

ALTERNATE SPACER DEVICES IN THE TREATMENT OF ASTHMA IN CHILDREN

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Asthma is the most common chronic illness in children in low and middle income countries (LMICs) including Africa, with prevalence rates that are similar or higher than those in high income countries^{1,2,3}. In these areas, the prevalence of childhood asthma is increasing and is associated with more severe disease than in high income countries³. Therefore availability of effective, affordable therapy for asthma is essential to ensure adequate control of disease and treatment of exacerbations.

Inhaled therapy is the treatment of choice for delivery of medication for both relief and prevention of asthma. Inhaled therapy given via metered dose inhaler (MDI) and spacer is the optimal delivery system recommended for treatment of acute and chronic asthma, rather than nebulisation. Bronchodilators given via MDI have been shown to be equivalent or superior to nebulised therapy for relief of bronchoconstriction in infants and children with acute asthma even when the degree of airways obstruction is severe⁴. A MDI-spacer delivery system has many other advantages over nebulisation including shorter and easier administration of drug, transportability, no need for a power source and lower risk of nosocomial infection. However, a spacer is essential to minimise dependence on the child's inhalation technique and optimise drug delivery.

Various commercially produced spacers have been developed but expense and unavailability have limited their use in developing countries. Moreover, while the current World Health Organisation's Essential Medicines List includes Beclomethasone (aerosol), Budesonide (aerosol), Ipratropium bromide (aerosol) and Salbutamol (aerosol), it does not include a spacer device. To enable widespread use of inhaler therapy in children, we undertook research to develop an appropriate spacer device for use in children. This research led to the development and widespread use of a plastic bottle as an alternative spacer device that is now recommended in national and global guidelines.

AEROSOL DEPOSITION STUDIES

Initial studies involved measuring aerosol deposition in children of different ages, using nebulised Tc99m-DTPA. Results showed that a 500 ml plastic bottle modified as a spacer produced equivalent or greater lung deposition than a conventional spacer^{5,6}. In these studies nebulised aerosol captured in a two litre anaesthetic 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, lung deposition obtained from a conventional spacer and sealed bottle was equivalent, but was less from an unsealed bottle⁵. However, a polystyrene cup produced the least amount of lung deposition, delivering between a third and a fifth of the dose that the other spacers were capable of delivering. Thereafter aerosol lung deposition from a modified bottle in younger children aged 3 to 5 years was measured; this was found to be twice that obtained with a conventional valved small volume spacer⁶. The amount of lung deposition was age dependent with a marked reduction occurring at around 50 months; this pattern occurred when either the conventional or bottle-spacer was used.

CLINICAL TRIALS

In a randomised clinical trial comparing the efficacy of home-made spacers (sealed 500 ml plastic bottle, unsealed 500 ml bottle, and polystyrene cup) to a conventional spacer (AeroChamber) in 88 children with acute asthma, a 500 ml bottle was confirmed to be an effective spacer for delivery of bronchodilators⁷. In this study, a sealed bottle and conventional spacer produced similar bronchodilation as measured by improvement in clinical score and pulmonary function. A polystyrene cup was the least effective for children with moderate to severe airway obstruction, producing only minimal bronchodilation. A nebulised 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 nebulisation in those who had previously used a conventional spacer or sealed bottle (indicating that maximal bronchodilation had been achieved with these) 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.

To investigate the efficacy of a home-made bottle-spacer in young children for administration of bronchodilator therapy, a second randomised clinical trial of a conventional, compared with a bottle-spacer was done in 400 young children (median age 12 months) with acute lower airways obstruction⁸. Bronchodilator therapy was given from a MDI via an AeroChamber or a bottle-spacer with mask. A clinical score and oximetry recording were done prior and 15 minutes after therapy. MDI-spacer therapy was repeated up to 3 times, dependent on clinical response, after which nebulisation was used. The primary outcome was hospitalisation; hospitalisations (60, 15%) were identical in the conventional and bottle-spacer groups. Secondary outcomes including change in clinical score, oxygen saturation, use of oral corticosteroids or number of bronchodilator treatments were similar in both groups⁸. Therefore, a low cost bottle-spacer was as effective as a conventional spacer for bronchodilator therapy in young children.

MODIFICATION AND USE OF A 500 ML PLASTIC BOTTLE

To modify a 500 ml plastic bottle for use as a spacer, the bottle was washed with soap and water and air dried for a minimum of 12 hours so as to reduce electrostatic charge on the side walls. A hole was then made in the base of the bottle through which the MDI was inserted. As the plastic base is 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 bottle⁹. The heated mould was held in position for approximately 10 seconds until the plastic had melted and then rotated 180 degrees and reapplied. The mouth of the MDI was inserted immediately after removal of the mould while the base of the bottle was still warm, so creating a tight fit. New bottle-spacers were primed initially with 15 puffs of medication to reduce electrostatic charge on the walls and increase aerosol

transit time.

