Home-made spacers for bronchodilator therapy in children with acute asthma: a randomised trial

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Summary

Background A metered-dose inhaler (MDI) with spacer is the best way to deliver bronchodilator therapy for treatment of acute asthma. In developing countries, commercially produced spacers are generally unavailable or too costly. We tested the efficacy of home-made spacers (500 mL plastic bottle, polystyrene cup) compared with a conventional spacer for delivery of a β_2 agonist via MDI for children with acute asthma.

Methods We studied children aged 5 to 13 years with acute asthma, stratified into those with mild airways obstruction (peak expiratory flow [PEF] 60–79% of predicted value) or moderate to severe airways obstruction (PEF 20–59% of predicted value). A β_2 agonist (fenoterol hydrobromide) was given via MDI and one of four randomly assigned spacers (conventional spacer, sealed 500 mL plastic bottle, unsealed 500 mL bottle, 200 mL polystyrene cup). Clinical score, pulmonary function tests, and oximetry were recorded at baseline and 15 min after treatment. If a second bronchodilator treatment was needed, nebulised fenoterol was given and the assessment repeated 15 min later. Primary outcome measures were changes in clinical score and pulmonary function, and need for and response to nebulisation.

Findings 88 children were eligible for study. In 44 children with moderate to severe airways obstruction, a cup gave significantly less bronchodilation (median increase in: forced expiratory volume in 1 s [FEV_1] 0%; PEF 12%) compared with the conventional spacer (37%; 59%), sealed bottle (33%; 36%), or unsealed bottle (18%; 21%, $p<0{\cdot}05$ for difference between groups). Nebulisation was required by ten of 11 who had used a cup, nine of 11 who had used an unsealed bottle, eight of 11 who had used a sealed bottle, and only four of 11 who had used a conventional spacer. After nebulisation, improvement in FEV_1 (15·5%) and PEF (26%) was more marked in children who had used a cup than in those who had used a conventional spacer (5·5% FEV_1; 4% PEF), sealed bottle (3%; 0%), or unsealed bottle (7%; 9%). For 44 children with mild airways obstruction, response to bronchodilator was similar for all spacers and need for nebulisation was not associated with use of a particular spacer.

Interpretation A conventional spacer and sealed 500 mL plastic bottle produced similar bronchodilation, an unsealed bottle gave intermediate improvement in lung function, and a polystyrene cup was least effective as a spacer for children with moderate to severe airways obstruction. Use of bottle spacers should be incorporated into guidelines for asthma management in developing countries.

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Introduction

Inhaled bronchodilator therapy is the recommended first-line treatment for episodes of acute asthma. Although nebuliser therapy is predominant, a pressurised metered-dose inhaler (MDI) with attached spacer can produce the same or better bronchodilation than a nebuliser even in the presence of severe airways obstruction.[1,2] Because of relative efficiency, ease of use, and low cost, an MDI with spacer may be preferable to a nebuliser for delivery of bronchodilators in acute asthma.[1–5] However, a spacer is essential to minimise dependence on the patient's inhalation technique and to optimise drug delivery.[1]

Several commercially produced spacers have been developed, but expense and lack of availability have limited their use in developing countries. Polystyrene cups and plastic cold-drink bottles have been adapted as home-made spacers, but little is known about their efficacy. Uncontrolled studies have reported that use of a cup or 1 L plastic bottle improves symptoms and pulmonary function in asthmatic children.[6–8] Despite the lack of data, home-made spacers such as a cup or 1 L bottle are endorsed for use in asthmatic children by the WHO and by the Global Initiative of Asthma guidelines, and are widely used in developing countries.[9,10]

We have shown that aerosol deposition of nebulised technetium-99m-labelled diethylene triamine penta-acetic acid (DTPA) was the same whether a conventional spacer or a sealed 500 mL plastic cold-drink bottle was used as a spacer, whereas a cup functioned poorly, delivering only about a fifth of the dose of other spacers.[11] We aimed to investigate the clinical applicability of these results by comparison of the response to bronchodilator of a conventional spacer with that of home-made spacers in children with acute asthma.

