

Comparison of terbutaline *via* the Nebuhaler and salbutamol *via* the Volumatic: theory and practice

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Comparison of terbutaline via the Nebuhaler and salbutamol via the Volumatic: theory and practice. B.J. Chapman, G.K. Crompton.

ABSTRACT: The bronchodilating efficacy of terbutaline (250 µg-puff) inhaled *via* the Nebuhaler and salbutamol (100 µg-puff) inhaled *via* the Volumatic has been studied in 30 patients with reversible obstructive airways disease in a randomized crossover study. The salbutamol/Volumatic combination produced significantly greater bronchodilatation than terbutaline/Nebuhaler (one puff, $p<0.001$; eight puffs, $p<0.01$). The findings are discussed with particular reference to the theories of spacer action. *Eur Respir J.*, 1990, 3, 584-585.

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Deposition studies [1, 2] and clinical comparisons [3, 4] have shown that a 750 ml pear-shaped spacer device (Nebuhaler, Astra Pharmaceuticals) significantly increases the delivery and bronchodilating effect of terbutaline administered from a metered dose inhaler (MDI). A similar spacer device (Volumatic, Allen and Hanbury Pharmaceuticals) is now available for use in conjunction with salbutamol MDIs, but its effectiveness has yet to be established. To compare the two spacer devices, we have measured the bronchodilating effects of equal numbers of actuations of terbutaline and salbutamol given *via* the Nebuhaler and Volumatic, respectively.

Patients and methods

Thirty subjects (17 male, 13 female; aged 20-74 yrs mean 50 yrs) with reversible chronic obstructive lung disease were studied on two separate days when they received terbutaline (Bricanyl) 250 µg-puff *via* the Nebuhaler and salbutamol (Ventolin) 100 µg-puff *via* the Volumatic in random order. On each visit, they inhaled one puff of bronchodilator *via* the spacer, followed 20 min later by a further seven puffs *via* the spacer. All patients were instructed in the correct use of the spacer devices by one of three experienced respiratory measurement technicians. With each dose they took two long, deep inspirations, each one being followed by a 5 s breath hold. The patients were closely observed throughout the study to ensure they were adhering to the instructions and also to ensure the spacer valves were opening and closing freely. Forced expiratory volume in one second FEV₁ (best of three) was measured before and 20 min after each dose. All subjects had an increase in FEV₁ of

at least 20% on day 1. Baseline FEV₁ values on the two days varied by less than 15% in all patients. The results were analysed using paired t-tests to compare the changes in FEV₁.

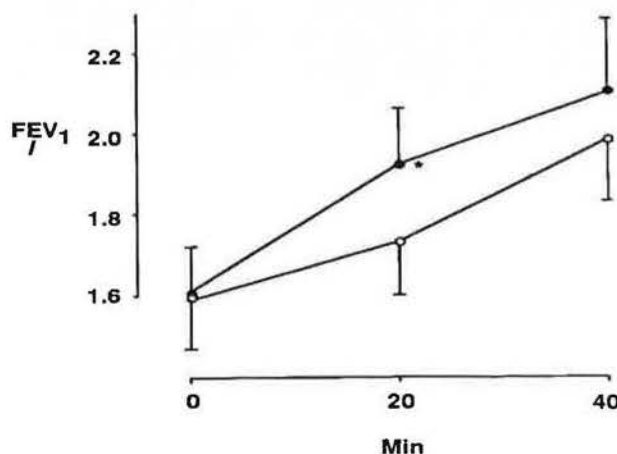


Fig. 1. - Mean forced expiratory volume in one second (FEV₁) values in 30 patients inhaling salbutamol *via* Volumatic and terbutaline *via* Nebuhaler. Mean FEV₁ ± SEM; *: $p<0.001$; **: $p<0.01$. —●— : salbutamol *via* Volumatic; —○— : terbutaline *via* Nebuhaler.

Results

The mean FEV₁ recordings for both study days are shown in figure 1. Salbutamol inhaled *via* the Volumatic produced significantly greater bronchodilatation than terbutaline *via* the Nebuhaler (mean increase in FEV₁; one puff, 20% vs 9%, $p<0.001$; eight puffs, 32% vs 25%, $p<0.01$).

Discussion

The development of spacer devices like the Nebuhaler and Volumatic was based on the principle that they would act as holding chambers in which aerosol particle size and velocity could decrease and thereby increase the penetration of particles to the airways [5]. The Nebuhaler is pear-shaped corresponding to the shape of the aerosol cloud emerging from the terbutaline MDI. In contrast, the Volumatic is symmetrical in outline and shorter than the Nebuhaler, despite the fact that the salbutamol MDI aerosol particles emerge at a higher velocity. *In vitro* studies have suggested that there is greater deposition of Ventolin in the Volumatic compared with Bricanyl in the Nebuhaler (78% vs 62%) (Andersson J., unpublished results. AB Draco, Lund, Sweden). The present study was designed to assess if the theoretical advantages of the terbutaline/Nebuhaler combination were reflected in practice. We chose to compare one actuation of each MDI in the belief that any increased efficiency of drug delivery would be more readily apparent with low doses of β_2 -agonist [2].

The finding that the salbutamol/Volumatic combination was more effective is surprising and the explanation is not at all clear. There was no evidence to suggest the Nebuhalers used were faulty with, for example, sticky valves. They were inspected carefully and the valves appeared to function normally. The fact this was an open study raises the possibility of observer bias. However, the respiratory measurement technicians were all experienced and reliable workers, and we know of no reason why any bias should have occurred. Also, the data were not analysed until the completion of the study.

This study has assumed that 100 μg salbutamol and 250 μg terbutaline have equal bronchodilating efficacy [6-9]. We know of no evidence to the contrary. A possible explanation lies in the higher velocity of the salbutamol MDI particles causing greater impaction of aerosol particles in the oropharynx with a corresponding reduction in bronchodilating efficacy. One puff of salbutamol may appear equipotent to one puff of terbutaline when inhaled directly from the MDI, but the addition of the spacer may reduce the negative effect of the higher salbutamol particle velocity and thus make the salbutamol/Volumatic combination appear more effective. However, this seems an unlikely explanation since when given by IPPV, 100 μg salbutamol appears equipotent with 200 μg terbutaline [10]. Further studies are required to identify the reasons for our surprising findings.

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Comparaison de la terbutaline administrée par le Nebuhaler et du salbutamol administré par le Volumatic: théorie et pratique. B. Chapman, G. Crompton.

RÉSUMÉ: L'efficacité bronchodilatatrice de la terbutaline (250 μg -bouffée) inhalée par le Nebuhaler, et du salbutamol (100 μg -bouffée) inhalé par le Volumatic, a été étudiée chez 30 patients atteints de maladie obstructive réversible des voies aériennes dans une étude randomisée avec permutation croisée. La combinaison Volumatic/salbutamol a provoqué une dilatation significativement plus marquée que terbutaline/Nebuhaler (une bouffée, $p < 0.001$; huit bouffées, $p < 0.01$). Les observations font l'objet d'une discussion orientée particulièrement sur la théorie d'intervention des espaceurs. *Eur Respir J.*, 1990, 3, 584-585.