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Original Research Article

The Role of Forced Expiratory Flow at 25-75 Measurement as A Predictor of Positive Reversibility Test in Asthmatic Patients with Normal Pulmonary Function Test

Safaa Jawad Kadhem
College of Medicine, University of Babylon, Hilla, IRAQ

E-mail: safaajawadk@yahoo.com

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Abstract

In the mild asthmatic attacks, partially treated asthma, early stages of bronchial asthma and in between the asthmatic attacks, sometimes we find patients with a history suggestive of asthma and normal PFT (FEV1 +FEV1/FVC > 80% of the predicted value).

This study investigated the value of FEF 25-75 measurement as a predictor of the presence of a reversible airway obstruction (RAO) in adult patients with clinical features of asthma and normal pulmonary function test.

64 patients with clinical features suggestive of asthma and normal pulmonary function test were included in the study. These patients were subdivided into three groups, group 1 were those with normal pulmonary function test and FEF 25-75>70%, group 2 were those with normal pulmonary function test and FEF 25-75< 70%>55% and group 3 are those with normal pulmonary function test and FEF 25-75<55%.each of the study group was compared with 35 sex and age matched healthy volunteers. Forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC), FEV1/FVC and FEF25 – 75 were measured before and 10-20 minutes after salbutamol administration (by nebulizer).

Of the 64 subjects, the percentage of subjects with RAO (FEV1 increase after bronchodilator >12 %) was lower (11%) in the group 1 (27 subjects) and higher (44%) in the subjects of the group 2 (23 subjects) and highest (52%) in the subject of group 3 (14 subjects). FEF25-75 percent predicted is a good predictor of the presence of reversible airways obstruction in asthmatic patient with normal PFT.

Key words: asthma, pulmonary function test, reversible airways obstruction

الخلاصة

قد نجد احيانا ان نتيجة فحص وظائف الرئة طبيعية لدى المرضى الذين لديهم تاريخ مرضي يشير لمرض الربو القصبي خاصة اثناء نوبات الربو الخفيفة، الربو المعالج جزئيا، المراحل المبكرة من مرض الربو القصبي، وبين نوبات الربو. صمم هذا البحث لدراسة الفائدة من قياس تدفق الزفير ألقسري بين ٢٥–٧٥ بوصفه مؤشرا على وجود انسداد مجرى الهواء قابل للانعكاس في المرضى البالغين الذين يعانون من المظاهر السريرية لمرض الربو و تظهر نتيجة وظائف الرئة لديهم طبيعية. شملت الدراسة ٦٤ من المرضى الذين يعانون من المظاهر السريرية التي تشير الى الربو وطبيعية اختبار وظائف الرئة في الدراسة. تم تقسيم هؤلاء المرضى إلى ثلاث مجموعات, نتائج وظائف الرئة لكل مجموعة تمت مقارنتها مع نتائج وظائف الرئة ل ٣٥ من المتطوعين الأصحاء. تم قياس وظائف الرئة لجميع المرضى والمتطوعين في بداية الدراسة وبعد ١٠–٢٠ دقيقة من استنشاق عقار السالبيوتامول عن طريق البخاخ. اظهر البحث ان تدفق الزفير ألقسري بين ٢٥–٧٥ هو مؤشر جيد على وجود انسداد مجرى الهواء قابل للانعكاس في المرضى البالغين الذين يعانون من المظاهر السريرية لمرض الربو و نتيجة وظائف الرئة طبيعية.

الكلمات المفتاحية : الربو القصبي , فحص وظائف الرئة, تدفق الزفير القصري بين ٢٥–٧٥

Introduction

Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. Chronic inflammation is associated with episodic airway obstruction characterized by expiratory airflow limitation [1].

The management guidelines of bronchial asthma [2–5] consider the use of a reversibility test with a bronchodilator to confirm the diagnosis of asthma and to asses the therapeutic effectiveness of β2-agonists. However, these guidelines do not define a threshold value of pulmonary function test results (forced expiratory volume [FEV1] or other) whether normal or abnormal, over which it is not important to perform a reversibility test to confirm the diagnosis of asthma.

Some patients present with symptoms of asthma but with a "normal" spirometry. A reversibility test with a bronchodilator could be useful in these subjects. Usually, the evidence of a FEV1/forced vital capacity (FVC) > 80% or FEV1/VC > 88%– 89% ratio by spirometry represents a cut-off to distinguish normal subjects from those with airflow obstruction [1, 3, 5]; and according to these references the use of a reversibility test in patients with "normal" lung function could be poorly important. But, a precise and normal FEV1 or FEV1/VC value, for every subject, does not exist [3, 4]; therefore, individuals with bronchial asthma symptoms and with a "normal" lung function test who must perform a reversibility test with a bronchodilator should be determined. In two recent reversibility test studies, using salbutamol or albuterol, approximately 25% of the adults and 26% of the children, with a "normal" pulmonary function test (FEV1 and FEV1/FVC > 80%) and asthmatic symptoms, showed a FEV1 increase greater than 12% [6,7]. This could avoid performing a bronchial provocation test or a PEF monitoring to confirm the diagnosis of asthma in these subjects.

