Received: 23 May 2020 | Revised: 10 October 2020 | Accepted: 13 October 2020

DOI: 10.1002/ppul.25123

ORIGINAL ARTICLE: ASTHMA

PEDIATRIC PULMONOLOGY WILEY

# Homemade valved holding chambers for children with airway hyperresponsiveness: A randomized crossover trial

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**Funding information**
Routine to Research Fund, Faculty of Medicine, Ramathibodi Hospital, Mahidol University

## Abstract

**Background:** During the COVID-19 pandemic, a metered-dose inhaler (MDI) with a valved holding chamber (VHC) is a preferred route of bronchodilator delivery. We have developed a new homemade VHC, made of a paper coffee cup, and a drinking water bottle. This study was conducted to compare the bronchodilator response in children with airway hyperresponsiveness after the use of our homemade VHC and that of a standard commercial one.

**Methods:** In a randomized, two-period, two-sequence crossover trial, we recruited 20 children, aged 6-15 years, who had a greater than 12% increase in $FEV_1$ after inhaled salbutamol. They were randomized into Group A and B. Group A used our VHC on the first day and Aerochamber® on the second day. Group B used the same VHCs but in alternate sequence. Spirometries were performed before and after 400 μg of salbutamol, MDI was administered via those VHCs.

**Results:** Baseline demographic data and spirometric values did not have statistically significant differences between group A and B and between the first and second day ($p > .05$). After giving salbutamol MDI, both VHCs produced significant increases in FVC, $FEV_1$, and $FEF_{25-75\%}$ ($p < .005$). The improvement in $FEV_1$ did not significantly differ between our homemade VHC and Aerochamber® ($p > .05$).

**Conclusion:** Our homemade VHC is effective for an MDI bronchodilator delivery. Since it is very cheap and easy to make, it may be used as a disposable device to minimize airborne transmission especially when commercial VHC is not available.

KEYWORDS

asthma, children, homemade, metered dose inhaler, spacer, valved holding chamber

## 1 | INTRODUCTION

The COVID-19 pandemic represents a massive global health crisis.[1] Recent evidence shows that this virus can also spread via airborne transmission.[2] Therefore nebulization which generates aerosols should be prohibited because of its potential to generate a high volume of respiratory aerosols that may be propelled over a longer distance. It is safest to minimize nebulized treatments in confirmed or suspected COVID-19 patients with increased risks of COVID-19 contamination. For this reason, if a bronchodilator is required, a metered-dose inhaler (MDI) with a spacer or valved holding chamber (VHC) is preferred.[3,4]

**Abbreviations:** $FEV_1$, forced expiratory volume in 1 s; $FEF_{25-75\%}$, forced mid-expiratory flow between 25% and 75% of forced vital capacity; FVC, forced vital capacity; MDI, metered dose inhaler; VHC, valved holding chamber.

  

Spacers and VHCs were developed to reduce the need for coordination of MDI actuation with inspiration[5] and decrease oropharyngeal deposition, which also decreases potential side effects of inhaled corticosteroids such as candidiasis and dysphonia.[6] Although the term "spacer" and "VHC" are frequently used interchangeably but they are not exactly the same. VHCs are special spacers manufactured with one-way valves, which regulate inspiratory flow and prevent exhaled gas with moisture into the spacer. Additional advantages of VHC over spacers include avoidance of leaking of the aerosol from the spacer and prevention of dilution of the aerosolized drug in the spacer.[7]

A Cochrane review of 10 randomized controlled trials comparing MDI with nebulizers showed that MDI with VHC produced outcomes that were at least equivalent to nebulizer delivery.[8] Another study showed that in children with severe asthma exacerbations MDI with VHC was more effective than by nebulizers.[9] When a pediatric hospital implemented the conversion from small volume nebulizers to MDIs with VHCs to administer beta-agonizts in the treatment of acute asthma exacerbations in children at the emergency room and inpatient wards, the number of asthma admissions did not change and the number of re-attendances for unresolved asthma symptoms within 72 h decreased.[10] Although the efficacy of non-valved spacers was demonstrated to be comparable to that of VHCs,[11] many experts still recommend using VHCs to deliver bronchodilators from MDIs.[3,5,13]

