



CLINICAL TRIAL PAPER

# Reversibility after inhaling salbutamol in different body postures in asthmatic children: A pilot study



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## KEYWORDS

Pediatric asthma;  
Reversibility;  
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## Summary

**Rationale:** Pulmonary medication is mostly delivered in the form of medical aerosols to minimize systemic side effects. A major drawback of inhaled medication is that the majority of inhaled particles impacts in the oropharynx at the sharp bend of the airway. Stretching the airway by a forward leaning body posture with the neck extended ("sniffing position") may improve pulmonary deposition and clinical effects.

**Methods:** 41 asthmatic children who were planned for standard reversibility testing at the pulmonary function lab, alternately inhaled 200 µgr salbutamol with an Autohaler<sup>®</sup> in the standard or in the forward leaning body posture. Forced Expiratory Volume in 1 s (FEV<sub>1</sub>), Forced Vital Capacity (FVC), Peak Expiratory Flow (PEF), Mean Expiratory Flow at 25% of vital capacity (MEF<sub>25</sub>) and Mean Expiratory Flow at 75% of vital capacity (MEF<sub>75</sub>) were analysed.

**Results:** The children in the forward leaning body posture group showed a significantly higher mean FEV<sub>1</sub> reversibility than the control group after inhalation of 200 µgr salbutamol (10.2% versus 4.1%,  $p = 0.019$ ). Additionally, mean MEF<sub>75</sub> was significantly more reversible in the forward leaning body posture group versus the standard body posture group (32.2% resp. 8.9%,  $p = 0.013$ ).

**Conclusion:** This pilot study showed a higher reversibility of FEV<sub>1</sub> and MEF<sub>75</sub> after inhaling salbutamol in a forward leaning body posture compared to the standard body posture in

**Abbreviations:** BAI, Breath Actuated Inhaler.

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asthmatic children. This suggests that pulmonary effects of salbutamol can be improved by inhaling in a forward leaning body posture with the neck extended. This effect is possibly due to a higher pulmonary deposition of salbutamol and should be confirmed in a randomized controlled trial.

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## Introduction

Inhaled bronchodilators are recommended as rescue medication for all children with asthma [1]. Deposition of inhaled medication in the upper airway can compromise deposition at the target area. This upper airway deposition is caused by the sharp angle between the pharynx and trachea [2,3]. In asthmatic children the loss of inhaled medication may even be greater as the upper airway is smaller and has a different geometry. Even with optimal inhalation via a breath actuated inhaler (BAI) 50–60% of the dose of beclomethasone dipropionate impacted in the oropharynx in children under the age of 12, as measured in a radio-labelling study [4]. In daily practice the inhalation technique is frequently less optimal leading to an even higher loss of medication [5].

Brandao et al. showed that inhaling nebulised bronchodilators in a forward leaning body posture during an asthma exacerbation in asthmatic young adults, led to a faster recovery of lung function compared to the conventional body posture [6]. They suggested that this could be caused by a higher pulmonary deposition of the nebulised medication in the forward leaning posture.

We hypothesized that stretching the bend in the upper airway during inhalation could improve the effect of salbutamol on lung function.

The aim of this study was to compare the reversibility of lung function in asthmatic children after a dose of 200 µgr salbutamol that was inhaled either in the forward leaning body posture with the neck extended, or in the standard body posture.

## Materials and methods

### Patients

Clinically stable patients aged 6 till 16 years old, with pediatrician diagnosed mild to moderate asthma, who underwent a planned spirometry in Medisch Spectrum Twente, Enschede from May to August 2013, participated in this prospective pilot study. Children were not allowed to use long acting bronchodilators 24 h before testing, or short acting bronchodilators 8 h before testing.

The medical ethical committee reviewed our study protocol and declared that our study did not meet the criteria necessary for an assessment by a medical ethical committee according to the Dutch law, because the children were not subjected to procedures deviating from the normal procedures. All children and parents received verbal information and their participation was voluntarily.

