ORIGINAL REPORT

Spirometric Indices after Bronchodilator Test in Obstructive Lung Disease

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Abstract- Bronchial responsiveness to bronchodilator medications is usually tested to establish reversibility of airflow obstruction. Among the various tests to establish bronchodilator response, FEV_1, $FEF_{25-75\%}$ or $FEF_{50\%}$, and FVC are the most widely used. In a cross-sectional study, we assessed spirometric responses after administration of bronchodilator in 187 workers with obstructive pattern in spirometry. Considering responsiveness to bronchodilator (200cc and 12% increase in FEV_1 or FVC), the study cases were divided into responsive or non-responsive groups, and the average increase in spirometric indices were measured and compared between two groups. 35.8% of cases were responsive to bronchodilator. Among responsive cases, FEV_1 was the most frequent index increased significantly; And PEF and FVC were the least frequent ones. The highest mean increase from baseline after administration of bronchodilator was observed in $FEF_{75\%}$. Increases in all indices were significantly higher in responsive group. The increase in FEV_1% predicted was inversely correlated with baseline FEV_1. In conclusion, we consider that FEV_1 is the most reliable spirometric index for assessing bronchodilator response. And Bronchial reversibility has an inverse relationship with baseline measures.

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Key words: Spirometry; bronchodilator agents; lung disease; obstructive

Introduction

Spirometry is a medical test that measures the volume of air an individual inhales or exhales and the rate at which the volume is changing as a function of time. Results of the test are usually compared with reference values to make an assessment (interpretation) of them (1).

The most important spirometric indices used are: forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1), FEV_1/FVC ratio, peak expiratory flow (PEF), forced expiratory volume between 25% and 75% of FVC ($FEF_{25-75\%}$), forced expiratory volume at 25%, 50% and 75% of FVC ($FEF_{25\%}$, $FEF_{50\%}$, $FEF_{75\%}$).

An obstructive ventilatory defect is a disproportionate reduction of maximal airflow from the lung in relation to the maximal volume that can be displaced from the lung and is defined by a reduced FEV_1/FVC ratio below the 5th percentile of the predicted value (2). This definition contrasts with other definitions which utilize a fixed FEV_1/FVC ratio at 0.7 rather than at the 5th percentile (3). However, in practice FEV_1 and FVC measurements that are > 80% of predicted values and FEV_1/FVC ratio > 70-75% are typically considered normal (4).

A method of categorizing the severity of lung function impairment based on the FEV_1% predicted is: Mild: >70, Moderate: 60–69, Moderately severe: 50–59, Severe: 35–49, and Very severe: <35 (2, 3).

Bronchial responsiveness to bronchodilator medications is an integrated physiological response. Short-acting β_2-agonists, such as salbutamol, are recommended for testing bronchial responsiveness (2, 3). Bronchodilator response is usually tested to establish reversibility of airflow obstruction, to aid in diagnosis, and to help plan long-term bronchodilator therapy. Among the various tests to establish bronchodilator response, FEV_1, $FEF_{25-75\%}$ or $FEF_{50\%}$, and FVC are the most widely used (5).

Studies show a tendency for the calculated bronchodilator response to increase with decreasing baseline FVC or FEV_1, regardless of whether the response was considered as an absolute change or as a percent of the initial value (2).

Values 12% and 200 mL compared with baseline during a single testing session suggest a ‘‘significant’’ bronchodilatation. (2, 3). But for other spirometric indices there isn't a consensus about significant increase. Some authors recommend a 30 percent increase in

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isovolume $FEF_{25-75\%}$ or $FEF_{50\%}$ above baseline are acceptable criteria for bronchodilator response (5).

We designed this study to assess the amount of increase in all spirometric indices in patients with obstructive spirometric pattern and compare it between responsive and non-responsive cases to bronchodilator.

Patients and Methods

In a cross-sectional study, we assessed spirometric responses after administration of bronchodilator in workers referred to Yazd occupational medicine clinic with obstructive pattern in spirometry (regardless of diagnosis) in a period of one year (from May 2007 till May 2008).