The criteria commonly used to define a reversibility test positive (using salbutamol) are increases in FEV1 and/or FVC_12% (from the theoretical or from the basal) and at least 200 mL of these, 15 to 20 minutes after the bronchodilator inhalation [5,6]. Also, an increase in PEF over than 15%, after bronchodilator, is considered significant [1]. In the subjects with FEV1 and FEV1/FVC > 80%, the evidence of increasing forced expiratory flow (FEF25−75) >35% (calculated to the iso volume) can be also considered significant to assess positive a reversibility test using salbutamol [6- 8].

FEF25-75 has also been used as a measure of small airways function [8, 9]. It has been shown to be an early marker of bronchial impairment in patients with seasonal allergic rhinitis and can predict bronchial hyper-esponsiveness in allergic individuals with airway disorders [9, 12]. In patients with mild asthma and normal FEV1, FEF25-75 can be impaired either at baseline or can decrease in response to exercise without any decline in FEV1 [10, 11, 13].

Bronchial hyper-responsiveness (BHR) is one of the cardinal features of asthma that serves as main diagnostic criteria [14-19]. Patients with symptoms suggestive of asthma whose spirometry is normal and do not respond to bronchodilators (BD), defined as less than 12% improvement in FEV1, are referred to the metacholine challenge test (MCT) [15]. The metacholine challenge test, the gold-standard for the diagnosis of BHR, is both time-consuming and costly [16] and unfortunately this test is not available in our country.

The aim of this study was to assess if the measurement of forced expiratory flow (FEF25−75) could be useful to determine the group of patients with asthmatic symptoms and normal pulmonary function test in whom a reversibility test using salbutamol, can be used to confirm the diagnosis of asthma, as it is not practical to perform reversibility test in all patients with normal PFT.

The Aim of the study was to evaluate the usefulness of FEF 25-75 measurement as a predictor of the presence of a reversible airway obstruction (RAO) in adult patients with clinical features of asthma and normal pulmonary function test.

Materials and Methods

The study was conducted in the pulmonary function test unit in Merjan

teaching hospital between march 2011 to august 2012.

Sixty four patients (mean age 30.21 ± 10.51; 33 males and 31 female; non smokers) with clinical features suggestive of asthma (dyspnea and/or cough and/or chest tightness and/or wheezing), who were referred for pulmonary function testing for the first time and their pulmonary function test results are normal were included in this study. All the patients in the study group underwent pulmonary function testing at baseline (table 1) and 10-20 minutes after inhaled b2-agonist (nebulised salbutamol). according to the baseline results the study group were subdivided into three groups:

Group 1 are those with normal pulmonary function test and FEF 25-75>70%,

Group 2 are those with normal pulmonary function test and FEF 25-75< 70%>55%

Group 3 are those with normal pulmonary function test and FEF 25-75<55%.

Each of the study group was compared with 35 sex and age matched non smoker healthy volunteers (mean age 29.5 ± 7.43; 19 males, 16 females).

The study was performed by using MIR spirolab III spirometer which can be used as standalone or computer based spirometer. Testing was based on a complete FVC test according to the ERS guidelines and repeated three times after adequate instruction of the persons being tested [21]. In this study, the following parameters were obtained: FVC, FEV1, PEF, FEF25 75, and FEV1/ FVC ratio. Parameters were expressed as percentages of predicted values [22]. The pulmonary function test results were considered normal if FEV1>80 % and FEV1/FVC > 80%.

For each subject, a second FVC test was performed, similar to the first one, 10-20 minutes after inhalation of salbutamol by nebulizer (reversibility test). For the forced expiratory volume in first second (FEV1), the increase obtained after inhaling salbutamol was expressed as a percentage of the prebronchodilator value: postbronchodilator value (mL) prebronchodilatator value (mL)/ prebronchodilator value (mL)*100.These values were calculated automatically by the spirometer.

The reversibility test with salbutamol was considered positive (subjects with reversible airflow obstruction = RAO) when an increase in FEV1>12% over baseline was found [20].

