

Salbutamol via Metered-Dose Inhaler With Spacer Versus Nebulization for Acute Treatment of Pediatric Asthma in the Emergency Department

Javier Benito-Fernández, MD, María González-Balenciaga, MD, Susana Capapé-Zache, MD, Miguel A. Vázquez-Ronco, MD, and Santiago Mintegi-Raso, MD

Objectives: To assess the effectiveness of salbutamol delivered via a metered-dose inhaler with spacer versus a nebulizer for acute asthma treatment in the pediatric emergency department.

Methods: All consecutive children younger than 14 years old who required treatment of acute asthma exacerbation in the emergency department during May 2002 (prospective cohort, n = 321) and May 2001 (retrospective cohort, n = 259) were included. Inhaled salbutamol was administered by metered-dose inhaler with a spacer (and a face mask in children younger than 2 years old) in the prospective cohort and by nebulizer in the retrospective cohort.

Results: There were no significant differences between the two cohorts in the mean (\pm SD) age (44.50 ± 38.64 vs. 48.37 ± 43.55 months) and asthma treatment, arterial oxygen saturation ($96.34 \pm 2.12\%$ vs. $96.19 \pm 6.32\%$), and heart rate (123.71 ± 23.63 vs. 129.41 ± 34.55 beats/min) before emergency department consultation. The number of doses of inhaled bronchodilators was also similar (1.42 ± 1.01 vs. 1.45 ± 0.98) as well as the number of children that required a stay in the observation unit, admission to the hospital, or returned for medical care. The overall mean length of stay in the emergency department was slightly shorter in the prospective cohort (82 ± 48 vs. 89 ± 52 minutes).

Conclusions: The administration of bronchodilators using a metered-dose inhaler with spacer is an effective alternative to nebulizers for the treatment of children with acute asthma exacerbations in the emergency department.

Key Words: Albuterol, administration and dosage, Bronchodilator agents, administration and dosage, metered dose inhalers, nebulizers and vaporizers, asthma, Emergency service, hospital

Asthma is the most common chronic illness in children, with a prevalence estimated at 5% to 10% in developed countries, and is a major reason for pediatric emergency

department visits (6–7% of all annual emergency visits in our hospital)^{1,2} and hospital admissions. Inhaled albuterol is the first-line bronchodilator agent most frequently used to treat acute asthma exacerbations in children.^{3–5} The β_2 -agonist, terbutaline, and the anticholinergic drug, ipratropium bromide, are other alternatives that can be administered by inhalation in the management of these patients.^{6,7} Whereas metered-dose inhalers (MDIs) with a spacer is commonly used for home management of mild exacerbations of asthma,^{3–5} for moderate and severe asthma and in the emergency department setting, the bronchodilator is typically administered by a nebulizer. Results of several studies carried out in pediatric populations indicate that MDIs with spacers are as effective as nebulizers in the treatment of mild and moderate acute asthma exacerbations.^{8–12} There are additional benefits of fewer side effects and less time required to administer the treatment. MDI-spacers are also cheaper, more portable, and easier to use than nebulizers.^{11–13}

However, while there is good evidence for the use of the spacer/MDI combination, there are many barriers to the successful reversal of the “nebulizer culture” in the emergency departments. In our hospital, based on clear evidence to support the use of MDI-spacer in preference to a nebulizer, in May 2002 it was decided to modify the routine in the treatment of asthma attacks and to substitute the nebulization by MDI with a spacer as the method of choice for the administration of bronchodilators. The objective of this study was to assess the effectiveness of salbutamol delivered via an MDI with a spacer versus a nebulizer for the treatment of children with acute asthma seeking medical care at the pediatric emergency department. The hospitalization rate was the primary end point of the study.

METHODS

This was a comparative prospective-retrospective cohort study. The study group consisted of the prospective cohort that included all consecutive children younger than 14 years with acute asthma exacerbation treated in the pediatric emergency department of an acute-care teaching hospital in

Division of Pediatric Emergency Medicine, Department of Pediatrics, Hospital de Cruces, Barakaldo, Bizkaia, Spain.

Address correspondence and reprint requests to Javier Benito-Fernández, MD, Division of Pediatric Emergency Medicine, Hospital de Cruces, Plaza de Cruces s/n, E-48903 Barakaldo, Bizkaia, Spain. E-mail: jbenito@hcru.osakidetza.net.

