Exercise induced airway obstruction in children: Patho-physiology and diagnostics

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Chapter 5

Detecting exercise induced bronchoconstriction in temperate and cold air with the forced oscillation technique

Work in Progress

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ABSTRACT

Aim
The aim of this study was to analyze the addition of the forced oscillation technique to spirometry to identify EIB in temperate air, in children with EIB.

Methods
Ten children (age 11.2 ± 1.5 years) with mild-moderate asthma performed exercise challenges on 2 separate days in cold and in temperate air.

Results
All children showed a fall in FEV₁ > 10% after exercise in cold air, whereas only 6 of 10 showed a fall in FEV₁ > 10% after exercise in temperate air. All children showed an increase in Rrs₅ > 20% after exercise in cold air, 8 of 10 children showed an increase in Rrs₅ > 20% after exercise in temperate air. Combining spirometry and the FOT allowed detection of 9 out of 10 children with EIB.

Conclusion
This study shows that the addition of the forced oscillation technique is helpful in detecting EIB in asthmatic children when testing in temperate air.
INTRODUCTION

Exercise induced bronchoconstriction (EIB) is considered to be an index of bronchial hyperresponsiveness and is highly specific for asthma. EIB is characterized by a fall in the forced expiratory volume in one second (FEV₁) of more than 10% after exercise compared to baseline. Analyzing EIB with FEV₁ requires repetitive, effort dependent, forced breathing maneuvers that may influence airway mechanics. The forced oscillation technique (FOT) is an effort independent technique that measures airway resistance and reactance and has been used to analyze EIB.

It is well known that the humidity and temperature of the inspired air influences the outcome of exercise challenges. Therefore, guidelines for exercise challenges limit the humidity of the inspired air to 10 mg·l⁻¹ H₂O. In most moderate climates however the outdoor air humidity is significantly lower than 10 mg·l⁻¹ H₂O for most of the year, reducing real life sensitivity for exercise tests in temperate air, measured with spirometry. Recent studies suggest that FOT measurements are relatively unaffected by differences in air quality.

The aim of this study was to analyze the addition of the FOT to spirometry to identify EIB in temperate air, in children with EIB.

MATERIALS AND METHODS

Study design
The study had an open cross-sectional design. Asthmatic children performed two exercise challenges on 2 separate days with a time interval of 2 to 6 weeks. Exercise challenges were performed in cold and in temperate air.

Subjects
Asthmatic children with exercise induced symptoms were selected from the outpatient clinic of the pediatric department of the Medisch Spectrum Twente. All of the children were informed and the local Ethics Committee was consulted, who filed no objection to perform the study.

Interventions
Exercise challenges were performed in the local skating rink, to obtain cold air (1-5°C; water content: 1.7 mg·l⁻¹ to 4.8 mg·l⁻¹), and in the exercise challenge lab to obtain temperate air (22-25°C; water content: 7.7 mg·l⁻¹ to 9.1 mg·l⁻¹). Exercise challenges were performed on a treadmill with a 10 degree slope. Children ran for a total of 6 minutes with a 2 minutes period to reach the targeted heart rate of 90 percent of predicted maximum (210-age). The nose was clipped to accommodate equal testing circumstances for all subjects. All exercise tests were performed by JD and EP.
Spirometric measurements

A Masterscope® Jaeger® (Hoechberg, Germany) was used to measure spirometry. Flow-volume loops were recorded using standard ERS protocol, in temperate air. Before exercise, flow volume loops were duplicated. After exercise flow volume loop measurements were repeated in duplex at 1, 3, 6, 9, 12, 15, 20, 25 and 30 minutes. The highest value for FEV₁ was used for analysis.

Oscillometric measurements

Measurements using FOT (R.O.S., Oscilink®, Sensormedics®) were performed 3 times with nose clipped and with hands supporting cheeks and mouth floor, measuring range 4-32 Hz. FOT measurements were repeated before exercise and at 5, 14 and 24 minutes after exercise. The average of three resistance at 5 Hz (Rrs₅) measurements were used for analysis.[4]

Statistical analysis

Best values of spirometric measurements and average FOT measurements were used for statistical calculations. Results were expressed as mean values ± standard deviation (SD) for normally distributed data, as median (minimum; maximum) for not normally distributed data or as numbers with corresponding percentages if nominal or ordinal.

RESULTS

Ten children (age 11.2 ± 1.5 years) with pediatrician diagnosed mild-moderate asthma performed an exercise challenge test in cold air and in temperate air in February 2005 to April 2005. No adverse events were observed.

Characteristics and baseline lung function are shown in table 1; body mass index (BMI z-score) was adjusted for age and gender and calculated as standard deviation from the mean. Before exercise, baseline lung function between tests in cold and temperate air were statistically similar. All children showed a fall in FEV₁ of more than 10% after exercise in cold air.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (%)</td>
<td>8 (80)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>11.2 ± 1.5</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>147.6 ± 9.8</td>
</tr>
<tr>
<td>BMI z-score</td>
<td>0.8 ± 1.1</td>
</tr>
<tr>
<td>FEV₁ (% of pred)</td>
<td>92.4 ± 9.8</td>
</tr>
<tr>
<td>Rrs₅ (% of pred)</td>
<td>96.8 ± 28.6</td>
</tr>
</tbody>
</table>

BMI z-score: age and gender corrected body mass index; FEV₁: Forced expiratory volume in the first second; Rrs₅: Resistance at 5Hz.
Detecting EIAO in warm and cold air with FOT

...whereas only 6 of 10 showed a fall in FEV₁ of more than 10% after exercise in temperate air (mean fall 15.1 ± 12.1%).

