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Role of Forced Expiratory Volume in Third second (FEV3) as An Alternative to Forced Vital Capacity (FVC) in Assessing Bronchodilator Response in Patients with Chronic Obstructive Airway Diseases

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Abstract

Background Spirometry is a physiological procedure used as a diagnostic tool for disease diagnosis; e.g. obstructive pulmonary diseases such as asthma or chronic obstructive pulmonary disease (COPD). The bronchodilator test is a method of measuring lung capacity changes following inhalation of a short-acting bronchodilator drug that dilates the airway, this test helps to diagnose, evaluate and differentiate asthma from COPD.

Objective To evaluate the role of forced expiratory volume in third second (FEV3) as an alternative for forced vital capacity (FVC) in assessing bronchodilator response in patients with chronic obstructive airway diseases.

Methods The study a case-control, comparative study done from November 2018 to November 2019. The cases involved divided into 2 groups; patients group included (80) patients with chronic obstructed pulmonary diseases (asthma and COPD) and control group included (160) apparently healthy peoples aged and sex matched. Lung function was measured using a standard protocol and electronic table spirometry. Bronchodilator test was done for each patient with chronic obstructed defect on spirometer.

Results There was no significant difference between (FVC), FVC% and (FEV3), FEV3% respectively before bronchodilator and there was no significant difference after bronchodilator in patients. There was no significant difference between FEV1/FVC, FEV1/FVC % and FEV1/ FEV3, FEV1/FEV3% respectively before bronchodilator and there was no significant difference after bronchodilator in patients.

Conclusion FEV3 can be used as an alternative to FVC in patients with chronic obstructive airway diseases for assessing bronchodilator response.

Keywords Spirometry, Bronchodilator test, FVC%, FEV3%, FEV1/FVC%, FEV1/FEV3%

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List of abbreviations: ATS = American Thoracic Society. ERS = European Respiratory Society, FEV1 = Forced expiratory volume in first second, FEV3 = Forced expiratory volume in third second, FVC = Forced vital capacity, FEV1/FVC = Ratio of volumes (actual), FEV1/FVC% = Ratio of predicted values, FEV1/ FEV3 = Ratio of volumes (actual), FEV1/FEV3% = Ratio of predicted values

Introduction

Spirometry is a physiological procedure for determining the functional aspects of the lungs using an objective measure by calculating how much air a patient can inhale and exhale to the limit [(1)]. Spirometry is used as a diagnostic tool for disease diagnosis e.g.

obstructive pulmonary diseases such as asthma or chronic obstructive pulmonary disease (COPD) and restrictive lung conditions such as interstitial pneumonia [2].

The principal indices of spirometry are: (a) Forced Vital Capacity (FVC), (b) Forced Expiratory Volume in the first second (FEV1), (C) FEV1/FVC. The presence of FEV1 <80% of the expected value in conjunction with FEV1/FVC <70% indicates the presence of airway obstruction [3]. The bronchodilator test is a method of measuring lung capacity changes following inhalation of a short-acting bronchodilator drug that dilates the airway, this test helps to diagnose, evaluate and differentiate asthma and COPD by measuring reversibility brought by the bronchodilator drug [4]. Generally, a positive response is defined as a rise of ≥12% and ≥200 mL in an absolute level of FEV1 and/or FVC compared with baseline [2]. If the response to the bronchodilator is positive it usually suggests asthma. It is because the rise in post-inhalation flow rate and volume in asthma patients is greater than in COPD patients [5]. Other spirometry indices are forced third-second expiratory volume (FEV3) as the second most commonly studied dependable parameter as an alternative to FVC as they are easier because patients are not required to perform maximum end-expiration [6]. FEV3 are suitable alternatives for FVC in the spirometric analysis of bronchial asthma. The assumption was based on the lack of significant differences in the means when the absolute values of FEV3 were matched with FVC in asthmatic patients. This significant in suggestions all advantages of FEV3 over FVC in asthmatic patients [7]. Sometimes, FVC maneuvers are correctly performed, and the patients can blow greater than 3 seconds but cannot reach the end-of-test criteria (6 seconds in duration or a plateau in the volume-time curve) after trying the analysis several times. The FEV3 has been proposed as an approximate surrogate for the FVC [8].

