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Wet Nebulizer Versus Spacer and Metered Dose Inhaler Via Tidal Breathing

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Nebulized beta$_2$-adrenergic drugs are widely used for treating acute asthma in children. Studies have shown that as much bronchodilatation is achieved by delivering the medication via a spacer attached to a metered dose inhaler (SMD) than via a wet nebulizer (WN) in either acute or chronic asthma in adults (1,2) and children (3-5). The SMD increases the deposition of aerosolized particles in the lungs (6,7) over the MDI without spacer and, like the WN, it reduces problems of coordination (8). In these studies, tidal breathing from a WN was compared with a deep inspiration and breathholding from a SMD. However, this may require more cooperation than can be expected from an acutely distressed child. Therefore, the study was designed to compare the effect of *tidal breathing* salbutamol from either SMD or WN in a double-blind randomized fashion in hospitalized moderately severe older asthmatic children (aged 7-18 years). The 750 ml pear-shaped Nebuhaler spacer (Astra Pharmaceuticals) which has a unidirectional valve, and which has been shown to be the most efficient in delivering aerosol in vitro (9) and in vivo (6) among various types of spacers was chosen for this study.

PATIENTS AND METHODS

Twenty-seven patients, 15 boys and 12 girls (mean age 11.9 years, range 7-18 years) diagnosed to have acute asthma were studied within the first 24 hours following their admission to Sainte-Justine Hospital. The protocol was approved by the hospital ethics committee and informed consent was obtained for each patient.

The treating physicians prescribed continuous intravenous aminophylline and

nebulized salbutamol at 3-hourly intervals for all patients and no child received other forms of β_2-adrenergic drugs within 8 hours prior to the study.

Forced vital capacity, FEV_1, and FEF_{25-75} were measured on a 9-liter automated water seal spirometer (Eagle One, Warren Collins, Braintree, MA). The best of three forced expirations (highest FEV_1 plus FVC) performed three hours following the last salbutamol administered via wet aerosol was recorded and the results were expressed as percent of the predicted value (10). All asthmatic children who had a baseline FEV_1 $<65\%$ of that predicted were accepted for the study.

Immediately following the baseline spirometry, subjects were entered in a double-blind randomized manner into one of two treatment groups. Group WN received 1 ml (5 mg) salbutamol added to 1 ml 0.9% saline solution via mouthpiece and Hudson Nebulizer (Up-Draft II Nebu-Mist, Temecula, CA) driven by continuous-flow oxygen output of 6 L/min (particles mass median diameter 3.18 μm), immediately followed by tidal breathing placebo via the SMD. Group SMD (n=14) received 2 ml 0.9% saline solution via mouthpiece and Hudson Nebulizer immediately followed by continuous tidal breathing of 2 puffs of salbutamol every 10 seconds (total 12 puffs = 1.2 mg salbutamol) via the Nebuhaler spacer. Patients were withdrawn from the study if the treating physician felt that it was clinically indicated. No child had ever previously seen the Nebulizer. Patients were simply instructed to breathe through the mouthpiece in a normal calm fashion with either apparatus.

Pulmonary function, pulse, blood pressure, respiratory rate, and tremor were assessed before (−11 minutes) and at 10, 30, 60, 90, 120, and 180 minutes after inhalation from the SMD.

Overall comparisons between groups were made using an ANOVA test. A p value <0.05 was taken to indicate significant differences between groups.

RESULTS

All patients completed the study. There were 14 in the SMD group and 13 in the WN group.

Table 1 shows the baseline characteristics of the groups. Despite the double-blind nature of the study, it is probable ($p<0.02$) that the SMD group had worse baseline pulmonary function tests than the WN group. Both groups improved significantly from baseline during the study ($p<0.002$) as shown in Figures 1 and 2. (Similar results were seen when examining the FEF_{25-75}.) Despite the graphical appearances, there was no significant difference in the response with regard to FEV_1 ($p<.5$), but there was with regard to FVC ($p<.05$). The maximum mean increase from baseline in FEV_1 was 36% at 10 minutes in the SMD group and 24% at 90 minutes in the WN group.

Side effects were comparable in the two groups for all parameters measured (SMD: nausea 2, headache 3, palpitations 3 patients; WN: mild tremor 2, headache 2, palpitations 2 patients) except for an increased pulse at 10 minutes in 17 of the SMD compared with 10 of the WN patients ($p<0.05$).

