

# Homemade valved holding chambers for children with airway hyperresponsiveness

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## Abstract

**Background:** During 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 design, we recruited 20 children, aged 6-15 years, who had greater than 12% increase in FEV1 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 microgram 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 ( $P > 0.05$ ). After giving salbutamol MDI, both VHCs produced significant increases in FVC, FEV1 and FEF25-75% ( $P < 0.005$ ). The improvement in FEV1 did not significantly differ between our homemade VHC and Aerochamber® ( $P > 0.05$ ). **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 are not available.

## KEYWORDS:

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

## 1. Introduction

COVID-19 pandemic is the most serious global health crisis in this century which impacts people around the world, like the World War III. COVID-19 virus is primarily transmitted between people through respiratory droplets and contact routes. Recent evidence shows that this virus can also spread via airborne transmission.<sup>1</sup> 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. For this reason if a bronchodilator is required, a metered dose inhaler (MDI) with a spacer or valved holding chamber (VHC) is preferred.<sup>2,3</sup>

Spacers and VHCs were developed to eliminate the need for co-ordination of MDI actuation with inspiration and decreases oropharyngeal deposition, which also decrease potential side effects of inhaled corticosteroids such as candidiasis and dysphonia.<sup>4</sup> 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, prevention of dilution of the aerosolized drug in the spacer, and elimination of the cold-Freon effect.<sup>5</sup>

In children with severe asthma exacerbations administration of bronchodilators by MDI with VHCs and face masks was found to be more effective than by nebulizers.<sup>6</sup> When a pediatric hospital implemented the conversion from small volume nebulizers to MDIs with VHCs to administer beta-agonists 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 hours decreased.<sup>7</sup> Although a number of studies showed that the efficacy of non-valved spacers were comparable to that of VHCs,<sup>8</sup> many experts still recommend using VHCs to deliver bronchodilators from MDIs.<sup>2,9-11</sup>

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.<sup>12</sup> 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.<sup>12</sup> 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 which are common household waste products. The water bottle acts like a chamber while the paper cup acts as a facemask. On the cup we made two one-way valves using pieces of plastic cut from a grocery shopping bag. Since our VHC costs less than one dollar, it is 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. How to make a homemade valved holding chamber (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 1x1 cm square 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 electrostatic 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 that is ready to use is shown in Figure 1. Watch the video clip how to make the VHC at <https://youtu.be/V2NmwmRQvk>.

### 2.2. Study populations

We recruited children, aged 6-15 years, who performed spirometries at the Pediatric Chest Outpatient Clinic at Ramathibodi Hospital, Bangkok, Thailand, who showed an increase of 12% or more in forced expiratory volume in 1 second (FEV<sub>1</sub>) following administration of 400 microgram of salbutamol MDI. We excluded the children, who did not pass the acceptable and reproducible criteria of spirometric forced expiratory maneuvers,<sup>13</sup> or who has 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 prior to 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 randomized, two-period, two-sequence crossover design. The two period was separated by 24-hour washout period. Children were randomized into two groups, A and B. Group A used the homemade VHC on the first day and Aerochamber Plus Flow-Vu<sup>®</sup> with medium mask for children aged 1-5 years (Trudell Medical International, London, Ontario, Canada) on the second day. Group B used Aerochamber<sup>®</sup> 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 hours, and to stop using the long acting bronchodilators for at least 24 hours prior to performing spirometries. Inhaled corticosteroids and leukotriene antagonists were not stopped.

### 2.4. Spirometry and administration of salbutamol

Spirometry (Viasys Healthcare FlowScreen Spirometer, California, United States) was performed with the child in 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.<sup>13</sup> We used the reference equations proposed by Polgar & Promadhat<sup>14</sup> to calculate percent predicted FEV<sub>1</sub>. Each child performed spirometry at baseline prior to receiving 4 puffs of salbutamol MDI (Ventolin<sup>®</sup>, 100 microgram/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 seconds after the previous one. Four puffs were delivered to achieve 400 microgram of salbutamol. A good seal between the child's face and a paper cup of the homemade VHC or a face mask of Aerochamber<sup>®</sup> was ensured by seeing the movement of exhalation valve or Flow-Vu indicator respectively. Post-bronchodilator spirometry was carried out in the same manner as baseline spirometry 15 minutes after salbutamol administration. The technician who performed spirometry did not know the type of VHC being used.