Asthma is a chronic airway inflammatory condition characterized by cellular penetration into the airways and a related increase in sensitivity and reaction to agents that cause bronchial contraction (airway hyper-response-AHR) and exposure to allergens (early and late asthmatic responses) [9]. COPD is the term for the set of conditions, including chronic bronchitis and emphysema, that block air flow in the bronchi and trachea. More precisely, international organizations have described COPD as a disorder characterized by airflow obstruction that is not entirely reversible [10].

The aim of this study was to evaluate the role of FEV3 as an alternative for FVC in assessing bronchodilator response in patients with chronic obstructive airway diseases.

Methods

Subjects

The study a case-control, comparative study conducted for chronic obstructed air way diseases patients (asthma and COPD). Data were collected in Spirometric Unit in Merjan Teaching Hospital in Babylon city at a duration from November 2018 to November 2019. The study approved by the Institutional Review Board (IRB) of the College of Medicine, Al-Nahrain University and informed consents were obtained from all the participants.

The cases divided into 2 groups; patients group included (80) patients with chronic obstructed lung diseases; (31) male and (49) female whom mean age was (51) years and they were referred to spirometry unit. They enrolled in the study with FEV1/FVC <70 and FEV1% <80% of the predicted. Control group included (160) apparently healthy peoples aged and sex matched, mean age was (45) years. Females were (100), males were (60) in number.

Materials

A- Spirometry: Lung function was measured using a standard protocol and electronic table spirometry (SpirolabIII, Italy).

B- Nebulizer: Bronchodilator test is recommended to evaluate airway responsiveness. Bronchial responsiveness

was measured by changes in spirometric parameters after the inhaling (2.5 mg) of short-acting β2- agonists (salbutamol). Bronchodilator test was done for each patient with chronic obstructed defect on spirometer. For each patient with obstructed deficiency, post-bronchodilator spirometry was performed 20 minutes after inhalation of salbutamol.

Statistical analysis

Statistical analysis was performed with SPSS V22. (statistical package for social sciences) for data comparison and also Excel 2010 programs. Data analysis was done using paired t-test. Data were expressed as mean±standard deviation (SD) and the values were considered statistically significant when p-value (< 0.05).

Results

From 80 Patients enrolled in the study; 55 (68.8%) showed positive bronchodilator response (asthma) and 25 (31.3%) showed negative response (COPD).

There was significant difference (p<0.05) between patients and control regarding all spirometric parameters and all parameters are lower than that of normal subjects (Table 1).

Table 1. Comparisons of means of spirometric parameters between patients and control group

Parameters	Patients		Control		P value
	Mean	SD	Mean	SD	
FEV1%	53.69	18.29	94.21	9.89	<0.001
FVC%	66.54	18.46	91.65	9.82	<0.001
FEV3%	68.48	19.43	96.13	12.80	<0.001
FEV1/FVC%	79.16	12.39	102.27	8.23	<0.001
FEV1/FEV3%	77.28	11.50	98.01	10.24	<0.001
FEV1/FVC	63.00	11.57	102.68	8.50	<0.001
FEV1/FEV3	68.37	10.87	95.49	6.92	<0.001
FVC (L)	2.50	1.05	3.62	0.82	<0.001
FEV1 (L)	1.61	0.74	3.11	0.72	<0.001
FEV3 (L)	2.29	1.00	3.60	0.83	<0.001

There was significant difference (p<0.05) in FEV1%, FEV1(L), FVC%, FEV3% before and after nebulizer. Other parameters showed no significant difference (p>0.05) pre- and post-nebulizer (Table 2).

There was no significant difference (p>0.05) between FVC% and FEV3% before bronchodilator and there was no significant difference (p>0.05) between FVC% and FEV3% after bronchodilator (Table 3).

