

A 500-ml plastic bottle: An effective spacer for children with asthma

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Inhaled therapy using a metered-dose inhaler (MDI) with attached spacer has been increasingly recognized as the optimal method for delivering asthma medication for acute attacks and chronic prophylaxis. However, in developing countries the cost and availability of commercially produced spacers limit the use of MDI-spacer delivery systems. A 500-ml plastic bottle has been recently adapted to function as a spacer. This article reviews the current data on the efficacy of this bottle-spacer and discusses its advantages and limitations. It is concluded that a modified 500-ml plastic bottle is an effective spacer; modification and use of this device should be incorporated into international guidelines for the management of children with asthma.

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A metered-dose inhaler (MDI) with attached spacer is an effective delivery system for bronchodilators and for anti-inflammatory therapy in patients with asthma (1). A wide variety of commercially produced spacers are available; these differ in shape, size, material out of which they are constructed, and the presence of valves. The primary purpose of any spacer is to compensate for some of the inherent shortcomings associated with MDI use alone. All spacers allow 'space' for the MDI propellant to evaporate after each actuation and they act as a surface for impaction of high-inertia aerosol droplets (2). Evaporation of MDI propellant promotes the formation of smaller aerosol particles liable to be carried into the small airways. Large, high-inertia particles travelling rapidly from the MDI would probably impact into the oropharynx in the absence of a spacer. In addition, some spacers are designed to function as a reservoir from which the aerosol can be inhaled. This ability to briefly hold suspended aerosol prior to inhalation helps to minimize the detrimental effects of poor timing between MDI

actuation and patient inhalation. This benefit may be especially important during an acute asthma attack when correct use of a MDI can be extremely difficult.

Although bronchodilator therapy via a nebulizer has been widely used for the treatment of acute asthma attacks, increasing evidence supports the use of a MDI with attached spacer in this situation (3). In asthmatic children, delivery of bronchodilators via a MDI-spacer results in equivalent bronchodilation with fewer side-effects and less hypoxia compared to the nebulized route (4,5). Even when the degree of airways obstruction was severe, β_2 -sympathomimetic bronchodilators given via a MDI with attached spacer have been shown to be equivalent or superior to nebulized therapy for relief of bronchoconstriction in infants and children with acute asthma (6–9).

A MDI with attached spacer has a number of important advantages over nebulized therapy in clinical scenarios, including a shorter administration time, lower cost, and ease of administration (10). Moreover, a MDI with attached spacer

does not require an electrical power source and is easily portable, enabling its use in even the poorest of households.

Despite the fact that MDI-spacer use should be regarded as essential for adequate delivery of all types of inhaled medications to children with asthma, high cost and unavailability have limited their use in developing countries. The development of a low-cost, effective spacer device has received relatively little attention despite an urgent need for such technology. Earlier small, uncontrolled studies evaluated a polystyrene cup (11,12), a large-volume plastic bottle (13,14), and a plastic zip-up bag (15), as possible spacers. These studies reported improvements in symptoms or lung function in asthmatic patients given inhaled bronchodilators via MDI and the particular spacer. However, these studies are limited by their small sample sizes and the lack of suitable control groups (11–15).

Recently, adaptation and testing of a 500-ml plastic cold-drink bottle to function as a MDI spacer for children with asthma has been undertaken (16,17). This article summarizes the evidence for the efficacy of this modified spacer device and discusses the place and limitations of this spacer in providing care for children with asthma.