### 2.5. Statistical analysis

Continuous variables are presented as mean + SD. Categorical variables are presented as percentage. The comparisons between the demographic data of Group A *vs.* B, spirometric parameters measured before *vs.* after bronchodilator inhalation, spirometric parameters measured on the first *vs.* the second days, and the percent increase in FEV<sub>1</sub> above baseline when using the homemade VHC *vs.* that of Aerochamber<sup>®</sup> were conducted using the paired t-test or independent t-test, or chi-square independence test, as appropriate. All analyses were conducted by using SPSS for Windows version 18.0. A *P* value of < 0.05 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 youngest child was 6 years old.

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<sub>1</sub>, FEF<sub>25-75%</sub>) 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<sub>1</sub> and FEF<sub>25-75%</sub> comparing between the two VHCs as shown in Table 2.

Both VHCs produced significantly increases in FVC, FEV<sub>1</sub> and FEF<sub>25-75%</sub> after giving bronchodilator (paired t-test, *P* < 0.005). Percent increases in all parameters did not show statistically differences between the two VHCs (independent t-test, *P* > 0.05). The proportion of children who had a positive post bronchodilator

response (a cutoff point  $> 12\%$ )<sup>13</sup> with the use of the homemade VHC was similar to that of those who used Aerochamber<sup>®</sup> (6/20 vs. 6/20, chi-square independence test,  $P = 1.0$ ). In addition, both VHCs showed significant increases in FEV<sub>1</sub> percent predicted after bronchodilator administration (paired t-test,  $P < 0.005$ ). And the degree of improvement did not differ between both VHCs (independent t-test,  $P > 0.05$ ) 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<sup>®</sup>) in children with airway hyperresponsiveness. Both VHCs were effective as shown by significant increases in FEV<sub>1</sub> after administration of 400 microgram 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 are 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 mould 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.<sup>15</sup> 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.<sup>16</sup> 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.<sup>17</sup> 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 which 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 electrostatic charge on the side walls and increase aerosol deposition to the lungs.<sup>18</sup> Another way to reduce the electrostatic charge inside the dry water bottle is to prime the bottle initially with 15 puffs of MDI medication.<sup>19</sup> This later method is faster but more expensive than washing the bottle with soap and let it dry. In addition to electrostatic charge, 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.<sup>9,20</sup> 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 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 homemade spacers and commercial VHCs.<sup>12</sup> Aerochamber<sup>®</sup> was used as a reference of commercial VHCs in 4 out of the 6 trials. In this current study we also used Aerochamber<sup>®</sup> as a reference not only because it is available in our country but it also has considerably scientific data especially in young children.<sup>4,21,22</sup> The findings of our study are 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<sub>1</sub> were increased significantly after bronchodilators delivered through either our VHC or Aerochamber<sup>®</sup> 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 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 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.<sup>23</sup> Herbes et al 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.<sup>24</sup> Therefore we would suggest to observe 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. 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 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.<sup>2,3,10</sup> In addition, the VHC should not be shared in order to prevent the spreading of virus. 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 solutions 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 coffee cup and water bottle. 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 of 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. This VHC would be most helpful in COVID-19 crisis when nebulization is prohibited due to concerns that nebulizers may help disseminate COVID-19 to other patients and to physicians, nurses and other personal. 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.

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### **Conflict of interests**

The authors declare that there are no conflict of interests.