Due to high cost, lack of reimbursement, and availability of commercial VHCs, a variety of homemade spacers have been implemented with the use of plastic cold-drink bottles, plastic mineral water bottles, polystyrene cups, plastic zip-up bags, cardboard tubes, empty plastic saline solution bottles, and paper spacers.[14] Their efficacies have been tested and demonstrated the improvements in symptoms or lung function of patients with asthma. The degree of improvement did not differ significantly when comparing those homemade spacers with nebulizers or commercial VHCs.[14] Unfortunately, none of these homemade spacers have combined with one-way valves.

Our team have developed a new homemade VHC using a clear drinking water bottle and a paper coffee cup that costs less than one dollar. It may be a perfect substitute for a standard commercial VHC and can be easily disposed of.

The aim of this study was to compare the bronchodilator response in children with airway hyperresponsiveness when we used salbutamol MDI attached to our homemade VHC as against the response obtained when salbutamol MDI was attached to a standard commercial VHC.

## 2 | METHODS

### 2.1 | Construction of the homemade VHC

Prepare the following items: a paper coffee cup (200 ml in volume, bottom diameter 50 mm, brim diameter 70 mm), a drinking water bottle (350 ml in volume, bottom diameter 60 mm, orifice diameter 25 mm), a grocery plastic bag, a ruler, a paper cutter and a sellotape. Draw a small $1 \times 1$ cm$^2$ 2–3 cm below the brim of the cup and another one at the bottom of the cup. Make two holes by cutting along the two squares. From the grocery plastic bag cut two pieces of flap slightly larger than the holes. Outside the cup tape one piece over the hole near the edge of the cup. This will serve as the exhalation valve. Inside the cup tape the second piece over the bottom hole to create the inhalation valve. The first flap will open when breathing out while the second one opens when breathing in. Make a slit of 1 cm down the cup's edge and place it tightly over the nose. Breathe in and out to test the valves. Soak the water bottle in detergent (dishwashing liquid) to avoid electrostatically and leave to dry. Cut the bottom of the water bottle to create a 15 cm long chamber and place it tightly over the cup. Unscrew the bottle cap and place the MDI over it and use it as a VHC. The homemade VHC with a total volume of 395 ml that is ready to use is shown in Figure 1. Watch the video clip how to make the VHC at https://youtu.be/V2NmwzmRQvk.

### 2.2 | Study populations

This study was conducted from May 2017 to December 2019. We recruited children, aged 6–15 years, who performed spirometries at

