Original Article

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ISSN: 1735-0344 *Tanaffos 2013; 12(2): 28-33*

TANAFFOS

Assessment of Bronchodilator Response in Various Spirometric Patterns

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Received: 9 January 2013
Accepted: 2 May 2013

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Background: Spirometry is a physiologic test that measures the volume of air an individual inhales or exhales and the rate at which the volume is changed as a function of time. Bronchodilator response, as a beneficial test for diagnosis of bronchial responsiveness is measured using the percent change from baseline and absolute changes in forced expiratory volume in 1 second and/or forced vital capacity. In this study we aimed to assess the increase in spirometric parameters in patients with symptoms of asthma regardless of spirometric pattern.

Materials and Methods: In this cross-sectional study bronchodilator test was performed in individuals with dyspnea, cough or wheezing and the mean increase in various spirometric parameters was measured and compared among individuals with different spirometric patterns.

Results: Among all individuals 24.5% responded to bronchodilator. Forced expiratory volume in 1 second was the parameter with the most frequent response to bronchodilator. Patients with mixed pattern had the highest frequency of response to bronchodilator. Response to bronchodilator was more than 50% in most mid flow volumes.

Conclusion: Some patients with symptoms of asthma may show restrictive or mixed pattern in spirometry which may respond to bronchodilator administration.

Key words: Spirometry, Bronchodilator test, Obstructive lung disease, Restrictive lung disease

INTRODUCTION

Spirometry is a physiologic test that measures the volume of air an individual inhales or exhales and the rate at which the volume is changed as a function of time (1). Asthma is a chronic disorder characterized by inflammation, hyperresponsiveness, and intermittent obstruction of the airways (2, 3).

Obstructive and restrictive spirometric patterns are defined as a reduction of FEV_1/FVC ratio and forced vital capacity (FVC) below the 5th percentile of the predicted value i.e. lower limit of normal (LLN) (4-6). However, in practice forced expiratory volume in 1 second (FEV_1) and FVC measurements that are more than 80% of predicted values and FEV_1/FVC ratio of more than 70-75% are typically considered normal (7).

In order to examine airway responsiveness, bronchodilator test is recommended. Bronchial responsiveness is assessed by changes in spirometric parameters after the administration of short-acting β_2-agonists, such as salbutamol, or anticholinergic drugs such as ipratropium bromide (4, 5). Among the various spirometric parameters for identification of bronchodilator response, FEV_1, FVC, forced expiratory volume between 25% and 75% of FVC (FEF_{25-75}%) and forced expiratory volume at 50% ($FEF_{50\%}$) are the most widely used (8). FEV_1 has been shown to be the best spirometric variable in terms of statistical power and reproducibility (2, 3). Some studies propose at least 30% increase in FEF_{50}% or $FEF_{25-75\%}$ isovolume as the criteria for responsiveness to bronchodilator (5,8). Another study has found larger increases for spirometric parameters to be significant after bronchodilator, e.g. 61% for $FEF_{25-75\%}$ and 23% for PEF (3).

According to ATS/ERS taskforce bronchodilator response is measured using the percent change from baseline and absolute changes in FEV_1 and/or FVC (4). Twelve percent and 200 mL increase in FEV_1 or FVC compared to baseline suggest a significant response to bronchodilator (4, 5). Other spirometric parameters such as peak flows are not considered precisely in bronchodilator response (8). Recently some studies have proposed other criteria for positive bronchodilator response (2, 9). Kainu et al. proposed that FEV_1 response to bronchodilation by around 9% from the baseline is significant (2).

Bronchodilator test is usually used in obstructive spirometric pattern, but nowadays there are some studies which have shown that bronchial reversibility and asthma may be accompanied by normal, restrictive or mixed patterns of spirometry (10-13). In some individuals this restrictive pattern may be due to extrapulmonary causes (10, 13), but some studies have shown a true restrictive pattern in these patients. Miller and Palecki showed an 8% frequency of true restrictive pattern among asthmatic patients (10).

We designed this study to assess and compare the amount of increase in all spirometric indices in patients with dyspnea, cough or wheezing regardless of diagnosis and pattern of spirometry.

MATERIALS AND METHODS

In a case series during September 2009- September 2010, we assessed bronchodilator response in a group of individuals referred to Yazd Occupational Medicine Clinic with intermittent dyspnea, cough and wheezing.

Obstructive pattern was defined as $FEV_1/FVC < LLN$; restrictive pattern was defined as FVC <LLN and FEV1/FVC> LLN and mixed pattern was defined as FVC<LLN and $FEV_1/FVC<LLN$ (4). We could not perform body plethysmography to confirm restrictive respiratory pattern due to monetary limitations. We could only use spirometric indices (FVC and FEV_1/FVC) for identification of subjects with probable restrictive or mixed patterns, which do not necessarily show a restrictive respiratory pattern.

