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The Effect of Priming new Plastic Spacers with 20 Puffs Salbutamol on Bronchodilator Response in Asthmatic Children

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ABSTRACT

The static charge on the plastic body of spacers attracts drug aerosols, reducing the drug available for inhalation from plastic spacers. Some instructions exist to decrease the electric charge on plastic spacers, such as priming them with salbutamol (20 puffs) before use. This study investigates whether priming plastic spacer devices with this method can improve the bronchodilator test result.

This study included children with stable mild to moderate asthma. All subjects underwent two pulmonary function tests to evaluate their bronchodilator response on separate days at 24-48 hours intervals. On each day, spirometry was performed at the baseline and 15 min after inhalation of four puffs of salbutamol (100 μg/puff) through either a primed or a new spacer. The change in forced expiratory volume in the first second (FEV1) after inhaling salbutamol was the primary outcome measure.

When the patients used a new spacer, the mean baseline FEV1 (% predicted) and FEV1/FVC (forced vital capacity) were 89.56±11.95 and 86.17±6.87, respectively. However, the mean increase in FEV1 from the baseline was 10.87±8.99 in this group. On the other hand, with the primed spacer, the respective mean baseline FEV1 and FEV1/FVC values were 89.41±12.14 and 85.49±6.76, while it increased by 12.1±11.01 after salbutamol inhalation. There were no significant differences between the techniques regarding the variation in FEV1 before and after bronchodilator use via a new spacer or primed spacer.

Priming new plastic spacers with 20 puffs of salbutamol did not cause additional bronchodilation in asthmatic children, suggesting this practice is inefficient in clinics.

Keywords: Bronchodilator response; Paediatric asthma; Plastic spacers; Salbutamol

INTRODUCTION

Aerosol-based drug therapy is the best and most effective treatment for asthma.[1] Pressurized metered-dose inhalers (pMDIs) are still the most common devices for delivering aerosol medication with low cost, portability, effectiveness, and relatively simple application without any required drug preparation.[2] However, they need hand-breath coordination, for which valved holding chambers (VHCs) are widely used to make them easier to use and reduce the deposition of

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large drug particles in the oropharynx.[3] Most VHCs are made of plastic and have an internal electrostatic charge that attracts drug aerosols to their walls. This will significantly reduce the drug aerosol available for inhalation from plastic spacers and the aerosol half-life in the spacer.[4] Two methods have been suggested to reduce the electrostatic charge on plastic spacers: washing them with ionic detergents and then air drying them or priming the chamber by administering multiple actuations of the drug.[5]

Multiple in vitro and in vivo studies demonstrate that drug delivery from VHCs is typically improved by pre-washing in a detergent solution followed by air-drying.[3-6] This method is more cost-effective than priming spacers with multiple doses of salbutamol. However, in emergency situations, it may not be possible to wash and dry spacers immediately. The second method is more practical for situations without the time and opportunity to do the first one. However, the clinical effect of multiple drug actuation has remained undetermined.

Accordingly, this study aims to investigate whether priming plastic spacer devices with salbutamol (20 puffs), as mentioned by some studies and guidelines,[1] is under question and may improve the bronchodilator test results compared with the usual technique (application of a new spacer).

MATERIALS AND METHODS

Twenty-six subjects diagnosed with mild to moderate asthma according to GINA criteria (age range: 7 to 15 years) were recruited from the outpatient Allergy and Clinical Immunology Clinic of Imam Ali Hospital, Karaj, Iran. All selected patients were familiar with spacer inhalations. The ethics committee approved the study protocol, and the patients or their parents signed the informed consent forms before participating in the study. We excluded patients with symptoms indicative of severe asthma, those who had an acute exacerbation, and if the baseline FEV1(Forced expiratory volume in the first second) at the second visit differed from that of the first visit by more than 10%.

The tests were performed between January 2017 and February 2018 in the Pulmonary Function Laboratory of Imam Ali Hospital, Karaj, Iran. All subjects underwent two pulmonary function tests evaluating their bronchodilator response on separate days with 24-48 hours intervals. On each day, spirometry was performed at the baseline and 15 minutes after inhalation of four puffs of salbutamol (100 μg/puff) through either a primed or a non-primed new spacer. Two new spacers were used for each patient. For priming the spacer, 20 single actuations were introduced into a new spacer with 5-second intervals between each actuation 20 minutes before starting the test. The pMDI was shaken between the actuation intervals.

The change in FEV1 after salbutamol inhalation **(**Bronchodilator response) was considered as the primary outcome measure.

The patients stopped all short-acting bronchodilators at least 8 hours and long-acting bronchodilators at least 48 hours before the study. All of the tests were performed in the morning. The children used a nose clip and were given detailed instructions on using the spacer. Polycarbonate nonvolumatic valved holding chamber devices (140 mL, DamYar; Fanava Teb Espadana Co, Isfahan, Iran) were used in this study. Each valved holding chamber used salbutamol 100 mg per dose of pMDIs (Ventalex HFA, Sina Daru, Iran).

