

Therapeutic and Diagnostic Methods

Reliable Salbutamol Administration in 6- to 36-Month-Old Children by Means of a Metered Dose Inhaler and Aerochamber With Mask

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Summary. A double-blind study was performed to demonstrate that bronchodilator can be administered reliably to infants and children under 3 years of age from a metered-dose inhaler (MDI) by means of an economical valved aerosol-holding chamber device (Aerochamber®) fitted with a mask. Symptoms of cough and breathlessness were compared for two 1-week crossover periods with the child either taking active drug or placebo. The MDI and Aerochamber with mask is an effective delivery system for respiratory therapy in these young children. *Pediatr Pulmonol.* 1989; 6:263-267.

Key words: Cough and breathlessness score; Aerosol therapy; MDI add-on device; pediatric asthma.

INTRODUCTION

Aerosols have become the mainstay of asthma therapy.¹ In adults, metered-dose inhalers (MDIs) are widely recognized to provide an inexpensive, effective, and readily portable means for administration of bronchodilators, cromolyn, and steroids. Until recently, such efficient, relatively simple aerosol therapy has not been available to those unable to coordinate canister discharge with aerosol inhalation.^{2,3} The patient groups least able to achieve good compliance with MDIs include the elderly, the handicapped, and children, particularly those under the age of 6 who may not comprehend the instructions or whose hand-inspiration coordination may not yet be adequately developed. Under the age of 3, successful MDI aerosol therapy has been unsatisfactory even when the aerosol is parent-administered because of the difficulty of aerosol discharge during inhalation and particularly during an asthmatic attack when the child is tachypneic and agitated.

It has previously been demonstrated that effective administration of aerosol bronchodilator drugs from standard aerosol inhalers is facilitated both in children⁴ and in adults^{5,6} by means of a valved aerosol-holding chamber device (Aerochamber®).⁷ In children, administration of aerosol medications by unaided MDI devices depends on the cooperation of the child, who must put his or her mouth around the actuator mouthpiece and inhale at the time of release of the dose. However, although children

over 5-6 years of age can usually be taught to inhale from MDIs, attempts to use metered-dose aerosols in infants and in young children have been largely ineffective, despite attempts to use styrofoam cups⁸ and other inhalation aids.⁹ Recently, a 500 ml plastic bottle, shaped to fit an infant's face, was shown to be effective for delivering relatively large doses of MDI-generated aerosol therapy.¹⁰ Pediatricians typically resort to using the less desirable systemic route or find it necessary to prescribe cumbersome and expensive compressor-driven nebulizers for delivering aerosols to infants and young children. Unfortunately, this limits the therapeutic possibilities because steroid solutions for nebulization are not available in many countries. Other limiting factors include the cost of wet aerosol delivery devices, the need for a power source to operate them, nosocomial infections if there is failure to clean nebulizers regularly,¹¹ and the potential delivery of excessive doses of bronchodilator. These and other problems of nebulizer therapy have recently been reviewed.¹²

The Aerochamber with mask is a simple, reliable, and inexpensive new device that attaches to any MDI. Experience indicates that it enables parents or health-care workers to provide MDI aerosol therapy to infants, chil-

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Received May 5, 1988; (revision) accepted for publication November 20, 1988.

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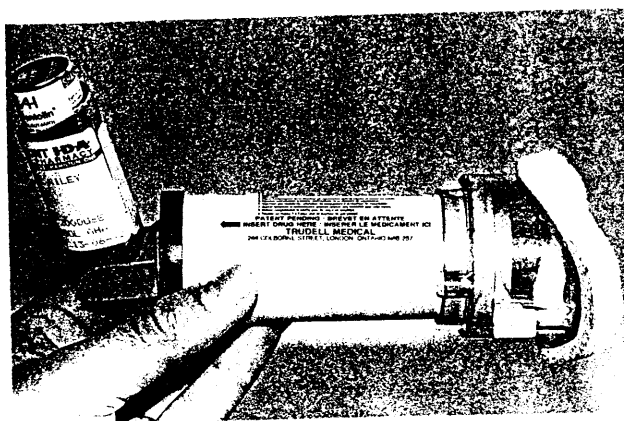


Fig. 1. Prototype Aerochamber-with-mask used in this study. The adult Aerochamber was modified to accommodate a pediatric tracheostomy mask, fitted with a foam seal.

dren, and others unable to effectively use an unaided MDI.

We have performed a double-blind trial of the Aerochamber-with-mask to determine whether effective aerosol therapy can be given reliably to infants and small children by their parents and to assess the magnitude of response and acceptability to the families of these patients. The protocol was approved by the hospital ethics committee, and parents gave written informed consent prior to entry.

