ORIGINAL ARTICLE
Iran J Allergy Asthma Immunol
September 2012; 11(3): 259-266.

Exercise Induced Changes in Spirometry and Impulse Oscillometry Measurements in Persistent Allergic Rhinitis

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Received: 15 August 2011; Received in revised form: 5 February 2012; Accepted: 26 February 2012

ABSTRACT

The Link between allergic rhinitis and asthma is well known. Bronchial hyperreactivity (BHR) may be present in rhinitis. The present study was aimed to compare airway responses in patients with rhinitis symptoms alone following exercise challenge, and to determine relationship of two different respiratory function tests.

98 subjects with rhinitis were investigated by spirometry and impulse oscillometry before and after exercise challenge.

No significant difference was detected between spirometry and impulse oscillometry measurements before and after exercise challenge in subjects with rhinitis alone. No correlation between spirometry and impulse oscillometry indices was found in pre and post-exercise stages.

We therefore conclude that exercise challenge is not an appropriate test to determine airway hyperresponsive in subjects with rhinitis symptoms alone and findings of spirometry and impulse oscillometry are not interrelated.

Keywords: Bronchial provocation tests; Oscillometry; Respiratory tract diseases; Rhinitis; Spirometry

INTRODUCTION

In recent years there has been expanding knowledge on the relationship between inflammatory diseases of the upper and lower airways. Both epidemiological and physiological data suggest that the upper and lower respiratory tract behave as an integrated unit. In other words, pathophysiological processes that affect one component of this unified system can concurrently impact other portions of the airway and presence or exacerbations of disease in one component of the airway may worsen the airway disease.[1] As a result, an updated international multidisciplinary consensus guideline recommended that ‘‘when considering a diagnosis of rhinitis or asthma, an evaluation of both the upper and lower airways should be made’’.[2]

Allergic rhinitis is the most frequent IgE-mediated disease. Epidemiologic studies show that 78% of patients who have asthma, experience symptoms of rhinitis, both allergic and nonallergic and 38% of

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Published by Tehran University of Medical Sciences (http://ijaai.tums.ac.ir)

patients who have rhinitis have asthma.[3,4] Nasal airflow limitation and inflammation are closely associated with bronchial function, mainly concerning FEV1 values, in patients with respiratory allergy.[5]

Allergic rhinitis has been demonstrated as a strong risk factor for the onset of asthma in adults.[6]

Reversible airflow obstruction is characteristic of asthma and forced expiratory volume/1 second (FEV1) is considered the gold standard in evaluation of bronchial obstruction.[7,8] There is increasing interest to consider small airways dysfunction in the pathogenesis of asthma.[9] To assess small airways, it has been considered that the forced expiratory flow at the 25% and 75% of the forced vital capacity (FEF25–75) might be more sensitive to reveal obstruction in small airways compared to FEV1[10]. Both FEV1 and mainly FEF25–75 have been demonstrated to be impaired in patients with allergic rhinitis who showed no asthma symptoms[11] and FEF25–75 has been considered to be a reliable marker of early bronchial impairment in allergic rhinitis.[12]

Bronchial hyperreactivity (BHR) is a paramount feature of asthma and may be seen in a high proportion of rhinitics.[13] It has been hypothesized that a positive bronchial challenge to methacholine could be a predictive value for those rhinitics that would progress to develop asthma.[14] BHR was reported both in patients with perennial and seasonal allergic rhinitis.[15,16] In a large cohort (>2000) of patients with allergic rhinitis it was demonstrated that 70% of them had BHR.[11]

Recently ARIA group revised the classification of allergic rhinitis defining two types: intermittent and persistent; the new classification does not consider the type of allergen, but the duration (days/week and consecutive weeks) and the severity of symptoms (mild or moderate-severe).[2] According to this new classification of ARIA, in a recent study, BHR by methacholine challenge is considered as a frequent presentation in patients with chronic rhinitis and it is suspected in the presence of defined risk factors.[17]

The small airways only account for 10% of the total airways resistance, which means that conventional tests of the lung function (FEV1) fail to accurately reflect changes in peripheral resistance.[18-20] Impulse oscillometry (IOS) is a forced oscillation technique (FOT), [21,22] which only requires passive cooperation of the test subject to measure lung function.[23-26] Furthermore, it allows for discrimination between central and peripheral obstruction.[27-29] It is considered that patients with allergic rhinitis and symptoms of asthma manifested greater peripheral airway obstruction compared to those with allergic rhinitis only with BHR.[30] Although the clinical efficacy of measuring respiratory resistance and impedance in inflammatory respiratory diseases using spirometry and impulse oscillometry respectively after methacholine challenge has been demonstrated,[30] its usefulness in measuring changes in airway caliber by exercise challenges in rhinitis patients has not been established.

