity (FRC), head tilted backwards, 10 s breath-holding; ■: from FRC, head not tilted backwards, no breath-holding.

To ensure that the inhalations were performed correctly and that only one manoeuvre changed at a time, the patients inhaled through a Turbuhaler in series with a pneumotachygraph. The differential pressure signal from the pneumotachygraph (proportional to the flow rate of inspired air) was fed to a pressure transducer, from which the analogue signal was integrated to give the inhaled volume. Throughout the inhalation, the children could see the variation with time of both inspiratory flow rate and inhaled volume on the screen of an oscilloscope. This was used as a teaching aid so that all the children, after practising in the morning, were able to make reproducible, standardized inhalations. Inspiratory flow rates and volume were recorded for analysis.

FEV_1 , forced mid-expiratory flow rate (FMEF), forced vital capacity (FVC), and peak expiratory flow rate (PEF). The best of three measurements was studied.

Statistics

Both absolute ventilatory function values, percentage change and area under the time/pulmonary function curves (AUC_{0-180}) were evaluated. Friedman's test was applied to determine whether there was any overall difference between the treatments. If significant effects for treatment or time were found, the results were analysed by Wilcoxon's rank sum test.

Results

All 14 patients completed the study. No period ($p=0.93$) or carry-over ($p=0.76$) effects were found and no side-effects observed.

On all occasions the children made reproducible inhalations, and peak inspiratory flow rate (PIF) measured during the various treatments showed little variation (mean PIF being 53, 53, 54, and 53 $l \cdot min^{-1}$ during the four treatments, and the biggest difference observed in any individual being 8 $l \cdot min^{-1}$). When the children inhaled from RV mean inhaled volumes were 1.4 (range 0.8–2.0) and 1.4 (range 0.7–2.2) l . On inhalation from FRC the mean inhaled volumes were 1.0 (range 0.5–1.6) and 0.9 (range 0.4–1.5) l .

FEV_1 measurements after the four treatments are shown in figure 1. There was no statistically significant difference between pretreatment ventilatory functions on the four days. Pretreatment FEV_1 varied from 29–70% (mean 54%) of the predicted value. All treatments resulted in a significant bronchodilation, which lasted throughout the study period. At no time was there any significant difference in measured ventilatory function, percentage change in pulmonary function or in AUC_{0-180} between the four treatments.

Table 1. — Mean maximum percentage increase in pulmonary functions (compared with baseline) after treatment with 0.25 mg terbutaline from a Turbuhaler (Turbu), followed by 0.25 mg terbutaline from a Nebuhaler (Neb 1) and 0.75 mg terbutaline from a Nebuhaler (Neb 2)

	FEV_1 %			FVC %			PEF %			FMEF %		
	Turbu	Neb 1	Neb 2	Turbu	Neb 1	Neb 2	Turbu	Neb 1	Neb 2	Turbu	Neb 1	Neb 2
Treatment 1	48	63*	78**	29	36	46*	73	106*	149**	83	106	149**
Treatment 2	44	64*	75*	28	37	46*	80	120*	145**	83	120	145**
Treatment 3	52	68*	81**	31	37	45*	95	133*	160**	95	133*	160**
Treatment 4	46	63*	80**	29	36	44*	86	114*	144**	86	114*	144**

*: significantly different from Turbu; **: significantly different from Turbu and Neb 1; FEV_1 : forced expiratory volume in one second; FVC: forced vital capacity; PEF: peak expiratory flow; FMEF: forced mid-expiratory flow.

Ventilatory functions were measured on a Vitalograph with a pulmonary function analyser, and the bronchodilator response was assessed by measuring changes in

After all four modes of inhalation the Nebuhaler treatments given at the end of the day resulted in significant additional increases in FEV_1 as compared with

maximum FEV₁ after Turbuhaler treatment ($p < 0.01$) (table 1 and fig. 1.) indicating that maximum bronchodilation had not been achieved by any of the Turbuhaler treatments.

The results were similar for FVC, PEF and FMEF (table 1).

Discussion

When designing this study we tried to avoid pitfalls which might influence the results in such a way that important differences between treatments were not detected [3]. Analysing the data afterwards indicated that this had been achieved. Pretreatment ventilatory functions on the four days showed very little intra-individual variation, and all patients had highly reversible asthma on all test days. In no child did 0.25 mg terbutaline (half the normal dose) from the Turbuhaler result in maximum bronchodilation, indicating that the comparison of the four treatments took place at the steep part of the dose-response curve, where differences would be detected more easily than if maximum bronchodilation had been achieved. The control of the inhalations was successful so that only one variable differed from treatment to treatment. Statistical evaluation of the relative differences between the various pulmonary function measurements showed that the probability of a more than 4% difference in response between the various treatments was less than 5%. We, therefore, believe that our findings can be safely adopted for clinical use.

When patients are taught to exhale deeply before the inhalation there will always be a risk that they will do this through the inhaler. When a powder inhaler is used, it may increase the humidity of the powder or blow some powder out of the inhaler with a subsequent reduction in effect. To our knowledge, the importance of a deep exhalation to RV has not previously been studied with powder inhalers. In the present study it did not improve bronchodilation. This is in accordance with the results reported with other inhalation devices [4, 5].

The finding that the response was not improved by 10 s breath-holding after inhalation, or by tilting the head back during inhalation so that the particles could follow a straight path to the trachea, is in accordance with earlier findings with other powder inhalers [6, 7]. Therefore, these manoeuvres can also be omitted from the instructions. This means that the Turbuhaler, which has been found simple to operate, can be used with a very simple inhalation technique. Hopefully, this will facilitate teaching and improve compliance.

The importance of inspiratory flow rate was not investigated. Clinical studies with other powder inhalers have found rapid inhalations to be preferable to slow inhalations [6-8], and an earlier study in our own laboratory showed that this is also the case with the Turbuhaler (inspiratory flow rates higher than 30 l·min⁻¹ resulting in significantly better response than in-

spiratory flow rates lower than 30 l·min⁻¹). Therefore, the children inhaled as fast as possible in the present study.

Conclusion

Children with asthma need not exhale to RV before inhalation, tilt the head backwards during inhalation or hold their breath afterwards when they inhale as fast as possible through a Turbuhaler.

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RÉSUMÉ: La réponse bronchodilatatrice obtenue avec quatre modalités différentes d'inhalation de 0.25 mg de terbutaline par un Turbuhaler, a été explorée dans une étude en double anonymat avec permutation croisée, chez 14 enfants asthmatiques âgés de 8 à 14 ans (âge moyen 11.6 ans). Les enfants ont inhalé aussi rapidement que possible (débit inspiratoire maximum de pointe moyen=53 l·min⁻¹), parce que les inhalations rapides s'avèrent plus efficaces que les inhalations lentes lorsque l'on emploie le Turbuhaler. Le fait de pencher la tête en arrière pendant l'inspiration et de tenir une pause respiratoire de 10 secondes après l'inhalation n'a pas d'effet significatif sur la bronchodilatation. De plus, la réponse s'avère identique, que les enfants inhalent à partir du volume résiduel ou de la capacité résiduelle fonctionnelle. Ces résultats suggèrent que ce nouvel inhalateur peut être utilisé avec une technique d'inhalation très simple, sans aucune perte d'efficacité. Une technique d'inhalation simple est susceptible de faciliter les instructions au patient et d'améliorer sa compliance.

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