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A Comparison of Impulse Oscillometry to Spirometry in the Evaluation of Exercise Induced Bronchoconstriction in Children with Asthma

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Abstract

Rationale: Impulse Oscillometry (IOS) is a noninvasive method to measure respiratory impedance. The use of IOS as an indirect measure of airflow obstruction compared to spirometry in the evaluation of Exercise-Induced Bronchoconstriction (EIB) has not been fully explored in children. In this study we aim to describe the IOS values, resistance at 5 Hz (R5rs) in subjects with EIB and without EIB. We also aim to compare whether IOS variables correlate with spirometry variables following exercise challenge test in asthmatic subjects.

Methods: We designed a cross sectional study involving subjects between 6-18 years old with a diagnosis of asthma who were referred to the pediatric pulmonary function lab for an exercise challenge test to rule out EIB. Spirometry and IOS were performed at baseline and at 5 minute intervals up to 20 minutes post exercise and again post bronchodilator.

Results: 43 subjects were enrolled. Of the 43 subjects, 15 had a 10% fall in FEV1 after exercise significant for EIB. Demographic characteristics (gender, age and ethnicity) were not different comparing subjects with EIB to those without EIB. There was a significant correlation between spirometry and IOS measurements at baseline, 1 minute, 5 minutes, 10 minutes, 15 minutes, 20 minutes and post bronchodilator after exercise (r= -0.75, -0.72, -0.72, -0.76, -0.75, -0.72 and -0.75 respectively, p<0.01) in asthmatic subjects without EIB. In asthmatic subjects with EIB, there was a significant correlation between spirometry and IOS measurements at baseline, 1 minute, and post bronchodilator after exercise (r=-0.55, -0.79 and -0.63 respectively p<0.05). There was weak correlation between spirometry and IOS measurements at 5 minutes, 10 minutes, 15 minutes and 20 minutes after exercise for asthmatic subjects with EIB.

Conclusion: A significant correlation was found between spirometry and IOS measurements of change in airway function in asthmatic patients both with EIB and without EIB.

Keywords: Asthma; Exercise; Pulmonary function testing

Background and Significance

Exercise Induced Bronchoconstriction (EIB), is a transient narrowing of the airways that follows strenuous exercise. It may appear with or without asthma. In the general population its prevalence is 5-20% whereas it is 30-70% among elite athletes. It occurs in 50-90% of asthmatics and 40% of subjects with allergic rhinitis [1-3] EIB is documented by a 10% baseline to post challenge fall in forced expiratory volume in one second (FEV1) [4]. Spirometry and exercise testing is the mainstay in the diagnosis of EIB. Since spirometry is effort dependent and requires active coaching, this may present clinical difficulties with younger children [5] and the elderly, or with cognitively or neurologically impaired individuals [6,7].

Impulse Oscillometry (IOS) is a noninvasive and validated technique that measures respiratory resistance and reactance at different oscillation frequencies. It was introduced as an alternative modality to the conventional pulmonary function test. IOS is effort independent. The pressure-flow oscillations are applied at the mouth superimposed on the subject's tidal breaths to measure respiratory system resistance and reactance [8,9]. IOS has been used to measure post-bronchodilator (Pb) changes in asthmatic airways [10,11]. Respiratory resistance at lower frequencies, particularly at 5 Hz (R5rs) has been shown to correlate with FEV1 [5,11-19]. Several works have been published showing that IOS can be used in adults as well as in preschool children [11,17] to diagnose and evaluate pulmonary disease such as asthma17,18 and cystic fibrosis [20].

In a recent study Arshi et al. [21] compared airway responses in patients between 12-44 years old with allergic rhinitis but without asthma symptoms following exercise challenge [21]. No significant difference were revealed between spirometry and impulse oscillometry measurement before and after exercise challenge. In the same study no correlation was found between spirometry and impulse oscillometry. In this study, we plan to compare airway responses following exercise challenge in asthmatic children and whether IOS variables are associated with spirometry variables.

Design and Methodology

Study design

We performed a cross sectional study involving asthmatic patients who were referred to pediatric pulmonary function lab for an Exercise Challenge Test (ECT).

Study subjects

Subjects between 6-18 years old with a diagnosis of asthma who were referred to the pediatric pulmonary function lab at for an ECT between June 2008 and June 2009 were recruited for the study. An informed consent and assent were obtained from parents/guardians and subjects.

Inclusion criteria

Children between 6-18 years old with a diagnosis of asthma

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confirmed by a validated asthma questionnaire18 and who fulfills the American Thoracic Society (ATS) standards for performing spirometry and ECT [4].

