Lung function changes in non-asthmatic allergic rhinitis patients: a case series

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Received 16th May 2011; revised 9th August 2011;
accepted 16th August 2011; online 17th November 2011

http://dx.doi.org/10.4104/pcrj.2011.00089

Dear Sirs,

Is allergic rhinitis (AR) a marker for subclinical asthma or a predictor for the future development of asthma? Firstly, there is evidence that the lower airways of patients with AR show evidence of inflammation.[1] Secondly, pulmonary function tests in AR patients with no symptoms suggestive of asthma have shown alterations in forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), FEV_1/FVC ratio, and forced expiratory flow between 25-75% of forced vital capacity (FEF_{25-75}).[1,2] Both FEV_1 and FVC are normally associated with overt airway obstruction, whereas FEF_{25-75} is reduced in patients with small airways inflammation, may be altered before FEV_1, and is considered a predictor of airway obstruction.[3,4] We wanted to track the profile of airway obstruction in a case series of non-asthmatic AR patients presenting to a general medicine practice in a developing country, aiming to investigate the role and limits of spirometry at the primary care level.

We therefore conducted a prospective cross sectional observational study and investigated the lung function of all AR patients who presented consecutively to the General Medicine outpatient clinic of the University Hospital in Lattakia, Syria, between October 1st 2008 and August 1st 2009. The main inclusion criterion was a clinical diagnosis of AR as noted in the patient's medical record. Exclusion criteria included a past history of asthma and bronchitis, a history of current or previous smoking, immunotherapy, anatomic nasal abnormalities, and AR treatment in the last four weeks. We obtained ethics approval from the hospital Ethics Board and obtained signed informed consent from every participant.

The diagnosis of AR was confirmed by clinical history and positive skin prick tests. Patients were classified into intermittent or persistent rhinitis, and stratified into mild, moderate or severe categories. Treatment was administered according to the ARIA-WHO report of 2008.[1] The treatment protocol included two nasal inhalations of 50 µg beclometasone twice-daily.[1]

Patients had pulmonary function tests conducted upon enrolment and after two weeks of therapy. Pulmonary function tests were interpreted using European Respiratory Society guidelines.[3,4] Specifically, a flow volume loop was performed at baseline for all included patients using Vmax Sensor Medics Body Box. FEV_1 and FVC were expressed as % predicted and were considered abnormal if < 80% predicted using ECSC reference equations.[3] FEF_{25-75} was considered abnormal if less than 65% predicted,[4-6] especially if the shape of the expiratory curve was concave.[3] In patients showing a reduction in FEV_1, FVC or FEF_{25-75}, reversibility test (after inhalation of 200 µg of salbutamol via Aerochamber) was performed and was considered positive if FEV_1 improved by 12% and 200 ml or FEF_{25-75} improved by > 30% of baseline values.[3-4] Flow volume loop was repeated after two weeks of treatment for patients who showed alteration of any spirometric value at baseline. Statistical analysis was carried out with Stata version 6. We considered p values <0.05 to be significant.

Sixty patients were enrolled, 34 women and 26 men; mean age was 28 ±9 years. AR was intermittent in (23%), persistent in (77%), mild in (73%) and moderate/severe in (27%). Pulmonary function tests revealed that the mean FEV_1% was 105±17% of predicted, FVC was 114±17% of predicted, and FEF_{25-75} was 92±25% of predicted. Four patients had FEV_1% <80% predicted, two patients had FVC<80%, while 21 patients had FEF_{25-75} below 65% predicted. FEV_1% predicted was the highest in mild intermittent AR patients and the least in moderate to severe AR patients (120±11% versus 89±14%, p<0.001). Similar findings were observed for FEF_{25-75} (see Table 1). We did not find any functional abnormalities in intermittent AR.

FEV_1% predicted and FEF_{25-75}% predicted were inversely correlated with the degree of severity of AR. These associations were independent of potential confounding factors (age, gender, allergic rhinitis duration) as shown by multiple linear regressions (see Table 2). For the 21 patients who showed alteration of any spirometric value at baseline, reversibility testing was positive in all cases for both FEV_1 and FEF_{25-75}. FEV_1 improved by 22±11% (p <0.001), FVC by 5±9% (p=0.03) and FEF_{25-75} improved by 30±11% (p<0.001) after treatment.

In this study, we provide evidence that the presence of a reduced FEF_{25-75} in patients with AR, even in the absence of a reduction in FEV_1 or FVC, may signify airway obstruction in these patients. Alteration in FEF_{25-75} reflects inflammation of small airways less than 2mm diameter,[3,4] so FEF_{25-75} may well be an early predictor of airway obstruction.[2-7] Using a definition of reduced FEF_{25-75} as <80% of predicted, Ciprandi found that 87% of patients with persistent moderate/severe AR had a reduction in

Table 1. Characteristics of patients included in the analysis, according to the category of allergic rhinitis

Allergic Rhinitis	Mild intermittent	Moderate to severe intermittent	Mild persistent	Moderate to severe persistent	
	11	3	33	13	p
Women, n (%)	4 (36.4)	1 (33.3)	19 (57.6)	10 (76.9)	0.20
Age, year, mean±SD	26.7±4.3	23.3±8	28.7±9.9	26.5±7.7	0.68
AR duration, mean±SD	5.5±4.0	9±5.6	4.7±4.1	3.7±2.6	0.18
FEV_1% predicted,					
• mean±SD	120±11	111±21	105±15	89±14	<0.001
• <80%, n (%)	0	0	2(6.1)	2(15.6%)	0.46
FVC% predicted,					
• mean±SD	119±11	124±17	110±16	116±23	0.30
• <80%, n (%)	0	0	1(3)	1(7.7)	0.74
FEF 25-75%,					
• mean±SD	114±17	102±21	94±23	66±15	<0.001
• < 65%, n (%)	0	0	9(27.3)	12(92.3)	<0.001