### Pulmonary function measurements

Spirometry was performed by standard pulmonary function tests before and after the administration of 200 µgr salbutamol, administered with an Autohaler®. All pulmonary function measurements – Forced Expiratory Volume in 1 s (FEV<sub>1</sub>), Forced Vital Capacity (FVC), Peak Expiratory Flow (PEF), Mean Expiratory Flow at 25% of vital capacity (MEF<sub>25</sub>) and Mean Expiratory Flow at 75% of vital capacity (MEF<sub>75</sub>) – were performed in the same standard upright body posture. Percentage of predicted baseline FEV<sub>1</sub> was measured with the aid of the Koopman formulas [7]. Reversibility was calculated as follows: (value after salbutamol – value at baseline)/value at baseline [8]. All spirometry measurements consisted of duplicated full flow volume loops, using standard ERS protocol [9]. The best values for all variables were used for analysis. Visual incentives such as blowing out candles or knocking down bowling pins were used to optimize spirometric effort.

### Inhalation technique

Patients inhaled alternately in the standard upright body posture described on the standardized checklists designed by the Dutch Asthma Foundation [10] or in the alternative body posture: a forward leaning body posture with the neck extended (Fig. 1).

The inhaled medication was administered to all children by the same investigator who did not perform the pulmonary function measurements. The pulmonary function technician was not blinded to the body posture during inhalation.

### Sample size calculation

No sample size calculation was performed, because this study was deemed a pilot study. This study was conducted between May 2013 and August 2013 (12 weeks). Results were analysed after the inclusion of 41 children.

### Statistical analyses

Data was expressed as mean values ± standard deviation (SD), and 95% Confidence Intervals (95CI), where appropriate, for normally distributed data, as median (Inter Quartile Range; IQR 25th–75th) for not normally distributed data or as numbers with corresponding percentages if nominal or ordinal. Continuous variables were visualised with histograms. When applicable, between-group comparison of continuous, normally distributed data was



**Figure 1** Standard and forward leaning body posture. 90° bent airway in standard body posture (left); stretched airway in forward leaning body posture with the neck extended ("sniffing" position) (middle); forward leaning posture (right).

performed using a t-test. In the case of not normally distributed data a Mann–Whitney U test was performed. Between-group comparison of nominal or ordinal variables was performed by Chi-square tests.

Best values of spirometry measurements were used for statistical calculations. Data was analyzed with SPSS® for Windows® version 15 (IBM, Chicago, IL, USA) analytical software. A two-sided value of  $P < 0.05$  was considered statistically significant.

## Results

Forty-one consecutive children, 6–16 years of age, 21 boys, participated in the study, none were excluded. Baseline characteristics did not significantly differ between the two body postures groups. There was a trend towards a younger median age ( $p = 0.109$ ), a better baseline  $FEV_1$  ( $p = 0.091$ , 95CI –1.3; 17.1) and a greater proportion of newly referred patients ( $p = 0.160$ ) in the standard body posture group. Table 1 summarizes the baseline characteristics of the two groups subdivided on body posture during inhalation.

## Spirometry

The children in the forward leaning body posture group showed a 10.2% reversibility in  $FEV_1$  after inhalation of 200 µgr salbutamol, while in the standard body posture group this was 4.1% ( $p = 0.019$ ). Mean  $MEF_{75}$  reversibility was 32.2% in the forward leaning group versus 8.9% in the standard body posture group ( $p = 0.013$ ). Reversibility in VC, PEF and  $MEF_{25}$  was numerically, but not significantly, higher in the forward leaning group as well (see Table 2).

## Discussion

This pilot study indicates a significantly higher reversibility of lung function expressed as  $FEV_1$  and  $MEF_{75}$  if 200 µgr salbutamol is inhaled in a forward leaning body posture, compared to the standard body posture in asthmatic children. These results suggest that a forward leaning body

posture can improve pulmonary effects of salbutamol, probably by a higher pulmonary deposition.

To our knowledge, this is the first study investigating the effect of a forward leaning body posture compared to the standard body posture during inhalation of salbutamol on lung function reversibility in clinically stable asthmatic children.

Our findings are in line with the study of Brandao et al. that showed a greater clinical effect of a forward leaning body posture compared to the conventional body posture during the inhalation of nebulised bronchodilators in young adults during an asthma exacerbation [6]. They suggested this difference was due to a higher pulmonary deposition of inhaled medication in the forward leaning body posture.

The significant higher reversibility of the  $FEV_1$  and  $MEF_{75}$  and not of the PEF, VC and  $MEF_{25}$  in the forward leaning body posture, as observed in our study, suggests mainly the conductive airways profited of the different body posture.