The purpose of this study was to compare airway responses in patients with rhinitis symptoms alone following room temperature exercise challenges and to determine whether impulse oscillometry variables relate to spirometry variables.

MATERIALS AND METHODS

Study Design

The study was performed from the October 2010 till March 2011 in Tehran (Allergy and Clinical Immunology Unit at the Rasoul Akram Hospital, Tehran University of Medical Sciences). To evaluate pulmonary function and the presence of BHR in patients with pure allergic rhinitis, we included subjects with sensitization to pollens, perennial allergens or both kinds of allergens.

We excluded all the subjects who met the following exclusion criteria: asthma symptoms including cough, wheezing, dyspnea, and shortness of breath, previous or current smoking, acute or chronic respiratory infections, anatomic abnormalities (nasal polyposis, sepatal deviation), patients with unilateral nasal symptoms, use of nasal or oral corticosteroids, antihistamines and drugs that cause nose symptoms (nasal decongestants, oral contraceptives, antihypertensives, aspirin and NSAIDS) within the previous 4 weeks.

Subjects

Ninety-eight rhinitis patients were prospectively and consecutively evaluated, 48 females and 50 males with mean age of 26 (±11.98) years (12-44 years old). All of them were inhabitants of Tehran who referred to our allergy clinic for rhinitis evaluation and management.

All of them were evaluated with performing both spirometry and impulse oscillometry before and after exercise challenge test. A detailed clinical history and a complete physical examination including allergy evaluation were performed. The patients were included in the study on the basis of a clinical history of persistent rhinitis (rhinorrhea, nasal obstruction, nasal itching, and sneezing for >4 days/week and >4 weeks [2]). All patients were sensitized to at least one of indoor or outdoor allergens (such as trees, grasses, weeds, fungi, pets and house dust mite). None of the patients was a previous or a current smoker.

Impulse Oscillometry (IOS)

The IOS MasterScreen device (E. Jaeger GmbH, Wurzburg, Germany) consists of a loudspeaker as a pulse generator to send the pressure impulses to the respiratory system.[31]

During tidal breathing, through a plastic mouthpiece, the impulse generator produces brief pressure pulses at intervals of 0.2 s. The superimposed pressure oscillations during normal spontaneous breathing are composed of several frequencies allowing assessment of R and X at several frequencies simultaneously. A fast Fourier analyzer is employed within the system to determine Rrs and Xrs at these frequencies.

The impedance (Zrs) representing a complex airway resistance, which includes two components, the real resistance (Rrs) and the imaginary reactance (Xrs), has also been determined. The frequency range of the signal was from 0 to 100 Hz, and we recorded R5–20 and X5. Rrs at 5 and 20 Hz represent the low (total resistance) and high (central resistance) frequency range, respectively.

During IOS measurements, subjects sat upright with the head in neutral position and a nose clip in place, while supporting their cheeks with their hands.[22] Monitoring took place for 30 seconds over a few respiratory cycles of quiet breathing and when the subjects got used to the forcing signal, baseline impedance measurements were recorded over 90 seconds before challenge testing. The results were averaged over the entire 90 s during which 450 impulses were applied. IOS measurements were systematically applied prior to any forced respiratory maneuver and repeated in the same order after exercise challenge.

Forced Flow volume Measurements in Spirometry

Before bronchial challenge testing, maximal flow volume measurements were performed using a Jaeger-Masterlab (E. Jaeger GmbH, Wurzburg, Germany). The following parameters were measured: FEV1, FVC, FEV1/FVC, PEF and the maximal expiratory flows at 25% and 75% of vital capacity (MEF25 and MEF75). The largest FEV1 value from three acceptable maneuvers was used as the baseline FEV1.[7,8]

Exercise Challenges

Mode of exercise was motor-driven treadmill in which speed and grade were chosen to produce 4-6 min of exercise at near-maximum targets with a total duration of exercise of 6-8 min.

Starting at a low speed and grade, both were progressively advanced during the first 2-3 min of exercise until the heart rate reached to 80-90% of the predicted maximum (calculated as 220 - age in years).[32]

The test accomplished by conducting the study in an air-conditioned room (with ambient temperature of 20-25” C) with low relative humidity (50% or less). Due to better compatibility of the subjects with the procedure, no nose clip used during running.