Table 1. Baseline Results

	GROUP SMD (N = 14)	GROUP WN (N = 13)	P
Age (year ± SD)	11.2 + 3.0	12.7 + 3.6	0.3
Height (cm ± SD)	141.2 + 15	150.5 + 19	0.2
VC (% ± SD)	53.1 + 9.0	67.5 + 18	<0.02
FEV_1 (% ± SD)	38.2 + 7.9	49.8 + 14	<0.02
FEF_{25-75} (% ± SD)	15.5 + 5.6	21.1 + 9.4	<0.09

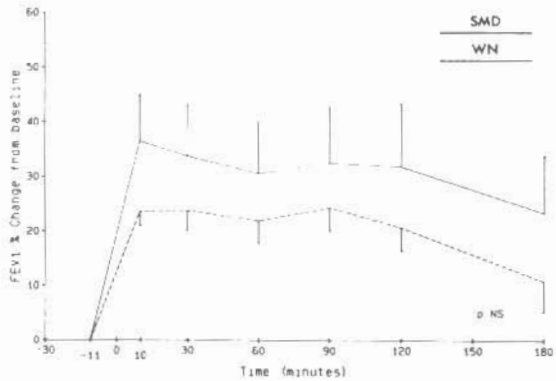

Figure 1. Percent change from baseline in FEV_1 (±SD) vs. time for the two groups. There was no significant difference (p = NS, ANOVA) in the degree of improvement between groups.

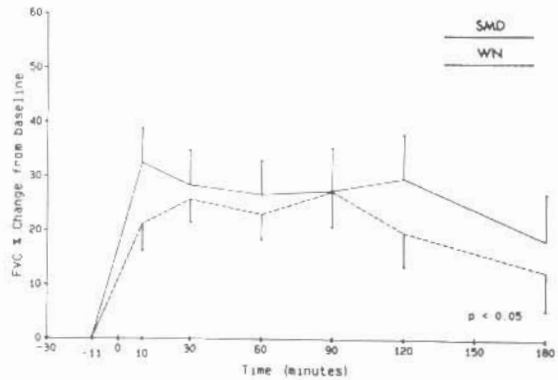

Figure 2. Percent change from baseline in FEV (±SD) vs. time for the two groups. There was a greater improvement in the SMD than the WN group (p < 0.05, ANOVA).

DISCUSSION

This study demonstrates that the SMD system performs at least as efficaciously as the standard WN in a moderately severe acute asthmatic episode. Among various types of spacers, it appears that the Nebuhaler is the most efficient (6,9), increasing the deposition of aerosol particles in the whole lung, while at the same time decreasing drug deposition in the oropharynx (6).

Despite the double-blind nature of the study, our two groups were probably different. However, the more severely affected patients were in the SMD group, and despite presumably narrower airways, they improved more than the WN group. The significant increase in pulse at 10 minutes in the SMD compared with the WN group also confirms that more medication was deposited despite the lower dose in the apparatus.

Tarala et al. showed that, in adults with acute asthma, an average dose of six puffs salbutamol (600 μg), given two puffs at the time at intervals of 15 minutes, did not result in further improvement in pulmonary function with an additional 5 mg of wet aerosol (11). Freedlander and Van Asperen, using half as much medicine in the Nebuhaler as in the wet nebulizer, have shown similar bronchodilatation in asthmatic children (5). Several previous studies have shown the efficiency of spacer devices using $beta_2$adrenergics (1,8,12). In all of those studies, the drug was released into the spacer and slowly inhaled from FRC followed by breathholding for 10 seconds. In the only previous study where the medication was distributed over more than a few puffs, Fuglsang and Pederson demonstrated significantly greater bronchodilation using a Nebuhaler than the wet nebulizer (3). Their results were very similar to ours, and we speculate that division of 12 puffs over 1 minute may be another reason for this seemingly improved efficacy of the SMD versus WN.

In the present study, both techniques used a mouthpiece and drug inhalation was performed using tidal breathing. Although it may not be the optimal technique, this study demonstrates that tidal breathing is more than adequate for $beta_2$adrenergic administration in this clinical situation.

The SMD technique seems to have several practical advantages over the WN. It is cheaper, more convenient to use, easier to clean, and it shortens inhalation time considerably.

We conclude that the very simple and time-saving technique of *tidal breathing* using a metered dose inhaler via a spacer is a very practical method for delivering $beta_2$-adrenergic medicines in the older hospitalized

child (aged 7–18) with acute moderately severe asthma and achieves at least as good bronchodilatation as the standard wet nebulization of the medication.

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