Table 2. Relationship between allergic rhinitis respiratory function by multivariate† linear regression

	Regression coefficient	95% Confidence Interval	p value ‡
FEV_1 % predicted			
Allergic rhinitis, %			
• Mild Intermittent	0	reference	
• Moderate to severe intermittent	-0.11	(-0.30, 0.08)	0.24
• Mild persistent	-0.12	(-0.23, -0.02)	0.02
• Moderate to severe persistent	-0.28	(-0.40, -0.15)	<0.001
FVC % predicted			
Allergic rhinitis, %			
• Mild Intermittent	0	reference	
• Moderate to severe intermittent	0	(-0.22, 0.22)	0.99
• Mild persistent	-0.08	(-0.20, 0.04)	0.20
• Moderate to severe persistent	-0.03	(-0.17, 0.12)	0.70
FEF (25-75%)			
Allergic rhinitis, %			
• Mild Intermittent	0	reference	
• Moderate to severe intermittent	-0.14	(-0.40, 0.11)	0.24
• Mild persistent	-0.16	(-0.30, -0.02)	0.02
• Moderate to severe persistent	-0.42	(-0.59, -0.25)	<0.001

†Adjustment for sex, age and allergic rhinitis duration. ‡ for regression coefficient

FEF_{25-75}.[7] We believe that using a definition of reduced FEF_{25-75} as <65% is more clinically relevant and would result in better identification of the concomitant presence of airway obstruction in AR. The rationale for our cut-off value is that FEF_{25-75} is a highly variable spirometric test and needs a very good technique and normal FVC.[3-5] McFadden comments on technical problems and the non-standardisation of normal value of FEF_{25-75},[5] referring to the NHLBI cut-off of 65%.[6]

Our data are consistent with published reports advocating the use of FEF_{25-75} as a predictor of airway obstruction in selected patients.[2-7] In the medical literature, "positive reversibility test" refers to reversibility in FEV_1. The reversibility of FEF_{25-75} is difficult to interpret, but a cut-off of more than 30% improvement from baseline covers the normal over-time changes.[4] For example, air trapping in asthma patients in the presence of normal FEV_1 has been documented;[6] in these

patients, FEF_{25-75} has been shown to be better correlated with air trapping than FEV_1%, which explains the ability of FEF_{25-75} to predict response to bronchodilator administration.[6]

Our results support the one airway/one disease hypothesis,[1,2,8] linking AR and asthma. This is plausible for several reasons. First, genetically, there are common atopic predispositions for AR and asthma. Second, AR and asthma share common pathological aspects; in biopsy studies, there was a high eosinophil count in AR even without asthma, with thickness of the bronchial reticular basement membrane in isolated AR. Third, from the pathogenesis point of view, the systemic release of IL-5 and the stimulation of bone marrow eosinopoiesis after allergen inhalation (challenge test) are important factors involved in the process of global airway allergy.[8]

One limitation of our study is the small numbers. We do not recommend spirometry testing for patients classified as intermittent allergic rhinitis. This could save time and money in primary care, but we do need a larger sample to confirm this finding.

Data from our study raise some additional questions that require further research. First, what is the appropriate cut-off for a clinically relevant reduction in FEF_{25-75}? There is a need to reach consensus on interpretation of FEF_{25-75},[3] including technical recommendations, the normal cut-off normal values, the methods and reference for a positive reversibility test using FEF_{25-75}, and consensus regarding its utility in practice and its significance as a risk factor for asthma in AR patients. Secondly, can early treatment of AR prevent the onset of asthma? Several pharmacological trials have shown that intranasal inhaled steroids improve asthma control. However, the role in preventing the allergic march from rhinitis to asthma has not been investigated.[8]

Acknowledgments

We are grateful to Prof. Mounir Osman, the director of the Lattakia hospital, and to Prof. Bassim Dubaybo from Wayne State University for his help in reviewing the manuscript before submission.

Conflicts of interest

The authors declare that they have no conflicts of interest in relation to this article.

Contributorship

Dr Yousser Mohammad participated in the study design, writing the manuscript and supervising. Dr Rafea Shaaban participated for the statistical analysis, and the writing of the manuscript. Dr Mustafa Ibrahim participated in the study design and nose examination. Moussa Ismail is a post graduate medical student, he did the data collection and performed plethysmography, and also participated in the drafting of the manuscript.

Funding

None.

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Knowledge of pulse oximetry among general practitioners in South Australia

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Received 8th August 2011; accepted 14th August 2011;
online 24th October 2011

http://dx.doi.org/10.4104/pcrj.2011.00088

Dear Sirs,

Pulse oximetry is a non-invasive, reliable technology for measuring arterial oxygen saturation (SpO2).[1] Pulse oximeters are part of standard care and it is hard to imagine emergency departments, intensive care units and general hospital wards without them. Recently, portable, user-friendly and relatively non-expensive pulse oximeters have become available, making them