Exclusion criteria

Subjects with other chronic respiratory conditions (e.g., cystic fibrosis, or brochopulmonary dysplasia) and subjects who does not fulfills the ATS standards for performing spirometry and ECT.

Asthma questionnaire

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Obtain informed consent and assent

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Exercise	Post challenge					
Baseline	1 min	5 min	10 min	15 min	20 min	Pb
IOS	IOS	IOS	IOS	IOS	IOS	IOS
Spiro	Spiro	Spiro	Spiro	Spiro	Spiro	Spiro

Exercise Challenge Test

The exercise challenge test was performed as per ATS guidelines in 1999. 4 The consent and assent were obtained. All subjects were examined to exclude the presence of wheezing. A motor-driven treadmill with adjustable speed and grade was used. Heart rate was monitored from a 3-lead ECG configuration and a pulse oximeter as back-up measure. Baseline IOS and spirometry were performed. Starting at a low speed and grade, both were progressively advanced during the first 2-3min of exercise until the heart rate is 80-90% of the predicted maximum (calculated as 220-age in years). The test was ended when the subject did exercise at the target heart rate for at least 4 min. Measurements of FEV1, resonant frequency (Fres), reactance at 5 Hz (X), and low frequency reactance area (AX; area of reactance integrated from 5 Hz up to Fres) were recorded at 1, 5, 10, 15 and 20 min after challenge and post-bronchodilator at the end of the test.

IOS

A Master Screen Impulse Oscillometry system (Jaeger Co, Wurzburg, Germany) was used to make the IOS measurements. The system was calibrated through a single volume of air (3L) at different rates and also with a reference resistance device (2cmH2O/l/s) per manufacturer. The machine was calibrated before each study. During IOS measurement, the subjects were instructed to sit in upright, heads in neutral position. The subjects were instructed to use nose clips and to support cheeks with hands to reduce loss of energy in the upper airways. Multi-frequency impulses were applied over a 30-second interval to the airway through the mouthpiece while the subjects were breathing quietly. Each observation consisted of an optimum of 3 reproducible (i.e., R5rs within 5% of highest obtained value) maneuvers with coherence values are 0,6 or greater at 5 Hz [22,23]. Each effort should not have artifacts caused by coughing; breathe holding, swallowing or vocalization. Impulse oscillometry measures pulmonary impedance which consists of pulmonary resistance and reactance. Pulmonary resistance is the energy required to propagate the pressure wave through the airways whereas pulmonary reactance is the amount of recoil generated against that pressure wave. 5 The mean resistance and reactance values were calculated at discrete frequencies ranging from 5 to 35 Hz. Low frequency signals penetrate out to the lung periphery, giving us information about the entire respiratory tract, whereas highfrequency signals reach the proximal, giving us information about the larger airways. Measurements from the 3 efforts for each IOS parameter were then averaged for the final result.

Spirometry

We used a Vmax 229 spirometry system (Cardinal health, Yorba Linda, California) to record the spirometry measurements. This system also was calibrated for body temperature and pressure of saturated gas and volume, as per ATS standards [24]. Spirometry was performed in the seated position before exercise and then serially after exercise, utilizing the test method recommended by the ATS. Three acceptable tests were obtained at each testing interval. As a goal, the highest and second highest FEV1 values should differ by no more than 0.2L. The highest FEV1 value from three acceptable maneuvers was used as the representative value within each interval. Polgar reference values were used for this study [25]. Percent predicted values for spirometry measurements are based on age, height, gender and ethnicity.

Exercise induced Bronchoconstriction. The presence of exerciseinduced bronchoconstriction was defined by plotting FEV1, as a percentage of the pre-exercise baseline FEV1, at each post-exercise interval. A decrease of 10% of FEV1 from baseline was accepted as EIB [4].

Variables

Demographic variables were collected such as age, gender and ethnicity

IOS measurements (Rsr5) were collected pre and post ECT

Spirometry measurements(FEV1) were collected pre and post ECT

Statistical Method

Descriptive statistics were computed for the IOS and spirometry data for each group (EIB, not EIB) separately and for each time point. Spearman correlations and linear regression analysis were used to examine the association of IOS values with spirometry values. Subjects were classified into EIB or not EIB groups based on the spirometry values (standard). Analysis of variance models were used to test for groups (EIB or not EIB) and time differences on the percent IOS change from baseline. We further used a students' t-test to compare the maximum change in IOS values between the groups. A α level of 0.05 was used for all statistical tests. The SAS version 9.1 software package was used for all data analysis.