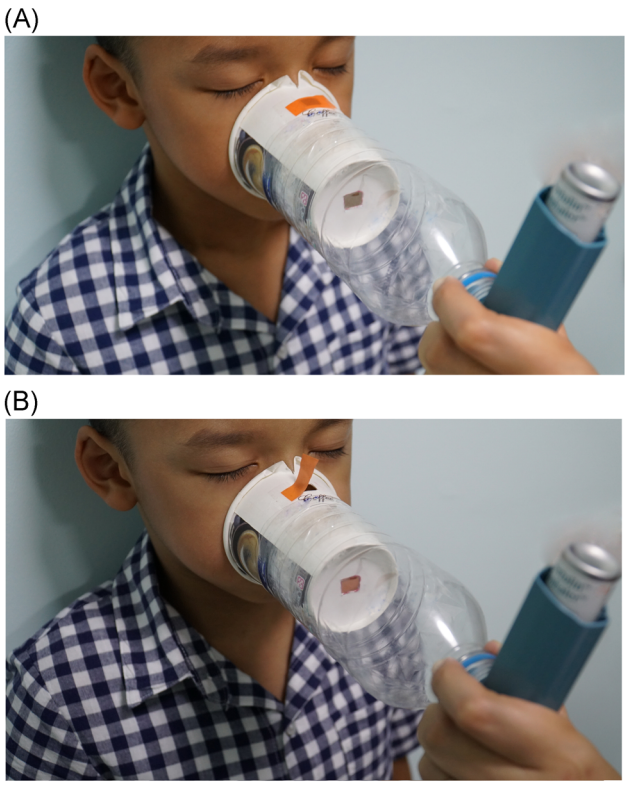


**FIGURE 1** A child using a homemade valved holding chamber (VHC). (A) Inhalation. (B) Exhalation. Parental consent was obtained for publication of this figure [Color figure can be viewed at wileyonlinelibrary.com]

the Pediatric Chest Outpatient Clinic at Ramathibodi Hospital, Bangkok, Thailand, who showed an increase of 12% or more in forced expiratory volume in 1 s ($FEV_1$) following administration of 400 μg of salbutamol MDI. We excluded the children, who did not pass the acceptable and reproducible criteria of spirometric forced expiratory maneuvers[12] or who have had an acute asthma exacerbation during the preceding 6 weeks, or whose breathing effort was not strong enough to see the movement of the exhalation valve. All parents or guardians of the children provided their informed consent before enrollment in the study. The study was approved by the Committee on Human Rights Related to Research Involving Human Subjects, Faculty of Medicine, Ramathibodi Hospital, Mahidol University. No. MURA2016/260.

## 2.3 | Study design

The study was conducted as a prospective randomized, two-period, two-sequence crossover design. The two-period was separated by 24-h washout period to eliminate the effect of the inhaled bronchodilator delivered on the first period. Children were randomly assigned following simple randomization procedures (computerized random numbers) to one of two groups: Group A and Group B. Group A used the homemade VHC on the first day and Aerochamber Plus Flow-Vu® with multiple mask sizes (Trudell Medical International, London, Ontario, Canada) on the second day. Group B used Aerochamber® on the first day and the new VHC on the second day. The diagram of our study design is shown in Figure 2.

Demographic data of the recruited children were recorded. We informed all recruited children to stop using salbutamol and other short-acting bronchodilators for at least 6 h, and to stop using the long-acting bronchodilators for at least 24 h before performing spirometries. Inhaled corticosteroids and leukotriene antagonists were not stopped.

## 2.4 | Spirometry and administration of salbutamol

Spirometry (Viasys Healthcare Flowscreen Spirometer, California, USA) was performed with the child in a standing position and wearing a nose clip. All performances fulfilled the criteria for acceptability and reproducibility of the American Thoracic Society and the European Respiratory Society.[15] We used the reference equations provided by the Global Lung Function Initiative (GLI) Network[16] to calculate percent predicted $FEV_1$. Each child performed spirometry at baseline before receiving 4 puffs of salbutamol MDI (Ventolin®, 100 μg/puff; GlaxoSmithKline, Boronia, Australia).

For the administration of salbutamol, children were told to breathe at tidal volume for 10 breaths after each puff. The MDI was shaken between each dose. Repeat doses were delivered 30 s after the previous one. Four puffs were delivered to achieve 400 μg of salbutamol. A good seal between the child's face and a paper cup of the homemade VHC or a face mask of Aerochamber® was ensured by seeing the movement of the exhalation valve or Flow-Vu indicator respectively. Post-bronchodilator spirometry was carried out in the same manner as baseline spirometry 15 min after salbutamol administration. The technician who performed spirometry was blinded to what type of VHC being used.

