

Delivery of albuterol aerosol by aerochamber to young children

R. Michael Sly, MD; Jeanne M. Barbera, MD; Helen B. Middleton, RN; and Donna M. Eby

Inhalation of albuterol aerosol, 200 µg, delivered from metered dose inhalers via Aerochamber, elicited a highly significant improvement in peak expiratory flow rate from 70% to 84% and 91% predicted normal 5 and 20 minutes after treatment, respectively, in 30 asthmatic children 3 to 6 years of age. No significant increase in peak expiratory flow rate followed inhalation of placebo by a similar group of 16 asthmatic children. Use of the Aerochamber permits effective delivery of medication from metered dose inhalers to children as young as 3 years of age.

INTRODUCTION

Inhalation of a beta adrenergic agonist is the treatment of choice for acute asthma.¹⁻³ Advantages of the inhalational route include rapid onset of action and a requirement for relatively small doses for effective bronchodilation with consequent lessening of the frequency and severity of adverse side effects.^{4,5}

Delivery from metered dose inhalers is popular because of convenience, but optimal response requires actuation of the canister at the start of a slow inhalation from functional residual capacity to total lung capacity followed by breathholding for ten seconds.⁶⁻⁹ Many adults and children are unable to master the technique required for optimal use of a metered dose inhaler.¹⁰⁻¹² Use of a spacer tube or chamber can enhance response by obviating the need for synchronization of actuation of the canister with inhalation as well as by permitting a decrease in the velocity of the aerosol particles before reaching the patient, de-

creasing oropharyngeal deposition by impaction, and allowing for a decrease in particle size to a size more consistent with delivery to the lower airways through evaporation of the propellant that encloses the bronchodilator particles.^{9,13} Various spacers and chambers have been reported to enhance pulmonary response to inhaled bronchodilators.¹³⁻²⁴

The Aerochamber (Monaghan Medical Corporation, Plattsburgh, NY) as modified from the original design is a 9-cm plastic cylinder 4 cm in diameter with a port at one end into which the standard metered dose inhaler is inserted (Fig 1).²⁵ A one-way inhalation valve and exhalation ports are at the other end with the mouthpiece. Within three seconds after actuation of the metered dose inhaler to release a single dose into the Aerochamber, the patient inhales slowly through the mouthpiece from functional residual capacity to total lung capacity and then holds the breath for ten seconds.

We have evaluated further the effectiveness of the Aerochamber in delivering a bronchodilator from metered dose inhalers to young children.

METHODS

Thirty children who had had recurrent episodes of reversible airway obstruction ascribed to asthma, 3 to 6 years of age, with peak expiratory flow rates 40% to 90% predicted

normal* were otherwise selected for study only by willingness to participate and ability to cooperate with testing. Their mean age was 4.8 years. Five subjects were 3 years old, and four were 4 years old. There were nine girls and 21 boys.

After instruction in the use of the Aerochamber each child received two doses of albuterol, 100 µg each, at an interval of five minutes. Pulse rate and peak expiratory flow rate were measured in that order before treatment and 5 and 20 minutes after administration of the second dose. Peak expiratory flow rate was determined with a Low Range Wright Peak Flow Meter as the best of three efforts that agreed within 10%.

A similar group of 16 asthmatic children was evaluated before and after inhalation of placebo to control for changes in peak expiratory flow rate due to possible effects of learning. Their mean age was 4.6 years. There were eight boys and eight girls.

RESULTS

Results are indicated in Tables 1 through 4 and Figures 2 through 4.

It was not necessary to exclude any patient because of inability to learn testing or treatment procedures.

* Data of Polgar and Promadhat;²⁶ predicted normal estimated by extrapolation for three children in control group and six in experimental group with height <110 cm.

From the Department of Allergy and Immunology, Children's Hospital National Medical Center, and the Department of Child Health and Development, The George Washington University School of Medicine and Health Sciences, Washington, DC. Dr. Sly is Director of Allergy and Immunology, Children's Hospital National Medical Center, and Professor of Child Health and Development, The George Washington University School of Medicine and Health Sciences. Dr. Barbera was a Fellow in Allergy and Immunology, Children's Hospital National Medical Center.