Methods

Patients

Children aged 5 to 13 years with a known history of asthma who presented to the Red Cross Children's hospital with an acute asthma attack were enrolled in the study. An acute asthma attack was defined as increased cough, wheezing, or difficulty in breathing, and a peak expiratory flow (PEF) of less than 80% of the predicted normal value for height, race, and sex.[12] Exclusion criteria were: inability to use an MDI and spacer or to reliably undergo pulmonary function tests; PEF of less than 20% of the predicted normal; arterial oxygen saturation of less than 92% in air; underlying cardiac or other chronic pulmonary disease; treatment with oral corticosteroids for more than 5 days before presentation; use of β_2 agonist within 4 h of presentation. Patients were stratified by PEF into two groups according to severity of airways obstruction: mild (PEF 60–79% of predicted normal value) and moderate (PEF 20–59% of predicted normal value). Informed consent was obtained. The study was approved by the ethics committee of the University of Cape Town.

Study design

We assessed four types of spacer. Conventional spacers (Aerochamber, Trudell Medical, Canada) were cylindrical 145 mL valved spacers with attached mouthpieces. Sealed 500 mL plastic cold-drink bottles were used as spacers by making a

Figure 1: **Use of MDI and 500 mL plastic bottle spacer**

hole in the base to fit the size and shape of the MDI.[13] The bottle-MDI perimeter was sealed with glue, and the opposite end was held in the mouth to simulate a mouthpiece (figure 1). Unsealed 500 mL plastic cold-drink bottle spacers were constructed in the same way as the sealed bottle spacers, but no glue was used to seal the perimeter. Spacers were also made from 200 mL polystyrene cups by cutting a hole in the base to fit the MDI tightly. The cup was held over the nose and mouth to simulate a facemask. Newly constructed spacers were primed with 15 puffs of fenoterol before use.

We used block randomisation for the two groups of children to randomly assign a spacer to a patient. Allocation of spacer was by sealed envelope. The investigators who did the clinical examination, pulmonary function testing, and oximetry were unaware as to which spacer was used, because treatment was given in a separate room.

We undertook baseline assessment immediately before use of the MDI-spacer. Assessment included a history, examination, pulmonary function test, and arterial oxygen saturation. A clinical score[14] was calculated for each child based on heart rate, respiratory rate, accessory muscle use, wheezing, and pulsus paradoxus. Pulmonary function tests used a portable spirometer (Microloop II, Micro Medical, Kent, UK), and the best of three tests was recorded. We used the forced expiratory manoeuvre to measure forced vital capacity, forced expiratory volume in 1 s (FEV_1), PEF, and mean flow rate between 25% and 75% of vital capacity. Measurements were expressed as a percentage of the predicted normal value for height, race, and sex.[12,15] We measured arterial oxygen saturation with a pulse oximeter (Ohmeda Biox 3760, BOC Health Care, Louisville, USA).

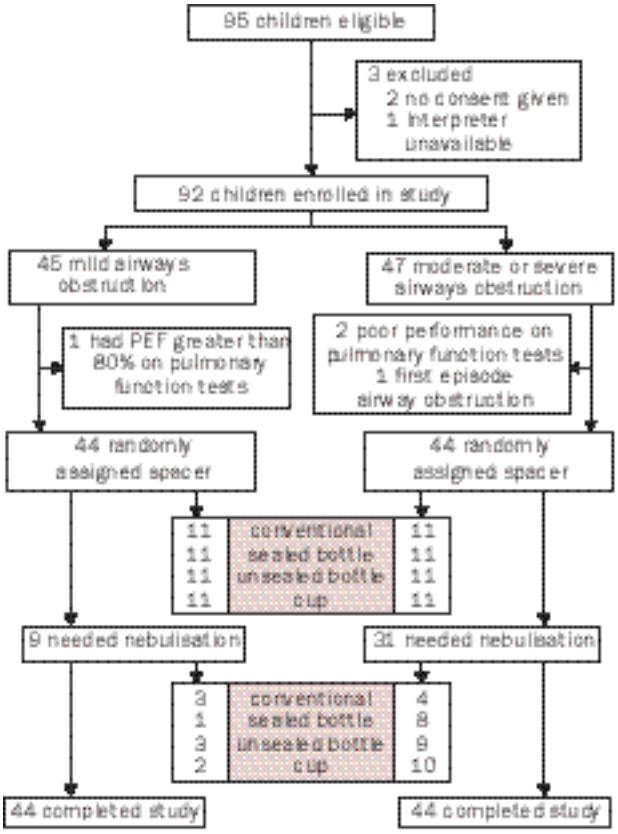

Figure 2: **Trial profile**

Fenoterol hydrobromide (100 μg/puff) was given via MDI-spacer at a rate of one puff every 10 s at a dose of 400 μg for children who weighed 25 kg or less, and 600 μg for children who weighed more than 25 kg. Normal tidal breathing was encouraged, and we made no attempt to synchronise actuation of the MDI with the child's inspiration. Clinical score, pulmonary function test, and oxygen saturation were repeated 15 min after fenoterol was given. If a child had a repeat PEF of less than 70% of the predicted value, fenoterol 1000 μg in 2 mL normal saline was given via a jet nebuliser (GRS Medical, Intersurgical, Berkshire, UK) together with oxygen at a flow rate of 5 L per min, and the child was reassessed 15 min after nebulisation.