Statistical Analysis

Descriptive statistics for resting lung function were calculated for IOS and spirometry lung function measurements. Airway responses were analyzed by analysis of variance, followed by paired t tests. Pearson correlations were used to evaluate relationships between resting and post challenge measurements of spirometry and impulse oscillometry measurements and their related changes (post – pre exercise challenge). Analysis was performed using NCSS statistical analysis software 2007. $P<0.05$ was considered significant.

RESULTS

Patients' Characteristics

During the study period, 98 patients entered the study (48 females, 50 males) with the mean age of 26±11.98 years, weight 63.06±18.76 kg, height 1.62±0.15 m and BMI 23.49±4.78 kg/m^2.

Frequency of rhinitis and its associated symptoms were as follows: rhinorhea 82%, Nasal obstruction 80%, nasal itching 58%, sneezing 58%, abnormal sleep 21%, impairment of daily activities 47%, impaired work and school 8%, troublesome symptoms 94%. Totally, 95% of patients fulfilled the moderate to severe rhinitis criteria based on ARIA guidelines.

Table 1. Mean (±SD) of pre and post-exercise lung function measurements (spirometry and impulse oscillometry) and their correlation and differences

TYPE of PFT	Variable	Pre-Exercise Mean (SD)	Post-Exercise Mean (SD)	Correlation (Cronbach Alpha)	Paired t-test (*p* value)
SPIROMETRY	FEV1	3.16 (0.99)	3.18 (1.00)	0.96*	0.49
	FEV1%	97.78 (13.95)	98.15 (13.63)	0.83*	0.64
	FVC	3.57 (1.14)	3.53 (1.14)	0.94*	0.27
	FVC%	94.58 (15.56)	93.50 (16.48)	0.80*	0.29
	FEV1/FVC%	88.90 (6.64)	90.54 (7.62)	*0.63*	0.01**
	PEF	6.58 (1.98)	6.66 (2.03)	0.95*	0.15
	PEF%	93.53 (11.30)	94.83 (12.36)	*0.77*	0.11
	FEF25-75	3.70 (1.23)	3.79 (1.38)	0.89*	0.11
	FEF25-75%	99.91 (19.70)	102.16 (25.09)	*0.78*	0.16
IMPULSE OSCILOMETRY	VT	0.75 (0.37)	0.78 (0.33)	0.59	0.38
	VT%	157.31 (82.26)	161.23 (67.72)	0.53	0.60
	Z5	0.45 (0.34)	0.43 (0.24)	0.91*	0.22
	Z5%	115.39 (51.03)	113.73 (43.50)	*0.76*	0.61
	R5	0.42 (0.24)	0.40 (0.20)	0.82*	0.25
	R5%	109.43 (42.89)	107.13 (39.23)	*0.74*	0.44
	R20	0.28 (0.12)	0.27 (0.10)	*0.75*	0.25
	R20%	93.08 (35.97)	91.12 (33.93)	*0.74*	0.43
	X5	(-)0.15 (0.27)	(-)0.13 (0.13)	0.92*	0.23
	X5%	140.01 (3540.08)	220.10 (3184.63)	0.97*	0.35
	rfreq	17.13 (4.93)	16.44 (4.87)	0.80*	0.02**
	Rcent	0.20 (0.11)	0.21 (0.11)	*0.74*	0.80
	Rperi	0.30 (0.28)	0.29 (0.24)	0.87*	0.34

*correlation indices ≥ 0.8 were considered excellent **p value < 0.05 was considered significant

Pre and Post-exercise Lung Function

Mean (SD) of pre and post-exercise lung function measurements (spirometry and impulse oscillometry) and their correlations and changes are presented in Table 1.

There was no significant differences between pre and post-exercise lung function studies except for FEV1/FVC% in spirmetry which was significantly greater in post challenge stage (p=0.01) and resonant frequency (rfreq) which was significantly greater in the pre challenge stage (p=0.02).

Pre and post-exercise measurements were significantly correlated specially for the indices which are related to airway resistance (FEV1 and FEF25-75 in spirometry and R5 and R20 in impulse oscillometry).

Relationship between Spirometry and Impulse Oscillometry

Correlations of spirometry and impulse oscillometry values in pre and post-exercise stages and the changes between these two stages are summarized in table-2 (r≥8.0=excellent and 0.6≤r<0.8=good correlations).

In pre-exercise stage, there were excellent correlations between (FEV1 and FVC, Z5 and R5, Z5 and R20, R5 and R20) and good correlations between (FEV1 and PEF, FEV and FEF25-75, FVC and PEF).