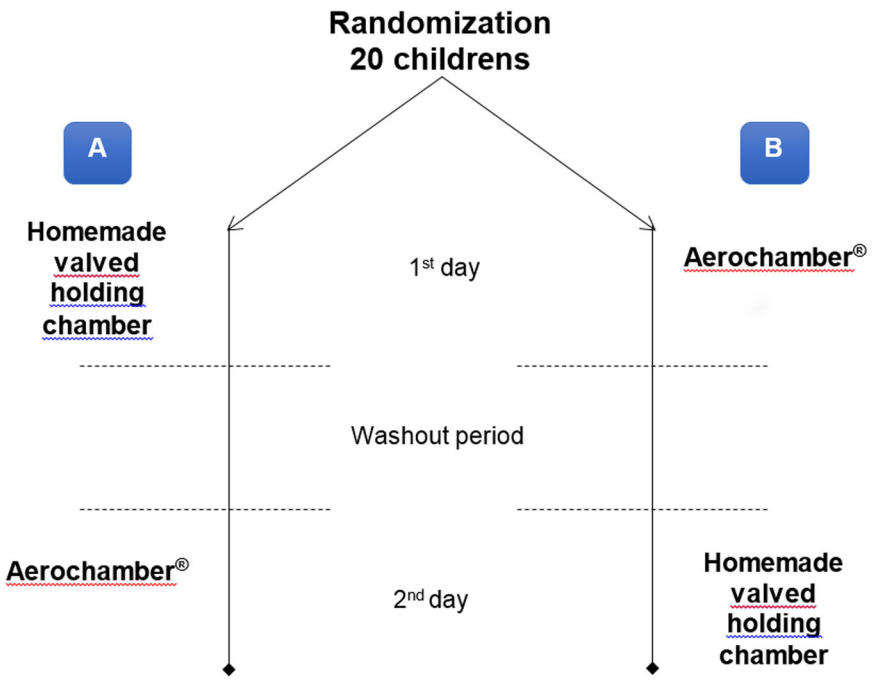


**FIGURE 2** Crossover trial with two treatment arms A and B separated by a 24 h washout period [Color figure can be viewed at wileyonlinelibrary.com]

## 2.5 | Statistical analysis

The sample size was determined by power analysis (power = 0.8, significance level = .05) using the G*Power Program.[17] An effect size of 0.7 based on the study conducted by Rodriguez-Martinez et al.[11] Approximately 5% was added to the calculated 19 children to compensate for incomplete data, bringing the final sample size to 20 children.

Continuous variables are presented as mean ± SD. Categorical variables are presented as percentage. The comparisons between the demographic data of Group A versus B, spirometric parameters measured before versus after bronchodilator inhalation, spirometric parameters measured on the first versus the second days, and the percent increase in $FEV_1$ above baseline when using the homemade VHC versus that of Aerochamber® were conducted using the paired *t*-test or independent *t*-test, or $\chi 2$ independence test, as appropriate. All analyses were conducted by using SPSS for Windows version 18.0. A *p* value of < .05 was considered statistically significant.

# 3 | RESULTS

Twenty children met the inclusion criteria. None were excluded. Therefore 20 children were randomized into two groups; 10 in Group A and 10 in Group B. Demographic characteristics and baseline spirometric parameters is shown in Table 1.

The demographic data and the absolute spirometric values at baseline on the first day and the second day did not have statistical significance between Group A and Group B. In addition, there were no significant differences between baseline spirometric indices (FVC, $FEV_1$, $FEF_{25-75\%}$) of the first day and the second day suggesting that the one-day washout period was sufficient. Since the carryover effect was not present, we used the spirometric data of Group A and B obtained in the two study days to determine the magnitude of the change in FVC, $FEV_1$ and $FEF_{25-75\%}$ comparing between the two VHCs as shown in Table 2.

Both VHCs produced significant increases in FVC, $FEV_1$, and $FEF_{25-75\%}$ after giving bronchodilator (paired *t*-test, $p < .005$). Percent increases in all parameters did not show statistical differences between the two VHCs (independent t-test, $p > .05$). The proportion of children who had a positive post-bronchodilator response (a cutoff point ≥12%)[18] with the use of the homemade VHC was similar to that of those who used Aerochamber® (6/20 vs. 6/20, $\chi 2$ independence test, $p = 1.0$). In addition, both VHCs showed significant increases in $FEV_1$ percent predicted after bronchodilator administration (paired *t*-test, $p < .005$). And the degree of improvement did not differ between both VHCs (independent *t*-test, $p > .05$) as shown in Figure 3.

