

Pressure gradient and inspiratory times required for valve opening of various holding chambers

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ABSTRACT

This study was designed to determine whether infants generate sufficient inspiratory pressure gradient to open the unidirectional valve of various commercially available holding chambers, as well as the time required to reach this gradient. A prospective, cross-sectional study was performed of 80 healthy infants (aged 1–24 months) seen in the childcare outpatient clinic of a pediatric hospital, from October to December of 2007. Using the same inhalation technique recommended for treatment of respiratory diseases and asthma in this age group, four holding chambers were analyzed: Flumax Baby, AlergoChamber, LuftChamber, and ACE (n = 20 infants per analysis group). The variables measured were gradient of inspiratory pressure and time for the valve to open. The holding chambers did not differ in gradient of inspiratory pressure (p = 0.382) or time to open the valve (p = 0.199). Fifteen of 80 infants were not able to generate sufficient inspiratory pressure to open the valve (1 using AlergoChamber, 5 using Flumax Baby, 6 using ACE, and 3 using LuftChamber), with no significant differences between devices. The holding chambers were similar regarding pressure gradient and time required to open the valve. The fact that 19% of the sample was unable to open the valve suggests that it would be useful to determine the ability of small children (<24 months of age) to use holding chambers before prescribing them.

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Pressurized metered-dose inhalers (MDI) are the most used devices for the treatment of asthma in all pediatric age ranges and are recommended by international guidelines.^{1–9} Holding chambers are accessories of various shapes, sizes, and materials that are placed between the mouth of the patient and the MDI. The holding chamber induces physical alterations in the aerosol that produce a greater proportion of respirable particles and linearized flow, facilitating the aerosol's deposit in the airway.¹⁰

A unidirectional valve at the end of the holding chamber ensures the flow of the medication to be delivered to the airway of the patient. Such valves should be of low resistance, allowing their opening at low inspiratory pressures. As previously stated, valved holding chambers are meant to facilitate the use of MDIs. However, some patients may have coordination problems or have difficulty with inhalation.¹¹ If the device is not opened by the patient's inspiratory force, the medication will not pass through the holding

chamber and, consequently, will not be delivered. In the pediatric literature, there are no studies reporting on the inspiratory force necessary to open holding chamber valves. In infants that can not achieve a valve-opening inspiratory pressure, the removal of the valve can lead to increased quantities of medication available for inhalation.¹² Therefore, infants might benefit from a valve with a minimal inspiratory flow for opening adjusted to their respiratory mechanics. The objective of this study was to determine whether infants generate sufficient inspiratory pressure gradient to open the valve of various commercially available holding chambers, as well as the time required for this pressure to be achieved.

METHODS

A prospective, cross-sectional study was performed with 80 infants aged 1–24 months. The subjects were consecutively selected from patients visiting the childcare outpatient clinic of Santo Antonio Children's Hospital, Porto Alegre, Brazil, from October to December 2007. Excluded from the study were infants who showed signs of respiratory illness, had chronic diseases (respiratory, cardiovascular, or neuromuscular), or showed signs of any other condition that would interfere with their using a holding chamber. All subjects' parents gave informed consent. The study protocol was approved by the Committee of Ethics in Research of the Federal University of Health Sciences of Porto Alegre, registered under the project number 622-8.

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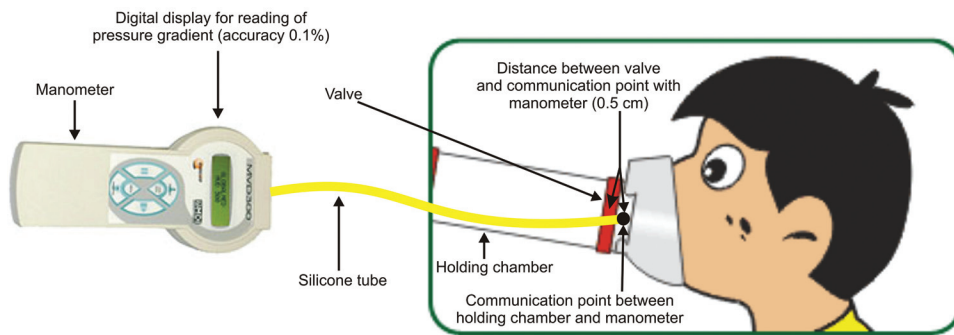


Figure 1. Experimental setup.