In the post-exercise stage there were excellent correlations between (FEV1 and FVC, Z5 and R5, R5 and R20) and good correlations between (FEV1 and PEF, FEV1 and FEF25-75, FVC and PEF, Z5 and R20).

In considering the changes of values between pre and post-exercise stages, there were excellent correlations between (ΔFEV1 and ΔFEV1/FVC, ΔR5 and ΔR20) and good correlations between (ΔZ5 and ΔR5, ΔZ5 and ΔR20).

Interestingly, there was not any correlation among spirometry and impulse oscillometry measurements in pre and post-exercise stages or their changes between the two measurements.

Table 2. Correlations of spirometry and impulse oscillometry values in pre and post-exercise stages and the changes between these two stages

PRE EXERCISE	FEV1	FVC	FEV1/FVC	PEF	FEF25-75	VT	Z5	R5	R20	X5	rfreq	Rcent
FEV1	-	-	-	-	-	-	-	-	-	-	-	-
FVC	0.92	-	-	-	-	-	-	-	-	-	-	-
FEV1/FVC	0.02	-0.43	-	-	-	-	-	-	-	-	-	-
PEF	0.72	0.61	0.15	-	-	-	-	-	-	-	-	-
FEF25-75	0.79	0.55	0.35	0.59	-	-	-	-	-	-	-	-
VT	0.13	0.12	0.02	0.01	0.09	-	-	-	-	-	-	-
Z5	0.17	0.11	0.03	0.08	0.25	0.09	-	-	-	-	-	-
R5	0.23	0.12	0.06	0.08	0.39	0.09	0.95	-	-	-	-	-
R20	0.08	0.04	0.04	0.03	0.25	0.16	0.80	0.89	-	-	-	-
X5	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	-	-	-
rfreq	0.23	0.11	0.08	0.04	0.24	0.00	0.14	0.17	0.09	0.00	-	-
Rcent	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.04	-
Rperi	0.00	0.00	0.01	0.00	0.00	0.00	0.01	0.01	0.00	0.00	0.08	0.31
POST EXERCISE												
FEV1	-	-	-	-	-	-	-	-	-	-	-	-
FVC	0.86	-	-	-	-	-	-	-	-	-	-	-
FEV1/FVC	0.00	-0.57	-	-	-	-	-	-	-	-	-	-
PEF	0.76	0.65	0.09	-	-	-	-	-	-	-	-	-
FEF25-75	0.72	0.36	0.41	0.50	-	-	-	-	-	-	-	-
VT	0.10	0.06	0.01	0.00	0.11	-	-	-	-	-	-	-
Z5	0.26	0.30	0.03	0.21	0.09	0.26	-	-	-	-	-	-
R5	0.12	0.13	0.01	0.10	0.04	0.32	0.92	-	-	-	-	-
R20	0.02	0.05	0.00	0.06	0.06	0.25	0.77	0.87	-	-	-	-
X5	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	-	-	-
rfreq	0.46	0.22	0.09	0.21	0.24	0.05	0.13	0.16	0.03	0.00	-	-
Rcent	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.03	-
Rperi	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.01	0.00	0.00	0.07	0.49
DIFFERENCE	**Δ FEV1**	**Δ FVC**	**Δ FEV1/FVC**	**Δ PEF**	**Δ FEF25-75**	**Δ VT**	**Δ Z5**	**Δ R5**	**Δ R20**	**Δ X5**	**Δ rfreq**	**Δ Rcent**
Δ FEV1	-	-	-	-	-	-	-	-	-	-	-	-
Δ FVC	0.80	-	-	-	-	-	-	-	-	-	-	-
Δ FEV1/FVC	0.05	-0.67	-	-	-	-	-	-	-	-	-	-
Δ PEF	0.29	0.07	0.22	-	-	-	-	-	-	-	-	-
Δ FEF25-75	0.55	0.28	0.26	0.10	-	-	-	-	-	-	-	-
Δ VT	0.05	0.05	0.07	0.07	0.07	-	-	-	-	-	-	-
Δ Z5	0.07	0.05	0.15	0.01	0.01	0.08	-	-	-	-	-	-
Δ R5	0.02	0.05	0.12	0.05	0.01	0.17	0.78	-	-	-	-	-
Δ R20	0.02	0.03	0.01	0.02	0.02	0.10	0.76	0.88	-	-	-	-
Δ X5	0.00	0.00	0.00	0.00	0.00	0.05	0.01	0.01	0.00	-	-	-
Δ rfreq	0.20	0.30	0.15	0.01	0.01	0.00	0.07	0.04	0.00	0.00	-	-
Δ Rcent	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-
Δ Rperi	0.00	0.00	0.03	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.03

DISCUSSION

In this study, we compared the spirometry and impulse oscillometry findings in patients with persistent rhinitis alone (without any asthma symptoms) who had undergone exercise challenge test.

