

What is the efficacy of home-made spacers compared to wet nebulizers in the delivery of beta agonists in children?

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The World Health Organization has produced guidelines for the management of common illnesses in hospitals with limited resources. This series reviews the scientific evidence behind WHO's recommendations. The WHO guidelines, and more reviews are available at http://www.who.int/child-adolescent-health/publications/CHILD_HEALTH/PB.htm

This review addresses the question: What is the efficacy of home-made spacers compared to wet nebulizers in the delivery of beta agonists in children?

The WHO Pocketbook of Hospital Care for Children recommends to give rapid acting bronchodilator via one of:

- * nebulized salbutamol
- * salbutamol by a metered dose inhaler with spacer device

If a commercial device is not available then a spacer device can be made from a plastic cup or

1L plastic bottle. (Pocketbook chapter 4.4.2, page 89).

INTRODUCTION:

Administration of aerosol bronchodilators is the cornerstone of treatment of symptomatic airflow obstruction. The use of a spacer (or holding chamber) with metered dose inhaler (MDI) for the delivery of beta-agonist medication in the treatment of asthma has long been held to be as efficacious as delivery via an oxygen-driven 'wet' nebuliser, with some studies showing a reduction in the number and degree of side effects [1]. They also confer the advantages of not requiring a power source, having minimal ongoing maintenance requirements, being comparatively cheaper and less complicated to use. This is important in the context of under-resourced areas given the lack of access to such devices as nebulisers and oxygen delivery systems.

Unfortunately the cost of supplying standardised mass produced spacer devices precludes this as a feasible option for many areas of the world. For this reason, several places have been using home-made spacer devices for beta-agonist delivery. Several different devices are used throughout the world; however the most common variation seems to be a non-valved plastic drink bottle cut in half. This review aims to answer the question of

whether or not these devices are as efficacious as 'wet' nebulisers for the delivery of beta-agonist medication.

METHODOLOGY

Initial evaluation was undertaken looking for an answer to the specific question on the Cochrane database using the keywords as outlined in the search below. This yielded one Cochrane Review looking at manufacturers holding chambers versus nebulisers for beta-agonist treatment of acute asthma [1]. No Cochrane Review has been done looking at home-made spacers.

Secondary evaluation was undertaken using Haynes et al. PubMed Clinical Enquiries with the search parameters of ('home-made' OR 'home made') AND ('spacer' or 'holding chamber') AND ('Ventolin' OR 'salbutamol' OR 'beta-agonist' OR 'bronchodilator') AND 'nebuli*'. A narrow, specific search identified 18 articles and a broad, sensitive search identified 32 articles. All abstracts were read, and if relevance was still in question, the complete article was sourced. Of the articles identified, most were excluded due to lack of relevance to the question. The remaining two articles were reviewed and included, both being type 1b [2, 3], although one study had a low study power given a small sample size [3].

RESULTS

Efficacy of proprietary spacers

A Cochrane review of 25 trials with 2066 children and 614 adults has concluded that the holding chamber devices are as efficacious as wet nebulisers for the administration of bronchodilator in the acute management of asthma [1]. Another study concurs with this looking at 42 young children (aged 10 months to 4 years) using a facemask to connect the baby/child to the spacer device [4].

Features of a holding chamber that may affect delivery of drug to the lung include volume, shape, valve design and electrostatic charge. Additional factors in young children that may be important are the increased respiratory rate, small tidal volumes and reduced flow rates. Studies have now been undertaken that provide some evidence for optimal use of holding chamber devices. Wildhaber et al demonstrated that reducing the electrostatic charge on the surface of plastic spacers led to a significant increase in small particle delivery, and that single actuations increased drug delivery compared

with multiple actuations of MDIs [5]. Pierart et al found that holding chambers washed with detergent resulted in a mean increase of 37.4% in small particle salbutamol output compared with washing with water, with the effect lasting four weeks [6]. Clark et al found that single actuations of an MDI increased salbutamol delivery by two-fold compared with multiple actuations with or without delays [7], and Everard et al has demonstrated that small chamber devices may enhance delivery with low tidal volumes [8].

Home made spacers compared to commercial spacers

Several studies have looked at this question, with Zar et al finding that the efficacy of a commercial spacer and sealed plastic bottle were better than an unsealed bottle, which in turn was better than a polystyrene cup, in the treatment of severe airway obstruction [9]. One study found greater bronchodilation when using a 1 litre plastic bottle compared with placebo [10], another showing similar with a coffee cup [11], with neither study demonstrating increased side effects. Zar et al found that equivalent lung deposition occurs whether a mask or mouthpiece is used with a commercial spacer and that a 500ml plastic bottle produced greater lung deposition than a commercial spacer device [12].

