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To cite this article: Niki Mitselou MD, Gunilla Hedlin MD, PhD & Carl-Axel Hederos MD, PhD (2016) Spacers versus nebulizers in treatment of acute asthma – a prospective randomized study in preschool children, Journal of Asthma, 53:10, 1059-1062, DOI: [10.1080/02770903.2016.1185114](https://doi.org/10.1080/02770903.2016.1185114)

To link to this article: <http://dx.doi.org/10.1080/02770903.2016.1185114>



Accepted author version posted online: 17 May 2016.
Published online: 17 May 2016.



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PHARMACOTHERAPY

Spacers versus nebulizers in treatment of acute asthma – a prospective randomized study in preschool children

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Abstract

Objective: To compare administration of bronchodilators by nebulizers with delivery by metered dose inhalers (MDIs) with spacers and to evaluate the clinical effect of the treatment of acute asthma in preschool children. **Methods:** A prospective randomized clinical trial in a pediatric emergency department (PED). Preschool children who were admitted for virus induced wheezing or acute asthma exacerbation were randomly allocated to receive bronchodilator treatment by nebulizer or by metered dose inhaler. The accompanying parents completed a questionnaire. **Results:** The length of stay in the PED and the hospitalization rate were similar and no difference was seen in the parents' view of ease of use and device acceptance. Baseline data were similar for both groups apart from the family history of asthma and atopic disease that was greater in the nebulizer group. No significant differences were seen in heart rate, respiratory rate and oxygen saturation at baseline and after the treatment. According to the parents 40% of the participants had asthma diagnosis though up to 66% had some kind of asthma medication. **Conclusions:** Our data suggests that MDIs with spacers are at least as effective as nebulizers in the delivery of beta agonists to treat preschool children with virus induced wheezing or acute exacerbations of asthma in the PED. Parents may underestimate the gravity of their children's asthma. It is mandatory to provide adequate information to the staff and parents in order to treat pediatric acute asthma successfully.

Keywords

Emergency department, pediatric, information, wheezing, bronchodilators, metered dose inhalers, hospitalization rate

History

Received 11 February 2016

Revised 24 March 2016

Accepted 26 April 2016

Introduction

Asthma is a common chronic disease in childhood and may potentially have a major impact on health and quality of life for both children suffering from it as well as their families [1]. Virus infection associated wheezing and acute asthma exacerbation are leading causes of emergency department visits [2, 3] and hospital admissions among children [2].

Inhaled beta-2-agonist is the drug of choice for the treatment of acute asthma [2–5]. The methods used for administering bronchodilators to treat preschool wheezing in the pediatric emergency department (PED) setting are mainly two: inhalation by metered-dose inhalers (MDIs) with spacers and by drug nebulizers [2, 6]. The literature has revealed that the efficacy of beta-2-agonists delivered by MDIs through a spacer device is equivalent to that of the nebulizer for the emergency department treatment of acute asthma exacerbations in pediatric patients [5, 7, 8] and no significant differences have been reported between the commercially available spacer devices [9].

Clinical research suggests that MDIs with spacers may have some significant advantages compared to nebulizers for the treatment of acute asthma in children. In particular, studies have demonstrated shorter stay in the PED [7], less increase in heart

rate [2, 7, 8], lower admission rate [2, 9, 10]. Two randomized double-blind placebo-controlled studies from France and New Zealand reported that both children and parents preferred spacers over nebulizers [5, 10]. Apart from the clinical advantages, using MDIs with spacers could lead to significant cost savings [10–13]. Following proper introduction of a spacer device, Breuer et al found that replacing nebulizers by MDIs with spacers is achievable if performed in cooperation with the staff, hospital authority and patients. Up to 92.5% of the children used this method throughout their hospital stay, while the costs were reduced by 63% after a 2-year follow-up [12].

Osmond et al. conducted a survey in 10 PEDs across Canada that evaluated the barriers and supports to implementation of MDIs with spacers. The study revealed that while most physicians and nurses were aware of the fact that the spacer was equivalent to the nebulizer, only a few actually used this method of treatment in their everyday clinical practice [14]. The educational interventions in addition to information and training of the medical and nursing staff are considered necessary for a successful implementation of a new treatment mode in the PED [3, 4, 14, 15].