Plastic bottle-spacer

A standard 500-ml plastic cold-drink bottle was adapted, as follows, for use as a MDI-spacer (18). A used, empty bottle was washed with soap and water and air-dried, as this has been shown to reduce electrostatic charge on the side walls (19). To modify the bottle to function as a spacer, a hole was made in the base of the bottle through



Fig. 1. Child using a modified 500-ml plastic bottle as a spacer. The neck of the bottle is held in the mouth, simulating a mouthpiece.

which the MDI was inserted. As the plastic base was difficult to cut, a hole was melted by applying a heated mould of steel wire (of similar shape and size as the end of the MDI) to the base of the bottle (18). The heated mould was held in position for approximately 10 s until the plastic had melted and then rotated 180° and re-applied. The plastic MDI actuator was inserted immediately after removal of the mould while the base of the bottle was still warm, in order to create a tight fit. The MDI actuator may either be sealed in the hole by applying glue between the insertion area of the MDI and the perimeter of the hole (sealed bottle), or left unsealed. For a sealed bottle, the MDI actuator may be left *in situ* and only the MDI canister removed and replaced when empty. New bottle-spacers were primed initially with 15 puffs of medication to reduce electrostatic charge on the walls, as priming a spacer has been shown to diminish the adverse effects of static charge (20). In children older than 3 years of age, the neck of a bottle-spacer was held in the mouth, simulating a mouthpiece (Fig. 1). In younger children, a small, well-fitting facemask (Cipla BabyMask; Cipla-Medpro, Bombay, India) can be attached to the neck of a modified bottle-spacer to enable use of this device as a spacer in those who are too young to use a mouthpiece (Fig. 2).

Efficacy of a bottle-spacer

The efficacy of a 500-ml plastic bottle modified to function as a spacer has been investigated using *in vitro* methods and in clinical trials. In all these studies, a bottle-spacer performed similarly or better than control, conventional spacers. In a recent *in vitro* aerosol-deposition study of 'home-made' spacers combined with a Flovent®



Fig. 2. Young child using a modified 500-ml plastic bottle as a spacer. A facemask is attached.

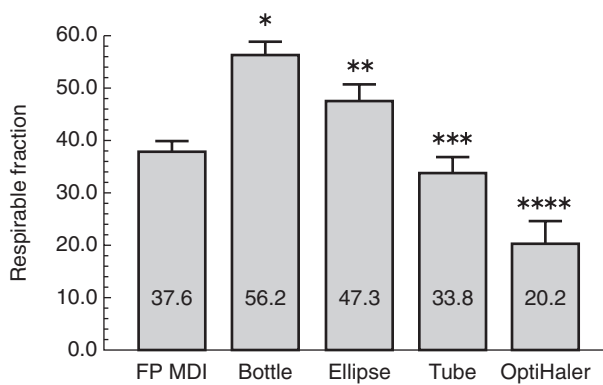


Fig. 3. Mean $\pm$ standard deviation fine-particle fraction (between 1 and 5 μm in aerodynamic size) of fluticasone aerosol emitted from the metered-dose inhaler (MDI) actuator, from a Flovent[®] inhaler (i.e. fluticasone MDI) containing 250- μg actuation (GlaxoWellcome, Research Triangle Park, NC, USA), and from an MDI with different spacers attached. The bottle-spacer was a 500-ml cold drink plastic bottle adapted for use as an MDI spacer (18). The tube spacer was a 6-inch (15-cm) piece of corrugated plastic tubing (1-in [2.5 cm] internal diameter). The Ellipse[®] (GlaxoWellcome) and OptiHaler[®] (Respir-onics, Cedar Grove, NJ, USA) are spacer devices commercially available in the United States. * $p < 0.01$ bottle vs. any; ** $p < 0.01$ Ellipse vs. MDI, tube, OptiHaler; *** $p < 0.01$ tube vs. bottle, Ellipse, OptiHaler, $p > 0.05$ vs. MDI; **** $p < 0.01$ OptiHaler vs. any. This figure was constructed from data published by Asmus et al. (21,22). *

(GlaxoWellcome, Research Triangle Park, NC, USA) MDI, the fine-particle fraction (i.e. percentage of fluticasone-emitted dose between 1 and 5 μm) of fluticasone from a 500-ml bottle-spacer was greater than that obtained from the other 'home-made' spacer tested (corrugated tube) and from an MDI alone (21). The fine-particle fraction, collected into a cascade impactor operating at 28.3 l/min, was 56% for the 500-ml bottle ($p < 0.01$), 38% from the MDI alone, and 34% from a 6-inch (15-cm) piece of corrugated tubing (1-in internal diameter [2.5 cm]) as a spacer ($p > 0.05$ Fig. 3) (21). Comparison of these results to *in vitro* deposition data obtained in a similar manner from commercially available spacers revealed that the fine-particle fraction of fluticasone from this 500-ml bottle-spacer was significantly larger than from any non-valved spacer available in the United States ($p > 0.01$, Fig. 3) (22).

