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The Bronchodilator Test on FEF 25%-75% in 34 Children and Adolescents with Asthma Sensitized and Non-Sensitized to House Dust Mites

Davisson do Sacramento de Lucena Tavares[1], Cyro Teixeira da Silva Junior[2*], Adriana Alvarez[1], Priscilla Filippo Alvim de Minas Santos[1], Patricia Siqueira Silva[1], Eduardo Vieira Ponte[3], Joeber Bernardo Soares de Souza[2], Selma Maria de Azevedo Sias[2]

[1]Pediatric allergist, Hospital Municipal Jesus, Rio de Janeiro, State of Rio de Janeiro, Brazil
[2]Professional Masters in Maternal and Children's Health. Federal Fluminense University, Niterói, State of Rio de Janeiro, Brazil
[3]Professor Adjunto do Departamento de Clínica Médica, Disciplina de Pneumologia da Faculdade de Medicina de Jundiaí, State of São Paulo, Brazil

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***Corresponding author:** Cyro Teixeira da Silva Junior
Professional Masters in Maternal and Children's Health. Federal Fluminense University, Niterói, State of Rio de Janeiro, Brazil

Abstract **Original Research Article**

The aim of this case series report was to assess the bronchodilator response on forced expiratory flow at 25%–75% of the vital capacity of children and adolescents with asthma, sensitized and non-sensitized to house dust mites (HDM). A retrospective study was evaluated in the Hospital Municipal Jesus, Rio de Janeiro, Brazil, with 34 participants enrolled as asthma *sensitized (n=26)* and non-*sensitized (n=8)* to HDM. In spirometry tests had not obstructions in large airways. Only the FEF 25%-75% values were found reduced in relation to the reference ranges (62% vs. 38%, X^2=1.39, P=0.2383) for HDM and non-HDM, respectively. The bronchodilator test with salbutamol was statistically significant in both groups (P<0.005). The measure of bronchodilator response from FEF 25%-75% values was important to evaluate the reversibility of the small airways in children and adolescents with asthma who were sensitized and non-sensitized to HDM.

Keywords: Asthma, children, adolescents, spirometry, FEF25%-75%, bronchodilator test.

INTRODUCTION

The asthma in children and adolescents resulting in important direct and indirect costs for the society, including the influence of the domiciliary economy (Soares *et al*., 2022). The bronchodilator test supports an asthma diagnosis. It is a method for evaluating the changes in reversibility from the airways after inhaling a short-acting β-agonist bronchodilator (Sim *et al*., 2017). The aim of this case series report was to assess the bronchodilator response of the small or peripheral airways, defined as those with a diameter smaller than 2 mm, on forced expiratory flow at 25%–75% of the vital capacity of children and adolescents with asthma, sensitized and non-sensitized to house dust mites (HDM).

METHODS

The 34 participants eligible for bronchodilator tests had asthma without other chronic conditions (**GINA, 2021**). All were notified about no use of medications before the test and confirmed it at the time of the exam **(**Aggarwal *et al*., 2019). The appropriate assays were used to determine sensitization to one or more allergens from HDM using specific serum IgE testing. It was defined by a specific IgE concentration of 0.35 kU/L (Tavares *et al*., 2022). The spirometry was performed after accurate measurements of age, height, and weight with Vitalograph Spirotrac® equipment in participants with controlled asthma considering the last 4 weeks **(**Pizzichini *et al*., 2020**).** Spirometry was repeated between 10 and 20 minutes after fully and slowly inhaling 200 mcg to 400 mcg of salbutamol. The statistical tests were performed after the dataset distribution was observed. A 2-tailed P-value of 0.05 or less was considered to indicate statistical significance. There was no missing data.