Table 1 :Features of controls and the study groups at baseline

	Control group	**Group1**	**Group2**	**Group3**
No. of subjects (M/F)	35 (19/16)	27 (14/13)	23 (12/11)	14 (7/7)
Age (mean ± SD)	29.5 ± 7.43	30.65±12.23	30.44±6.77	29.84 ± 11.21
FVC	110.9 ± 6.86	89.34 ± 8.23	88.85 ±9.66	84.95 ±9.96
FEV1	108.7 ± 5.89	90.91 ± 5.66	89.44 ± 9.04	83.84 ± 2.98
FEV1/FVC	102.6± 7.12	89.87 ± 1.84	90.1 ± 6.11	91.12 ± 7.15
FEF25 – 75	105.3± 44.2	83.9 ± 89.13	60.6 ± 2.56	53.23 ± 8.65
PEF	119.1± 3.55	96.75 ± 68.88	95.98 ± 64.44	86.98 ± 89.08

At baseline, lung function tests are expressed as mean percentage of the predicted value ± standard deviation.

Statistical analysis

Statistical analysis was done using a student t-test for independent group (two-tailed). The level of significance was taken as $p<0.05$.

Results

The results of post bronchodilators changes of variable PFT parameters in the

three study groups and the control group were shown in tables 2,3,4 respectively.

Table 2: Percent increase in PFT parameters after bronchodilator in controls and group 1 patients (Results are expressed as mean and standard deviation).

	Control (no.35)	Group 1 (no. 27)
FVC	0.72 ± 2.8	2.8 ± 1.8
FEV1	3.1 ± 2.2	4.99 ± 4.1
PEF	3.32± 0.9	4.19 ± 3.9
FEF25 – 75	17.91 ± 4.1	18.1 ± 17.9

Of group 1 patient only 3 patients (11%) shows significant increase in FEV1 in post bronchodilators FVC test.

Table 3: Percent increase in PFT parameters after bronchodilator in controls and group 2 patients (Results are expressed as mean and standard deviation).

	Control (no.35)	Group 2 (no. 23)
FVC	0.72 ± 2.8	3.49 ± 3.31
FEV1	3.1 ± 2.2	8.12 ± 7.9
PEF	3.32± 0.9	4.98 ± 4.12
FEF25 – 75	17.91 ± 4.1	27.78 ± 24.9

Of group 2 patient 10 patients (44%) shows significant increase in FEV1 in post bronchodilators FVC test.

Table 4: Percent increase in PFT parameters after bronchodilator in controls and group 3 patients (Results are expressed as mean and standard deviation).

	Control (no.35)	Group 3 (no.14)
FVC	0.72 ± 2.8	4.26 ± 4.01
FEV1	3.1 ± 2.2	9.75 ± 8.1
PEF	3.32± 0.9	5.08 ± 4.92
FEF25 – 75	17.91 ± 4.1	29.94 ± 26.1

The most significant increase in FEV1 in post bronchodilator FVC test occur in group 3 patients in which 7 patients shows evidence of reversible airway obstruction (FEV1 increase > 12% after bronchodilators) which represent 57% of the group patients.

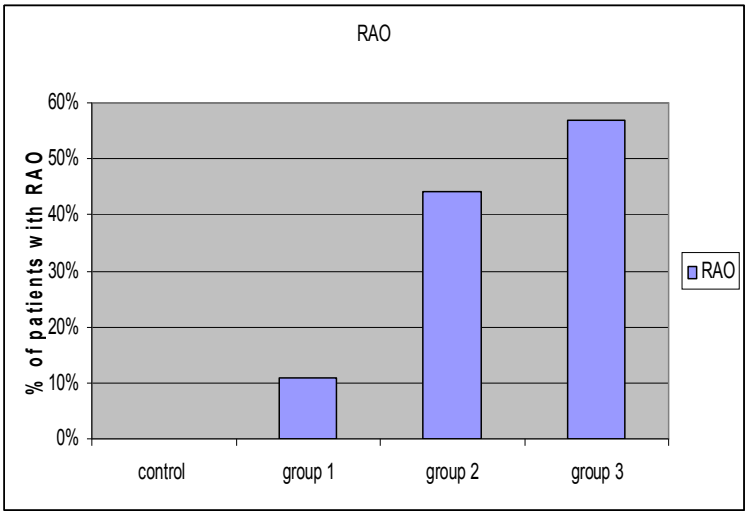

Figure 1: Percentage of patients with RAO in each of the study group and the control group