All children showed an increase in Rrs₅ of more than 20% after exercise in cold air (mean increase 191.1 (23.3; 261.5) %), 8 of 10 children showed an increase in Rrs₅ of more than 20% after exercise in temperate air (mean increase 96.2 (9.4; 146.5) %). Individual data for the children are shown in table 2.

**DISCUSSION**

This study shows that the addition of the FOT increases the detection of EIB in temperate air exercise challenge, for children with EIB in cold air. Combining spirometry and the FOT allows detection of 9 of 10 children with EIB in cold air compared to 6 of 10 for spirometry alone.

To our knowledge, this is the first study that analyzes changes in lung function after exercise using both spirometry and the FOT in both cold, and temperate air. As expected the fall in FEV₁ was more profound in cold air. Two children (ID 7 and ID 10) showed a fall in FEV₁ of less than 10% in temperate air but a fall of more than 40% in cold air. The fact that the fall in FEV₁ can be severe in real life, outdoor situations in moderate climates when compared to testing conditions using ATS protocol, leads to a search for other lung function parameters that can accurately diagnose EIB in temperate air conditions.

Repeated deep inspiration, needed for spirometric measurements, influences airway mechanics and may cause bronchodilation³. The observed diminished response to exercise in temperate air may be further reduced by this phenomenon as we measured forced expira-

### Table 2. Individual response of asthmatic children to exercise.

<table>
<thead>
<tr>
<th>ID</th>
<th>Sex</th>
<th>Height (cm)</th>
<th>BMI z-score</th>
<th>Age (years)</th>
<th>Change in FEV₁ (%)</th>
<th>Change in Rrs₅ (%)</th>
<th>Change in FEV₁ (%)</th>
<th>Change in Rrs₅ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>135.00</td>
<td>−0.45</td>
<td>8.7</td>
<td>−13.7</td>
<td>24.3</td>
<td>−0.6</td>
<td>26.3</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>149.00</td>
<td>−0.70</td>
<td>10.9</td>
<td>−17.1</td>
<td>87.0</td>
<td>0.5</td>
<td>33.8</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>153.00</td>
<td>0.45</td>
<td>11.4</td>
<td>−58.5</td>
<td>261.5</td>
<td>−43.1</td>
<td>146.5</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>157.00</td>
<td>1.30</td>
<td>11.7</td>
<td>−60.5</td>
<td>176.9</td>
<td>−23.9</td>
<td>138.1</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>169.00</td>
<td>1.80</td>
<td>14.6</td>
<td>−34.5</td>
<td>168.7</td>
<td>−18.2</td>
<td>102.8</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>143.00</td>
<td>1.55</td>
<td>11.2</td>
<td>−16.9</td>
<td>23.3</td>
<td>−16.4</td>
<td>39.5</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>149.00</td>
<td>1.30</td>
<td>10.6</td>
<td>−40.6</td>
<td>226.6</td>
<td>−9.5</td>
<td>65.9</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>137.00</td>
<td>−0.65</td>
<td>12.0</td>
<td>−38.6</td>
<td>72.0</td>
<td>−17.0</td>
<td>9.4</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>145.00</td>
<td>2.80</td>
<td>11.4</td>
<td>−40.8</td>
<td>56.3</td>
<td>−24.7</td>
<td>62.4</td>
</tr>
<tr>
<td>10</td>
<td>M</td>
<td>139.00</td>
<td>0.70</td>
<td>9.8</td>
<td>−50.3</td>
<td>66.2</td>
<td>−4.7</td>
<td>16.2</td>
</tr>
</tbody>
</table>

BMI z-score: age and gender corrected body mass index; FEV₁: Forced expiratory volume in the first second; Rrs₅: Resistance at 5Hz. M: Male, F: Female.

(mean fall 35.4 ± 16.2%), whereas only 6 of 10 showed a fall in FEV₁ of more than 10% after exercise in temperate air (mean fall 15.1 ± 12.1%).

All children showed an increase in Rrs₅ of more than 20% after exercise in cold air (mean increase 191.1 (23.3; 261.5) %), 8 of 10 children showed an increase in Rrs₅ of more than 20% after exercise in temperate air (mean increase 96.2 (9.4; 146.5) %). Individual data for the children are shown in table 2.
tions. However, as FOT measurements preceded the forced deep inspiration we may have partly prevented this phenomenon which may explain the sensitivity of the FOT measurements. This idea is further enhanced by the work of Malmberg et al. who found a weak relation ($r^2=0.25$) between change in $Rrs_5$ and temperature but did not measure forced expiration in wheezing pre-school children.

Some remarks should be made about this study. The time interval (2-6 weeks) between cold air and temperate air tests may have influenced the outcome of the exercise challenge. However there were no changes in medication regimen in that period and lung function measurements were comparable before exercise tests.

We chose a relatively mild cut-off value for EIB in cold air, 10%. This cut-off however has been used previously and is advised when analyzing EIB in a trial set-up.

Due to the intensity of exercise and the cumbersome nature of head gear we chose not to use head gear when measuring forced oscillations, leading to an expected upper airway shunt. The upper airways shunt causes energy from the oscillating air to be absorbed by the relative high compliant upper airways (cheeks and the base of the mouth). We therefore used only lower frequency measurements for analysis (5 Hertz), which are least affected by the upper airway shunt.

We tested in the ice rink with electric driven ice resurfacing machines, providing a child friendly environment allowing a reduction in temperature and humidity of the inspired air. However, water content was not fully controllable.

In conclusion, this study shows that the addition of FOT measurements to spirometry when testing EIB in temperate air is helpful to identify the response to exercise in real life, outdoor situations. In the future, more research needs to be done to further outline the use of the FOT in analyzing EIB in temperate air.
REFERENCES