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ISSN: 0749-5161/04/2010-0656

Barakaldo, Basque Country, Spain, between May 1 and May 30, 2002. In these patients, bronchodilator medication was delivered using MDI-spacers and doses were adjusted to the patient's weight. According to the bronchodilator agent and the spacer device used at home, children weighing less than 20 kg received 1 mg of salbutamol (10 puffs) or 1 mg terbutaline (4 puffs) and children weighing more than 20 kg received 2 mg of salbutamol (20 puffs) or 2 mg terbutaline (8 puffs). Patients with severe asthma received 0.08 mg ipratropium bromide (4 puffs). Medications were delivered using the following spacer devices, Nebuchamber, Babyhaler, and Aerochamber in children younger than 6 years (with a face mask in children under 2 years) and Volumatic, Nebuhaler, and Aerochamber in children aged 6 years or older. Treatments were given 2 to 3 times at 20-minute intervals. Treatment was associated with a first dose of oral prednisone (1 mg/kg) depending on severity.

The control group included a retrospective historic cohort of all consecutive children younger than 14 years with acute asthma exacerbation treated in the pediatric department between May 1 and May 30, 2001. Bronchodilators were delivered as nebulization as follows: nebulized salbutamol using standard doses according to the body weight, children weighing less than 20 kg received 2.5 mg salbutamol (0.5 mL of 5% solution), and children weighing more than 20 kg received 5 mg salbutamol (1 mL of 5% solution) by an oxygen-driven nebulizer using a pneumatic jet system at a flow rate of 7 L per minute. The interval between the first and the second doses of salbutamol was 20 minutes. Successive doses of inhaled salbutamol were administered until the patient was judged by the attending clinician to need no further doses. Treatment was associated with ipratropium bromide (0.25 mg) and a first dose of oral prednisone (1 mg/kg) depending on severity.

In all patients, epidemiological data, clinical data before presentation to the emergency department, management at the emergency department, method of delivery of bronchodilators, length of stay in the emergency department, discharge destination, and return for medical care because of the same asthma episode within 1 week of the initial visit were recorded.

The study was approved by the hospital ethics committee. Informed consent was not obtained because no intervention was planned.

Statistical Analysis

Statistical analysis and the calculations were performed using the Statistical Package for the Social Sciences (SPSS) for Windows, version 10.0 (SPSS, Chicago, Ill). The Mann-Whitney *U* test and the Student *t* test were used for the analysis of continuous variables and the χ^2 test (with Yates correction when necessary) and the Fisher exact probability test for the analysis of categorical data. Quantitative variables

are expressed as mean \pm standard deviation (SD). Statistical significance was set at $P < 0.05$.

RESULTS

A total of 580 children younger than 14 years were enrolled: 321 in the nebulizer group and 259 in the MDI-spacer group. Seven of the 259 patients in the MDI-spacer group received inhaled bronchodilator by nebulizer due to severity of their clinical condition. Demographic characteristics of both groups were similar in respect to gender distribution and mean age (44.50 ± 38.64 vs. 48.37 ± 43.55 months for patients treated in May 2001 and May 2002, respectively). A total of 154 (48%) children in the control group had received inhaled bronchodilator therapy before emergency department consultation versus 125 (49%) in the study group. Arterial oxygen saturation ($96.34 \pm 2.12\%$ vs. $96.19 \pm 6.32\%$) and heart rate (123.71 ± 23.63 vs. 129.41 ± 34.55 beats/min) before the index emergency room admission were also similar in both groups.

As shown in Table 1, there were no statistically significant differences in the percentage of children that were not treated, number of doses of β -agonist, and percentage of patients who received ipratropium bromide and oral steroids. On the other hand, the retrospective and prospective cohorts were similar in the mean length of stay in the emergency department and in the observation unit, hospitalization rate,

TABLE 1. Treatment and Outcome of the Study Cohorts of Children Younger Than 14 Years with Acute Asthma Attended at the Emergency Department

Data	Retrospective Cohort	Prospective Cohort	<i>P</i>
	May 2001	May 2002	
No. patients	321	259	
No treatment	52 (16.2)	26 (10)	NS
A single dose of bronchodilator	145 (45.2)	102 (39.4)	NS
Dose of bronchodilator, mean \pm SD	1.42 ± 1.01	1.45 ± 0.98	NS
Treatment with oral steroids	115 (35.8)	93 (35.9)	NS
Treatment with ipratropium bromide	62 (19)	49 (18.9)	NS
Emergency room, mean length of stay, min	89 ± 52	82 ± 48	NS
Observation unit			
No. patients	30 (9)	28 (10.8)	NS
Mean length of stay, min	924 ± 350	788 ± 555	NS
Hospital admission	5 (1.6)	4 (1.5)	NS
Return for medical care	24 (7.5)	15 (5.8)	NS

Percentages in parenthesis.

and percentage of patients who returned for consultation after discharge.

Among children in the prospective cohort, 226 received inhaled bronchodilator therapy in the emergency department, 143 (63.3%) salbutamol and 83 (36.7%) terbutaline. Differences in the clinical outcome in these subsets of patients were not observed. The mean length of stay in the emergency department was 89 minutes for salbutamol-treated children and 90 minutes for those treated with terbutaline.