Peak expiratory flow rates improved in 29 of the 30 children who received albuterol. Paired *t* tests disclosed the increases from a mean of 70% predicted normal before treatment to 84% at 5 minutes and 91% at 20 minutes were highly significant ($P < .0005$, Table 1, Fig 2). The small increases in mean peak expiratory flow rate from 70% to 73% and 75% in the children who received placebo were not significant ($P > .05$). Analysis of covariance disclosed a highly significant difference in peak expiratory flow rate due to treatment ($P < .0001$).

Mean pulse rates increased from 90 to 104 after inhalation of albuterol and from 93 to 102 after inhalation of placebo (Table 2). Analysis of covariance disclosed no significant effect of treatment on changes in pulse rate ($P = .0975$).

Highly significant increases in peak expiratory flow rate 5 and 20 minutes after inhalation of albuterol occurred among both the five 3-year-old children ($P < .0005$ and P

$< .0025$, paired *t* tests) and the eight 6-year-old children ($P < .0125$ and $P < .005$). Among the 3-year-old children mean peak expiratory flow rate increased from 73% to 96% and 109% predicted normal; among the 6-year-olds, from 66% to 75% and 80% (Table 3, Fig 3). There was no significant difference in pretreatment peak expiratory flow rates for these two groups (two sample *t* test, $P = .45$). Analysis of covariance confirmed a highly significant effect of age on increases in peak expiratory flow rate after inhalation of albuterol ($P = .004$).

Seventeen children held their breath for ten seconds after each inhalation of albuterol. Their mean peak expiratory flow rates increased from 69% predicted normal to 82% and 88% 5 and 20 minutes after treatment (Table 4, Fig 4). These increases were highly significant (paired *t* tests, $P < .0005$). The increases in peak expiratory flow rate from a mean of 79% to 100% and 114% for the four children who did

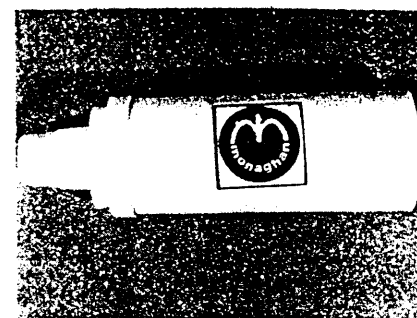


Figure 1. The Aerochamber.

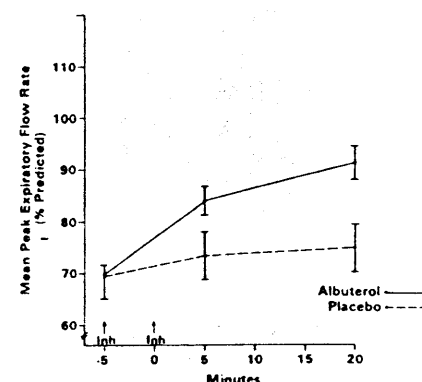


Figure 2. Mean peak expiratory flow rates expressed as percent predicted normal with standard errors of the mean in 30 asthmatic children before and after inhalation of albuterol via Aerochamber and in 16 asthmatic children before and after inhalation of placebo via Aerochamber.

Table 1. Mean Peak Expiratory Flow Rates Expressed as Percent Predicted Normal with Standard Errors of the Mean in 30 Asthmatic Children Before and After Inhalation of Albuterol via Aerochamber and in 16 Before and After Inhalation of Placebo

	N	Pretreatment	5 Minutes	20 Minutes
Albuterol	30	69.7 ± 2.1	84.1 ± 2.8	91.3 ± 3.3
Placebo	16	69.6 ± 4.3	73.4 ± 4.8	75.0 ± 4.6

Table 2. Mean Pulse Rates with Standard Errors of the Mean in 30 Asthmatic Children Before and After Inhalation of Albuterol via Aerochamber and in 16 Before and After Inhalation of Placebo

	N	Pretreatment	5 Minutes	20 Minutes
Albuterol	30	90 ± 1.7	99 ± 2.0	104 ± 2.0
Placebo	16	93 ± 2.3	98.9 ± 3.9	101.9 ± 4.0

Table 3. Mean Peak Expiratory Flow Rates Expressed as Percent Predicted Normal with Standard Errors of the Mean in Five 3-Year-Old and Eight 6-Year-Old Asthmatic Children Before and After Inhalation of Albuterol via Aerochamber

Age	N	Pretreatment	5 Minutes	20 Minutes
3	5	73.0 ± 5.0	96.0 ± 6.1	108.8 ± 7.5
6	8	66.4 ± 4.9	75.0 ± 3.3	80.0 ± 2.8