We considered FEV_1/FVC ratio< 75% as obstructive spirometry. Then post-bronchodilator responses were assessed among them. Female workers (because of little sample size, only 5 persons) and cases with mixed pattern of lung function in spirometry were excluded from the study. At last 187 male individuals entered the study. Spirometry was performed for all of them (spirometer: spirolab II, MIR, Italy) in our respiratory lab in a standard situation (in a sitting position, in the morning, at BTPS) by an occupational medicine resident with direct supervision of an occupational medicine specialist. The highest of three technically acceptable recordings was taken (1). After baseline test, they were administered bronchodilator (salbutamol, 400µg, inhalational) and were tested again after 15 minutes (1). Before performing the test, all factors intervening or contraindicating spirometry were questioned. Considering responsiveness to bronchodilator (200cc and 12% increase in FEV_1 or FVC), the study cases were divided into two groups: responsive or non-responsive (2). The average increase in main spirometric indices (*i.e.* FVC, FEV_1, FEV_1/FVC, and PEF) and volumes of isoflow ($FEF_{25\%}$, $FEF_{50\%}$, $FEF_{75\%}$, and $FEF_{25-75\%}$) were measured and compared between two groups. We used SPSS (ver.11.5) for data analysis. Descriptive indices such as mean, median, standard deviation, standard error and range were used for quantitative data, and independent samples t test and also one-way ANOVA were used for comparing means. *P* values of 0.05 were deemed to be statistically significant, and 95% confidence intervals (CI) were calculated. We obtained an informed consent from all participants. We didn't have any conflict of interest.

Results

The mean age, height, and weight of the subjects was 37.43±10.61 (range: 16-69), 170.26±6.23 (range: 155-189), and 74.50±13.75 (range: 46-117), respectively.

Descriptive statistics of spirometric indices before and after administration of bronchodilator are shown in table1.

The cases were divided into two groups considering their responsiveness to bronchodilator: 67 persons (35.8%) were responsive and 120 persons (64.2%) were non-responsive to bronchodilator.

The mean age in responsive and non-responsive group was 36.37±11.37 and 38.03±10.15, respectively and the difference was not statistically significant (P = 0.3). And also the average height and weight were not significantly different between two groups (P = 0.7 and P = 0.2 for weight and height, respectively).

Among responsive cases, FEV_1 was the most frequent index increased significantly. In our study, among 67 responsive cases, 44 persons (65.7%) showed significant increase in FEV_1 only, 5 persons (7.5%) in FVC only and 18 persons (26.9%) in both FEV_1 and FVC. If we consider 30% increase as positive response for other indices, frequency of responsiveness in each index is as following: 19 persons (28.35%), 60 persons (89.55), 51 persons (76.12%), 61 persons (91.04%), and 55 persons (82.08%) showed significant increase in PEF, $FEF_{25-75\%}$, $FEF_{25\%}$, $FEF_{50\%}$, $FEF_{75\%}$, respectively.

Mean baseline spirometric indices (*i.e.* before bronchodilator administration) in responsive group were significantly lower compared with non-responsive group (Table 2).

The highest mean increase from baseline after administration of bronchodilator in responsive group was observed in $FEF_{75\%}$. Generally increases seen in volumes of isoflow were more than FEV_1 and FVC (*i.e.* 80.55% in $FEF_{75\%}$, 61.21% in $FEF_{25-75\%}$, 60.92% in $FEF_{50\%}$, 47.30% in $FEF_{25\%}$ versus 23.20% for PEF, 21.03% for FEV_1, 11.11% for FEV_1/FVC and 9.35% for FVC). Besides main indices (*i.e.* FEV_1 and FVC), increases in all other indices were significantly higher in responsive group. Mean increases of spirometric indices in both groups are shown in table 3.

According to baseline FEV_1, all cases were divided into 5 groups of severity. The most frequent severity observed was mild obstruction (144 persons, 74.9%); and 22 persons (11.8%), 7 persons (3.7%), 15 persons (8%), and 3 persons (1.6%) showed moderate, moderately severe, severe, and very severe obstruction, respectively.

Table 1. Descriptive statistics of spirometric indices before and after bronchodilator administration.