A modified 500 ml plastic bottle should be used in a similar way to a conventional spacer. The neck of a bottle should be held in the mouth simulating a mouthpiece (Figure 1). For a young child who cannot form a tight seal with the spacer in their mouth, a small commercially available facemask that fits on the open end of the bottle can be applied, thus enabling it to be used as a spacer in young children (Figure 2). Single actuations of the MDI should be used until the desired amount of medication is given so as to improve drug delivery.



Figure 1. Child using a homemade bottle-spacer by holding the neck of the bottle in their mouth



Figure 2. Mom using a homemade bottle-spacer to give bronchodilator therapy to her infant. A mask is attached to the neck of the bottle-spacer

An estimate of the cost of a modified 500 ml plastic bottle in South Africa is approximately R1.00 which is 30 to 180 times less expensive than various commercially available devices in this country.

CONCLUSION

Low cost, effective spacer devices are essential for delivery of good asthma care in LMICs and should be regarded as essential equipment. A modified 500 ml plastic bottle is an effective spacer for delivery of bronchodilator therapy in children of all ages, shown by in vitro and in vivo studies. Subsequent studies using a homemade spacer have been done in other parts of the world; a Cochrane review reported similarly efficacy for homemade and commercially produced spacers.¹⁰

Modification and use of a bottle-spacer has now been included in national and international asthma guidelines. Homemade bottle-spacers are now widely used throughout the world. The use of the bottle-spacer has enabled delivery of optimal inhaled asthma therapy in the poorest households, empowering children and their families to

provide such care.

REFERENCES

1. Mallol J, Crane J, von Mutius E, Odhiambo J, Keil U, Stewart Aatl. The International Study of Asthma and Allergies in Childhood (ISAAC) Phase Three: a global synthesis. *Allergol Immunopathol (Madr)* 2013;41(2):73-85.
2. Ait-Khaled N, Odhiambo J, Pearce N, Adjoh KS, Maesano IA, Benhabyles B et al. Prevalence of symptoms of asthma, rhinitis and eczema in 13- to 14-year-old children in Africa: the International Study of Asthma and Allergies in Childhood Phase III. *Allergy* 2007;62(3):247-58.
3. Lai CKW, Beasley R, Crane J, Foliaki S, Shah J, Weiland S et al. Global variation in the prevalence and severity of asthma symptoms: Phase Three of the International Study of Asthma and Allergies in Childhood (ISAAC). *Thorax* 2009;64(6):476-83.
4. Cates CJ, Crilly JA, Rowe BH. Holding chambers (spacers) versus nebulisers for beta-agonist treatment of acute asthma. *Cochrane Database Syst Rev*. 2006 Apr 19;(2):CD000052.
5. 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.
6. Zar HJ, Weinberg EG, Binns HJ, Gallie F, Mann MD. Lung deposition of aerosol--a comparison of different spacers. *Arch Dis Child* 2000;82:495-498.
7. Zar HJ, Brown G, Donson H, Brathwaite N, Mann MD, Weinberg EG. Home-made spacers for bronchodilator therapy in children with acute asthma: a randomised trial. *Lancet* 1999;354:979-82.
8. Zar HJ, Streun S, Levin M, et al. Randomised controlled trial of the efficacy of a metered dose inhaler with bottle-spacer for bronchodilator treatment in acute lower airway obstruction. *Arch Dis Child* 2007;92:142-6.
9. 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);1-4.
10. Rodriguez C, Sossa M, Lozano JM. Commercial versus home-made spacers in delivering bronchodilator therapy for acute therapy in children. *Cochrane Database Syst Rev* 2008;2(CD005536).

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Ciclovent 160	Ciclesonide	120 doses	3	720735001	R 349.40	R 398.31	50%

REFERENCES:

1. Berger WE. Ciclesonide: a novel inhaled corticosteroid for the treatment of persistent asthma - a pharmacologic and clinical profile. *Therapy* 2005; 2(2):167-178.
2. Hoshino M. Comparison of Effectiveness in Ciclesonide and Fluticasone Propionate on Small Airway Function in Mild Asthma. *Allergol Int* 2010; 59(1):59-66.
3. Newman S et al. High lung deposition of 99mTc-labeled ciclesonide administered via HFA-MDI to patients with asthma. *Respir Med* 2006; 100:375-384.
4. Nave R, et al. In Vitro Metabolism of Ciclesonide in Human Lung and Liver Precision-cut Tissue Slices. *Biopharm Drug Dispos* 2006; 27: 197-207.
5. Nonaka T et al. Ciclesonide uptake and metabolism in human alveolar type II epithelial cells (A549). *BMC Pharmacol* 2007; 7:12.
6. DoH Price Approval.