Table 4. Mean Peak Expiratory Flow Rates Expressed as Percent Predicted Normal with Standard Errors of the Mean Before and After Inhalation of Albuterol via Aerochamber for Children Who Held Their Breath Not More Than Five Seconds after Inhalation and Those who Held Their Breath Ten Seconds

Duration of Breathholding	N	Pretreatment	5 Minutes	20 Minutes
≤5 seconds	4	79.2 ± 5.4	100.0 ± 6.3	114.2 ± 8.4
10 seconds	17	68.8 ± 3.8	82.3 ± 4.2	88.4 ± 4.4

not hold their breath for more than five seconds were also highly significant (paired *t* tests, $P < .01$ and $P < .005$). Pretreatment peak expiratory flow rates did not differ significantly for these two groups (two sample *t* test, $P > .2$). Analysis of covariance disclosed no significant effect of duration of breathholding on changes in peak expiratory flow rate.

DISCUSSION

The highly significant increases in peak expiratory flow rate that followed inhalation of albuterol delivered by Aerochamber confirm that this mode of therapy can be effective in asthmatic children as young as 3 years of age.^{15,23} The lack of any significant difference in the increase in pulse rate that followed inhalation of albuterol as compared with

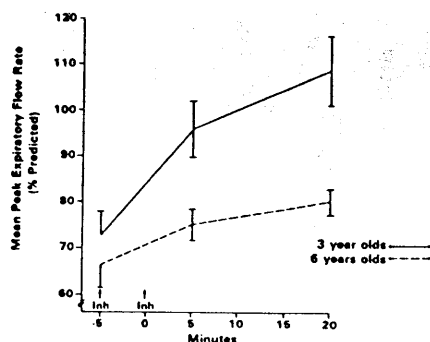


Figure 3. Mean peak expiratory flow rates expressed as percent predicted normal with standard errors of the mean in five 3-year-old and eight 6-year-old asthmatic children before and after inhalation of albuterol via Aerochamber.

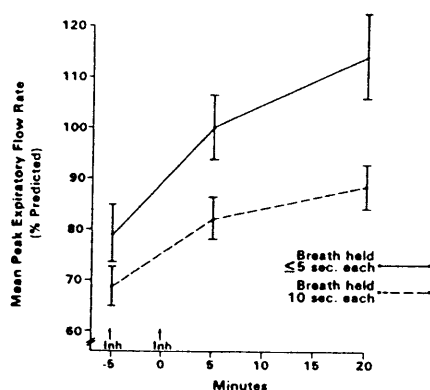


Figure 4. Mean peak expiratory flow rates expressed as percent predicted normal with standard errors of the mean before and after inhalation of albuterol via Aerochamber for four children who held their breath not more than five seconds after inhalation and 17 who held their breath ten seconds.

inhalation of placebo by a similar group of asthmatic children confirms that delivery of 200 μ g albuterol by this system to asthmatic children 3 to 6 years of age is safe. The increase in mean pulse rate from 91 to 100 five minutes after treatment and to 109 20 minutes after treatment was somewhat higher for the five 3-year-olds. The significantly better bronchodilation that occurred in the younger children was probably due to the larger dose they received relative to size.

The suggestion of somewhat better bronchodilation among the children who held their breath not more

than five seconds after each treatment was probably due to the fact that these included two 3-year-old children, one 4-year-old, and one 5-year-old, whereas the children who could hold their breath for ten seconds were 5 and 6 years old except for a single 4-year-old. It appears that those who held their breath not more than five seconds received relatively larger doses for size. Relatively small doses of an inhaled beta agonist are probably required for satisfactory response in children who have not been receiving continual treatment with beta agonists.

ACKNOWLEDGEMENT

We thank Norman Leong, PhD, Research Fellow, Laboratory of Behavioral Medicine, Children's Hospital National Medical Center for assistance with statistical analyses.