Home made spacers compared to nebuliser

Both articles included were prospective single blinded randomized controlled trials using patients in an emergency department setting in different hospitals of Brazil, with the primary aim being efficacy of salbutamol delivered via a home-made spacer with metered dose inhaler (MDI) versus an oxygen driven nebuliser. Duarte et al also looked at comparative safety (incidence and severity of side effects) [2], whereas Vilarinho et al also looked at cost-effectiveness, time to prepare and deliver doses as well as parent satisfaction [3]. The first study looked at well established asthma, with severe exacerbations (PEFR <50% predicted) being excluded, whereas in the latter study 22 children (out of 54) were under the age of two, where asthma was difficult to definitively diagnose. Similar home made devices were used in both studies, with similar treatment regimens.

Primary outcomes were based on analysis of clinical features, oxygen saturation and, in one study, peak expiratory flow rate [2], with both studies evaluating these parameters after three 20 minutely salbutamol administrations from initial evaluation (time zero). Both studies showed no statistical significance ($p < 0.05$) between the observed changes in efficacy parameters in the nebuliser versus home-made spacer groups at time zero or any of the three intervals, despite obvious improvement in both groups with treatment. Duarte et al also used time to discharge from emergency as an evaluation parameter, with total length of stay in minutes being 66.9 +/- 31.4 (nebuliser) versus 41.1 +/- 17.7 (home made spacer), CI 18.6-33.0, $p < 0.05$ [2]. The comparative safety (incidence and severity of side effects) showed side effects in 17.2% (nebuliser) versus 4.1% (home-made spacer), $p = 0.003$, although not severe enough to discontinue treatment in either group. The nebuliser group also showed a higher increase in heart rate at all three intervals ($p = 0.02$). These findings would suggest not only a comparative safety, but a relative reduction in the incidence of unwanted effects with home-made spacer devices [2].

The cost effectiveness and time to prepare and deliver doses with a home-made spacer was also found by Vilarinho et al to be significantly lower [3]. The former observation supports other studies evaluating cost effectiveness of spacers versus nebulisers [13, 14]. Parent satisfaction in the same study was equal with both the nebuliser and home-made spacer groups.

DISCUSSION

It appears that when comparing the two methods for delivery of salbutamol, a home-made spacer offers comparative efficacy to that of a nebuliser, with considerably less cost to the consumer. Although one study found a relative reduction in time to discharge from an emergency setting using the home-made spacer, it must be taken into account that a nebuliser is a more time consuming device to prepare and deliver. Thus, the time to discharge parameter does not necessarily reflect a greater or quicker clinical effect from the home-made spacer. In practical terms, however, it does still seem to limit the total time a child spends in emergency.

With regards to safety, in neither study was there any cessation of treatment to suggest an excessive amount of side effects that would limit clinical use of a home-made spacer device. One study actually found a smaller rise in heart rate using a home-made spacer versus the nebuliser, with the Cochrane Review [1] certainly supporting this trend of fewer side effects with commercial spacers compared to nebulisers. Studies looking at home made spacers compared with commercial spacers also support this [9-12].

Of note, neither study looked at assessing the use of a home-made spacer device in cases of severe asthma. Severe asthma was defined in both studies using a points system encompassing 1 to 3 points for several similar objectively measured clinical parameters.

SUMMARY

The existing data are limited but provide sufficient evidence to recommend the use of home-made spacer devices in children with an acute exacerbation of asthma as it appears home-made spacer devices with MDIs are as effective as nebulisers in the delivery of salbutamol in children with mild to moderate asthma. The safety of a home-made spacer device has been looked at in these studies and appears to be adequate. They may indeed offer a lower rate of side effects, although the lower dosing required may, in part, explain this. Further studies with larger numbers are required to further define these recommendations.

These recommendations carry the following limitations:

- Given the lack of current evidence, recommendations cannot be made for similar use in severe exacerbations of asthma.
- There are insufficient data in children who cannot use a mouthpiece (generally less than 4 years of age). In these children limited data suggests some form of mask would be required with a home made spacer although this has not been well tested.
- The spacer should be a 500 ml litre plastic container and be regularly rinsed in detergent (or soap and water) and allowed to dry.

Further controlled trials are needed, especially for young children. These trials should precisely define the type of spacer, method of actuation/breathing recommended, the dose administered and washing practice. A more detailed systematic review focussing on the efficacy of home-made spacers compared with commercial spacers would also be warranted, given further evidence that has not yet been analysed completely here [15-20].

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