Spirometry was performed for all subjects (Spirolab III, MIR, Italy) in our respiratory lab in a standard condition (in a sitting position, in the morning, at BTPS) by an occupational medicine resident with direct supervision of an occupational medicine specialist. Acceptability criteria were considered according to ATS/ERS taskforce (a satisfactory start of test i.e. extrapolated volume of less than 0.5% of FVC or 0.150 L and a satisfactory end of test criteria i.e. a 1s plateau in the volume–time curve, without coughing during the first second of the maneuver, without early termination of expiration, and without glottis closure) (1).

The highest of three technically acceptable recordings was taken (1). After baseline test, bronchodilator was administered (salbutamol, 400µg, inhalational) and spirometry was repeated again after 15 minutes. Before performing the test, all factors intervening or contraindicating spirometry were questioned (1). We used our population reference equations according to Golshan et al. (14).

A 200cc and 12% increase in FEV_1 or FVC was considered as the positive response to bronchodilator (4).

The average increase in spirometric parameters [*i.e.* FVC, FEV_1, FEV_1/FVC, peak expiratory flow (PEF), forced expiratory volume at 25% ($FEF_{25\%}$), $FEF_{50\%}$, forced expiratory volume at 75% of FVC ($FEF_{75\%}$), and $FEF_{25-75\%}$] was measured and compared between groups.

We used SPSS (version 19) for data analysis using t test, chi square and ANOVA tests. Level of significance was set at 0.05. An informed consent was obtained from all participants. The study was approved by the ethics committee of research of Shahid Sadoughi University of Medical Sciences.

RESULTS

Totally 403 male subjects entered the study. According to their baseline spirometry, they were divided into four groups: 180, 109, 89 and 25 individuals in normal, obstructive, restrictive and mixed groups, respectively. Table 1 shows the demographic information of subjects.

Table 2 shows the frequency of responsiveness in all groups according to FEV_1 or FVC increase after bronchodilator administration. FEV_1 was the parameter with the most frequent response in all 4 groups. Among all responsive subjects 69.7%, 6%, and 24.3% showed increase in FEV_1 only, FVC only and both FEV_1 and FVC, respectively. The group with the most frequent responsiveness was the mixed group.

Table 3 shows the mean increase in spirometric parameters among the subjects of four groups.

We also compared the mean increase in spirometric parameters between subjects with obstructive spirometric pattern and other subjects (Figure 1).

Table 4 shows the mean increase in spirometric parameters among responsive individuals (99 subjects).

The mean increase in all spirometric parameters was significantly higher in responsive subjects ($p<0.001$ for all parameters).

Table 1. Demographic information of subjects

	Spirometric pattern	Mean	SD*	Min	Max	p-value
Age	Obstructive	39.54	9.65	18	68	< 0.001
	Restrictive	37.27	8.15	23	54	
	Mixed	36.15	8.07	22	57	
	Normal	44.56	8.27	26	60	
BMI	Obstructive	25.23	4.51	16.60	42.72	0.076
	Restrictive	26.70	4.81	17.04	38.10	
	Mixed	25.94	4.56	15.55	39.91	
	Normal	27.20	4.29	17.63	39.55	

* SD: standard deviation

Table 2. Frequency of responsiveness to bronchodilator according to the parameter with a significant increase

Spirometric pattern	Total number	Parameter with significant increase		
		FVC or FEV1	FVC	FEV1
		No. (%)	No. (%)	No. (%)
Obstructive	109	42 (38.5)	6 (5.5)	39 (35.5)
Restrictive	89	19 (21.3)	10 (11.2)	16 (18.1)
Mixed	25	15 (60)	12 (48)	15 (60)
Normal	180	23 (12.7)	2 (1.1)	23 (12.7)
Total	403	99 (24.5)	30 (7.4)	93 (23.1)

* 200cc and 12% increase in FEV1 or FVC after bronchodilator administration

Table 3. Comparison of mean increase in spirometric parameters among the subjects of the four groups