A potential limitation of this pilot study was the way we included the children into the study. Children were

**Table 1** Baseline characteristics subdivided on body posture during inhalation.

|                                           | Standard       | Forward leaning |
|-------------------------------------------|----------------|-----------------|
| Number of patients                        | 20             | 21              |
| Age, years                                | 9.0 (7.4–11.7) | 12.4 (8.3–13.8) |
| Boys                                      | 9 (45%)        | 12 (57%)        |
| First spirometry                          | 10 (50%)       | 6 (29%)         |
| $FEV_1$ baseline<br>(mean % of predicted) | 94.2% ± 13.5%  | 86.3% ± 15.5%   |
| Exacerbation <6<br>months prior to study  | 2 (10%)        | 2 (10%)         |
| Maintenance medication                    | 20 (100%)      | 17 (81%)        |

Data expressed as mean ± SD, median (IQR) or numbers (percentage).

$FEV_1$ : forced expiratory volume in 1 s, percentage of predicted based on the reference values of Koopman et al. [7].

Exacerbation was defined as hospital admission or use of systemic corticosteroids.

**Table 2** Change in pulmonary function after inhaling 200 µgr salbutamol in different body postures.

|                                 | Standard body posture | Forward leaning body posture | Difference (95%CI) | P value |
|---------------------------------|-----------------------|------------------------------|--------------------|---------|
| FEV <sub>1</sub> reversibility  | 4.1 (7.4)             | 10.2 (8.5)                   | −0.111; −0.011     | 0.019   |
| VC reversibility                | 0.8 (3.9)             | 2.2 (3.9)                    | −0.039; 0.010      | 0.241   |
| PEF reversibility               | 9.4 (14.7)            | 11.1 (16.3)                  | −0.116; 0.083      | 0.740   |
| MEF <sub>25</sub> reversibility | 9.9 (15.2)            | 18.3 (24.0)                  | −0.212; 0.045      | 0.194   |
| MEF <sub>75</sub> reversibility | 8.9 (30.5)            | 32.2 (25.8)                  | −0.414; −0.052     | 0.013   |

Data expressed as mean ± SD.

FEV<sub>1</sub>: Forced Expiratory Volume in 1 s, FVC: Forced Vital Capacity, PEF: Peak Expiratory Flow, MEF<sub>25</sub>: Mean Expiratory Flow at 25% of vital capacity, MEF<sub>75</sub>: Mean Expiratory Flow at 75% of vital capacity.

alternately included in the standard or the forward leaning body posture group, in order to exclude selection bias. However, there was an imbalance in experience with spirometry and baseline FEV<sub>1</sub>: 50% of the children in the standard body posture group performed their first spirometry versus 29% in the forward leaning group. The difference was not significant and all children performed technically appropriate spirometries. In contrast to a significant difference in reversibility of MEF<sub>75</sub> and FEV<sub>1</sub>, no significant difference in reversibility of PEF between the groups was observed, suggesting technique of performing spirometry was comparable between groups. An additional limitation was that the pulmonary function technician was not blinded to body posture during inhalation. These limitations could have resulted in bias, however, we regard the observed differences as clinically relevant.

We purposely chose a low dose of salbutamol so as to be on the steep slope of the dose response curve. Perhaps higher doses such as 400 µgr or 800 µgr salbutamol could be used to discover the top of the dose response curve.

Our observation suggests that inhaling in a forward leaning body posture improves medication delivery to the lower airways. A higher pulmonary deposition of inhaled medication may lead to a reduction in dose and consequently a reduction in side effects, especially when inhaling corticosteroids. Dubus et al. showed that approximately 60% of asthmatic children using beclomethasone dipropionate or budesonide reported local side effects such as coughing, hoarseness, dysphonia and oral candidiasis [11].

In the future, the effect of a forward leaning body posture during inhalation in asthmatic children should be assessed in a randomized controlled trial with different doses of salbutamol, preferably radio-labeled. Less impaction of inhaled medication in the upper airway may be more relevant for other medication than bronchodilators, such as corticosteroids and antibiotics.

## Conclusion

This pilot study showed a higher reversibility of FEV<sub>1</sub> and MEF<sub>75</sub> after inhaling salbutamol in a forward leaning body

posture compared to the standard body posture in asthmatic children. This suggests that pulmonary effects of salbutamol can be improved by inhaling in a forward leaning body posture with the neck extended, possibly due to a higher pulmonary deposition of salbutamol.

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