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Evaluation of airway responsiveness using colored three-dimensional analyses of a new forced oscillation technique in controlled asthmatic and nonasthmatic children

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ABSTRACT

Background: Bronchodilator response (BDR) is routinely used in asthma management. A new forced oscillation technique (FOT) is able to quickly measure respiratory system resistance (Rrs) and reactance (Xrs) at each tidal breath phase. The present study evaluated bronchial changes by using the new FOT.

Methods: Respiratory resistance and reactance were measured using FOT in 132 children (age, 10.86±4.78 years; M:F=88:44), including asthmatic (n=98) and nonasthmatic children (n=34), pre- and post-bronchodilator inhalation in an asymptomatic state. Whole-breath or within-breath changes in Rrs and Xrs were measured and compared pre- and post-bronchodilator inhalation and between each group. All patients performed spirometry and forced expiratory nitric oxide pre- and post-bronchodilator inhalation.

Results: Spirometric parameters showed significant positive changes at V_{50} and V_{25} in both groups; however, these changes were not significantly different between the groups. eNO was significantly higher in the asthmatic group than in the nonasthmatic group; however, there was no significant change pre- and post-inhalation in either group. Rrs in the asthma group was significantly higher in the expiratory phase than in the inspiratory phase. Rrs and Xrs before and after bronchodilator inhalation were significantly different in

Abbreviations: BDR, bronchodilator response; FEV_1, forced expiratory volume in 1 s; FOT, forced oscillation technique; Rrs, respiratory system resistance; Xrs, reactance; eNO, forced expiratory nitric oxide; Fres, resonant frequency

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the asthma group alone, except for the expiratory–inspiratory phase of each of these parameters. Changes in Rrs and Xrs at 5 Hz (R5 and X5) in a whole-breath and the inspiratory phase were significantly different between the groups.

Conclusions: Changes in X5 and R5 reflect bronchial reversibility. The new FOT is useful for asthmatic children.

1. Introduction

The reversibility of airways is one of the major criteria of asthma in children [1,2], and responses to bronchoconstrictors, bronchodilators, or both are routinely used in asthmatic pediatric patients to make a diagnosis and evaluate the severity of asthma [3,4]. Bronchodilator provocation has been recommended for the measurement of bronchial reversibility in children because of its safety. Reactions to bronchoconstrictors and bronchodilators are commonly characterized by a decrease or increase in forced expiratory volume in 1 s (FEV_1) from the baseline value and a decrease in airway resistance [5,6]. In adults, increases in baseline FEV_1 values of at least 12–15% and an absolute change of 200 mL have been defined as a significant response. However, bronchodilator responses may not be as large in younger children because of smooth muscle immaturity. Furthermore, most asthmatic children have FEV_1 values that are close to those of normal children who may exhibit smaller changes in FEV_1 than those obtained in previous reports [7].

The forced oscillation technique (FOT) has been increasingly used in children because it is a noninvasive method that can quickly measure respiratory system resistance (Rrs) and reactance (Xrs) over a wide range of frequencies while breathing at rest [8]. Recently, Kurosawa et al. developed a new method for the FOT using three-dimensional color images with an added time axis to visualize respiratory cycle dependence; Rrs was shown to be higher and Xrs was more negative in the expiratory phase than in the inspiratory phase [9,10]. Three-dimensional colored images could potentially become a tool with which to understand the complex oscillatory properties of the respiratory system.

However, there have been no reports on the evaluation of airways using the new FOT in which respiratory cycle dependence may be visualized during the bronchodilator provocation test in children. The aim of the present study was to assess bronchial reversibility by using the new FOT between asthmatic children receiving treatment and nonasthmatic children. We performed the bronchodilator provocation test in these children during an asymptomatic state.

2. Materials and methods

2.1. Study subjects

Table 1 shows the characteristics of the study subjects comprising 132 pediatric outpatients at the Minami Wakayama Medical Center. All participating individuals were divided into 2 groups: asthmatic ($n=98$; mean age, 10.9±6.3 years; M:F=59:34; height, 138.4±18.0 cm; weight 35.1±12.8 kg) and nonasthmatic ($n=34$; mean age, 10.7±3.6 years; M:F=29:10; height, 141.6±19.7 cm; weight, 36.6±13.6 kg). There were no significant differences between the ages, heights, weights, and body surface areas of each group. The asthmatic diagnoses and classifications were performed according to international guidelines [11,12]. Children with mild persistent asthma and moderate persistent asthma were treated with continuous medication, including inhaled corticosteroids, leukotriene receptor antagonists, or both. Seventy asthmatic children were treated with inhaled corticosteroids. All drugs were withdrawn 12 h before the test. Asthmatic children had no asthmatic symptoms for at least 3 months before the test. Children in the nonasthmatic group had never had wheezing episodes or other respiratory diseases. Written informed consent was obtained from all children or their legal guardians, and the study protocol was approved by the Ethics Committee of our institution.

2.2. Respiratory impedance [13]

Respiratory impedance was measured with FOT using a commercially available machine (MostGragh-01; Chest M.I., Co Ltd, Tokyo, Japan), which was developed by Kurosawa et al. [9,10] and met the standard recommendations [8].

By using this machine, both random noise and Hanning impulses were available as oscillation signals. Impulse oscillatory signals generated by a loud speaker at intervals of 0.25 s were applied to the respiratory system through the mouthpiece while tidal breathing at rest. Mouth pressure and flow signals were measured and calculated to obtain the Rrs and Xrs properties against oscillatory frequencies ranging from 5 to 35 Hz. During measurements, subjects firmly supported their cheeks to reduce upper airway shunting while sitting with their neck in a comfortable neutral posture. As the curves of Rrs and Xrs frequencies could be obtained every 0.25 s, they were serially lined up by assigned color gradients along the time axis, resulting in colored three-dimensional imaging patterns. The oscillatory properties results were available as the mean values of inspiration or

Table 1 – Characteristics of study patients.

N=132	Asthmatic $n=98$	Nonasthmatic $n=34$
Age, years	10.9±6.3	10.7±3.6
Gender (M:F)	59:34	29:10
Height, cm	138.4±18.0	141.6±19.7
Weight, kg	35.1±12.8	36.6±13.6
Body surface area	1.1±0.2	1.2±0.3

Values are mean±SD or numbers.