Spirometric indices	Mean	SD	Median	Range
FEV_1 before bronc. (lit)	2.92	0.78	3.01	0.86-4.59
FEV_1 after bronc. (lit)	3.19	0.81	3.24	0.93-5.35
FEV_1% pred. before bronc.	77.63	16.78	80	29-130
FEV_1% pred. after bronc.	85.06	16.12	88	35-135
FVC before bronc. (lit)	4.31	0.96	4.32	1.57-6.67
FVC after bronc. (lit)	4.41	0.86	4.39	2.18-6.64
FVC% pred. before bronc.	95.72	16.18	97	45-169
FVC% pred. after bronc.	98.32	13.46	99	61-152
FEV_1/FVC before bronc.	67.21	8.48	70	30.80-84.60
FEV_1/FVC after bronc.	71.83	9.00	74.15	35.10-93
PEF before bronc (lit/s)	6.41	1.88	6.71	1.31-10.48
PEF after bronc (lit/s)	7.11	1.86	7.35	1.53-11.84
PEF% pred. before bronc	71.12	19.72	72.50	17-117
PEF% pred after bronc	79.09	18.66	81	22-119
$FEF_{25-75\%}$ before bronc (lit/s)	2.077	0.72	2.12	0.39-3.59
FEF_{25-75}% after bronc (lit/s)	2.66	0.89	2.69	0.47-5.10
$FEF_{25-75\%}$% pred. before bronc	47.10	14.57	49	10-82
$FEF_{25-75\%}$% pred. after bronc	60.47	17.89	61	13-112
$FEF_{25\%}$ before bronc (lit/s)	4.29	1.53	4.34	0.64-7.94
$FEF_{25\%}$ after bronc (lit/s)	5.22	1.74	5.42	0.82-8.66
$FEF_{25\%}$% pred. before bronc	55.26	18.72	58	9-109
$FEF_{25\%}$% pred. after bronc	67.31	20.56	70	13-103
$FEF_{50\%}$ before bronc (lit/s)	2.21	0.79	2.26	0.34-4.21
$FEF_{50\%}$ after bronc (lit/s)	2.82	0.97	2.78	0.44-4.82
$FEF_{50\%}$% pred before bronc	44.28	14.61	47	8-84
$FEF_{50\%}$% pred after bronc	56.77	17.77	58	10-100
$FEF_{75\%}$ before bronc (lit/s)	0.84	0.34	0.84	0.16-1.93
$FEF_{75\%}$ after bronc (lit/s)	1.12	0.44	1.08	0.16-2.43
$FEF_{75\%}$% pred. before bronc	39.22	13.35	40	11-101
$FEF_{75\%}$% pred. after bronc	51.84	17.09	51	10-103

Pred.: precidted, bronc: bronchodilator administration

Table 2. Comparison of predicted spirometric indices before bronchodilator administration between two groups.

Pred. indices	Mean (SD)		SE		Significance* (95% CI)
before bronch.	R	N-R	R	N-R	
FEV_1	66.24 (17.63)	84.00 (12.40)	2.15	1.13	<0.001 (13.40-22.12)
FVC	87.52 (17.49)	100.30 (13.44)	2.14	1.23	<0.001 (8.26-17.30)
FEV_1/FVC	62.83 (10.22)	69.62 (6.18)	1.25	0.56	<0.001 (4.41-9.15)
PEF	59.60 (16.92)	77.31 (18.34)	2.09	1.66	<0.001 (12.29-23.13)
$FEF_{25-75\%}$	37.84 (14.75)	52.28 (11.66)	1.81	1.07	<0.001 (10.54-18.33)
$FEF_{25\%}$	42.43 (17.52)	62.34 (15.34)	2.17	1.41	<0.001 (14.98-24.82)
$FEF_{50\%}$	34.95 (14.65)	49.43 (11.81)	1.81	1.08	<0.001 (10.54-18.40)
$FEF_{75\%}$	33.32 (15.55)	42.47 (10.71)	1.92	0.98	<0.001 (5.29-13)

Pred.: precidted, SD: standard deviation, SE: standard error of mean, R: responsive to bronchodilator, N-R: non-responsive to bronchodilator, CI: confidence interval * *P* value for difference between means

Table 3. Copmparison of average increase in spirometric indices after bronchodilator administration between two groups.