Aerosol deposition studies in children using nebulized Tc99m-DTPA have reported that a 500-ml cold-drink bottle modified to become a spacer produced equivalent or greater lung deposition than a conventional spacer (16,23). In these studies, nebulized aerosol captured in a 2-l anesthetic bag was inhaled and the amount of aerosol deposited in the lungs was expressed as a percentage of the available aerosol. Although the aerosol produced differed from that obtained

using a MDI, the delivery system was kept constant except for the variation in the spacer, making a valid comparison of aerosol deposition with different spacers possible. In children older than 5 years of age, lung deposition obtained from a conventional spacer and sealed bottle was equivalent, but was less from an unsealed bottle (16). However, a polystyrene cup produced the least amount of lung deposition, delivering between one-third and one-fifth of the dose that the other spacers were capable of delivering. More recently, aerosol lung deposition from a modified bottle in younger children (3–5 years of age) was found to be twice that obtained with a conventional valved small-volume spacer (23). The amount of lung deposition was age dependent with a marked reduction occurring at around 50 months of age; this pattern occurred when either the conventional-spacer or bottle-spacer was used.

In a randomized clinical trial comparing the efficacy of home-made spacers (sealed 500-ml plastic bottle, unsealed 500-ml bottle, and polystyrene cup) with a conventional spacer (Aero-Chamber[®]; Trudell Medical International) in 88 children with acute asthma, a 500-ml bottle was confirmed to be an effective spacer for delivery of bronchodilators (17). In this study, a sealed bottle and conventional spacer produced similar bronchodilation, as measured by improvement in clinical score and pulmonary function (17). A polystyrene cup was the least effective for children with moderate-to-severe airway obstruction, producing only minimal bronchodilation (17). A nebulized bronchodilator was administered to children whose peak expiratory flow rate was less than 70% of the predicted value after MDI-spacer treatment; minimal improvement in pulmonary function occurred post-nebulization in those who had previously used a conventional spacer or a sealed bottle (indicating that maximal bronchodilation had been achieved with these subjects), while a significant increase occurred in those who had used a polystyrene cup. Therefore, use of a modified 500-ml plastic bottle as a spacer for delivery of bronchodilators in children can be recommended; however, a polystyrene cup provided sub-optimal drug delivery and cannot be recommended for use as a spacer.

Factors accounting for efficacy of the bottle

The bottle used in these studies has a cylindrical shape and volume of 500 ml. This shape and volume resemble the optimum chamber dimensions (which have been experimentally shown to be a cylinder approximately 11 cm in length by 3.5 cm in diameter) for a spacer in children (24).

In a few, small, uncontrolled trials in older patients, larger-volume bottles have been reported to be effective for delivery of bronchodilator medication (13,14). A 1-litre plastic bottle was found to produce bronchodilation when used to administer salbutamol to 22 children with acute asthma (14). In five adults with stable asthma, a 1.5-l bottle was reported to be as effective for administration of a β_2 -agonist as a 750-ml valved conventional spacer and produced a similar incidence of side-effects, as measured by changes in the forced expiratory volume in 1 s (FEV_1), heart rate, and serum potassium (13). However, a 500-ml bottle may be a more efficient spacer resulting in increased availability of drug in young children, as they have relatively small tidal volumes (25).