Four valved holding chambers for the treatment of asthma were tested: Flumax Baby (Flumax Equipamentos Médicos Ltda., Belo Horizonte, MG, Brazil), AlergoChamber (Farmaqui Industria eComercio Ltda., São José dos Campos, SP, Brazil), LuftChamber (Luft, São Paulo, SP, Brazil), and ACE (DHD Healthcare, Wampsville, NY). All of the holding chambers were classified as small volume. All examinations were conducted by the same individual. The order of the holding chambers to be used was determined by randomization in 4 groups of 20, with each group using only one holding chamber.

Gradient of inspiratory pressure was determined using a digital vacuum manometer (MVD300a; Globalmed, Porto Alegre, Brazil) connected to a silicone tube. For each holding chamber, the end of the manometer tube was inserted at a distance of 0.5 cm from the holding chamber valve (Fig. 1). The mask of the holding chamber was individually fitted to each subject. Before the measurements were obtained, the system was calibrated at zero pressure. The detection of a measurable pressure gradient inside the holding chamber meant that the valve had been opened. The time required for the patient to reach a sufficient pressure gradient to open the valve was measured. Measurements were taken for 15 seconds (~10 respiratory cycles), during which the mask remained tight fitting to the subject's face.

The holding chamber groups were compared with respect to the time and minimum inspiratory pressure for opening the valve. Quantitative variables were described by medians and interquartile range. Performances of holding chambers were compared using the Kruskal-Wallis test. In case of statistical significance, the Mann-Whitney test was used. Associations between the holding chambers and the time and pressure to open the valve were determined using Pearson's chi-square test. The level of significance for all tests was set at $p < 0.05$.

RESULTS

Of the 80 subjects, 45 (56.3%) were boys and 35 (43.8%) were girls; mean age was 15 ± 7.1 months. The

four holding chamber groups were homogeneous regarding demographic characteristics (Table 1).

The minimum pressure gradient measured inside the chamber was $1 \text{ cmH}_2\text{O}$. There were no statistical differences between the holding chambers in terms of opening pressure ($p = 0.382$; Fig. 2). It was observed that 15 infants (19%) could not generate sufficient inspiratory pressure to open the valve (Table 1): 1 of 20 patients using the AlergoChamber, 5 of 20 patients using the Flumax Baby, 6 of 20 patients using the ACE, and 3 of 20 patients using the LuftChamber. There was no statistical difference between the groups in terms of the number of patients unable to open the valve ($p = 0.19$). Similarly, no statistical difference was observed ($p = 0.14$) for the comparison of age in patients who were able to open the valve ($n = 65$; 15.4 ± 7 months) versus those who were unable to open it ($n = 15$; 12.71 ± 7.93 months).

In our series, the minimum time required to open the valve was 3 seconds, and the maximum time was 15 seconds. The median time for each brand was as follows: Flumax, 8.5 seconds (5.3–13.8 seconds); Luftchamber, 5.5 seconds (4.0–10.0 seconds); ACE, 10.0 seconds (4.3–15.0 seconds); AlergoChamber, 5 seconds (3.0–10.0 seconds). There were no statistical differences between the holding chambers in time to open the valve ($p = 0.199$; Fig. 3).

DISCUSSION

Various types of holding chambers are commercially available for the treatment of pediatric asthma. The choice of device is guided by various factors: age of the child, cost, ability of family members to assist with administration, etc..^{7–10}

This study found that a large proportion of infants were not capable of opening the inspiratory valve in the time recommended for use of an inhalation system (time between application of the mask/activation of the MDI and beginning of the respiratory cycles that trigger the opening of the valve). The use of a device without a holding chamber is an alternative that may, in theory, reduce the problem of low inspiratory pressure. However, nonvalved holding

Table 1 Sex and age of children using four different commercially available holding chambers

Holding Chamber							
Flumax		LuftChamber		ACE		AlergoChamber	
Sex	Age (mo)	Sex	Age (mo)	Sex	Age (mo)	Sex	Age (mo)
F	24	M	13	F	7*	M	24
M	24	M	3	F	24*	M	18
F	24	M	8	M	24	F	7
F	22	F	20	F	10	F	20
F	4*	M	24	M	20	F	5
F	5	M	14	M	15*	M	12
F	24*	M	4	M	8	M	14
M	10*	F	21	F	7	M	13*
F	24	F	15	M	3	M	24
F	12	M	14	F	23	M	12
M	19*	F	24*	M	2*	F	18
F	5	M	12	F	17	F	8
M	17	F	12	M	4	F	12
M	16	F	24	M	14	M	12
F	22	M	7	M	19	M	12
M	24	M	7*	M	15*	F	24
F	24	M	13	F	17	M	22
F	23	M	12*	M	5	M	22
M	24	F	18	F	10*	M	23
M	5*	F	16	M	21	M	2
Mean	17.6 (± 7)		14.05 (± 6)		13.25 (± 7)		15.2 (± 7)

*Children who were unable to generate sufficient inspiratory pressure to open the valve after 15 s.