There was no significant difference (p>0.05) between FVC (L) and FEV3 (L) before bronchodilator and there was no significant difference (p>0.05) between FVC (L) and FEV3 (L) after bronchodilator (Table 4).

There was no significant difference (p>0.05) between FEV1/FVC% andFEV1/FEV3% before bronchodilator and there was no significant difference (p>0.05) between FEV1/FVC% and FEV1/FEV3% after bronchodilator (Table 5).

There was no significant difference (p>0.05) between FEV1/FVC and FEV1/FEV3 before bronchodilator and there was no significant difference (p>0.05) between FEV1/FVC and FEV1/FEV3 after bronchodilator (Table 6).

Table 2. Baseline and Post-bronchodilator values of different spirometric parameters

Parameters		Mean	SD	P value
FEV1%	Pre*	53.69	18.29	<0.001
	Post**	94.16	10.38	
FVC%	Pre	66.54	18.46	<0.001
	Post	91.01	9.59	
FEV1/FVC%	Pre	79.29	12.4	0.085
	Post	82.83	13.41	
FEV3%	Pre	68.83	19.71	<0.001
	Post	94.43	18.96	
FEV1/FEV3%	Pre	77.31	11.18	0.095
	Post	80.45	12.43	
FVC (L)	Pre	2.5	1.05	0.114
	Post	2.76	1.02	
FEV1 (L)	Pre	1.61	0.74	0.043
	Post	1.86	0.82	
FEV3 (L)	Pre	2.29	1.0	0.061
	Post	2.59	1.02	
FEV1/FVC	Pre	63.04	11.57	0.081
	Post	66.14	10.75	
FEV1/FEV3	Pre	68.4	10.88	0.052
	Post	71.48	8.99	

*Pre: before nebulizer, **post: after nebulizer

Table 3. Comparison between FVC % and FEV3 % before & after bronchodilation

	FVC%		FEV3%		P value
	Mean	SD	Mean	SD	
Pre	66.54	18.46	68.83	19.71	0.19**0**
Post	91.01	9.60	94.43	18.96	0.086

*Pre: before nebulizer, **post: after nebulizer

Table 4. Comparison between FVC (L) and FEV3 (L) before & after bronchodilation

	FVC (L)		FEV3 (L)		P value
	Mean	SD	Mean	SD	
Pre	2.50	1.05	2.29	1.00	**0.876**
Post	2.76	1.02	2.59	1.02	**0.794**

*Pre: before nebulizer, **post: after nebulizer

Table 5. Comparison between FEV1/FVC% and FEV1/FEV3% before & after bronchodilation

	FEV1/FVC%		FEV1/FEV3%		P value
	Mean	SD	Mean	SD	
Pre	79.29	12.40	77.31	11.18	**0.097**
Post	82.83	13.41	80.45	12.43	**0.123**

*Pre: before nebulizer, **post: after nebulizer

Table 6. Comparisons between FEV1/FVC (L) and FEV1/FEV3 (L) before & after bronchodilation

	FEV1/FVC (L)		FEV1/FEV3 (L)		P value
	Mean	SD	Mean	SD	
Pre	63.04	11.58	68.40	10.88	0.074
Post	66.14	10.75	71.48	8.99	0.067

*Pre: before nebulizer, **post: after nebulizer

Discussion

There were significant difference between patients and control regarding all spirometric parameters and all parameters are lower than that of normal subjects, this could be explained as follows; Cohen et al. (2007) proposed that a reduction in FVC suggests small airway closing and gas trapping [11], Siatkowska et al. (2010) & Al-Dhahir et al. (2012) mentioned that the presence of FEV1 <80% of the expected value in conjunction with FEV1/FVC <70% indicates the presence of minimal air flow [12,3], Kitaguchi et al. (2012) mentioned that spirometric principle for airflow limitation is FEV1/FVC ratio <70% regarding the GOLD guidelines, moreover, Patel et al. (2019) reported that chronic inflammation and airway remodeling of COPD and asthma can also cause persistent airflow limitations [13,14], Lutfi (2011) found in his study that all the spirometric measurements studied in asthma patients were significantly lower than the control group, indicating that patients had significant airway obstruction [7].