DISCUSSION

The present results indicate that the use MDI-spacers is an effective alternative for the administration of bronchodilator agents in the pediatric emergency setting. The introduction of this modality in our department was not associated with modifications in the management of acute asthma as there were no changes in the number of doses of bronchodilator administered or in the use of ipratropium bromide and systemic steroids. Doses of bronchodilators were similar in both study periods. Although there is some controversy regarding the equivalence between doses administered through a spacer device and a nebulizer,^{14,15} according to studies of drug deposition in the lower airways, the albuterol dose ratio of MDI dose to nebulized dose of 1:3 ratio is recommended by most authors. In the study group (prospective cohort), because salbutamol and terbutaline were equivalent,^{16,17} both drugs were administered indistinctly, which in turn had no effect on the results obtained. Therefore, the method of delivery was the only difference between the study periods but the use of an MDI-spacer had no effect on an increase in the length of stay in the emergency department or in the rate of hospital admission and return for care after the initial visit.

Recently, different studies have provide evidence of the efficacy of MDI with spacers in all age groups including children younger than 2 years.^{18,19} Compared with a nebulizer, a spacer and MDI is a more efficient means of drug delivery: less total dose is required for the same degree of bronchodilation, the time to delivery a complete dose is shorter, and there are fewer side effects. Delivery by nebulizer results in greater facial and oropharyngeal deposition of medication, with consequent systemic absorption and side effects, particularly tachycardia, vomiting, and tremor.^{9,12,19} Delivery with a spacer improves targeting of medication to the lung and reduces the dose delivered elsewhere, thus reducing the amount of medication available for systemic absorption. In addition, a spacer and MDI is compact, relatively cheap, and because it requires no external power source, it can be used in most settings.

In our study, the number of doses of bronchodilators administered was very similar in both cohorts and although the mean length of stay in the emergency department was shorter in the MDI-spacer group than in the nebulizer group, the

difference was not statistically significant. In the study of Delgado et al¹⁸ in children aged 2 to 24 months, slightly more children using the nebulizer than children using the spacer were admitted to the hospital, but the groups did not differ significantly. Similar findings have been reported by others.^{13,17,19} In our study, about 15% of asthma children attended at the emergency department during the study periods were not treated, nearly 50% received a single dose of bronchodilators, and in more than 60% the use of combined systemic steroids was not considered necessary. Overall, almost 70% of asthma-related consultations can be considered mild episodes and susceptible to be managed in the outpatient setting. It may be argued that the fact that the study took place during the month of May could have contributed to the low asthma severity of the study population. However, the episodes of asthma attended in the emergency department during the month of May, although smaller in number than the episodes attended during the months of September or October, show a similar degree of severity with a comparable hospitalization rate for asthma during the two periods.

Substitution of nebulization by a spacer-holding device for treating asthma in the emergency department can be considered a significant change since for more than 20 years nebulization has been the only efficient mode of delivery of inhaled bronchodilators for the treatment of acute asthma in the emergency department and in other settings. Nebulizers, however, are still very important in the treatment of severe asthma attacks and in the management of other conditions, such as laryngitis and bronchiolitis, for the administration of adrenaline. In our study, like others,²⁰ more than 97% of acute asthma episodes attended at the emergency department can be successfully treated with the use of the MDI-spacer combination. Prior to effective introduction of spacer-holding devices in clinical practice, it was necessary to inform primary care physicians and to run interactive educational meetings focusing on medical and nursing staff of the emergency department and on ward for the correct use of this mode, as well as to solve logistic aspects related to procurement and proper cleaning of the MDI-spacers until children began to bring their own devices at the time of emergency department consultation. With regard to acceptability of the MDI-spacer by the families, Delgado et al¹⁸ and Rubilar et al¹⁹ reported percentages of satisfaction higher than 65% and 80%, respectively. In our study, no objections were raised to the use of the MDI-spacer as the mode of delivery bronchodilator medications. On the other hand, it is well known that many asthmatic children use their inhaler devices too poorly to result in reliable drug delivery.²¹ In this respect, the possibility of providing inhalation instructions of proper technique is an additional advantage of the introduction of MDI with spacers in the emergency department setting.

It should be noted that the main limitation of our study is the use of retrospective historical controls. However, it

seems improbable that other factors affecting the condition under study (effectiveness of salbutamol according to mode of delivery) may have changed to an unknown extent in the time elapsed.

CONCLUSIONS

The administration of bronchodilators in the pediatric emergency department using an MDI with spacer is an effective alternative to nebulizers for the treatment of children with acute asthma exacerbations. Advantages of this mode of delivery include a shorter time to deliver a complete dose of the drug and a more rapid effect of medication, as well as the possibility to teach the proper use of inhaled bronchodilators during the patient's stay in the emergency department.

ACKNOWLEDGMENT

The authors thank Marta Pulido, MD, for editing the manuscript and editorial assistance.

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