	EIB (n=15)	Non-EIB (n=28)	+ 1/2	
	Mean ± SD	Mean ± SD	ι, χΖ	ρ
Age (year)	14,00 ± 1,96	13,25 ± 2,80	t:-0,922	a0,362
Height (cm)	160,27 ± 11,39	158,61 ± 12,15	t:-0,436	a0,665
	n (%)	n (%)		
Sex			χ2:0,897	b0,343
Male	5 (33,3)	5 (33,3)		
Female	10 (66,7)	10 (66,7)		
Ethnicity			χ2:6,970	c0,125
Caucasian	4 (26,7)	4 (26,7)		
African American	3 (20,0)	3 (20,0)		
Hispanic	1 (6,7)	1 (6,7)		
Asian	3 (20,0)	3 (20,0)		
Other	4 (26,7)	4 (26,7)		

aStudent's t Test; bYates' Continuity Correction; cFisher-Freeman-HaltonExact Test **Table 1:** Baseline Demographic characteristics of study subjects.

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Results

The technique was well accepted by children and exhibited good within test repeatability, with coefficient of variation (5% for R5rs) and coherence >0.6 at 5 Hz. Forty three subjects were enrolled. Of the 43 subjects, 15 had a 10% fall in FEV1 after exercise. Demographic data of the subjects with EIB and without EIB have been shown in Table 1. The mean age of subjects with EIB was 14.0 ± 1.96 years and the mean age of subjects without EIB was 13.2 ± 2.80 years. Demographic characteristics (gender, age, height and ethnicity) were not different those subjects with EIB and those without EIB.

Baseline Lung Function

The mean baseline lung function values from IOS and spirometry are presented in Table 2. Baseline FEV1, FEV1%, FVC, FVC%, FEV/ FVC, FEF 25-75, and FEF 25-75% values and R5rs values were not statistically different in asthmatic children with EIB compared to asthmatic children without EIB. Five patients in EIB group and 15 patients in non-EIB group showed obstructive changes at baseline spirometry.

Airway response to exercise and relationship between spirometry and IOS

Of the 43 subjects, 15 had a 10% fall in FEV1 after exercise. The mean changes in lung function and spearman's correlation coefficient between measurements FEV1 and R5rs values after exercise in the study groups have been shown in Table 3. A significant correlation was found between baseline FEV1 and R5rs in subjects with EIB (r=-0.55, p: 0.03) and those with non-EIB (r=-0.66, p: 0.001). Significant correlation was found between FEV1 and R5rs at baseline, 1 minute, 5 minutes, 10 minutes, 15 minutes, 20 minutes and post bronchodilator after exercise in non-EIB group (asthmatic subjects without EIB) (r=-0.66, -0.59, -0.66, -0.69, -0.70, -0.71 and -0.61 respectively, p<0.01).

	EIB (n=15)	Non-EIB (n=28)	р	
	Mean ± SD (Median)	Mean ± SD (Median)		
R5rs FVC	4,57 ± 1,10 (4,17) 3,53 ± 0,92 (3,54)	4,95 ± 1,72 (4,43) 3,5 ± 0,61 (3,52)	0,516 0,970	
FVC (%)	104,68 ± 11,99 (102)	102,27 ± 12,71 (99)	0,436	
FEV1	2,9 ± 0,76 (2,87)	2,86 ± 0,5 (2,85)	0,929	
FEV1 (%)	95,5 ± 12,5 (94,5)	93,2 ± 7,27 (94)	0,750	
FEV1/FVC	82,57 ± 8,03 (83)	82,2 ± 8,17 (81)	0,858	
FEF 25-75	2,99 ± 1,14 (2,84)	2,9 ± 0,85 (2,73)	0,949	
FEF 25-75 (%)	85,54 ± 25,87 (82,5)	80,87 ± 18,8 (83)	0,628	
PEF	6,16 ± 1,62 (5,93)	5,92 ± 0,66 (5,59)	0,524	
PEF (%)	98,43 ± 12,71 (97)	95,07 ± 13,33 (91)	0,499	

Mann Whitney U Test

Table 2: Baseline lung function values from IOS and Spirometry.