Absence of a valve in a bottle-spacer may also have increased pulmonary aerosol deposition compared to a valved conventional spacer. This may be especially true in young children or those with airways obstruction, as overcoming the resistance of a valve on inspiration may be difficult in such patients. As evidence of this, a valveless spacer has been reported to enhance the delivery of aerosol to the lungs of infants with chronic lung disease when compared to the delivery obtained with the same spacer with a valve (26). The absence of valves may also minimize the amount of dead space in the spacer.

Reducing the electrostatic charge on the side walls of a bottle by washing it in detergent and priming new bottles with aerosol may also maximize pulmonary drug delivery (19,20). Increasing aerosol transit time and reducing deposition on the side walls of the spacer may result in a larger fraction of fine particles for delivery to the airways (27). In a clinical trial (17), drug delivery was further optimized by actuating the canister every few breaths until the desired dose of medication had been given, as multiple actuations of the MDI have been reported to decrease the amount of drug available (28).

Finally, careful attention to the way in which a bottle-spacer is made and used may contribute to its efficacy. Patients, or their parents, are instructed in the use of these devices, as should occur when using any spacer device. In young children, care is taken to ensure a tight seal between the child's face and a facemask; in older children, patients are instructed to seal their lips tightly around the neck of a bottle-spacer.

Advantages

Although a number of commercially produced MDI-spacers are available, their cost is prohib-

itive for most people in developing countries. A bottle-spacer is significantly cheaper than any of the commercially produced varieties. Use of a bottle-spacer therefore makes inhaled asthma therapy a possibility for many children in whom oral therapy has been widely used owing to the lack of a low-cost delivery system. Furthermore, many of the commercially produced spacers fit only specific MDIs made by a single company. As the shape of the MDI can vary between products, MDIs may be developed in conjunction with a particular spacer for optimal use of a product. However, as a result cheaper, generic MDIs may not fit particular spacers, further limiting their affordability and use. The brand of MDI prescribed in public hospitals may change according to the lowest tender received for supply of MDIs each year. Therefore, commercially produced spacers that do not have a universal adapter may become useless if the hospital changes to products manufactured by a different company. However, a new bottle-spacer can be easily and cheaply provided.

Use of a bottle-spacer enables prompt use of bronchodilators via a MDI in children with acute asthma. This is especially important in poor communities where access to the nearest health facility is limited by time, distance, and cost. Use of a bottle-spacer empowers children or their caregivers to obtain appropriate inhaled therapy for asthma at home. Furthermore, provision of an effective low-cost spacer enables asthmatic children or their caregivers to utilize effective bronchodilator therapy outside their homes, including at school.

Modification of a bottle to function as a spacer can be performed relatively easily and without sophisticated equipment (18). Caregivers or health care workers can be taught how to make such bottle-spacers. Replacement of a damaged or lost bottle-spacer is inexpensive and easy compared to one commercially produced. Finally, many children and their caregivers are familiar with 500-ml plastic bottles, as soda is frequently purchased and consumed from these bottles. A modified 500-ml plastic bottle is now used routinely at the Red Cross Children's Hospital in Cape Town, South Africa, for children who require inhaled therapy. This spacer has been well accepted and used by the children and their caregivers (H. J. Zar & E. G. Weinberg, unpublished observations). The widespread availability of these bottles makes them a useful source of low-cost spacers.

Limitations

A limitation of a modified bottle-spacer is the absence of a one-way valve that may allow exhaled air to enter the spacer, causing increased aerosol loss if exhalation (rather than inhalation) follows actuation of the MDI. However, a bottle is an effective spacer, as measured by clinical response to bronchodilator therapy. Nevertheless, the similar degree of bronchodilation obtained with a bottle and conventional spacer does not indicate equivalence of these devices, as patients were on the plateau of the dose-response curve. Thus, these results cannot be directly extrapolated to the use of inhaled corticosteroids. Furthermore, the aerosol-deposition studies should be interpreted with caution as the performance of a nebulized aerosol will probably differ from that obtained when a MDI is actuated into a spacer. Absence of a valve may result in contamination of the bottle-spacer with organisms from the mouth during exhalation. As for any spacer, a bottle-spacer should be frequently wiped down if any microbial growth is observed inside the spacer then the device should be replaced.