Statistical analysis

Primary outcome measures were changes in clinical score and pulmonary function, and need for and response to nebulisation. A 15% improvement in PEF is judged clinically significant, so we selected a sample size of 22 for each spacer to ensure detection of a 15% change in PEF at a significance level of 0·05 with a power of 90% for each type of spacer. We compared groups by means of Kruskal-Wallis one-way ANOVA, and the EpiInfo statistical package (version 6·04b) was used. When ANOVA showed significant differences, the same test was used for pair by pair comparison of the two groups.

Results

88 children were enrolled in the study: 44 with mild airways obstruction and 44 with moderate or severe airways obstruction (figure 2). Baseline characteristics of the children are shown in table 1. Demographic characteristics were similar in each group. The median improvement in clinical score for all patients was 1 (25th–75th percentile 0–1), and this improvement did not vary by type of spacer. Each type of spacer was judged effective in that it gave a median improvement in PEF of more than 15%. Improvement in FEV_1 was greater if a conventional spacer, sealed bottle, or unsealed bottle was used rather than a cup (table 2, p=0·02). Use of spacers gave consistent improvement in PEF, forced vital capacity, and mean flow rate between 25% and 75% of vital capacity. A conventional spacer or sealed bottle gave similar improvements, an unsealed bottle gave intermediate improvements, and a cup was least effective.

Patients with mild airways obstruction had a median improvement of 1 (0–1) in clinical score after MDI use, which did not vary by type of spacer. Improvement in pulmonary function in that group was similar for all spacers (table 2). Nine (20%) of children needed nebulisation; but this need did not vary according to the type of spacer used.

For children with moderate to severe airways obstruction, median improvement in clinical score (1 [0–2]) was similar to that with mild obstruction and did not vary according to the spacer used. Change in pulmonary function varied by the spacer used—a cup was least effective (table 2). Median PEF as a percentage of the predicted value after MDI use was 74% (25th–75th percentile 61–90), 62% (49–72), 56% (38–64), and 45% (38–55) for the conventional spacer, sealed bottle,

Characteristic	Conventional spacer (n=22)	Sealed bottle (n=22)	Unsealed bottle (n=22)	Cup (n=22)	p for difference between groups
All patients					
Age (years)	10·3 (8·9–12·4)	9·2 (7·9–10·7)	9·1 (7·9–10·7)	9·7 (7·5–11·3)	0·37
M/F	15/7	12/10	13/9	13/9	0·83
Clinical score	1 (1–2)	1·5 (1–3)	2 (1–3)	2 (1–3)	0·60
O_2 saturation (%)	97 (95–98)	96 (95–98)	97 (95–98)	97 (96–99)	0·52
Pulmonary function tests					
FEV_1*	67 (57–77)	67·5 (51–74)	64·5 (52–75)	65 (53–77)	0·89
PEF*	58·5 (45–69)	59·5 (43–68)	59 (32–73)	54·5 (44–67)	0·95
FVC*	78·5 (68–83)	74·5 (64–86)	77·5 (61–86)	75·5 (60–87)	0·91
FEF*	37 (27–52)	32 (24–47)	40 (26–50)	37·5 (27–51)	0·71
Mild airways obstruction†					
Age (years)	9·7 (7·7–14·4)	10·6 (8·6–12·7)	9·1 (7·9–11·4)	9·8 (7·9–11·9)	0·79
M/F	8/3	6/5	7/4	5/6	0·60
Clinical score	1 (1–1)	1 (1–1)	1 (0–2)	1 (0–2)	0·93
O_2 saturation (%)	97 (94–98)	96·5 (95–98)	97 (95–98)	97 (96–99)	0·57
Pulmonary function tests					
FEV_1*	76 (68–82)	74 (66–79)	75 (72–78)	77 (67–88)	0·78
PEF*	69 (61–74)	68 (62–70)	73 (65–74)	67 (65–71)	0·56
FVC*	79 (76–93)	86 (69–90)	86 (77–92)	87 (81–94)	0·53
FEF*	51 (40–65)	37 (34–51)	49 (40–58)	51 (38–57)	0·37
Moderate to severe airways obstruction†					
Age (years)	11·4 (8·9–12·4)	8·3 (7–12·7)	9·0 (7–9·5)	8·8 (7·3–11)	0·18
M/F	7/4	6/5	6/5	8/3	0·79
Clinical score	1 (1–3)	3 (2–3)	3 (2–4)	3 (2–4)	0·25
O_2 saturation (%)	98 (95–99)	95 (94–97)	96 (94–99)	96 (94–99)	0·45
Pulmonary function tests					
FEV_1*	57 (52–63)	51 (41–69)	52 (42–58)	53 (47–60)	0·52
PEF*	45 (41–56)	43 (34–51)	32 (26–47)	44 (37–51)	0·26
FVC*	78 (64–82)	64 (59–77)	61 (52–78)	60 (58–73)	0·08
FEF*	31 (24–37)	29 (22–30)	26 (19–40)	27 (23–37)	0·89