REFERENCES

1. Ben-Zvi Z, Lam C, Hoffman J, et al: An evaluation of the initial treatment of acute asthma. *Pediatrics* 1982;70:348-353.
2. Becker AB, Nelson NA, Simons FER: Inhaled salbutamol (albuterol) vs injected epinephrine in the treatment of acute asthma in children. *J Pediatr* 1983;102:465-469.
3. Fanta CH, Rossing TH, McFadden ER, Jr: Treatment of acute asthma. Is combination therapy with sympathomimetics and methylxanthines indicated? *Am J Med* 1986;80:5-10.
4. Pliss LB, Gallagher EJ: Aerosol vs injected epinephrine in acute asthma. *Ann Emerg Med* 1981;10:353-355.
5. Sly RM, Anderson JA, Bierman CW, et al: Adverse effects and complications of treatment with beta-adrenergic agonist drugs. *J Allergy Clin Immunol* 1985;75:443-449.
6. Newhouse MT, Ruffin RE: Deposition and fate of aerosolized drugs. *Chest* 1978;73(suppl):936-943.
7. Newman SP, Pavia D, Clarke SW: Improving the bronchial deposition of pressurized aerosols. *Chest* 1981;80(suppl):909-911.
8. Dolovich M, Ruffin RE, Roberts R, et al: Optimal delivery of aerosols from metered dose inhalers. *Chest* 1981;80(suppl):911-915.
9. Newman SP, Clarke SW: Therapeutic aerosols—physical and practical considerations. *Thorax* 1983;38:881-886.
10. Epstein SW, Manning CPR, Ashley MJ, et al: Survey of the clinical use of pressurized aerosol inhalers. *Can Med Assoc J* 1979;120:813-816.
11. Crompton GK: Problems patients have using pressurized aerosol inhalers. *Eur J Respir Dis* 1982;63(suppl 119):101-104.
12. Lee HS: Proper aerosol inhalation technique for delivery of asthma medications. *Clin. Pediatr* 1983;22:440-443.
13. Bloomfield P, Crompton GK, Winsey NJP: A tube spacer to improve inhalation of drugs from pressurized aerosols. *Br Med J* 1979;2:1479.
14. Newman SP, Moren F, Pavia D, et al: Deposition of pressurized suspension aerosols inhaled through extension devices. *Am Rev Respir Dis* 1981;124:317-320.
15. Hodges IGC, Milner AD, Stokes GM: Assessment of a new device for delivering aerosol drugs to asthmatic children. *Arch Dis Childhood* 1981;56:787-800.
16. Tobin MJ, Jenouri G, Danta I, et al: Response to bronchodilator drug administration by a new reservoir aerosol delivery system and a review of other auxiliary delivery systems. *Am Rev Respir Dis* 1982;126:670-675.
17. Pedersen S: Aerosol treatment of bronchoconstriction in children, with or without a tube spacer. *N Engl J Med* 1983;308:1328-1330.
18. Cushley MJ, Lewis RA, Tattersfield AE: Comparison of three techniques of inhalation on the airway response to terbutaline. *Thorax* 1983;38:908-913.
19. Newman SP, Millar AB, Lennard-Jones TR, et al: Improvement of pressurized aerosol deposition with Nebuhaler spacer device. *Thorax* 1984;39:935-941.
20. Lee H, Evans HE: Aerosol bag for administration of bronchodilators to young asthmatic children. *Pediatrics* 1984;73:230-232.
21. Rivlin J, Mindorff C, Reilly P, et al: Pulmonary response to a bronchodilator delivered from three inhalation devices. *J Pediatr* 1984;104:470-473.

-
22. Huntley W, Weinberger M: Evaluation of bronchodilation from aerosol beta₂ agonists delivered by the Inhal-Aid device to young children. *J Asthma* 1984;21:265-270.
23. Chang B, Sly RM, Eby D, et al: Delivery of albuterol aerosol by Inhal-Aid to young children. *J Allergy Clin Immunol* 1985;75:159.
24. Ellul-Micallef R, Moren F, Wetterlin K, et al: Use of a special inhaler attachment in asthmatic children. *Thorax* 1980;35:620-623.
25. Corr D, Dolovich M, McCormack D, et al: Design and characteristics of a portable breath actuated, particle size selective medical aerosol inhaler. *J Aerosol Sci* 1982;13:1-7.
26. Polgar G, Promadhat V: *Pulmonary function testing in children: Techniques and standards*, Philadelphia, W.B. Saunders Co, 1971, p 188.
- Request for reprints should be addressed to:*
R Michael Sly, MD
Director, Allergy & Immunology
Children's Hospital
National Medical Center
111 Michigan Ave, NW
Washington, DC 20010
-

Printed in U.S.A.