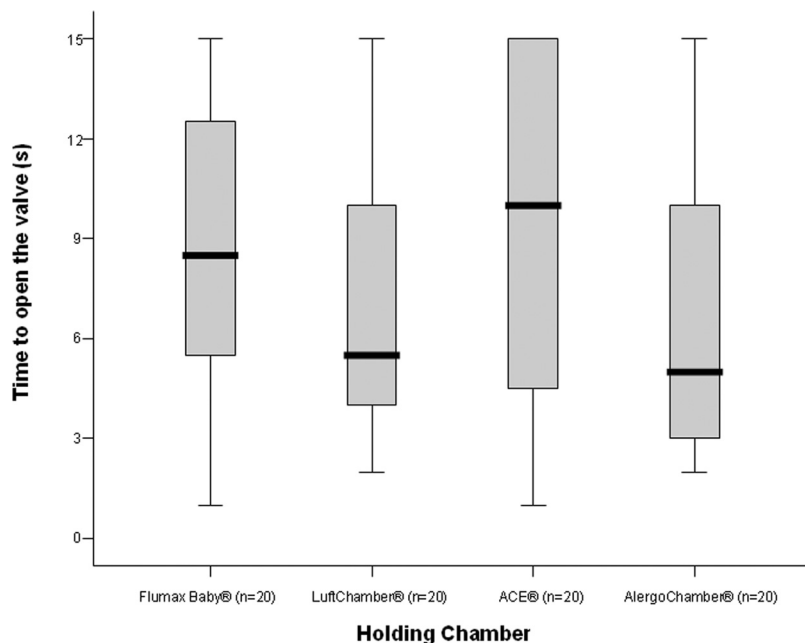


Figure 2. Time required to open the valve of various holding chambers. Results refer to all 80 patients, including those unable to open the valve.

chambers have been associated with less deposition of medication.¹²

These findings are relevant, because treatment with MDIs coupled to holding chambers is the preferential

technique for the administration of inhalation medication in the pediatric age range. In this situation, insufficient delivery of the medication might result in treatment failure.¹³

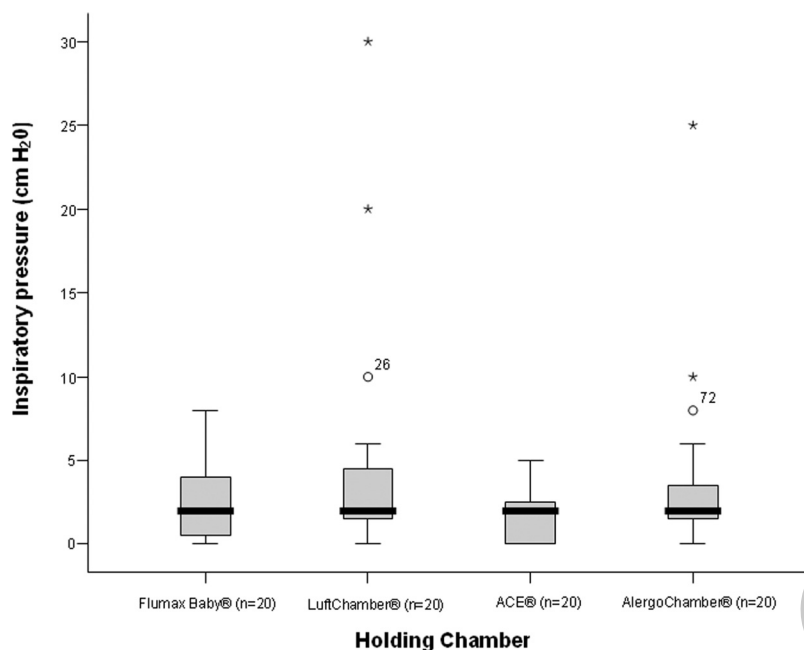


Figure 3. Pressure gradient indicating opening of the valve of various holding chambers. Results refer to all 80 patients. Asterisks indicate outliers (values outside the 25–75 interquartile range).