Spirometric parameters (%predicted)	Spirometric pattern	Mean	SD*	Min	Max	P-value
FEV_1	Obstructive	9.95	10.57	-6.93	68.42	< 0.001
	Restrictive	5.36	7.30	-7.75	31.64	
	Mixed	21.79	19.30	-4.30	58.58	
	Normal	5.24	5.74	-8.33	22.33	
	Total	7.53	9.69	-8.33	68.42	
FVC	Obstructive	2.18	5.19	-9.47	17.83	< 0.001
	Restrictive	3.13	6.08	-7.65	20.95	
	Mixed	12.12	13.39	-5.46	44.83	
	Normal	0.43	4.15	-9.78	21.87	
	Total	2.21	6.38	-9.78	44.83	
PEF	Obstructive	11.92	17.60	-19.69	123.56	0.268
	Restrictive	10.73	18.40	-20.55	85.51	
	Mixed	21.31	28.41	-13.37	103.05	
	Normal	9.78	15.67	-22.94	78.16	
	Total	11.25	17.90	-22.94	123.56	
$FEF_{25-75\%}$	Obstructive	27.20	28.78	-24.17	192.54	< 0.001
	Restrictive	20.05	26.53	-34.98	119.67	
	Mixed	52.96	58.01	-42.03	199.04	
	Normal	17.32	19.05	-28.14	70.41	
	Total	22.86	28.60	-42.03	199.04	
$FEF_{25\%}$	Obstructive	23.39	23.05	-24.42	120.90	0.014
	Restrictive	16.97	26.85	-16.04	146.03	
	Mixed	36.56	27.69	-42.03	199.04	
	Normal	16.52	16.12	-17.82	63.27	
	Total	19.73	22.27	-24.42	146.03	
$FEF_{50\%}$	Obstructive	28.25	29.62	-26.14	206.56	0.002
	Restrictive	17.83	21.59	-24.28	75.72	
	Mixed	44.01	46.26	-27.94	131.82	
	Normal	16.88	20.96	-25.19	99.02	
	Total	21.90	26.66	-27.94	206.56	
$FEF_{75\%}$	Obstructive	35.76	45.51	-31.82	345.83	0.016
	Restrictive	20.93	30.25	-30.51	116.33	
	Mixed	70.21	73.08	-52	221.05	
	Normal	29.14	58.92	-29.81	454.79	
	Total	31.49	51.65	-52.00	454.79	

* SD: standard deviation

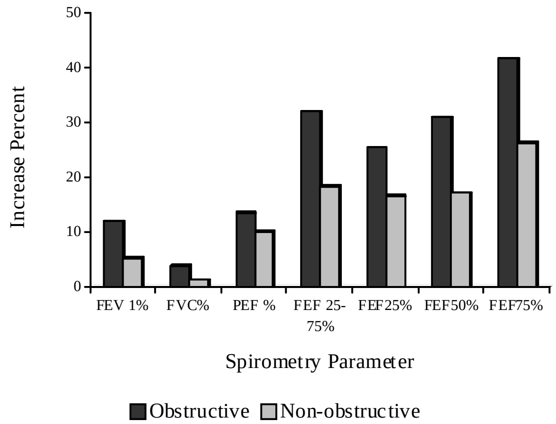

Figure 1. Mean increase in spirometric parameters (percent predicted) in obstructive and non-obstructive subjects

Table 4. Mean increase in spirometric parameters among responsive individuals.

	Mean	SD*	Minimum	Maximum
FEV1(ml)	450	200	50	1510
FEV1%predicted	19.22	11.57	2.20	68.42
FVC(ml)	270	260	-280	1040
FVC% predicted	8.11	8.76	-6.97	44.83
PEF(ml/s)	950	770	-1640	3440
PEF% predicted	20.43	21.47	-20.12	123.56
FEF25-75%(ml/s)	950	450	90	2140
FEF25-75% %predicted	55.51	32.17	4.71	199.04
FEF25%(ml/s)	1260	670	220	3170
FEF25%%predicted	38.18	22.68	3.58	120.90
FEF50%(ml/s)	900	470	-220	2130
FEF50%% predicted	49.95	29.59	-6.34	206.56
FEF75%(ml/s)	500	340	-50	1970
FEF75%%predicted	67.54	50.90	-4.29	345.83

* SD: Standard deviation

DISCUSSION

Spirometry, a physiologic test, is commonly used for evaluation of pulmonary function. One important application of spirometry is to show responsiveness of the airways to bronchodilator administration. Bronchodilator test is usually performed in subjects with obstructive spirometric pattern, but studies have shown some symptomatic patients with restrictive spirometric pattern. Thus, in this study we assessed bronchodilator response in 4 groups of individuals (with normal, obstructive, restrictive and mixed spirometric patterns).

Normal, obstructive, restrictive and mixed patterns respectively showed the highest frequency among all individuals which was almost consistent with the result of Miller and Palecki (10). Among the subjects, about 23% were responsive to bronchodilator. This rate was lower than the obtained value in our previous study (3); although in the previous study all individuals had obstructive spirometric pattern.

The parameter with the most frequent increase in all groups was FEV_1 which was consistent with our previous research and some other studies (3, 9, 16-19). The mean increase in FEV_1 was about 200 ml which was higher than some previous studies (9, 13); although the mentioned studies selected their samples from the general population whereas our sample consisted of individuals with respiratory symptoms.