Despite the research evidence supporting the use of MDIs with spacers for treatment of acute exacerbations of asthma in pediatric patients, the majority of PEDs in Sweden have not adopted this method. Only few studies involve patients under 6 years of age and those conducted prospectively include

low numbers of participants which indicates the need for performing further randomized large clinical trials in preschool children.

The aim of this study was to compare the two main methods of delivering bronchodilators, spacers with nebulizers, and evaluate the clinical effect of administration of inhaled beta-2-agonists in the emergency department treatment of acute wheezing and asthma in preschool children aged 0–6 years. The primary end points were the hospitalization rates and the length of stay at the PED.

Methods

In our pediatric emergency department setting at Central Hospital, Karlstad, Sweden, the bronchodilators have traditionally been administered by nebulizers like in the most PEDs in Sweden. In February 2012, we changed our protocol for acute asthma treatment from using nebulizers to MDIs with spacers (Nebunette, AstraZeneca, Södertälje, Sweden). Our aim was to familiarize the staff of the PED with both methods in order to make it possible to conduct this prospective study in a proper scientific way. During the implementation period November 2011–January 2012, physicians and nurses who worked in the PED received information, training and education. This process included several meetings with the medical and nursing staff, literature reviews on the equality of effectiveness of both methods, information about how to use MDIs with spacers properly and about the doses to be administered for the treatment of virus induced wheezing and acute asthma exacerbation in children.

Children were eligible for inclusion in this survey if they were 0–6 years of age and presented with virus infection associated wheezing or acute exacerbation of asthma to the emergency department at Central Hospital, Karlstad during the period 27 December 2012–27 April 2014. The participants were included consecutively and we had the intention to include at least 100 patients as power estimation found that we reached 80% with 95% significance if we had 49 children in each group and considered a 25% difference in hospitalization rate as clinical important. Exclusion criteria included symptoms consistent with pseudocroup, clinically suspected or laboratory confirmed Respiratory Syncytial Virus (RSV) bronchiolitis, multi-handicapped patients, life threatening asthma exacerbation and signs of impending respiratory failure.

The parents of the children who were considered eligible for inclusion in this clinical trial received written and oral information about the study and then they were asked to complete their consent form. The children were randomized in two groups, the nebulizer group (Group A) and the spacer group (Group B). The two treatment protocols were concealed in respective envelopes mixed in a box containing the same number of envelopes for each group (Group A and B). When a new patient was included in the study, the doctor picked a new envelope from the box in a blind manner. The assessors were also blinded. For patients in the nebulizer group, each treatment consisted of inhaled beta-2-agonist salbutamol (Ventoline 5 mg/ml) 4 ml delivered by an oxygen driven nebulizer. We used continuous nebulization for one minute for those weighed < 35 kg and for two minutes for those weighed > 35 kg. The process was repeated after 15 minutes. Children aged < 2 years in the spacer group received 4 puffs (10 breathes/puff) of salbutamol MDI (Airomir

100 µg/puff) with spacer (Nebunette) while older children aged >2 years received 6 puffs (5 breathes/puff). In both groups, treatment could be repeated up to three times during the first hour (with 20–30-minute intervals).

The accompanying parents were asked to complete a questionnaire during their stay in the PED. Demographic characteristics that were included in the analysis were age, gender distribution, maternal smoking during pregnancy and parental smoking in general as well as the presence of fur-bearing animals at home. Historical data included the percentage of patients for whom this was the first episode with wheezing, known asthma diagnosis, known allergies or eczema, asthma maintenance medications at home and medications received before attending the PED. Observations including heart rate, respiratory rate and oxygen saturation were recorded at baseline and after the last treatment. Before leaving the PED, the parents answered a question about how they experienced their child's treatment by using an evaluation scale 0–10 where 0 stood for "very simple" and 10 stood for "very inconvenient."