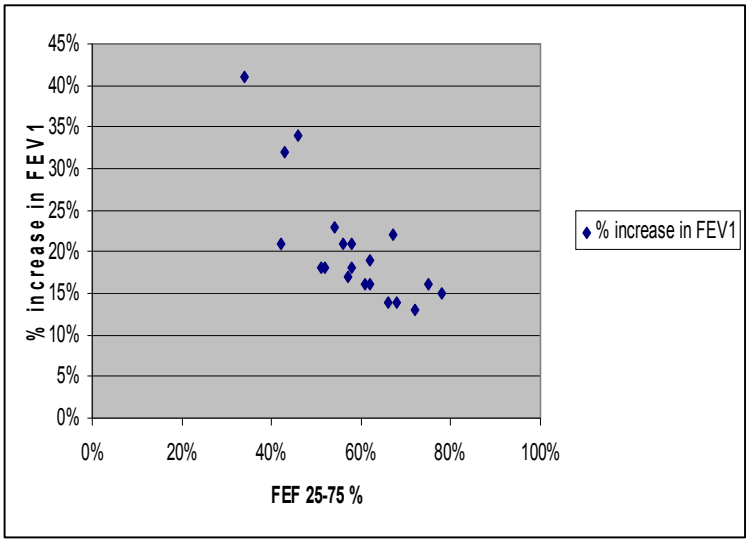

Figure 2 : Correlation between increases in FEV1 and FEF25 – 75 in the patients with RAO.

Discussion

Asthma is characterized by airflow obstruction reversibility. The gold standard to evaluate airways obstruction is forced expiratory volume/1 second (FEV1). [23,24]

There is also suggestion of a possible involvement of small airways in the pathogenesis of asthma. [25]Even though there is no direct parameter able to assess the obstruction/inflammation of small airways, it has been proposed that the forced expiratory flow at the 25% and 75% of the pulmonary volume (FEF25–75) might be a suitable parameter to determine a small airway obstruction rather than FEV1. [26] It has been demonstrated that impaired value of FEF25–75 is useful in predicting airway responsiveness, as it may also be a more sensitive indicator of chronic airflow obstruction than FEV1, as well as a risk factor for the persistence of respiratory symptoms in children suffering from allergic asthmatic symptoms. In addition, it has to be considered that subjects with mild asthma and normal FEV1 may show impaired FEF25–75 only [27].

Respiratory symptoms indicative for asthma suppose an obstructive impairment of airway caliber so that the reversibility of airway obstruction confirms the diagnosis [1, 12]. In this study, a considerable number of group 2 subjects (44%) & group 3 subjects (52%), showed a significant improvement in FEV1 (>12%) after bronchodilator administ-ration, thus revealing reversible bronchial obstruction.

The bronchodilator responsiveness is the simplest test for assessing a reversible bronchial obstruction. Usually, the test is carried out when the baseline assessment shows an FEV1 value or an FEV1/FVC ratio < 80% of the predicted value.

Considering these values as the cutoff of normality for all indices, it is commonly thought that the reversibility test is unnecessary and ineffective in subjects in whom these parameters are above 80%. In these cases, guidelines suggest PEF monitoring or bronchial provocation tests such as the methacholine challenge [1, 2]. It can be suggested that these asthmatic patients have pulmonary function tests higher than the lower limits of predicted values or that the obstruction of the airways is so little that in the earlier stages of the disease these indices are unable to pick up the functional impairment [28]. In

this setting, our controls showed functional indices significantly higher than the predicted values and than the values of asthmatics who were also within the normal range. Therefore, when subjects have symptoms indicative of asthma, even if their lung function tests are ''normal,'' the presence of an initial or limited bronchial obstruction should be suspected [8–25], and the reversibility test should be routinely performed.

We assumed that a value of FEF25–75 <70% of predicted constitutes proof of bronchial impairment, as previously validated [29].

Conclusion

FEF25-75 percent predicted is a good predictor of the presence of reversible airways obstruction in asthmatic patient with normal PFT. We strongly encourage careful assessment of FEF25-75 percent predicted in the clinical evaluation of possible asthmatic patients and might be of use in predicting the presence of clinically significant reversible airflow obstruction.

References

1. Global Initiative for Asthma. Global strategy for asthma management and prevention. Revised 2006.

2. British Thoracic Society Scottish Intercollegiate Guidelines Network. British guideline on the management of asthma. Thorax 2003; 58 (suppl 1):1–94.

3. American Thoracic Society. Lung function testing: selection of reference values and interpretative strategies. Am Rev Respir Dis 2001; 144:1202– 1218.

4. Quanjer PH, Tammeling GJ, Cotes FE, Pedersen OF, Peslin R, Yernault JC. Standardized lung function testing. Eur Respir J 2003; 6 (suppl 16):1–99.

5. National Heart, Lung and Blood Institute. National Asthma Education and Prevention Program. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma.