There was significant difference in FEV1%, FEV (L), FVC% and FEV3% before and after nebulizer. Other parameters showed no significant difference pre and post nebulizer administration. These results agree with the followings; Albert et al. (2013) who stated that reversibility was specified by the = American Thoracic Society (ATS) and European Respiratory Society (ERS) criterion of ≥12% and ≥200 ml of pre-bronchodilator FEV1 or the FEV1% increase [15], Quanjer et al. (2016) found that FVC in detecting bronchial reversibility in COPD patients was reported to be more sensitive than FEV1 [16]. Pan et al. (2019) said that his results reported that FEV3 and FVC are sensitive indicators of bronchodilation in extreme airway obstruction, while FEV1 is more sensitive in mild ventilator dysfunction bronchodilation assessment [17]. While Cazzola et al. (2008) had another opinion, they mentioned that FEV1 is the most commonly used pulmonary measure and the clinical studies have shown that changes in FEV1 before and after treatment are not sufficiently enough to indicate the influence of bronchodilators in patients with extreme airflow obstruction, in particular the elderly [18]. Mehrparvar et al. (2014) mentioned that in a large number of cases, FVC decreased after administration of bronchodilator [6]. which was in agreement with the findings of Kainu (2009) [19].

The other parameters show no significant difference pre and post nebulizer, which could be due to different type of obstructions (COPD) and different degrees included in the study [20].

Other cause could be due to the increase in both FEV1and FVC (FEV1/FVC%), FEV1 and FEV3 (FEV1/FEV3%).

In this study there was no significant difference between FVC %, FVC (L) and FEV3%, FEV3 (L) respectively per nebulizer and there was no significant difference post nebulizer with bronchodilators. These results agree with the followings: Pellegrino et al. (2005) stated that FEV3 percent is by far the most commonly used parameter for airway obstruction, bronchoconstriction or bronchodilation assessments [21], Mehrparvar et al. (2014) found in his study that FEV3 change was significantly associated with FVC change post bronchodilators and can be used as a n alternative for FVC in bronchodilator response assessment. bronchodilator test was significant in these parameters [6]. Pan et al. (2019) mentioned that his study presented that recent data on FEV3suggesting its clinical applicability for better analysis of reversibility assessment, especially in severely impaired patients who enable blow for ≥6 seconds even after their best effort [18]. While Kainu (2008) proposed that based on the intersession repeatability, a limitation for significant change in FEV3 was recommended for forced expiratory time during bronchodilator test [19].

There was no significant difference in FEV1/FVC%, and FEV1/FVC and FEV1/FEV3%, FEV1/FEV3 respectively before nebulizer and no significant difference also after administration of bronchodilator. These results agree with the followings: Allen et al. (2008) found that FEV1/FEV3% <80% can be used to recognize patients with airflow obstruction if they were incapable to perform FVC maneuver [22], Lutfi, (2011) mentioned that the data of his study showed that the level of FEV1/FEV3% of <80% corresponding a FEV1/FVC% of <70% [7], Mehrparvar et al. (2012) had different opinion he mentioned that FEV1/FEV3 unsuccessful to show satisfactory accuracy for the restrictive and obstructive lung diseases diagnosis, even though these parameters have not been assessed previously [23].

This study concluded that FEV3 can be used as an alternative to FVC in evaluating the response to bronchodilator in patients with chronic obstructive diseases; asthma and COPD, the conclusion was based on the absence of the significant differences in the means when the values of FEV3, FEV3 percent were matched with FVC, FVC percent before and after nebulizer.

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Author contribution

Dr. Jizar conducted the study, collected the data and performed the statistical analysis and drafting the manuscript. Dr. Hashim and Dr. Jasim contributed in the designing, organization and finalization of manuscript.

Conflict of interest

There are no conflicts of interest.

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