ORIGINAL ARTICLE

Asthma predictive index in relation to respiratory mechanics by impulse oscillometry in recurrent wheezers

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Abstract
Background: The identification of children who will have persistent asthma has become a focus of recent research. The aim of this study was to assess whether impulse oscillometry (IOS) has a diagnostic value to predict modified API (asthma predictive index) in pre-schoolers with recurrent wheezing.
Methods: Pre-school children aged 3–6 years with recurrent wheezing were enrolled. The study population was divided into two groups based on mAPI criteria. Lung function was assessed by IOS.
Results: 115 children were assessed; 75 (65.2%) of them were male. The median age was 39 months (min: 36, max: 68 months). 64 (55.6%) of the children were mAPI positive. The R5-R20% levels of children with positive mAPI were significantly higher compared to negative mAPI. Also, R5-R20% levels of children with parental asthma and R20% pred and resonant frequency (Fres) levels of children with inhalant sensitization were higher than those without. No significant differences were found in IOS indices between groups based on the presence of atopic dermatitis, food sensitization, eosinophilia, inhaled corticosteroid usage or wheezing without colds. R5-R20% and total IgE values were found to be significantly related to positive mAPI (aOR: 1.40, $p = 0.022$ and aOR: 1.02, $p = 0.001$, respectively). In the ROC analysis, R5-R20% levels >14.4 had a sensitivity of 75% and specificity of 53% for predicting a positive mAPI ($p = 0.003$).
Conclusion: IOS may help clinicians to identify the pre-school wheezers with a high risk of asthma.
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Introduction

Recurrent wheezing is a common problem in pre-school children. Approximately 40% of children wheeze in their first year of life. However, only 30% of pre-schoolers with recurrent wheezing still have asthma at the age of six years.[1,2] Despite the fact that asthma usually starts in the early life years during which the substantial alterations in lung structure develop, the actual pathopyhsiology of infant lung function in the progression of asthma is still limited.[3] Asthma is reported to be the most prevalent chronic respiratory disease in childhood and early detection of the children at potential risk in this crucial time may affect the natural course of the disease.[4,5]

The identification of pre-school children who will have persistent asthma has been the focus of interest.[6] The asthma predictive index (API), which is the most widely used model was originally developed in the Tucson cohort study.[7] A positive API requires recurrent episodes of wheezing during the first three years of life and one of two major criteria (physician-diagnosed eczema or parental asthma) or two of three minor criteria (physician-diagnosed allergic rhinitis, wheezing without colds or peripheral eosinophilia ≥4%). A positive API by the age of three years was associated with a 77% chance of active astma from ages 6 to 13, whereas a negative API at the age of three years had less than a 3% chance of having active asthma during the school years.[4] The API was modified by the incorporation of aeroallergen sensitization as a major criterion and food sensitization as a minor criterion, replacing physician-diagnosed allergic rhinitis.[7]

The assessment of respiratory mechanics in children with recurrent wheezing may provide an objective information about the progression and the need for and response to interventions.[3,8] However, detection of airway dysfunction in young children remains a challenge for clinicians because of the lack of methods easily applied in clinical care. Impulse oscillometry (IOS) can be easily done even in children who are unable to perform forced expiratory maneuvers.[9] It is a simple, non-invasive method that requires minimal patient cooperation. This method uses sound waves to measure respiratory mechanics and has the potential to evaluate airflow limitation during tidal breathing. It can be used in various chronic respiratory diseases in order to identify the underlying airway dysfunction more accurately.[10,11]

To date, there is limited data available on impulse oscillometry in children with recurrent wheezing.[12,13] The aim of the present study was to assess the diagnostic value of IOS to predict mAPI positivity in preschool children with recurrent wheezing.

Methods

Study population

The study included pre-school children aged three to six years who had attended to the department of Pediatric Allergy and Immunology of Mersin University with a history of recurrent wheezing between January 2014 and December 2016. Recurrent wheezing was defined as having more than three wheezing episodes confirmed by a doctor during the last one year. Children who were able to perform impulse oscillometry according to ATS/ERS recommendations were eligible for this study. Those children with prematurity, low weight for gestational age, airway malformations, cardiac, neurological diseases, chronic respiratory diseases such as cystic fibrosis, ciliary dyskinesia and bronchopulmonary dysplasia were excluded. Children who were experiencing an acute wheezing attack were not enrolled in the study.

A positive modified API requires four or more episodes of wheezing with at least one confirmed by a physician and one of three major criteria (physician-diagnosed eczema, parental asthma, aeroallergen sensitization) or two of three minor criteria (food sensitization, wheezing without colds or peripheral eosinophilia ≥4%).[7] The wheezy children were divided into two groups; 1) Group with positive API; if they had one major or two minor criteria and 2) Group with negative API; if they did not meet these criteria.

The study was approved by the ethics committee of the Mersin University.

Data collection

Medical records of the patients were reviewed to determine demographic characteristics, history of wheezing, atopy (food and inhalant sensitization determined by specific IgE levels and skin prick tests), atopic dermatitis and parental asthma. Serum total IgE levels, peripheral eosinophil counts, usage of inhaled corticosteroids and leukotriene receptor antagonists (LTRA) were also obtained from medical records.

Impulse oscillometry

Impulse oscillometry (IOS) was performed in compliance with the European Respiratory Society/American Thoracic Society (ERS/ATS) guidelines by MasterScreen IOS system (Jaeger Co., Germany).[14] IOS was performed during spontaneous breathing. The output pressure and flow signals were analyzed for 30 s in the frequency range of 5–20 Hz for their amplitude and phase differences to determine the resistance (R) and reactance (X) values. The IOS parameters obtained at the end of the application were resistances (R5, 20) at 5–20 Hz, R5-R20 (resistance at 5 Hz minus resistance at 20 Hz), reactance at 5 Hz (X5), resonant frequency (Fres, the frequency where the X value is zero), and area of the reactance curve (AX, integral of X values from 5 Hz to Fres).

Statistical analysis

The Shapiro–Wilk test was performed to test the suitability of the normal distribution of the numerical data. Descriptive analyses were presented using median or mean ± SD based on normal distribution or not. Unadjusted comparisons were made using the Independent samples t-test or Mann–Whitney U test for continuous endpoints and the Chi-Square test for categorical endpoints. In order to match the subgroups of pre-school wheezers for sample size equilibrium according to the clinical risk factors, the propensity score was used. A multivariate logistic regression model was used to identify independent predictors of API. Odds ratios with their 95% confidence intervals were estimated. For the variables with large measurement units, a regression