# 4 | DISCUSSION

In the present crossover trial, our homemade VHC yielded a similar bronchodilator response to a standard commercial VHC (Aerochamber®) in children with airway hyperresponsiveness. Both VHCs were effective as shown by significant increases in $FEV_1$ after administration of 400 μg of salbutamol MDI. Our study showed that the one-way valves on our homemade VHC were easy to open and close. All of the children participating in the study were able to breathe and show the movement of the valves; the youngest being 6 years old.

To our knowledge, this is the first study showing the effectiveness of a homemade VHC incorporated with two one-way valves. The material used to make the VHC is readily available in every home. A paper coffee cup is selected because it is relatively nonelectrostatic and easier to cut and make holes than a plastic cup. Zar et al. conducted a study using a 500-ml plastic bottle to make a spacer. They had to use a heated mold of steel wire to melt a hole at the base of the bottle. The hole must have the same size and shape as the mouthpiece of the MDI.[19] So Zar's spacer is a lot more complicated to make than ours. Another advantage is its quality to fit tightly and safely over the nose and mouth of the child by only making a short slit down the edge of the paper cup and place this slit over the nose bridge. The paper cup simulates a face mask of a commercial VHC. If the face mask fits well, it will minimize aerosol leakage into the environment and increase therapeutic aerosolized drug to the lungs.[20] Vilarinho et al. conducted a study using a saline bottle to make a spacer. They had to cover the cutting edge of the bottle with Band-Aid to soften the contact and prevent abrasions or other injuries to the child's face.[21] Contrary to Vilarinho's spacer, we do not need any other covering because the open round rim of the paper cup is soft and smooth.

The other essential part of our VHC is the drinking water bottle. We chose a drinking water bottle since it is clear and cylindrical like commercial VHC. When its base is cut out horizontally, the body of the bottle perfectly encases the coffee cup. After removing the cap from the bottle, the MDI actuator or mouthpiece is inserted into the orifice of the bottle. Typically the diameter of the actuator fits well with the orifice of the bottle, leaving a little gap that allows air to flow into the bottle when the patient inhales. Without this gap, the bottle would collapse during forceful inhalation. Since electrostatic charge from a plastic bottle can reduce drug delivery, we, therefore, eliminated the electrostatic charge by washing an empty bottle with detergent and water and air-dried which could reduce the electrostatic charge on the sidewalls and increase aerosol deposition to the lungs.[22] Another way to reduce the electrostatic charge inside the dry water bottle is to prime the bottle initially with 15 puffs of MDI medication.[23] This latter method is faster but more expensive than washing the bottle with soap and let it dry. In addition to electrostatic charge, the performance of each VHC may vary according to their size and volume. Theoretically, the VHC should ideally be 100–700 ml in volume and should provide a distance of ≥10 cm between the MDI and the patient's mouth.[5,24] So in this study we decided to use a drinking water bottle 350 ml in volume and cut it into 15 cm in length.

Rodriguez-Martinez et al. conducted a systematic review in 2008 comparing the bronchodilator response delivered through MDI using homemade spacers, to the use of commercial VHCs in children with