Increase in spirometric indices after bronch	Mean (SD)			SE			Significance* (95% CI)
	R	N-R	Total	R	N-R	total	
FEV_1 (mL)	476.26 (179.99)	169.50 (131.57)	279.41 (210.53)	21.99	12.01	15.39	<0.001 (257.09-356.44)
FEV_1% pred (%)	21.03 (11.39)	5.22 (3.91)	10.88 (10.66)	1.39	0.35	0.77	<0.001 (12.95-18.67)
FVC (mL)	280.00 (251.79)	6.58 (151.58)	104.54 (233.40)	30.76	13.83	17.06	<0.001 (206.43-340.39)
FVC% pred (%)	9.35 (10.02)	0.35 (3.49)	3.58 (7.88)	1.22	0.31	0.57	<0.001 (6.47-11.52)
FEV_1/FVC (%)	11.11 (8.87)	5.01 (4.67)	7.17 (7.08)	1.09	0.42	0.52	<0.001 (3.75-8.41)
PEF (mL/s)	1032.72 (852.39)	518.17 (871.37)	700.57 (879.01)	104.92	79.54	65.77	<0.001 (253.11-776.01)
PEF% pred (%)	23.22 (24.55)	8.52 (15.24)	13.74 (20.27)	3.02	1.39	1.48	<0.001 (8.09-21.30)
$FEF_{25-75\%}$ (mL/s)	937.57 (346.52)	390.00 (452.30)	586.41 (458.66)	52.35	31.90	33.81	<0.001 (433.37-661.77)
$FEF_{25-75\%}$% pred (%)	61.21 (32.57)	16.57 (13.90)	32.58 (31.01)	4.01	1.28	2.28	<0.001 (36.25-53.01)
$FEF_{25\%}$ (mL/s)	1406.46 (728.17)	671.44 (698.00)	932.51 (789.98)	90.31	64.50	53.39	<0.001 (518.98-951.05)
$FEF_{25\%}$% pred (%)	47.30 (23.26)	13.91 (14.05)	25.77 (23.96)	2.88	1.29	1.77	<0.001 (27.10-39.67)
$FEF_{50\%}$ (mL/s)	946.92 (450.44)	429.55 (403.06)	613.32 (487.26)	55.87	37.10	36.02	<0.001 (389.22-645.50)
$FEF_{50\%}$% pred. (%)	60.92 (33.86)	16.72 (14.54)	32.42 (31.45)	4.20	1.33	2.32	<0.001 (35.41-52.97)
$FEF_{75\%}$ (mL/s)	483.84 (273.20)	167.79 (214.65)	280.05 (280.83)	33.88	19.76	20.76	<0.001 (238.9-393.80)
$FEF_{75\%}$% pred (%)	80.55 (60.29)	18.14 (21.10)	40.43 (49.69)	7.47	1.95	3.68	<0.001 (47.00-77.81)

Pred.: precidted, SD: standard deviation, SE: standard error of mean, R: responsive to bronchodilator, N-R: non-responsive to bronchodilator, CI: confidence interval, mL: Mili liter, mL/s: mili liter/second. * *P* value for difference between means

The increase in FEV_1% predicted was inversely correlated with baseline FEV_1 and the difference in FEV_1 increase among 4 groups (*i.e.* 7.79%, 13.23%, 19.85%, 27.66% for groups 1, 2, 3, and 4, respectively) was significant ($P < 0.001$); Because of low sample size in group 5 (*i.e.* very severe obstruction), we didn't considered this group in this analysis.

After bronchodilator administration, 85 persons (45%) had normal FEV_1/FVC ratio (without obstruction) and 101 persons (54%) remained obstructive.

Discussion

Spirometry measures the volume and flow of air into and out of the lungs as a function of time. Obstructive lung disease is shown by a reduced FEV_1/FVC ratio below the 5th percentile of the predicted value or (in practice) below 70-75%. (1, 2, 4, 6).

Bronchodilator response is usually tested to establish reversibility of airflow obstruction, to aid in diagnosis.

In our study, after administration of bronchodilator (salbutamol) we assessed responsiveness to the drug. Less than 40% of cases showed reversibility to bronchodilator. Age, height and weight didn't affect responsiveness, but baseline spirometric indices significantly affected responsiveness (*i.e* those with lower spirometric volumes showed more responsiveness), other studies also show a tendency for the calculated bronchodilator response to increase with decreasing baseline FVC or FEV_1, regardless of whether the response was considered as an absolute change or as a percent of the initial value (2, 4, 8).

Between spirometric indices (except for volumes of isoflow) FEV_1 was the one with most frequent increase after bronchodilator administration. From our data it seems that FEV_1 is the most reliable spirometric index for bronchodilator response (8, 9, 10, 11, 12), and PEF and FVC are the least reliable indices; although some studies has shown a positive correlation between increase in FEV_1 and FVC (13). Among other indices, $FEF_{25-75\%}$ and $FEF_{50\%}$ are the most reliable ones, which is consistent with the results of Ninković M, et al. study (9). In conclusion, we consider that FEV_1 is the most reliable spirometric index for assessing bronchodilator response. Among other indices, $FEF_{25-75\%}$ and $FEF_{50\%}$ are also useful (though with 30% increase from baseline), but PEF and FVC, because of high variability, are not useful for this test. Bronchial reversibility has an inverse relationship with baseline measures. Although, Further studies are required to determine the clinical significance of these findings.

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