ARTICLE

Metered-Dose Inhalers With Spacers vs Nebulizers for Pediatric Asthma

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Objective: To determine whether the administration of β-agonists by metered-dose inhaler (MDI) with a spacer device is as effective as the administration of β-agonists by nebulizer for the treatment of acute asthma exacerbations in children.

Design: Randomized trial with two arms.

Setting: Urban pediatric emergency department (ED) in Bronx, NY.

Patients: Convenience sample of 152 children 2 years and older with a history of at least two episodes of wheezing presenting to the ED with an acute asthma exacerbation.

Interventions: Patients were randomly assigned to receive standard doses of a β-agonist (albuterol) by an MDI with spacer or by a nebulizer. Dosing intervals and the use of other medications were determined by the treating physician.

Measurements/Main Results: Baseline characteristics and asthma history were recorded. Asthma severity score, peak expiratory flow rate in children 5 years or older, and oxygen saturation were determined at presentation and before admission or discharge. The groups did not differ in age, sex, ethnicity, age of onset of asthma, or asthma severity score at presentation. There were no significant differences between the groups in outcomes, including mean changes in respiratory rate, asthma severity score, and peak expiratory flow rate, oxygen saturation, number of treatments given, administration of steroids in the ED, and admission rate. Patients given MDIs with spacers required shorter treatment times in the ED (66 minutes vs 103 minutes, $P<.001$). Fewer patients in the spacer group had episodes of vomiting in the ED (9% vs 20%, $P<.04$), and patients in the nebulizer group had a significantly greater mean percent increase in heart rate from baseline to final disposition (15% vs 5%, $P<.001$).

Conclusions: These data suggest that MDIs with spacers may be an effective alternative to nebulizers for the treatment of children with acute asthma exacerbations in the ED.

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APPROXIMATELY 9 to 12 million people in the United States are affected by asthma.[1,2] Among the highest risk groups for asthma are inner-city poor children.[3] Many of these individuals receive their medical care from emergency departments (EDs), which are often overburdened and understaffed. The challenge facing urban EDs is to deliver quality care to children with asthma, given the limited resources and manpower available.

Traditionally, patients who present to EDs with symptoms of asthma are treated with nebulized bronchodilators.[4] With the increasing prevalence of asthma, acute management has become more time-consuming and costly.[3] Crowded EDs may have too few oxygen ports to meet the growing demand, leading to treatment delays. In addition, a concern in inner-city hospitals has been the potential for the spread of tuberculosis by aerosolized particles from nebulizers.[5]

A spacer device is a holding chamber with a port at one end to which a metered-dose inhaler (MDI) is attached and a mask or mouthpiece at the other end. Patients dispense medications into the holding chamber and inhale them by breathing normally through the mask or mouthpiece. In the ED, MDIs with spacers may be a useful alternative to nebuliz-

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METHODS

STUDY PROTOCOL

This study was conducted at the Bronx Municipal Hospital Center Pediatric Emergency Department, an inner-city facility with approximately 55 000 patient visits per year, of which nearly 6500 are for asthma. Between October 1, 1992, and April 30, 1993, a convenience sample of asthmatic patients who presented to the ED during daytime hours when the investigator (K.C.) was present was enrolled.

To be eligible for the study, a child had to be 2 years of age or older, have a history of at least two episodes of wheezing, and currently be wheezing. Exclusion criteria included a history of other chronic illnesses, altered mental status, an initial oxygen saturation of less than 90% while breathing room air in conjunction with an asthma severity score[16] of 12, or respiratory insufficiency requiring mechanical ventilation.

Informed consent for participation in the study was obtained for each patient enrolled, and baseline demographic data were collected from the parents of all eligible children. Prior to undertaking the study, consecutively numbered envelopes were prepared containing treatment group assignments that were randomized using a random number table. Each enrolled patient received the next numbered envelope in time order containing the assignment to one of the two treatment groups. Because of the seasonal decrease in asthma cases and unavailability of the primary investigator, enrollment was terminated before all assignments were made, resulting in slightly uneven groups.

A standard β-agonist, albuterol, was supplied by the hospital pharmacy either as an MDI or as a solution for nebulization.