Data are median (25th–75th percentile) except where indicated. FVC=forced vital capacity. FEF=mean flow rate between 25% and 75% of vital capacity. *% predicted normal value for height, race, and sex. †n=11 in each spacer group.

Table 1: **Baseline characteristics of children stratified by severity of airways obstruction and type of spacer**

unsealed bottle, and cup, respectively (p=0·001). Nebulisation was needed by ten of 11 who had used a cup, eight of 11 who had used a sealed bottle, nine of 11 who had used an unsealed bottle, and only four of 11 who had used a conventional spacer. Median improvement in FEV_1 and PEF after nebulisation was minimal in children who had previously used a conventional spacer (FEV_1 5·5% [2–7·5], PEF 4% [–4 to 12·5]) or sealed bottle (FEV_1 3% [0–8], PEF 0% [–7 to 6]), but was greatest in patients who had previously used the cup (FEV_1 15·5% [7–36], PEF 26% [1–32%], p=0·03 and 0·05 respectively for the four groups). A small increase of 7%(0–23) in FEV_1 and 99% (2–20) in PEF after nebulisation occurred in children who had previously used the unsealed bottle.

No significant change in arterial oxygen saturation occurred after bronchodilator use in any child. Minor side-effects occurred in 25% of children, including tremor in 18 (20·4%), nausea in five (5·7%), headache in three (3·4%), and dizziness in two (2·3%). There was no association between the type of spacer used and the development of side-effects. Median increase in heart rate was 4 beats per min (–4 to 13), and this increase did not vary according to the type of spacer used.

Discussion

A 500 mL plastic bottle and a conventional spacer gave a similar response to a β_2 agonist given via MDI in children with acute asthma. Each type of spacer was effective in that the median PEF of each group improved by a clinically important amount. However, changes in pulmonary function were lowest with the cup, and differences in response were most apparent in children with moderate to severe airways obstruction.

Many properties of a spacer may affect pulmonary deposition of aerosol and subsequent response to bronchodilator.[16] These include the volume and shape of the device, the electrostatic charge of the sidewalls, the volume of dead space, and the presence or type of valves.[17–19] The efficacy of the bottle may be due in part to its physical characteristics. In preference to a larger bottle, we chose a 500 mL bottle since its dimensions are similar to the optimum chamber dimensions for a spacer for children (a cylinder about 11 cm long and 3·5 cm in diameter).[17] The bottle was also modified carefully to create a good seal between the MDI and the hole in the base of the bottle. A heated wire mould of the same shape and size as the MDI was applied to the base of the plastic bottle to melt the plastic and make a hole.[13] The MDI canister was then inserted immediately, to create a tight fit