The data were analyzed with the SPSS statistical software for Windows (SPSS Inc., Chicago, IL). The intention to treat analysis was employed. The results are expressed as means, standard deviations (SD) and frequency and percentage distributions. $P \leq 0.05$ was considered statistically significant. The study was approved by the Uppsala University Ethics Committee.

Results

During the period 27 December 2012–27 April 2014 a total of 100 preschool children aged 0–6 years were enrolled into this trial. Two patients were excluded from data analysis for the following reasons: one because of their age (a 7-year-old child) and one because the parents decided to quit the study. Then, 53 children were randomized to the nebulizer group (Group A) and 45 to the spacer group (Group B).

The treatment groups were similar with respect to demographic characteristics as summarized in Table 1. The mean age of the children was 23.36 months (SD 15.77) in group A and 22.71 months (SD 11.85) in group B, $p = 0.82$. About two-thirds of the patients were boys, 64.2% of the children in group A and 73.3% in group B, $p = 0.33$. No significant differences between the two groups were seen in maternal smoking during pregnancy ($p = 0.19$), parental smoking in general ($p = 0.31$) and the presence of fur-bearing animals at home ($p = 0.64$).

Table 1. Demographic characteristics.

Demographic data	Group A (nebulizer) N = 53	Group B (spacer) N = 45
Age: mean in months ± SD	23.36 ± 15.77	22.71 ± 11.85
Male: n (%)	34 (64.2%)	33 (73.3%)
Parental smoking in general: n (%)	15 (28.8%)	7 (15.9%)
Maternal smoking during pregnancy: n (%)	8 (15.4%)	3 (6.8%)
Fur-bearing animals at home : n (%)	20 (38.5%)	19 (43.2%)

Table 2. Heart rate, respiratory rate and saturation at baseline and after the last treatment.

		Group A (Nebulizer) N = 53	Group B (Spacer) N = 45
Heart rate (beats/min): mean $\pm$ SD	at baseline	142.21 $\pm$ 21.68	139.52 $\pm$ 20.14
	after treatment	155.89 $\pm$ 22.63	148.35 $\pm$ 17.77
	difference	12.96 $\pm$ 17.63	6.23 $\pm$ 25.75
Respiratory rate (breaths/min): mean $\pm$ SD	at baseline	40.86 $\pm$ 11.16	39.92 $\pm$ 11.03
	after treatment	36.71 $\pm$ 10.95	35.75 $\pm$ 10.69
	difference	-4.69 $\pm$ 9.97	-3.52 $\pm$ 10.00
SaO ₂ (saturation %): mean $\pm$ SD	at baseline	96.00 $\pm$ 2.64	95.98 $\pm$ 2.44
	after treatment	96.50 $\pm$ 2.21	96.52 $\pm$ 2.26
	difference	0.63 $\pm$ 2.66	0.50 $\pm$ 2.65

No clinical differences were recorded in the baseline assessment of asthma severity on presentation to PED as shown in Table 2. Furthermore, there were no statistically significant differences in the histories of asthma ($p = 0.79$), allergy ($p = 0.75$) and eczema ($p = 0.39$) between the children in the two treatment groups. However, the family history of asthma and atopic disease (allergies or eczema) was greater in the nebulizer group, 84.6% versus 65.9% in the spacer group ($p = 0.03$), as presented in Table 3. Moreover, it is notable that 66% of the children had some kind of asthma medication, whereas only 40% had asthma diagnosis according to the parents.

Primary outcome measures

As shown in Table 4, the length of the stay in the PED was similar for both groups, 206.0 min (95% CI, 91.1–314.9) for group A and 209.4 min (95% CI, 110.6–328.2) for group B, $p = 0.86$. The admission rate was 11.3% (95% CI, 2.8–22.2) in the nebulizer group and 15.6% (95% CI, 5.0–26.2) in the spacer group, $p = 0.54$. With regard to how the parents experienced their child's acute asthma treatment in the PED, no significant differences were observed between the two groups with 3.5 (95% CI, 2.1–4.8) for group A and 3.7 (95% CI, 2.2–5.1) for group B, $p = 0.75$.