**TABLE 1** Demographic characteristics and baseline spirometric parameters

| | Total sample | Group A (n = 10) | Group B (n = 10) | *P*-value |
|---|---|---|---|---|
| Age (years) | 11.1 ± 3.37 (6-17) | 11.1 ± 3.64 (7-17) | 11.1 ± 3.03 (6-15) | .887 |
| Gender, M:F | 11:9 | 2:8 | 9:1 | .001 |
| Weight (kg) | 38.75 ± 20.59 | 39.4 ± 21.6 | 38.1 ± 20.67 | .896 |
| Height (cm) | 137.2 ± 16.88 | 137 ± 17.25 | 137.4 ± 17.43 | .953 |
| Current medications | | | | |
| Inhaled corticosteroids (*n*, %) | 11 (55%) | 6 (60%) | 5 (50%) | .591 |
| Long-acting bronchodilators + inhaled corticosteroids (*n*, %) | 9 (45%) | 4 (40%) | 5 (50%) | .678 |
| Leukotriene antagonists | 10 (50%) | 5 (50%) | 5 (50%) | .99 |
| Spirometry at baseline on the first day | | | | |
| FVC (L) | 1.82 ± 0.98 | 1.77 ± 0.84 | 1.87 ± 1.15 | .833 |
| FVC % predicted | 87.10 ± 20.76 | 87.45 ± 17.23 | 86.76 ± 24.75 | .949 |
| $FEV_1$ (L) | 1.50 ± 0.75 | 1.49 ± 0.75 | 1.48 ± 0.78 | .916 |
| $FEV_1$%predicted | 78.62 ± 18.54 | 81.12 ± 15.93 | 76.12 ± 21.41 | .583 |
| $FEV_1$/FVC ratio (%) | 0.84 ± 0.08 | 0.85 ± 0.07 | 0.81 ± 0.08 | .504 |
| $FEV_1$/FVC % predicted | 91.58 ± 8.42 | 92.77 ± 8.17 | 90.38 ± 8.93 | .653 |
| $FEF_{25-75\%}$ (L/s) | 1.53 ± 0.68 | 1.61 ± 0.79 | 1.45 ± 0.57 | .647 |
| $FEF_{25-75\%}$ % predicted | 62.13 ± 22.53 | 63.38 ± 20.83 | 60.87 ± 25.18 | .836 |
| Spirometry at baseline on the second day | | | | |
| FVC (L) | 1.86 ± 0.99 | 1.78 ± 0.77 | 1.94 ± 1.22 | .740 |
| FVC % predicted | 88.36 ± 22.34 | 88.84 ± 16.19 | 87.87 ± 28.11 | .928 |
| $FEV_1$ (L) | 1.55 ± 0.79 | 1.93 ± 1.21 | 1.59 ± 0.94 | .847 |
| $FEV_1$% predicted | 81.89 ± 20.77 | 82.47 ± 14.11 | 81.31 ± 26.67 | .902 |
| $FEV_1$/FVC ratio (%) | 0.85 ± 0.09 | 0.86 ± 0.09 | 0.85 ± 0.09 | .792 |
| $FEV_1$/FVC % predicted | 92.88 ± 9.16 | 92.98 ± 9.02 | 92.77 ± 9.79 | .970 |
| $FEF_{25-75\%}$ (L/s) | 1.67 ± 0.75 | 1.65 ± 0.68 | 1.68 ± 0.85 | .919 |
| $FEF_{25-75\%}$ % predicted | 68.17 ± 27.36 | 67.26 ± 24.27 | 69.09 ± 31.45 | .898 |

*Note*: Continuous data are presented as mean ± standard deviation, unless otherwise stated. Categorical data are *n* (%).
Abbreviations: $FEF_{25-75\%}$, forced mid-expiratory flow between 25% and 75% of forced vital capacity; $FEV_1$, forced expiratory volume in 1 s; FVC, forced vital capacity.

acute exacerbations of wheezing or asthma. In 6 trials with 658 participants included in their study, no significant differences in terms of clinical responses were demonstrated between the home-made spacers and commercial VHCs.[14] Aerochamber® was used as a reference of commercial VHCs in 4 out of the 6 trials. In this current study, we also used Aerochamber® as a reference not only because it is available in our country but it also has considerably scientific data especially in young children.[6,25,26] The findings of our study are

**TABLE 2** Comparison of the spirometric parameters between before and after salbutamol administration through our homemade VHC and Aerochamber®

| | Homemade VHC (*n* = 20) | | | Aerochamber® (*n* = 20) | | |
|---|---|---|---|---|---|---|
| | Before | After | Change (%) | Before | After | Change (%) |
| FVC (L) | 1.85 ± 1.02 | 1.94 ± 1.05* | 5.1 ± 5.71 | 1.82 ± 0.95 | 1.89 ± 0.94* | 4.85 ± 5.11 |
| $FEV_1$ (L) | 1.55 ± 0.83 | 1.68 ± 0.90* | 8.2 ± 5.73 | 1.50 ± 0.71 | 1.62 ± 0.74* | 9.10 ± 6.12 |
| $FEF_{25-75\%}$(L/s) | 1.65 ± 0.8 | 1.99 ± 1.01* | 22 ± 2.34 | 1.55 ± 0.62 | 1.81 ± 0.72* | 18 ± 4.34 |