We found a statistically significant difference in the increase in most spirometric parameters (e.g. FEV_1, FVC and $FEF_{50\%}$) among the 4 groups. The highest increase in main spirometric parameters was seen among individuals with mixed pattern in spirometry and the lowest increase was observed among normal subjects. The highest increase was seen in $FEF_{75\%}$ among all individuals which was consistent with our previous study finding (3). This was true as well when dividing the individuals into different groups. The mean increase in all mid flow parameters was higher than 50% consistent with our previous study (3). The lowest increase was observed in FVC in all four groups.

Our study had some limitations. We could not perform body plethysmography for confirmation of restrictive pattern due to monetary problems. All subjects were males; thus, we could not compare the results between the two genders.

It is concluded from the results of this study that some patients with respiratory symptoms like dyspnea, cough and wheezing may show restrictive or mixed pattern in spirometry which may respond to bronchodilator administration; although the response is significantly different among obstructive, restrictive, and mixed spirometric patterns.

Acknowledgment

The authors would like to thank Dr. Mahmoud Taheri, and Dr. Mohammad Heydari, occupational medicine residents, for their collaboration in this project.

REFERENCES

1. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, et al. Standardisation of spirometry. *Eur Respir J* 2005; 26 (2): 319- 38.
2. Kainu A, Lindqvist A, Sarna S, Lundbäck B, Sovijärvi A. FEV1 response to bronchodilation in an adult urban population. *Chest* 2008; 134 (2): 387- 93.
3. Mehrparvar AH, Mirmohammadi SJ, Sohrabi MM. Spirometric indices after bronchodilator test in obstructive lung disease. *Acta Med Iran* 2010; 48 (4): 226- 30.
4. Pellegrino R, Viegi G, Brusasco V, Crapo RO, Burgos F, Casaburi R, et al. Interpretative strategies for lung function tests. *Eur Respir J* 2005; 26 (5): 948- 68.
5. Stuart M, Garay MD. Pulmonary Function Testing. 4th ed. Environmental and Occupational Medicine. Philadelphia, Lippincott Williams & Wilkins, WN Rom; 2007; chapter 15; p. 200-235.
6. Teculescu D, Racineux JL. The analysis of bronchial obstruction and its reversibility after bronchodilators using a study of "density-effect" on maximum flow. *Rev Mal Respir* 1991; 8 (1): 29- 37.
7. Weir NA, Gulati M, Redlich CA. Diseases of the lung and pleura. 2nd ed. Textbook of clinical occupational and environmental medicine. Elsevier Saunders, L. Rosenstock; 2005. chapter 19, Lung volumes, p. 289.
8. Shim C. Response to bronchodilators. *Clin Chest Med* 1989; 10 (2): 155- 64.
9. Kainu A, Lindqvist A, Sarna S, Lundbäck B, Sovijärvi A. Responses of FEV6, FVC, and FET to inhaled bronchodilator in the adult general population. *Respir Res* 2009; 10: 71.
10. Miller A, Palecki A. Restrictive impairment in patients with asthma. *Respir Med* 2007; 101 (2): 272- 6.
11. Gill K, Jain B, Miller A. True restrictive impairment in bronchial asthma. *Am J Respir Crit Care Med* 1999; 159: A652.
12. Colp C, Williams MH Jr. Total occlusion of airways producing a restrictive pattern of ventilatory impairment. *Am Rev Respir Dis* 1973; 108 (1): 118- 22.
13. Rothe T. True restrictive ventilatory pattern in asthma. *J Asthma* 2010; 47 (5): 594- 6.
14. Golshan M, Nematbakhsh M, Amra B, Crapo RO. Spirometric reference values in a large Middle Eastern population. *Eur Respir J* 2003; 22 (3): 529- 34.
15. Dales RE, Spitzer WO, Tousignant P, Schechter M, Suissa S. Clinical interpretation of airway response to a bronchodilator. Epidemiologic considerations. *Am Rev Respir Dis* 1988; 138 (2): 317- 20.
16. Tweeddale PM, Alexander F, McHardy GJ. Short term variability in FEV1 and bronchodilator responsiveness in patients with obstructive ventilatory defects. *Thorax* 1987; 42 (7): 487- 90.
17. Brand PL, Quanjer PH, Postma DS, Kerstjens HA, Koëter GH, Dekhuijzen PN, et al. Interpretation of bronchodilator response in patients with obstructive airways disease. The Dutch Chronic Non-Specific Lung Disease (CNSLD) Study Group. *Thorax* 1992; 47 (6): 429- 36.
18. Chhabra SK, Vijayan VK, Gupta R, De S Expression of bronchodilator response: comparison of four indices. *Respir Med* 2002; 96 (8): 611- 4.
19. Kabondo P, Orehek J. Reversibility of airway obstruction in asthma and chronic bronchitis (author transl). *Bull Eur Physiopathol Respir* 1977; 13 (6): 829- 36.