Time	EIB			Non-EIB			
	R5rs	FEV1	R	R5rs	FEV1	r	
Baseline	4.72 ± 1.33	2.86 ± 0.56	-0.551*	5.05 ± 1.38	2.90 ± 0.76	-0.664**	
1 min	5.95 ± 1.97	2.40 ± 0.64	-0.793**	5.34 ± 1.94	2.82 ± 0.74	-0.597**	
5 min	4.95 ± 1.84	2.73 ± 0.58	-0.714	5.32 ± 1.78	2.86 ± 0.76	-0.660**	
10 min	4.88 ± 1.73	2.68 ± 0.74	-0.750	5.23 ± 1.56	2.88 ± 0.73	-0.696**	
15 min	5.14 ± 1.90	2.76 ± 0.87	-0.657	5.28 ± 1.61	2.87 ± 0.74	-0.701**	
20 min	5.02 ± 1.91	2.79 ± 0.86	-0.725	5.16 ± 1.60	2.90 ± 0.75	-0.716**	
PB	4.77 ± 1.74	2.85 ± 0.62	-0.634*	4.36 ± 1.22	3.04 ± 0.76	-0.616**	

 Table 3: Spearmen's correlation coefficient between measurements FEV1 and R5rs values in EIB and non-EIB group before and after exercise.



Figure 1: Correlation between FEV1 and R5rs in non-EIB group after exercise.



Figure 1 presents correlation between FEV1 and R5rs in non-EIB group. In EIB group only significant correlation was found between FEV1 and R5rs at baseline, 1 minutes and post bronchodilator after exercise (r= -0.55, -0,79, and -0,63 respectively, p=0.33, and 0.01) (Figure 2). Weak correlation was observed between FEV1 and R5rs at 5 minutes, 10 minutes, 15 minutes and 20 minutes after exercise for subjects with EIB. In all patients with asthma strong correlation was observed between FEV1 and R5rs at baseline, 1 minute, 5 minutes, 10 minutes, 15 minutes and post bronchodilator after exercise (r= -0,63, -0,73, -0,66, -0,75, -0,74, -0,75 and -0,65 respectively, p<0,001). Figure 3 presents the correlation between FEV1 and R5rs in all patients with asthma.

The mean changes in R5rs and FEV1 values in subjects with EIB and without EIB are shown in Figure 4. Table 4 presents correlation between mean percent change in R5rs and FEV1 after exercise. We found a strong correlation between mean percent change in R5rs and FEV1 at 1 minute, 5 minutes, 10 minutes, 15 minutes, 20 minutes and



Figure 3: Correlation between FEV1 and R5rs in all patients with asthma after exercise.



Figure 4: Mean changes in R5rs and FEV1 values in EIB and non-EIB groups.

	EIB (n=15)		Non-EIB (n=28)		Total (n=43)	
	r	р	r	р	r	р
Baseline – 1 min	-0,764	0,001**	-0,766	0,001**	-0,871	0,001**
Baseline – 5 min	-0,429	0,0337	-0,406	0,032*	-0,532	0,001**
Baseline – 10 min	-0,857	0,014*	-0,372	0,050*	-0,571	0,001**
Baseline – 15 min	-0,600	0,203	-0,675	0,001**	-0,745	0,001**
Baseline – 20 min	-0,829	0,042*	-0,700	0,001**	-0,719	0,001**
Baseline - Pb	-0,594	0,025*	-0,833	0,001**	-0,730	0,001**

 Table 4: The Correlation between mean percent change in R5rs and FEV1 after exercise challenge.

post bronchodilator after exercise in non-EIB group (r= -0.76, -0.40, -0,37, -0,67, -0,70, and -0,83 respectively, p<0,05). In EIB group a strong correlation was found between mean percent change in R5rs and FEV1 at 1 min, 10 minutes, 20 minutes and post bronchodilator after exercise (r=-0.76, -0.85, -0.82, and -0.59 respectively, p<0,05). The correlation between mean percent change in R5rs and FEV1 were strong at 1 minute, 5 minutes, 10 minutes, 15 minutes, 20 minutes and post-bronchodilator after exercise in all subject (r=-0.87, -0.53, -0.57, -0.74, -0.71, and -0.73, p<0,01).

We assessed the bronchodilator response after exercise challenge

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in subjects with EIB and those without EIB. FEV1 decreased 2.25% and R5rs decreased 6% in subjects with EIB. In subjects without EIB, FEV1 has improved 14% and R5rs decreased 65% after administration of bronchodilator.

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Discussion

In this study, we compared airway responses following exercise challenge test and examined whether baseline and post-challenge IOS variables correlated with corresponding spirometric variables. There are no previously published data that compare IOS and spirometry after ECT in children with asthma. We found a high correlation between spirometric measures of change in airway function and IOS measures of change after exercise challenge, indicating close equivalency of the two testing methods. The technique was well accepted by children and exhibited good within test repeatability, with coefficient of variation (5% for R5rs) and Coherence >0.6 at 5 Hz.