*Note*: Continuous data are presented as mean ± standard deviation.
Abbreviations: $FEF_{25-75\%}$, forced mid-expiratory flow between 25% and 75% of forced vital capacity; VHC, valved holding chamber; $FEV_1$, forced expiratory volume in 1 s; FVC, forced vital capacity.
*$p < .005$ when comparing between before and after salbutamol administration.

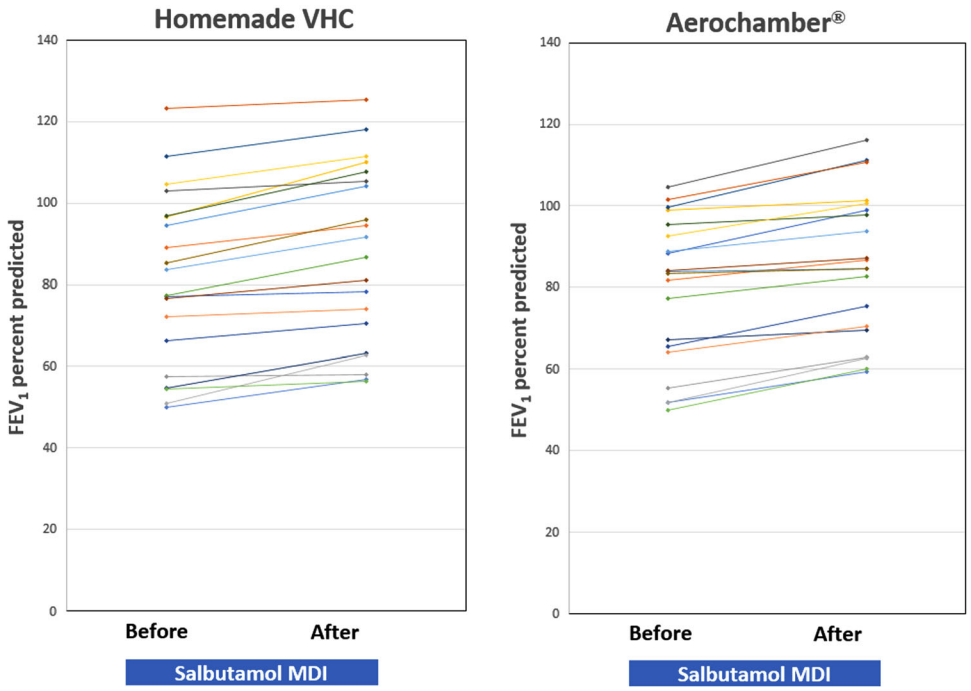


**FIGURE 3** FEV1% predicted before and 15 min after salbutamol administration via the homemade valved holding chamber (VHC) versus Aerochamber®. FEV, forced expiratory volume [Color figure can be viewed at wileyonlinelibrary.com]

consistent with those previously reported. But we did not measure the clinical outcomes. Only the spirometric parameters before and after bronchodilators were used for comparison. $FEV_1$ were increased significantly after bronchodilators delivered through either our VHC or Aerochamber® with the similar level of improvement. Since our study design aimed to compare our VHC with a commercial VHC, we could not address whether or not our VHC has more efficacy over the other homemade spacers without one-way valves. The long-term performance, clinical efficacy, aerosol delivery, and deposition of our VHC needs further studies.