MATERIALS AND METHODS

The prototype Aerochamber-with-mask^b used in this study consisted of a modified pediatric tracheostomy mask (Airlife, Inc. CA) adapted to one end of a modified adult Aerochamber (Fig. 1). The most important feature of the adaptation is the presence of a seal attached to the mask to assure a tight fit between the mask and the infant's face. Because the mask fits tightly over both the mouth and nose, the infant is obliged to breathe in and out through the Aerochamber (Fig. 2). By means of a low-pitched whistle built into the mask, breathing through the Aerochamber was signaled audibly, while at the same time, a visual signal was provided by mist on the inside of the mask during expiration. The device has a very low resistance (3 cm H₂O/L/s) one-way valve, and the mask has an extremely small dead space (35 ml). The Aerochamber-with-mask was kept in place over the nose and mouth during four complete breaths following delivery of one puff, 100 µg of salbutamol (albuterol) from a standard MDI.

Twenty-nine patients with childhood asthma as evi-



Fig. 2. One technique of administering MDI aerosol to an infant using the prototype Aerochamber-with-mask.

denced by symptoms of recurrent cough and wheezing, in whom other conditions had been excluded, were recruited. They had all received prior treatment with a variety of medications including oral bronchodilators and cough medicines by their primary-care physicians and were referred for management of their symptoms. In view of the young age, it was not possible to obtain objective lung function studies. Effectiveness was judged by the results of a double-blind symptom questionnaire. The parents knew that their child would undergo two treatment periods consisting of 1 week of treatment with salbutamol (albuterol). Identical, unmarked placebo and active drug canisters^c were provided to the hospital pharmacy, which distributed them in random order and identified them only by number. All parents were instructed in the use of the Aerochamber-with-mask and MDI by the same research assistant who also administered a standard questionnaire prior to each course of therapy. Where possible, all other drugs were discontinued during the trial, but the requirement to introduce other medications during the trial was recorded.

In most instances, the treatments were given for 1 week periods during recurrences of coughing or apparent breathlessness in association with upper respiratory tract infections, since, in this particular age group, symptoms potentially responsive to bronchodilators are usually sporadic rather than continuous and the double-blind nature of the trial addressed the issue that these symptoms are often self-limiting.

For symptoms of cough and breathlessness, a five-level scoring system was used (1—very severe, 2—severe,

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TABLE 1—Patient Response to Therapy Delivered by MDI and Aerochamber-With-Mask (n = 25)

Symptom	Treatment		P ^a
	Salbutamol	Placebo	
Cough improved	20	5	<0.001
Breathing improved	19	8	<0.01

^aChi-squared, 1 df.

3—moderate, 4—some, 5—none). Immediately prior to the trial and at the end of each week, parents were asked to record the score that they felt best represented the child's condition. A change in score from one time to the next was used to assess the response to each treatment course. An increase in the score indicated an improvement in symptoms, whereas a decrease indicated a worsening of the symptoms.

Possible side effects such as changes in activity level and sleep disturbances were noted at each visit, and parents' overall impression of response to treatment was recorded at each visit. Parents were also asked to compare one treatment course with the other with regard to the convenience and acceptability of this form of therapy.

RESULTS

Twenty-five of 29 children completed the course of treatment prescribed. Of the 4 children who did not complete the trial, 1 received no drug at all, 1 had lost the medications, and 2 recovered well before the trial was completed and stopped therapy.

The results of the trial are shown in Table 1. The values shown reflect the number of patients who had improved symptom scores after 2 weeks of treatment, thus indicating benefit. The remainder of the patients in each category showed either no change or a worsening of symptoms. Active drug administered via the Aerochamber-with-mask resulted in fewer symptoms than placebo given the same way. This indicated effective delivery of medication to the lung. None of the patients on salbutamol deteriorated whereas three patients on placebo had an exacerbation of symptoms. Twenty-eight of 29 parents asked to keep the Aerochamber-with-mask for continued use, and five of seven patients who previously used compressor-driven nebulizers were readily switched to the Aerochamber-with-mask.

DISCUSSION

Bronchodilator and anti-inflammatory/antiallergic aerosols are most effective in controlling chronic asthma, and adrenoceptor agonist aerosols, in relatively large doses, together with systemic steroids are first-line ther-



Fig. 3. Aerochamber-with-mask, available commercially.

apy for reversing bronchoconstriction in acute life threatening episodes in adults and children.^{13,14} In recent years, provision of aerosol therapy has been made more convenient and cost-effective by the increased use of Freon-pressurized metered-dose inhalers instead of nebulized drug solutions. Furthermore, valved add-on devices such as the Aerochamber have improved the reliability and efficacy of aerosol therapy, particularly in adults and in children over age 4 years who are unable to effectively use the unaided MDI.^{4,15-17} Previously, aerosol administration to infants and children under age 3 years required the use of drug solutions delivered from relatively inefficient and expensive compressor-driven or ultrasonic nebulizer systems. Another disadvantage of the latter is the lack of available steroid solutions for nebulization in some parts of the world, particularly in North America.