A bottle-spacer is not suitable for young children who cannot form a tight seal with their mouths around the neck of a bottle. However, small, commercially available facemasks can be fitted onto the open end of a bottle, thus enabling its use as a spacer in children younger than 2–3 years of age. Aerosol-deposition studies suggest that this is an effective delivery system in such young children (23).

A bottle-spacer is made of plastic and is therefore not as durable as some of the commercially produced spacers. However, replacement of a bottle-spacer is relatively easy and inexpensive. Nevertheless, the long-term performance and efficacy of these devices has not been studied. Long-term use may result in build up of the drug and impairment of drug delivery if the device is not washed. Even with washing it may be difficult to remove drug from the nozzle area. Once washed, it is important that the actuator area is allowed to dry completely, as any remaining dampness may also impair drug delivery. A further limitation is that only MDI devices of a similar size and shape as the original MDI may be used. However, this is a limitation that applies to many of the commercially available spacer devices where a particular spacer fits only the MDI containers manufactured by a single company. Nevertheless, a different spacer bottle can be relatively easily supplied if a new brand of MDI is used. A final limitation is that a bottle-

spacer has not been extensively studied. However, all available studies to date have reported that this spacer is as effective as control, conventional spacers (16,17,21–23).

Conclusion

Low-cost, effective spacer devices are essential for delivery of good asthma care in the developing world and should be regarded as essential equipment. A modified 500-ml plastic cold-drink bottle is an effective spacer for children with asthma, as shown by *in vitro* and *in vivo* studies. Modification and use of a bottle-spacer should be included in international asthma guidelines. Further research on low-cost spacers is needed and greater priority should be given to developing and testing low-cost devices.

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References

1. National Asthma Education and Prevention Program. Expert Panel Report 2. Guidelines for the Diagnosis and Management of Asthma. NIH Publication #97-4051A. Bethesda, MD: US Department of Health and Human Services, National Institutes of Health, 1997.
2. O'RIORDAN TG, SAMLDONE GC. Aerosols. In: MIDDLETON E, REED CE, ELLIS EF, ADKINSON NF, YUNGINGER JW, BUSSE WW, eds. Allergy Principles and Practice, 5th edn. St. Louis: Mosby, 1998, pp 532–43.
3. AMIRAV I, NEWHOUSE MT. Metered dose inhaler accessory devices in acute asthma: Efficacy and comparison with nebulizers. A literature review. Arch Pediatr Adolesc Med 1997; 151: 876–82.
4. IDRIS AH, McDERMOTT MF, RAUCCI JC, MORRABEL A, MCGORRAY S, HENDELES L. Emergency department treatment of severe asthma. Metered-dose inhaler plus holding chamber is equivalent in effectiveness to nebulizer. Chest 1993; 103: 665–72.
5. RAIMONDI AC, SCHOTTLINDER J, LOMBARDI D, MOLFINO NA. Treatment of acute severe asthma with inhaled albuterol delivered via jet nebulizer, metered dose inhaler with spacer, or dry powder. Chest 1997; 112: 24–8.
6. KEREM E, LEVISON H, SCHUH S, et al. Efficacy of albuterol administered by nebulizer versus spacer device in children with acute asthma. J Pediatr 1993; 123: 313–7.
7. PARKIN PC, SAUNDERS NR, DIAMOND SA, WINDERS PM, MACARTHUR C. Randomized trial spacer vs. nebulizer for acute asthma. Arch Dis Child 1995; 72: 239–40.
8. ROBERTSON CF, NORDEN MA, FITZGERALD DA, et al. Treatment of acute asthma: Salbutamol via jet nebulizer vs. spacer and metered dose inhaler. J Paediatr Child Health 1998; 34: 142–6.
9. MANDELBERG A, TSEHORI S, HOURI S, GILAD E, MORAG B, PRIEL IE. Is nebulized aerosol treatment necessary in the pediatric emergency department? Chest 2000; 117: 1309–13.
10. LEVERSHA AM, CAMPANELLA SG, AICKIN RP, ASHER MI. Costs and effectiveness of spacer versus nebulizer in young children with moderate and severe acute asthma. J Pediatr 2000; 136: 497–502.