There are some limitations to our VHC. The most difficult step to assemble the VHC is when we have to tape a piece of the flap over the bottom hole inside the coffee cup to create the inhalation valve. If the flap is too large or is not taped over the hole appropriately, the inhalation valve will not function well. The presence of the one-way valves may limit their use in small infants who have shallow breathing. Their breathing effort may be too weak to open the valves. Reginato et al[27] showed that approximately 20% of infants under 2 years of age were unable to open the one-way valve of various VHCs during their inspiratory cycles. Herbes et al.[28] found that more than half of the newborns were unable to generate an inspiratory flow capable of opening the one-way valve of a VHC, even when using an appropriate VHC and face mask. Therefore we would suggest observing the movement of the valves first. If the valves do not move with respirations even though the cup fits well without leakage, it is not suitable to use this homemade VHC in that patient. The second limitation of our VHC is that it is not as durable as commercial VHCs. The paper cup is easily damaged and needs to be replaced. The part of the water bottle is more durable and lasts much longer than the coffee cup. Although the water bottle can be washed with detergent, the paper cup cannot endure the same use. The valves made of tiny thin plastic cut from a disposable grocery shopping bag can be damaged when the cup is washed or wiped. So we recommend the cup to be air-dried after use. Since the coffee cup with one-way valves is very cheap and easy to make, frequent replacement is recommended. Our VHC may be considered as an alternative disposable device that parents can make easily and cheaply at home.

During the COVID-19 pandemic, nebulized bronchodilators for presumptive or confirmed COVID-19 patients may not be safe due to the generation of aerosols, which increases the risk that respiratory droplets will remain in the air and spread the virus. Bronchodilator delivery via MDI with VHC instead of nebulization is strongly recommended.[3,4,12] In addition, the VHC should not be shared to prevent the spreading of viruses. Therefore the VHCs are considered an essential accessory device in all hospitals in the face of COVID-19. Our homemade VHC should be an ideal solution to this problem. It is a lot cheaper than any other commercial VHCs. It is effective to deliver the bronchodilators and very easy to make. Since it is not durable, we would suggest to use it as a disposable medical device for an individual patient. For adult patients, our VHC can be enlarged by using larger sizes of a coffee cups and water bottles. Additional research may be needed to determine its efficacy in adults with asthma in the future.

In conclusion, a homemade VHC is a promising alternative option for a medical device for use with an MDI medication. It is made from a paper coffee cup and a drinking water bottle which costs less than

one dollar. To make this VHC is easy and fast. The coffee cup seals over the nose and mouth simulating a face mask. The movement of valves with respiration reassures medication delivery to the lungs. It is effective as shown by significant bronchodilator response. Due to its low-cost, this homemade VHC can be used as a disposable medical device for any patients, with or without COVID-19 infection, who suffer from bronchospasm, especially in developing countries where commercial VHCs are not reachable.

## ACKNOWLEDGMENTS

The authors would like to pay respect to Professor Allan Coates for his kind advice and encouragement towards our work on this homemade VHC. Likewise, we thank to M.L. Sirina Jittalan for her editorial assistance, Harutai Kamalaporn, MD, Teeradej Kuptanon, MD, and Thitida Chaisupamongkollarp for valuable suggestions, and also Kamonrat Kittipimpanon for the statistical analysis.

## CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

## AUTHOR CONTRIBUTIONS

*Study conception and design:* Kesanee Chaicoming and Aroonwan Preutthipan. *Developing the valved holding chamber*: Anusorn Adirekkittikun and Kesanee Chaicoming. *Acquisition of data*: Kesanee Chaicoming and Malinee Nugboon. *Analysis and interpretation of data*: Kesanee Chaicoming and Aroonwan Preutthipan. *Drafting of manuscript*: Kesanee Chaicoming and Aroonwan Preutthipan. *Critical revision*: Aroonwan Preutthipan.

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

**How to cite this article:** Chaicoming K, Preutthipan A, Adirekkittikun A, Nugboon M. Homemade valved holding chambers for children with airway hyperresponsiveness: a randomized crossover trial. *Pediatric Pulmonology*. 2021;56:49–56. https://doi.org/10.1002/ppul.25123