In adults, the particle-size selective characteristics of the Aerochamber serve to decrease upper airway steroid aerosol deposition eight- to tenfold and the total body dose by approximately 75% while providing a similar lower respiratory tract dose of medication as does an optimally used unaided MDI.⁵ As a result, oral candida albicans infections are virtually eliminated while systemic steroid side effects are minimized, a particularly important feature when large doses of inhaled steroids are administered.^{18,19} This reduction in the total body dose of inhaled medications would be especially useful in infants and young children who, unlike adults, are unable to expectorate the upper airway dose by gargling.

Measuring the effectiveness of aerosol therapy in children less than 4 years old with reversible airflow obstruction is difficult because of the variable natural history of this condition as well as problems in obtaining objective physiological evidence of benefit. Although scoring systems are not the ideal method for objectively assessing response to therapy, they have been used with some mea-

sure of success in pediatric populations.^{20,21} In the present double-blind trial, the symptom score could not have been influenced by foreknowledge of which drug was being used, either by the physician or the parents. Thus, in our opinion, the scoring system used reflected the actual clinical situation; efficacy was shown by the improved symptom scores and was further suggested by the high level of acceptance by the parents. Side effects were negligible but difficult to quantify. For example, it was impossible to know whether infants' increased activity was due to an improvement in symptoms or systemic effects of the medication. No patient discontinued therapy because of adverse effects. Those parents who decided to discontinue the trial did so because they found the randomly assigned initial treatment arm so effective that they were not willing to participate in the other (placebo) arm of the trial. Of the 29 patients who started the trial, only one left because of total lack of response to therapy.

In a similar study using a 480 ml spacer of their own design, Mallol et al.¹⁰ were able to provide effective MDI-generated aerosol bronchodilator therapy to infants with acute wheezing by triggering the MDI visually at end-expiration. This is likely to be difficult in breathless tachypneic infants, although, as they indicate, crying may facilitate coordination. The valved Aerochamber-with-mask makes precise coordination of MDI aerosol discharge with inspiration unnecessary because the closed valve of the aerosol-holding chamber prevents dispersal of the aerosol on exhalation, thus retaining the drug for inhalation with the next breath. The dimensions of the Aerochamber and its valve also act as a baffle for reducing the upper airway dose much more than other apparently similar add-on devices.²² An additional advantage of the Aerochamber system is its relatively small volume, so that even infants with low tidal volume can be given an effective aerosol dose in the course of approximately four breaths.

The question of appropriate MDI-generated bronchodilator aerosol dosage in infants and small children must be considered. Mallol et al.¹⁰ successfully treated acute wheezing episodes with 600 µg of fenoterol or 60 µg of ipratropium bromide administered hourly for 4 hours without unacceptable side effects. In another study, Freeland and Van Asperen¹⁴ showed that symptomatic benefit could be achieved with five puffs (1.25 mg) of terbutaline sulphate administered to asthmatic infants under 20 kg, and with 2.5 mg (10 puffs), to those over 20 kg. These doses and those administered by Mallol et al. are much lower than the five to ten times higher doses usually nebulized for infants and small children. It is nevertheless likely that approximately equivalent doses are delivered to the lower respiratory tract since nebulizers are only 10–30% as efficient as MDI.²³ The use of MDI doses similar to those for adults may appear exces-

sive. However, in infants, the rapid respiratory rate, the smaller airways, as well as breathing through the nose rather than the mouth predictably results in delivery of much smaller doses of medication to pulmonary airways.²⁴

In conclusion, salbutamol (albuterol), when administered by means of the Aerochamber-with-mask, appears to be effective in controlling symptoms of cough and shortness of breath in infants and children under the age of three years with bronchodilator-responsive bronchitis or asthma. The Aerochamber-with-mask provides a relatively inexpensive, readily manipulated, simple, and portable means by which virtually all MDI aerosols can be administered to infants and children who otherwise would require compressor-driven nebulizers if aerosol therapy is to be used at all. Although no direct comparison has yet been performed, possibly the Aerochamber-with-mask could for most patients in this age group safely replace, at approximately 40% of the cost, the currently prescribed aerosol delivery systems using compressor-driven nebulizers.⁶

ACKNOWLEDGMENTS

The modified pediatric Aerochambers were designed and produced in the Firestone Regional Chest and Allergy Unit by Don McCormack. The study design and scoring system were suggested by the Department of Epidemiology and Biostatistics, McMaster University. We thank Shirley Ramelan for typing the manuscript.

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