The experimental (spacer) group received albuterol by MDI with spacer, after a brief instruction in its use. A standard dose of three puffs per dose (90 μg per puff) was given based on current literature.[7-13] The spacer device used was the Aerochamber (Monaghan Medical Corporation, Plattsburgh, NY). Children under the age of 5 years or those who were unable to cooperate with the use of a mouthpiece were given the spacer with a face mask. For each dose, one puff by MDI was dispensed into the spacer, followed by the child's breathing normally five times through either the mouthpiece or the face mask. The process was repeated two more times for a total of three puffs per dose.

The control (nebulizer) group received a standard dose of 0.15 mg/kg of albuterol, to a maximum of 5 mg, in 3 mL of normal saline solution by an oxygen-driven nebulizer (Acorn II, Marquest Medical Products, Englewood, Colo) at a flow rate of 6 L per minute.

For both groups, the number of treatments, use of other medications, and final disposition were determined by the treating physician according to management protocols outlined by the National Asthma Education Program Expert Panel Report.[17] The approximate dosing interval was 20 minutes for both groups. Oxygen was given to all patients with an oxygen saturation of less than 94% while breathing room air. All discharged patients who received steroids in the ED were prescribed a short home course of prednisone.

This study was approved by the Committee on Clinical Investigations of the Albert Einstein College of Medicine and the Bronx Municipal Hospital Center.

ASSESSMENT

Demographic data included age, sex, ethnicity, and method of payment. Baseline characteristics included age at the diagnosis of asthma, the number of hospitalizations for asthma, whether there was a history of intensive care unit admissions or intubations, the number of days wheezing in the present illness, the presence of intercurrent illnesses, and whether asthma medications were used within the past 24 hours. Clinical measurements at presentation included an asthma severity score, peak expiratory flow rate (PEFR) using a Wright peak flowmeter (Ferraris Medical LTD, London, England) for children older than 5 years, and room air oxygen saturation measured by a pulse oximeter (Nellcor Inc, Hayward, Calif).

We used the pulmonary index (**Table 1**),[16] a validated asthma severity score composed of four items, each scored from 0 to 3, to assess severity of illness. We defined total scores of 0 to 3 as mild asthma, 4 to 7 as moderate asthma, and 8 to 12 as severe asthma.

Primary outcomes were measured before each treatment and at the time of final disposition. These included the percent change in asthma severity score, percent predicted PEFR for children older than 5 years, and oxygen saturation. Secondary outcome measures included the number of treatments given, whether steroids were used, the admission rate, and the treatment time in the ED. The percent change in heart rate (HR) was calculated using the following formula: $[(HR_{final} - HR_{initial})/HR_{initial}] \times 100$.

Vomiting or observed tremulousness was recorded, as well as whether the child complained of any side effects associated with β-agonist therapy.

STATISTICAL ANALYSIS

The Mann-Whitney *U* test was used to evaluate the differences between groups with respect to ordinal data and the χ^2 test to compare the groups on categorical variables. Where the expected frequency in any cell was five or less, Fisher's Exact Test was used to compare the groups on categorical variables. Statistical significance was considered at $P<.05$.

ers since treatments are not limited by the availability of oxygen ports and there is less risk of spreading respiratory pathogens. Results of several studies from the adult population indicate that MDIs with spacers are as effective as nebulizers in the treatment of asthma in both inpatient and outpatient settings.[6-15] The purpose of this study was to evaluate whether MDIs with spacers are as effective as nebulizers in the ED treatment of pedia patients with acute asthma exacerbations.

RESULTS

One hundred fifty-two patients were enrolled: 81 in nebulizer group and 71 in the spacer group. No patie

Table 1. Asthma Severity Score

Score	Respiratory Rate, Breaths per min	Wheezing*	I:E†	Retractions
0	<30	None	5:2	None
1	31-45	End expiratory	5:3 to 5:4	±
2	46-60	Entire expiratory	1:1	++
3	>60	Inspiratory and expiratory	<1:1	+++

*If no wheezing due to minimal air exchange, score 3.
†Inspiratory-expiratory ratio.
‡Plus/minus sign indicates mild wheezing; double plus signs, moderate wheezing; and triple plus signs, marked wheezing.