Table 3. Asthma, allergy and eczema history.

	Group A (Nebulizer) N = 53	Group B (spacer) N = 45
History of wheezing: n (%)	25 (49%)	27 (61.4%)
Asthma medication: n (%)	33 (64.7%)	32 (72.7%)
Asthma: n (%)	22 (42.3%)	17 (39.5%)
Allergies: n (%)	8 (15.7%)	8 (18.2%)
Eczema: n (%)	8 (15.7%)	10 (22.7%)
Family history of asthma and atopic disease: n (%)	44 (84.6%)	29 (65.9%)

Table 4. Medication received before presentation to the ED and oral steroids given in the PED.

	Group A (Nebulizer) N = 53	Group B (Spacer) N = 45
Oral beta2agonist: n (%)	13 (25.5%)	15 (34.1%)
Inhaled beta2agonist: n (%)	20 (39.2%)	13 (29.5%)
Inhaled steroids: n (%)	14 (27.5%)	9 (20.5%)
Leukotriene antagonist: n (%)	3 (5.9%)	4 (9.1%)
Oral steroids before presentation to the PED: n (%)	6 (11.8%)	1 (2.2%)
Oral steroids given in the PED: n (%)	35 (66.0%)	35 (77.8%)

Secondary outcome measures

The oxygen saturation ($p = 0.82$), respiratory rate ($p = 0.59$) and heart rate ($p = 0.16$) after the last treatment were similar in both groups (Table 2).

Discussion

Our data suggests that the efficacy of inhaled beta 2 agonists administered using the spacer device does not differ from that of the nebulizer. These findings are in agreement with those of earlier studies [5, 7, 8].

It is notable that there were no significant differences between the two groups in the length of stay in the PED, hospitalization rate and side effects. In addition, both methods were found similar as far as how the parents experienced their child's treatment were concerned. Yet, it is important to mention that in the present study the family history of asthma and atopic disease was greater in the nebulizer group. That is to take into consideration as it could suggest that these children run a higher risk of developing persistent asthma.

One interesting finding of our study arose from the comparison of the percentage of patients in both groups who had asthma medication at their disposal to the percentage of patients who were described as having asthma. Accordingly, these findings suggest that relying on parental reports may lead to underestimation of asthma prevalence and severity in preschool children. Accurate and repeated education of parents is of outmost importance in order to provide adequate treatment to children with acute asthma [16].

A valuable lesson to be learned here is that changing physician practice and pediatric emergency department culture can be really challenging. Thus, to be effective in the

Table 5. Length of stay, hospitalization rate and how the parents experienced their child's treatment.

	Group A (Nebulizer) N = 53	Group B (Spacer) N = 45
Length of stay (minutes) $\pm$ SD	153.33 $\pm$ 80.39	153.60 $\pm$ 97.57
Admission rate: n (%)	6 (11.3%)	7 (15.6%)
Parents' opinion on the acute asthma treatment: mean $\pm$ SD	3.46 $\pm$ 2.69	3.65 $\pm$ 3.04

long run, our experience has shown that this type of intervention requires teamwork combined with extensive preparation. The latter includes literature reviews as well as education and training of the medical and nursing staff which are of paramount importance before adopting the new technique [12, 13, 17]. Today MDI with spacer is standard treatment in our PED.

From a pedagogical point of view, using the spacer and MDI combination in the PED could probably provide extra support to the families that already use a spacer device for asthma treatment at home, seen as an extra training occasion. Moreover, a successful implementation of this technique could potentially lead to a decrease in hospital admissions and thus lower costs per child with acute asthma exacerbation. However, the potential economic benefits and cost savings of the implementation of spacers in the PEDs need to be further investigated.

Conclusions

Inhaled bronchodilators administered using the spacer device in the PED is an effective treatment not only for acute asthma but also for virus induced wheezing in preschool children. It is now standard treatment in our PED and the hospitalization rate is still very low. Parents may underestimate the gravity of their children's asthma. It is therefore mandatory to provide adequate information to the staff and the parents in order to achieve a successful treatment.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

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