Characteristic	Conventional spacer (n=22)	Sealed bottle (n=22)	Unsealed bottle (n=22)	Cup (n=22)
All patients				
FEV_1	23·5 (14–37)	20 (15–33)	16·5 (10–34)	13 (0–23)†
PEF	22·5 (14–59)	24·5 (10–44)	17 (1–42)	16 (2–23)
FVC	12·5 (6–20)	12·5 (8–26)	10 (4–23)	5 (0–8)†
FEF	46 (29–68)	48·5 (21–77)	33·5 (17–80)	33 (17–66)
Mild airways obstruction*				
FEV_1	20 (5–24)	16 (10–21)	15 (12–24)	16 (11–23)
PEF	17 (11–23)	19 (9–32)	2 (−2–36)	16 (9–23)
FVC	10 (5–13)	9 (3–9)	5 (3–20)	5 (0–7)
FEF	44 (19–55)	53 (26–64)	37 (25–80)	48 (37–73)
Needed nebulisation (n)	3	1	3	2
Moderate to severe airways obstruction*				
FEV_1	37 (19–53)	33 (18–55)	18 (9–57)	0 (−4 to 24)†
PEF	59 (22–69)	36 (21–102)	21 (16–99)	12 (−5 to 37)†
FVC	17 (8–22)	23 (14–36)	18 (5–26)	6 (−5 to 15)†
FEF	68 (29–91)	24 (13–161)	27 (14–102)	23 (−16 to 29)
Needed nebulisation (n)	4	8	9	10

Data are median (25th–75th percentile) of difference between actual pretreatment and post-treatment values as a % of the pretreatment value. FVC and FEF as in table 1. *n=11 in each spacer group. †p<0·05.

Table 2: **Response to bronchodilator according to severity of airways obstruction and type of spacer**

between the heated plastic of the bottle and the MDI, even in the unsealed spacer.

The technique of spacer use may also have affected response to bronchodilator therapy and contributed to the efficacy of the bottle. Plastic bottles were primed with 15 puffs of bronchodilator to reduce the electrostatic charge of the sidewalls and to optimise drug delivery. Electrostatic charge can also be reduced by rinsing the bottles in detergent.[19] Single rather than multiple actuations of the MDI also ensured maximum drug delivery.[18]

The relatively poor response to bronchodilator given via a cup in children with moderate to severe asthma is probably due to characteristics of the cup and the severity of airways obstruction. Studies of pulmonary deposition have shown marked loss of aerosol around the face where the cup fits over the mouth and nose, resulting in lower delivery of aerosol to the lungs compared with use of a conventional spacer or plastic bottle.[11] Moreover, pulmonary aerosol deposition decreases as the severity of airway obstruction increases.[20] Thus the combination of aerosol loss from the cup and increased airway obstruction may have resulted in minimal delivery of β_2 agonist. The reversibility of these children's asthma was shown by their excellent response to nebuliser therapy. This response did not occur in those who used a conventional spacer or bottle. Although similar numbers of children with moderate airways obstruction who had used a cup or a bottle needed nebulisation, minimal bronchodilator response occurred in those who had used a bottle, suggesting that maximum bronchodilation had been obtained with that type of spacer.

A cup was an effective spacer in children with mild airways obstruction, and may be of clinical use in this group of patients, particularly in infants or children too young to use a mouthpiece. However, these children may not be easy to distinguish clinically from those with more severe airways obstruction. Furthermore, aerosol deposition in the lung is substantially less in young children than in older patients.[21] Our study did not assess the therapeutic efficacy of a cup in children younger than 5 years. A bottle may also be adapted for use as a spacer for young children by attaching a facemask to the bottle neck.

The bottle is limited as a spacer because it has no one-way valve. Exhaled air may therefore enter the spacer, to dilute the aerosol inside the spacer. However, our results suggest that, in practice, absence of a valve does not adversely affect the response to bronchodilator. Spacers without valves enhance the delivery of aerosol to the lungs in infants with chronic lung disease.[22] Similarly, absence of a valve may benefit children with moderate to severe airways obstruction, since there is no need to overcome the resistance of the valve on inspiration. However, a bottle may be less efficient when lower doses of bronchodilator are given than the dose used in our study. Furthermore, our study lacks power to detect differences between a conventional spacer and bottle, because of the small number of children in each group; however, clinically important differences between these two spacers are unlikely given the similarity in response achieved with both.

A 500 mL plastic bottle is an effective alternative to a conventional spacer. Adaption and use of the bottle as a spacer should form part of asthma education programmes in developing countries, and should be incorporated into guidelines such as those produced by the WHO.

Contributors

Heather Zar designed and coordinated the study, did the data analysis, and was primarily responsible for drafting the paper. Gerry Brown was responsible for recruiting patients, giving bronchodilators, and data collection. Hilton Donson contributed to study design, and did pulmonary function tests and oxygen saturation measurements. Nicola Brathwaite recruited patients, and did clinical assessments. Mike Mann and Eugene Weinberg contributed to study conception, design, and analysis. All investigators contributed to writing of the final paper.

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