Statistical Analysis

Paired t-test was used to evaluate the differences between bronchodilator responses with each spacer. Pearson's correlation was used to quantify the relationship between baseline parameters. SPSS version 15 was used for the statistical analysis, and a *p*-value of < 0.05 was taken as statistically significant.

RESULTS

As mentioned earlier, 26 participants were initially randomized into the study, but three children were excluded as the baseline FEV1 at the second visit differed by more than 10%. The mean age of the subjects was 9.8±2.65, ranging between 7 and 15 years. They comprised seven girls and 16 boys.

The severity of asthma was intermittent in 4, mild persistent in 10, and moderate persistent in 9 subjects. Also, 19 patients took regular inhaled corticosteroids (ICS) or inhaled corticosteroids + long-acting β-agonists (ICS+LABA).

When the patients used a new spacer, the mean baseline FEV1 (% predicted), FEV1/FVC (Forced vital capacity), and percentage change in FEV1 from the baseline were 89.56±11.95, 86.17±6.87, and 10.87±8.99, respectively. On the other hand, with the primed spacer, the values were 89.41±12.14,

85.49±6.76, and 12.1±11.01, respectively (Table 1).

There was a significant correlation between the two spirometry tests in terms of the baseline FEV1 (p<0.001, r=0.83), while there were no significant differences between the techniques in terms of the variation in FEV1 before and after bronchodilator use via a new spacer or primed spacer (p>0.05).

Table 1. Spirometry parameters in two groups

Group	FEV1, mean±standard deviation (range)	FEV1/FVC, mean±standard deviation (range)	% change in FEV1 mean ±standard deviation (range)
New spacer	89.56±11.95 (71-112)	86.17±6.87 (71-93)	1087±8.99 (0-35)
Primed spacer	89.41±12.14 (70-117)	85.49 ±6.76 (73-94)	12.1 ±11.01 (0-40)

FEV1: Forced expiratory volume in the first second; FVC: Forced vital capacity

DISCUSSION

The electric charge on the plastic body of spacers can diminish the availability of the drug to the lungs.[4] A study indicated that when electric charge did not exist on the body of spacers, 35% of salbutamol particles could reach the lungs. However, the level of these particles diminished to 10% using electrically charged spacers.[7]

'Priming' VHCs with 20 actuations of pMDI before use to coat the internal surfaces of spacers with a layer of surfactant has been reported to cause increased lung deposition of budesonide (up to 37.7%) as compared with unprimed spacers with 26.7% of aerosol lung deposition.[7] However, clinical evidence for this practice is less clear. Our results did not show the effectiveness of this method in the clinical setting. To the best of our knowledge, no reported study examines the effect of priming spacers with multiple actuations on the bronchodilator response via spirometry. Nevertheless, some studies have investigated the influence of reducing the electrostatic charge on the patients' bronchodilator response by pre-washing them in a detergent solution. Some of these studies indicated that antistatic treatment of spacers did not affect bronchodilator response, while others found a significant response.[8-10]

Dompeling et al, reported that changes in bronchodilation were insignificant in asthmatic children given salbutamol with either detergent-coated or non-coated spacers based on measuring peak expiratory flow (PEF). They reported a dose-dependent bronchodilator response not influenced by washing the spacer with detergent. They suggested that the dosages chosen for this study were already at the higher part of the dose-response curve in children.[8] Similarly, Barben et al, found no significant difference in FEV1 using detergent-coated or non-coated spacers in stable asthmatic children.[9]

On the contrary, Wildhaber et al, showed improved bronchodilator response in adults with asthma after using the spacer device, which was already washed with dish-washing detergent.[10] Accordingly, the provocation dose required to cause a clinically significant improvement in FEV_1 (a minimum increase of 10%) was significantly lower than when the detergent-treated spacer was used.

The absence of a significant difference in FEV1 variation in our study might be related to our patients performing spirometry under stable and disease-controlled conditions. Indeed, although most children had airway hyperresponsiveness and evident response to bronchodilators in previous spirometries and at the time of attacks, FEV1 level increased to levels close to the normal limit, and airway hyperresponsiveness diminished with the initiation of inhaled anti-inflammatory treatments and control of the disease. Therefore, if patients had been evaluated during the attack, the difference in salbutamol consumption techniques could have been more obvious. However, more investigations are required to draw firm conclusions, and we cannot rule out the need for priming the spacers in acute asthma attacks according to the current study results. Nevertheless, our results showed that this strategy might not improve drug effects in stable asthmatic children, and there is no need for priming the spacers in this condition.

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The strong point of our study is that the control group was the patients themselves under the same conditions. In this regard, the comparison of the two methods was accurate. Furthermore, to our knowledge, this was the first study to evaluate the response to bronchodilators by priming the spacer with multiple actuations.

Priming new plastic spacers with 20 puffs of salbutamol did not cause additional bronchodilation in asthmatic children, suggesting that this technique may not be effective enough in clinical practice.

STATEMENT OF ETHICS

The Ethics Committee of Alborz University of Medical Sciences approved this study (ethics code: IR.ABZUMS.REC.1395.42). Written informed consent was obtained from all participants. all methods were performed under the relevant guidelines and regulations

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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