Table 2. Demographic Characteristics

Characteristic	Nebulizer Group (N=81)	Spacer Group (n=71)	P
Median age, y (25th-75th percentile)	8.8 (4.9-12.0)	7.1 (4.5-12.7)	.62
Male, %	53	59	.45
Latino and African American, %	94	94	.11
Medicaid payment, %	79	70	.47

Table 3. Baseline Characteristics*

Characteristic	Nebulizer Group (N=81)	Spacer Group (N=71)	P
Mean age at diagnosis of asthma, y	2.1	2.5	.60
Mean No. of past asthma hospitalizations	2.1	2.8	.69
No. of patients with history of ICU admissions	7	11	.19
Mean No. of days wheezing	3.2	2.9	.70
% With other illnesses	65	69	.64
% Given medications in past 24 h	90	82	.13
Steroids	12.3	14.1	.71
Theophylline	7.4	8.5	.79
β-agonists†			
Syrup	23.5	28.2	.51
Inhaler	54.3	32.4	<.01
Nebulizer	25.9	33.8	.26
Mean±SD asthma severity score	5.3±2.0	4.9±2.2	.24
Median asthma severity score (25th-75th percentile)	6.0 (4-7)	5.0 (3-7)	.24
Mean oxygen saturation, %	96	95	.29
Mean PEFR, % predicted‡	53	56	.55

*ICU indicates intensive care unit; PEFR, peak expiratory flow rate.
†Percents within groups may add to more than 100 because some patients were taking more than one medication.
‡For this analysis N=49 in the nebulizer group and N=39 in the spacer group.

Table 4. Outcomes*

Outcome	Nebulizer Group (N=81)	Spacer Group (N=71)	P
Mean final asthma severity score	1.1	1.1	.79
Severity score improvement, %			
Overall	80.9	79.4	.79
≤6 y	75.7	78	.73
>6 y	83.5	80.3	.95
Final PEFR, % predicted†	79	76	.61
Final oxygen saturation, %	97	97	.67
Mean No. of treatments	2.5	2.3	.55
Given steroids in ED, %	44	54	.26
Admission rate, %	6.2	5.6	.89
Mean treatment time in ED, min	103	66	<.001
Vomiting in ED, %	20	8	<.05
Mean increase in heart rate, %	15	5	<.001

*PEFR indicates peak expiratory flow rate; ED, emergency department.
†For this analysis, N=49 in the nebulizer group and N=39 in the spacer group.

who presented for asthma treatment during the hours when the primary investigator was present met the criteria for exclusion from the study. All of the patients completed the study and there was no crossover between groups. The groups did not differ significantly in demographics (**Table 2**). Baseline characteristics of both groups are shown in **Table 3**. While the groups did not differ in terms of the average number of home medications used per patient in the 24 hours prior to presentation to the ED, significantly more patients in the nebulizer group (n=44) reported using β-agonist inhalers at home than in the spacer group (n=23) ($P<.01$). When these patients were compared at baseline, there was no significant difference between their initial asthma severity scores.

Outcomes for the two groups are shown in **Table 4**. There were no significant differences between the groups in changes in asthma severity score or percent predicted PEFR from baseline to the time of final disposition. Furthermore, at disposition there were no significant differences in final oxygen saturation, mean number of treatments given, administration of steroids, or admission rate. No patients in either group received other bronchodilators.

There was a significant difference between the two groups in terms of treatment time in the ED. The mean ED treatment time for children in the nebulizer group was 103 minutes compared with 66 minutes for children in the spacer group ($P<.001$). Additionally, significantly fewer patients in the spacer group experienced episodes of vomiting during treatment: six of 71 (8%) vs 16 of 81 (20%) ($P<.04$). Finally, the nebulizer group had a significantly greater mean percent increase in heart rate at final disposition compared with the spacer group (15% vs 5%, $P<.001$).

COMMENT

Nebulized β-agonist therapy is the standard treatment for patients presenting to EDs with acute asthma exacerbations. In the past, the use of MDIs in children has been limited because of their inability to coordinate inspiration with aerosol delivery.[9] The development of spacer devices has allowed younger children with asthma to be treated with MDIs.[18] Several studies from the adult population have demonstrated the effectiveness of MDIs with spacers for the treatment of acute asthma exacerbations.[6-15] Many of these studies are limited by small

sample size, lack of a control group, difficulty in determining equivalent doses of bronchodilator agents via MDI vs nebulizer, and variations in patients with respect to bronchodilator responsiveness.[12] However, even with differences in the doses of the agents used, most studies found no significant differences in patient response to MDI therapy vs nebulizer therapy in EDs, inpatient wards, and intensive care units.[6-15] In addition, cost-analysis studies have indicated that for hospitalized adult patients with asthma exacerbations, treatment with either MDIs or nebulizers produced equivalent responses, and MDI use was not associated with longer hospital stays. The substitution of MDI therapy for nebulizer therapy was economically beneficial for both patients and hospitals.[10,12,14]