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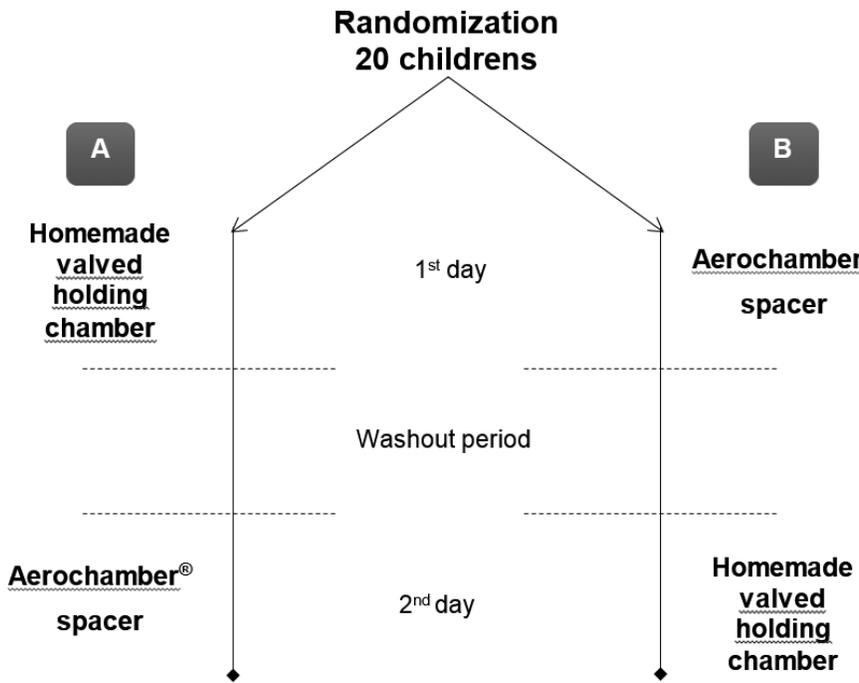
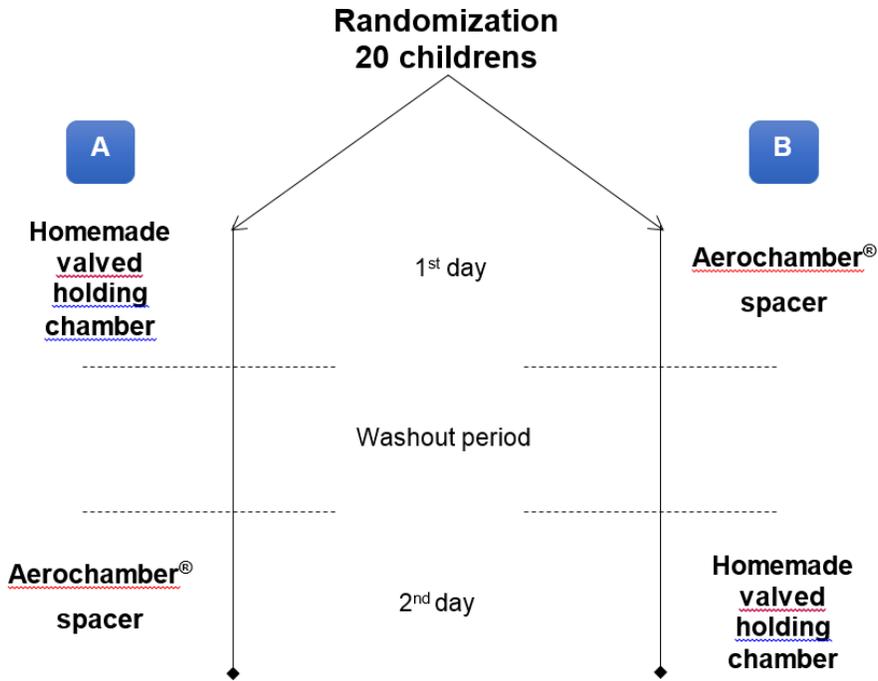
TABLE 1 Demographic characteristics and baseline spirometric parameters.docx available at <https://authorea.com/users/326387/articles/454235-homemade-valved-holding-chambers-for-children-with-airway-hyperresponsiveness>

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TABLE 2 Comparison of the spirometric parameters.docx available at <https://authorea.com/users/326387/articles/454235-homemade-valved-holding-chambers-for-children-with-airway-hyperresponsiveness>







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