11. HENRY RL, MILNER AD. Simple drug delivery system for use by young asthmatics. *BMJ* 1983; 286: 2021.
12. CARSON JW, HILLER EJ. 'Cup-mask' salbutamol in acute asthma in children. *Ir Med J* 1985; 78: 5–6.
13. WONG C, AYSON M, RAJASINGHAM S, BURGESS C, CRANE J. Efficacy of a simple DIY spacer with a metered dose inhaler in asthma. *N Z Med J* 1995; 108: 256–7.
14. TEO J, KWANG LW, YIP WCL. An inexpensive spacer for use with metered-dose bronchodilators in young asthmatic children. *Pediatr Pulmonol* 1988; 5: 244–6.
15. LEE H, EVANS HE. Aerosol bag for administration of bronchodilators to young asthmatic children. *Pediatrics* 1984; 73: 230–2.
16. ZAR HJ, LIEBENBERG M, WEINBERG E, BINNS HJ, MANN MD. The efficacy of alternative spacer devices for delivery of aerosol therapy to children with asthma. *Ann Trop Paediatr* 1998; 18: 75–9.
17. ZAR HJ, BROWN G, DONSON H, BRATHWAITE N, MANN MD, WEINBERG EG. Home-made spacers for bronchodilator therapy in children with acute asthma: A randomized trial. *Lancet* 1999; 354: 979–82.
18. ZAR HJ, GREEN C, MANN MD, WEINBERG EG. A novel method for constructing an alternative spacer for patients with asthma. *S Afr Med J* 1999; 89: 1–4.
19. PIERART F, WILDHABER JH, VRANCKEN I, DEVADASON SG, LE-SOUEF PN. Washing plastic spacers in household detergent reduces electrostatic charge and greatly improves delivery. *Eur Respir J* 1999; 13: 673–8.
20. KENYON CJ, THORSSON L, BORGSTROM L, NEWMAN SP. The effects of static charge in spacer devices on glucocorticosteroid aerosol deposition in asthmatic patients. *Eur Respir J* 1998; 11: 606–10.
21. ASMUS MJ, LIANG J, COOWANITWONG I, HOCHHAUS G. Home-made spacer *in vitro* performance with a fluticasone metered-dose inhaler (Abstr.). *J Allergy Clin Immunol* 2001; 107: S103.
22. ASMUS MJ, LIANG J, COOWANITWONG I, HOCHHAUS G. *In vitro* performance characteristics of rigid valved holding chambers (VHC) with fluticasone (Abstr.). *Am J Respir Crit Care Med* 2001; 163: A444.
23. ZAR HJ, WEINBERG EG, BINNS HJ, GALLIE F, MANN MD. Lung deposition of aerosol – a comparison of different spacers. *Arch Dis Child* 2000; 82: 495–8.
24. 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.
25. EVERARD ML, CLARK AR, MILNER AD. Drug delivery from holding chambers with attached facemask. *Arch Dis Child* 1992; 67: 580–5.
26. FOK TF, LAM K, CHAN CK, et al. Aerosol delivery to non-ventilated infants by metered dose inhaler: Should a valved spacer be used? *Pediatr Pulmonol* 1997; 24: 204–12.
27. WILDHALER JH, DEVADASON SG, HAYDEN MJ, et al. Electrostatic charge on a plastic spacer device influences the delivery of salbutamol. *Eur Respir J* 1996; 51: 985–8.
28. NEWMAN SP, PAVIA D, CLARKE SW. How should a pressurized beta-adrenergic bronchodilator be inhaled? *Eur J Respir Dis* 1981; 62: 3–21.