6. Mariotta S, Sposato B, Ricci A, Bruno P, Mannino F. Test of reversibility in the early stages of bronchial asthma. J Asthma 2005; 42:487– 491.

7. Galant SP, Morphew T, Amaro S, Liao O. Value of the bronchodilator response in assessing controller na¨ıve asthmatic children. J Pediatrics 2007; 151:457–462.

8. Bjermer L. History and future perspectives of treating asthma as a systemic and small airways disease. Respir Med 2001; 95:703–719.

9. Cirillo I, Klersy C, Marseglia GL, Vizzaccaro A, Pallestrini E, Tosca M, Ciprandi G. Role of FEF25%-75% as a predictor of bronchial hyperreactivity in allergic patients. Ann Allergy Asthma Immunol 2006; 96: 692– 700.

10. Lipworth BJ, Clark DJ. Effects of airway calibre on lung delivery of nebulised salbutamol. Thorax 1997; 52:1036–1039.

11. Bahc¸eciler NN, Barlan IB, Nuho˘glu Y, Bas¸ Ran MM. Risk factors for the persistence of respiratory symptoms in childhood asthma. Ann Allergy Asthma Immunol 2001; 86:449–455.

12. Ciprandi G, Cirillo I, Klersy C, Marseglia GL, Vizzaccaro A, Pallestrini E, Tosca M. Role of FEF25-75 as an early marker of bronchial impairment in patients with seasonal allergic rhinitis. Am J Rhinol 2006; 20:. 641–647.

13. Fonseca-Guedes CH, Cabral AL, Martins MA. Exercise-induced bronchospasm in children: comparison of FEV1 and FEF25-75% responses. Pediatr Pulmonol 2003; 36:49–54.

14. Mathur SK, Busse WW. Asthma: diagnosis and management. Med Clin North Am 2006; 90:39–60.

15. Murphy S, Bleecker ER, Boushey H, Evans D. Practical guide for the diagnosis and management of asthma: based on the expert panel report II; guidelines for the diagnosis and management of asthma. National Heart, Lungs and Blood Institute Bethesda, MD. National Institutes of Health Publication 97–4043, 1997.

16. Van Schoor J, Joos GF, Pauwels RA. Indirect bronchial hyperresponsiveness in asthma: mechanisms, pharmacology and implications for clinical research. Eur Respir J 2000; 16:514–533.

17. Godfrey S, Springer C, Bar-Yishay E, Avital A. Cut-off points defining normal

and asthmatic bronchial reactivity to exercise and inhalation challenges in children and young adults. Eur Respir J 1999; 14:659– 668.
18. NishWA, Schwietz LA. Underdiagnosis of asthma in young adults presenting for USAF basic training. Ann Allergy 1992; 69:239–242.
19. Siersted HC, Mostgaard G, Hyldebrandt N, Hansen HS, Boldsen J, Oxhoj H. Interrelationships between diagnosed asthma, asthma-like symptoms, and abnormal airway behaviour in adolescence: the Odense Schoolchild Study. Thorax.1996; 51:503–509.
20. American Thoracic Society. Lung function testing: selection of reference values and interpretative strategies. Am Rev Respir Dis 1991; 144: 1202– 1218.
21. Quanjer PH, Tammeling GJ, Cotes FE, Pedersen OF, Peslin R, Yernault JC. Standardized lung function testing. Eur Respir J 1993; 6(suppl 16):1–99.
22. Quanjer PH, Dalhuijsen A, Van Zomeren BC. Summary equations of reference values. Bull Eur Physiopathol Respir 1983; 19(suppl 5):45– 51.
23. Pellegrino R, Viegi G, Brusasco V, et al. Interpretativ strategies for lung function tests. Eur Respir J 2005;26: 948–968.
24. Miller MR, Hankinson J, Brusasco V, et al. Standardisation of spirometry. Eur Respir J 2005;26:319–338.
25. Hamid Q, Song Y, Kotsimbos TC, et al. Inflammation of small airways in asthma. J Allergy Clin Immunol 1997; 100:44–51.
26. Bjermer L. Past and future perspectives in the asthma treatment. Resp Med 2001;95:703–719.
27. Lipworth BJ, Clark DJ. Effects of airway calibre on lung delivery of nebulised salbutamol. Thorax 1997;52: 1016–1021.
28. Zomeren BC. Changing relationship between stature and lung volume during puberty. Respir Physiol 1986; 65:139–153.
29. Cirillo I, Pistorio A, Tosca MA, Ciprandi G. Impact of allergic rhinitis on asthma: effects on bronchial hyperreactivity. Allergy 2009;64:439–444.