In our study, we used a standardized exercise testing. Forty three subjects with asthma participated, with 15 (34.9%) having a decrease of \geq 10% in FEV1 after exercise challenge test significant for EIB. In literature the prevalence of EIB in asthmatic varies between 50-90%. This is most likely due to study-specific differences regarding the intensity of the exercise and in the methods used to detect the response [26].

We found a significant correlation between FEV1 and R5rs in subjects without EIB. We also found a significant correlation at baseline, 1 minute and post bronchodilator in subjects with EIB. However we did not find a significant correlation between FEV1 and R5rs at 5 minutes, 10 minutes, 15 minutes and 20 minutes after exercise. As per our pulmonary function laboratory protocol no further testing was done when FEV1 decreased more than 15%. Six subjects had a decrease in FEV1 from baseline more than 15%. We did not continue further testing in those six subjects. However we were able to get spirometry and IOS measurements in 7 subjects whose FEV1 decreased more than 10% but less than 15%. In those subjects there was no correlation between FEV1 and R5rs at 5 minutes, 10 minutes, 15 minutes and 20 minutes. This is possibly due to small sample size.

Evans et al published a study which involves 22 physically active adults with probable EIB has shown high correlation between spirometry and IOS variables measuring change in airway function following room temperature and cold temperature exercise challenges [27]. In that study subjects performed 6-minute of stationary cycle ergometry while breathing either cold or room temperature. Impulse oscillometry and spirometry were performed at baseline and for 20 minutes post-challenge at 5-minute intervals. Significant correlations were identified between baseline FVC, FEV1 and resistance (Raw). For room temperature exercise, postchallenge peak percentage change in isovolume forced expiratory flow at 50% of vital capacity (FEF50) was strongly correlated to peak percentage change in reactance (X).

In our study we used a standardized exercise testing. All subjects were diagnosed asthma confirmed by a validated asthma questionnaire.18Since previous studies have shown significant correlation between FEV1 and R5rs, we only described changes in R5rs. We did not describe the changes in resonance frequency and reactance in our study. LP Malmberg et al. assessed the exercise-induced responses of respiratory impedance by using IOS in young wheezy children and nonatopic controls after a free running test [28]. A significantly larger responses in respiratory resistance (R5rs), reactance (X5rs) and the resonance frequency (Fr) were observed in wheezy children compared to nonatopic subjects. In our study we found a strong correlation between mean percent change between R5rs and FEV1 after exercise challenge in subjects with non-EIB and in all subjects with asthma. We assessed the bronchodilator response after exercise challenge in subjects with EIB and those without EIB. FEV1 decreased 2.25% and R5rs decreased 6% in subjects with EIB. The lung functions of some of subjects with EIB did not recover after administration of bronchodilator whereas R5rs improved. We may speculate that IOS is more sensitive than spirometry measurements in detecting lung function changes. In subjects without EIB, FEV1 has improved 14% and R5rs decreased 65% after administration of bronchodilator.

JM Olaguibel et al. compared the bronchodilator response measured by IOS, spirometry and body plethysmography in asthmatic preschool children [29]. IOS indices (R5rs) were correlated with FEV1 and sRaw at both, baseline and post-bronchodilator. They reported 19% decrease in R5rs after bronchodilator from baseline. Nielsen in 2000 suggested 29% drop in R5rs is significant bronchodilator response whereas Hellinckx found 40% drop is significant bronchodilator response [30,18].

The lack of higher correlation in our study could be ascribed to the fact that IOS and spirometry are measuring different aspects of lung dynamics: while FEV1 is indirectly reflects airway resistance, IOS respiratory resistance, mainly determined by central airways caliber and respiratory reactance depends on the compliance of the airways, lung tissue and chest wall [8].

The major limitation of this study was small sample size. In addition for safety reasons we by protocol did not obtain neither IOS measurements nor spirometry measurements in subjects whose FEV1 decreased more than 15% after exercise challenge. Thus the number of subjects left with the full complement of measurements at 5 minute intervals following the challenge is not available for review.

In summary, impulse oscillometry is a noninvasive, safe and validated technique that provides valid indices to explore lung function. A significant correlation was found between spirometry and IOS measurements of change in airway function in asthmatic children both with EIB and without EIB. IOS may play a complementary role in the diagnosis of airway obstruction and bronchodilatation in asthmatic.

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