Numerous factors in addition to the holding chamber valve can influence deposition of medication in the lungs. These include the type of mask, diameter of the particles generated, other characteristics of the MDI, inspiratory flow, breathing rate, caliber of the airways, humidity, and cooperation of the patient.¹⁴ Our study only evaluated the pressure gradient generated inside the chamber by the opening of the valve and the time required for this gradient to be reached. It did not take into account any other characteristic that could have influenced the outcome. This is an important limitation of this study. We were able to determine differences in valve compliance, but not the minimum inspiratory pressure for opening the holding chamber valve. For this, it would be necessary not only to determine the pressure gradient inside the mask, but also to verify the inspiratory pressure inside the mask (before the valve).

Previous studies have established the importance of holding chamber characteristics for pulmonary deposition of medication. These include the proper functioning of the valve, size and electrostatic charge associated with the holding chamber, and characteristics of the mask.^{14–16} In a laboratory study, Berg and coworkers concluded that different types of holding chambers can show differences in the release of the medication, independent of the size of aerosol particles generated.¹⁶ If this is confirmed in clinical practice, we believe that the properties of the valve would be an issue to be addressed. In addition, further studies should extend the present work to include analysis of medication delivery.

In summary, although we did not examine the delivery of medication, we observed that many infants were unable to open the valve of the holding chamber. This finding may be of clinical importance. It is likely that infants with obstructive respiratory disease, which reduces inspiratory pressures, would have greater difficulty opening the holding chamber valves than our healthy subjects. Our findings suggest that use of an MDI coupled to a holding chamber requires clinical supervision to ensure the best fit between the mask and the patient's face. In addition, determining the patient's ability to open the valve before prescribing the use of valved holding chambers is an easy measure that could increase the efficacy of treatment in small children.

REFERENCES

1. Ariyananda PL, Agnew JE, and Clarke SW. Aerosol delivery systems for bronchial asthma. *Postgrad Med J* 72:151–156, 1996.
2. Yernault JC. Inhalation therapy: A historical perspective. *Eur Respir Rev* 4:65–67, 1994.
3. Fink JB, and Rau JL. New horizons in respiratory care: The pharmacology of inhaled aerosol drug therapy. *Respir Care* 45:824–825, 2000.
4. Global Initiative for Asthma (GINA). Global Strategy for asthma management and prevention. National Institutes of Health, Bethesda, MD. Available online at www.ginasthma.com; last accessed September 5, 2009.
5. The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema. *Lancet* 351: 1225–1232, 1998.
6. IV Diretrizes Brasileiras para o Manejo da Asma J Bras Pneumol 32: S447–S474, 2006.

7. Aickin RP, Asher MI, Campanella SG, and Leversha AM. Costs and effectiveness of spacer versus nebulizer in young children with moderate and severe acute asthma. *J Pediatr* 136:497–502, 2000.
8. Vilarinho LC, Cardeal Mendes CM, and de Freitas Souza LS. Metered-dose inhalers with home-made spacers versus nebulizers to treat moderate wheezing attacks in children. *J Pediatr* 79:403–412, 2003.
9. American Association for Respiratory Care (AARC) Clinical Practice Guideline. Selection of an aerosol delivery device for neonatal and pediatric patients. *Respir Care* 40:1325–1335, 1995.
10. Ribeiro JD. Aerossóis e espaçadores na crise aguda de asma. Evolução e hora de mudar a rotina. *J Pediatr* 4:274–276, 2005.
11. Chambers FE, Brown S, and Ludzik AJ. Comparative in vitro performance of valved holding chambers with a budesonide/formoterol pressurized metered-dose inhaler. *Allergy Asthma Proc* 30:424–432, 2009.
12. Amirav I, and Newhouse MT. Aerosol therapy with valved holding chambers in young children: Importance of the face-mask seal. *Pediatrics* 108:389–394, 2001.
13. Buchdahl R, and Summerfield A. Spacer devices in asthma. *Thorax* 55:1070–1071, 2000.
14. Fink JB. Aerosol device selection: Evidence to practice. *Respir Care* 45:874–885, 2000.
15. Dubus JC. Delivery of salbutamol pressurized metered-dose inhaler administered via small-volume spacer devices in intubated, spontaneously breathing rabbits. *Pediatr Res* 50:384–389, 2001.
16. Berg E. In vitro properties of pressurized metered dose inhalers with and without spacer devices. *J Aerosol Med* 3:3–11, 1995. □

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