Based on the above mentioned results there were not any significant differences in pre and post challenge spirometry findings except for FEV1/FVC% which was greater in the post-exercise stage, i.e. not only challenge did not increase airways resistance but also led to decreased overall resistance of these patients. In impulse oscillometry there was no significant difference in impedence (Z5), airway resistances (R5, R20, R-central, and R-peripheral), and reactance (X5) due to exercise. The only difference in impulse oscillometry was seen in resonant frequency (rfreq) which was decreased in the post-exercise stage maybe due to overall although insignificant decrease of lung resistance in patients after exercise with indirect effect on resonant frequency.

Correlation studies revealed that in both pre- and post-exercise stages during spirometry, good to excellent correlations were present among central resistance indices (FEV1 and FVC, FEV1 and PEF, PEF and FVC) and central and peripheral resistance indices with each other (FEV1 and FEF25-75).

In impulse oscillometry, good to excellent correlations were found between central and overall lung resistance (R5 and R20) and also between impedence (Z5) and resistance indices (R5 and R20). Interestingly, no correlations between R5 (), R20 (), R-central (), and R-peripheral () were seen. This unusual finding might be due to calculations which were done by software to produce R-central and R-peripheral values and it seems better to rely on R5 and R20 more than R-central and R-peripheral during exploring impulse oscillometry findings.

Another interesting finding was that significant correlations were seen only among spirometry and impulse oscillometry indices and their related pre- and post-exercise changes separately; in other words no significant correlation was found between spirometry and impulse oscillometry in this study and based on the findings of each test, it could not be possible to estimate appropriate changes in another one.

In multiple previous studies, the relationships of spirometry and impulse oscillometry findings were investigated in asthma. Evans et al concluded that correlations were found between spirometric and IOS measures of change in airway function for exercise challenge.[33] Mansur et al stated airway resistance measured by IOS during methacholine challenge correlated better with asthma symptoms than traditional spirometric measures implying a higher sensitivity index[34] and in a similar study, Malmberg et al found that increase of 35% in Rrs5 after a free running test could be regarded as an abnormal response and wheezy children showed an enhanced airway response, which was clearly distinguishable from the control subjects.[35]

Other studies investigated airway hyper responsiveness of rhinitis patients during spirometry after methacholine challenge. Ciprandi et al found that an impairment of spirometric parameters may be observed in patients with seasonal allergic rhinitis alone during the pollen season and a high percentage of these patients had BHR[36]. Cirillo et al evidenced that an impairment of spirometric parameters and BHR may be observed in patients with allergic rhinitis alone and careful evaluation of lower airways should be performed in patients with allergic rhinitis alone[37] and BHR was frequently present in patients with chronic rhinitis and should be suspected in the presence of defined risk factors.[17]

In a recent study Aronsson, et al compared the degree of involvement of the peripheral airways during metacholine challenge test in asthmatics and patients with allergic rhinitis with or without BHR by using the impulse oscillometry (IOS) and spirometry techniques and concluded that patients with allergic rhinitis and symptoms of asthma manifested greater peripheral airway obstruction compared to those with allergic rhinitis only with BHR.[30]

Although there have been many similar studies around the subject but it seems that the present study could be unique for exploring the role of exercise challenge before and after both spirometry and impulse oscillometry techniques simultaneously in patients with allergic rhinitis alone specially considering the relationship of the two techniques to each other.

This study produced two findings that are noteworthy. Our study indicated that there was no significant differences between pulmonary function tests (spirometry and impulse oscillometry) before and after exercise as a challenge test in patients with allergic rhinitis alone (without any asthma symptoms). The other important finding was that spirometry and impulse oscillometry were not correlated in this study and in other words oscillometric findings could not be extrapolated from spirometry and vice versa. It could be concluded that exercise challenge is not an appropriate test to determine airway hyperresponsiveness in subjects with rhinitis symptoms alone and findings of spirometry and impulse oscillometry are not interrelated.

ACKNOWLEDGEMENTS

We thank Dr. Ali Javad Mousavi and Dr. Kamran Kamrava for their feedback during this research.

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