FEWER STUDIES exist in the pediatric literature.[9,13,18-20] Recently, Kerem et al[20] randomly assigned patients to receive albuterol either by nebulizer or by MDI with spacer in a double-blinded, placebo-controlled study. The authors showed no significant differences between the groups in changes in respiratory rate, clinical score, and respiratory function values. They noted that patients treated with MDIs with spacers had significantly less increase in heart rate over time ($P<.05$). Their study was limited by the relatively small sample size (n=33) and brief study period (40 minutes). Benton et al[13] studied 13 patients with moderate symptoms of asthma. These subjects were given a bronchodilator by MDI with spacer (Aerochamber). A comparison sample of 25 patients treated with nebulized bronchodilators was selected by reviewing the medical records of known asthmatics. These authors found no significant differences between the two groups with respect to final PEFR measurements and change in heart rate, but found a significant difference in mean change in respiratory rate. The MDI with spacer group had a fall in respiratory rate while the nebulizer group experienced a rise. Several problems limited their study. The sample size of 38 patients may not have been large enough to permit the detection of a difference between the groups. The control group may have differed significantly in baseline characteristics from the study group. Additionally, because the control group was studied retrospectively, other unmeasured factors may have affected their response to the nebulized treatments.

In our study, MDIs with spacers were as effective as nebulizers in producing bronchodilation for children with acute asthma exacerbations. We found that both forms of delivery of albuterol resulted in similar improvements in clinical observations and objective parameters. Additionally, our study included younger patients (age ≤6 years), who traditionally have not been treated with MDIs due to difficulty in administration of the medication. For the children in this age group, we found no significant differences in baseline or final asthma severity scores between the nebulizer and spacer groups.

There were some limitations to our study. While our sample size was large in comparison to that in other published reports, only 8.6% of children in the nebulizer group and 8.5% of children in the spacer group had baseline asthma severity scores of 8 or above. Therefore, we cannot comment conclusively that MDIs with spacers would be as effective as nebulized treatment in children with the most severe symptoms of asthma. However, we believe that our sample was representative of children presenting to EDs with acute asthma exacerbations. In another study by DiGiulio et al,[21] 29 patients with asthma exacerbations, aged 2 to 16 years, who demonstrated insufficient improvement after ED treatment to allow discharge, were recruited. For these patients, the authors found a median baseline asthma severity score of 6 using a modified pulmonary index.[16]

We found a difference in admission rate of 0.6% between the nebulizer and spacer groups (6.2% vs 5.6%). We calculated a 95% confidence interval of 0% to 8.2% for the difference in admission rate between the two groups. Although the true difference may be as great as 8.2%, our result of 0.6% suggests that this difference is probably very small and close to zero.

Some outcome measurements were subjective, such as degree of wheezing and retractions. To avoid differences in interobserver reliability, we used a single data recorder.

Finally, although our study was a randomized controlled trial, it was not blinded. Spacers have already been studied as effective delivery devices for inhaled medications in adults and children. Our main question was whether spacers were useful for the delivery of asthma medication as an alternative to nebulizers in a busy pediatric ED setting, and blinding would have made the care substantially different from usual ED care. A few of the outcomes were vulnerable to investigator bias (ie, degree of wheezing and degree of retractions). However, these variables behaved the same as nonvulnerable objective variables (ie, respiratory rate and oxygen saturation).

In summary, in our study sample, patients treated with MDIs with spacers achieved the same degree of improvement in symptoms as patients treated with nebulizers, while spending significantly shorter treatment times in the ED. Although we did not perform a cost-benefit analysis, it may be reasonably assumed that shorter treatment times for asthmatics treated with MDIs with spacers would result in fewer number of personnel and resources utilized. In our study, significantly fewer patients treated with MDIs with spacers experienced vomiting while in the ED, and the mean percent increase in heart rate from baseline to final disposition was significantly greater in the nebulizer group, suggesting that there may be fewer systemic effects of β-agonist therapy with MDIs with spacers.

We conclude that an MDI with a spacer device is an effective alternative to nebulizers for the ED treatment of children with mild to moderate asthma exacerbations.

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