CASE SERIES

The bioethics committee from the Medical School approved a protocol under number 4. 605. 087. The participants were recruited from Hospital Municipal Jesus, Rio de Janeiro, Brazil, between

January 2016 and December 2019. All cases were participants with asthma sensitized (n=26) or non-sensitized (n=8) to HDM. The standard reference value for FEF25%-75% was considered abnormal if below 65% of what was predicted **(**Ciprandi *et al*., 2012). All participants had a FEV1/FVC ratio, forced vital capacity (FVC), and forced expiratory volume in one second (FEV1) above or equal to 80%. There was a statistical difference (t=2.19; P=0.0353) between the mean ages of the sensitized (9.8±2.53) and non-sensitized participants (7.75±1.28). The male sex was 66% (n=17/26) for HDM and 38% (n=3/8) for non-HDM. According to the FEF 25%-75% index, 62% of sensitized participants and 38% of non-sensitized participants with HDM had asthma with small airway disease (X2 = 1.39, P = 0.2383). **Table 1** and **Table 2** show our results.

Table 1: The bronchodilator test on FEF 25%-75% of 26 children-adolescents with asthma sensitized to house dust mites from Hospital Municipal Jesus, Rio de Janeiro, Brazil (January 2016-December 2019)

FEF 25%-75%, pre BD, Liters/s (% predict), mean±SD*	FEF 25%-75%, pos BD, Liters/s (% predict), mean±SD*	Test (P-value, 2 tail)
48.42±13.56	64.35±19.17	t=5.440 (P<0.0001)

Abbreviations: SD, standard deviation; BD, bronchodilator test; FEF 25%-75%, forced mid-expiratory flow or forced expiratory flow at 25%–75% of the vital capacity. *Reference value for FEF25%-75%: less than 65% of predicting. All participants had FEV1/FVC ratio, forced vital capacity (FVC), and forced expiratory volume in one second (FEV1) above or equal at 80% with negative responses to bronchodilator test.

Table 2: The bronchodilator test on FEF 25%-75% of 8 children-adolescents with asthma non-sensitized to house dust mites from Hospital Municipal Jesus, Rio de Janeiro, Brazil (January 2016-December 2019)

FEF 25%-75%, pre BD, Liters/s (% predict), mean±SD*	FEF 25%-75%, pos BD, Liters/s (% predict) mean±SD*	Test (P-value, 2 tail)
58.62 ±13.56	72.63±15.18	t=4.078 (P=0.0047)

Abbreviations: SD, standard deviation; BD, bronchodilator test; FEF 25%-75%, forced mid-expiratory flow or forced expiratory flow at 25%–75% of the vital capacity. *Reference value for FEF25%-75%: less than 65% of predicting. All participants had FEV1/FVC ratio, forced vital capacity (FVC), and forced expiratory volume in one second (FEV1) above or equal at 80% with negative responses to bronchodilator test.

DISCUSSION

A reversibility criterion ideally should be able to identify a true bronchodilator response, provide information on the severity of airway obstruction, and correlate well with clinical response (Aggarwal *et al*., 2019).

Several authors considered the FEF 25%-75% for a bronchodilator test response, despite important guidelines (GINA, 2021; ATS, 2019; Pereira, 2002) (Tavares *et al*., 2022; Pennock, 1981; Snider, 1974). The biomarkers FEF25%-75%, FEF50%, and a quantitative dosage of peripheral eosinophils can suggest asthma in subjects with compatible clinical signals **(**Bao *et al*., 2021).

Table 1 and Table 2 show reduced values of the FEF 25%-75%, according to reference ranges (Ciprandi *et al*., 2012). The FEF 25%-75% values after the bronchodilator test were statistically significant in participants sensitized (P<0.0001) and non-sensitized (P=0.0047) to HDM.

Despite being non-statistically significant, sensitized patients have a lower FEF of 25%-75% than non-sensitized patients.In relation to the treatment, the extra-fine particles in aerosolized puffs are more able to reach smaller airways than non-extra-fine particles, resulting in overall lung deposition and lower deposition in the oropharynx **(**Usmani *et al*., 2020**).**

CONCLUSION

The measure of bronchodilator response from FEF 25%-75% values is important to evaluate the reversibility of the small airways in children and adolescents with asthma who are sensitized and non-sensitized to HDM.

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