EVALUATION OF SPECIFIC AIRWAY CONDUCTANCE AND FLOWS IN ASSESSING BRONCHODILATOR RESPONSIVENESS IN OBSTRUCTIVE AIRWAY DISEASE BY BODY PLETHYSMOGRAPHY

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ABSTRACT

Background: Bronchodilator response is routinely assessed during pulmonary function tests to evaluate the therapeutic efficacy. Forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC) are the most commonly used parameters. However some studies have shown that bronchodilators may reduce symptoms, independent of any improvement in flows. It has been claimed that direct measurement of airway resistance (Raw) and specific conductance (sGaw) in body plethysmography is more reliable parameter of changes in airway calibre.

Aim: Aim of present work was to assess Raw, sGaw, flows before and after bronchodilator induction and to determine if the measurement of sGaw offers advantages over FEV_1 and FVC for the evaluation of bronchoreversiblity.

Methods: Study involved 40 patients with obstructive airway disease. Recordings were done before and 20 minutes after inhaling bronchodilator via a nebulizer. Raw and sGaw were measured in MEC-PFT Systems body plethysmograph along with standard spirometry according to American Thoracic Society standards.

Statistical analysis: Results were analyzed using Mean SD, student-t test in SPSS software version 15.

Results: Out of the 40 patients, seven were excluded who did not meet bronchoreversibilty criteria of FEV_1 or FVC or sGaw. The rest 33 patients showed statistical significant improvement in all the parameters after bronchodilatation. Spirometry alone identified bronchoreversibility in 66.7% of patients and sGaw identified remaining 33.3%.

Conclusion: Changes in spirometric parameters alone lack to reveal significant response to bronchodilator in some obstructive patients. Specific airway conductance must be included in deciding the therapeutic efficacy to obstructive airway disease patients.

Keywords: airway resistance, body plethysmography, specific airway conductance, spirometry, obstructive lung disease.

LIST OF ABBREVIATIONS

ATS/ERS	-	American Thoracic Society/ European Respiratory Society
FEV_1	-	Forced expiratory volume in 1 second
FVC	-	Forced vital capacity
$FEF_{25-75\%}$	-	Mean forced expiratory flow between 25% to 75%
GOLD	-	Global initiative for chronic obstructive lung disease.
MEC-PFT	-	Medical electronic construction-Pulmonary function test
PEF	-	Peak expiratory flow
Raw	-	Airway resistance
sGaw	-	Specific airway conductance

INTRODUCTION

Bronchodilator response is routinely assessed during pulmonary function tests to evaluate the therapeutic efficacy. Reversibility of airflow limitation implies a better prognosis and may have considerable significance in planning a treatment program.[1] Response of forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC) to inhaled bronchodilators is commonly used to assess the reversibility of airway obstruction.[2,3,4,5] Although FEV_1 improvement is routinely used to define bronchodilator response, it correlates poorly with clinical effects.[6] Some studies have shown that bronchodilators may reduce symptoms in obstructive lung disease

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patients, independent of any improvement in flows.[7,8,9] It has been claimed that direct measurement of airway resistance (Raw) and specific conductance (sGaw) in a body plethysmography is more reliable parameter of changes in airway calibre.[10,11] sGaw is possibly the most sensitive parameter for the identification of changes in airway calibre.[6] Another study suggests Raw and sGaw are seldom better than FEV_1 and FVC in defining the response.[12] Hence this study was undertaken to resolve the dispute between the two schools of thought.

The aim of present work was to assess Raw, sGaw and flows before and after bronchodilator induction and to determine if the measurement of sGaw offers advantages over FEV_1 and FVC for the evaluation of bronchoreversiblity in patients who do not meet FEV_1 and/FVC criteria for reversibility so as to enable the clinicians in deciding which parameters to be considered in evaluating the bronchoreversibilty in obstructive airway disease patients.

MATERIALS AND METHOD

Study involved 40 patients (28 males and 12 females) with obstructive airway disease referred to the Life style laboratory, Bangalore Medical College and Research Institute. Subjects who showed FEV_1/FVC ratio < 0.7 were included in the study.[13] Subjects were selected who reported no history of active pulmonary infection. If the patients were on therapy, to avoid the confounding results by the residual effects of previous therapy, short-acting bronchodilators were withheld for at least 4 hours, and long-acting bronchodilators for 12 hours and theophylline for 24 hours prior to testing.[13, 14] Smoking was avoided for more than or equal to 1 hour prior to procedure and throughout the procedure.[14]

The required manoeuvre for measurement of FEV_1 and sGaw was demonstrated and subjects were encouraged and supervised throughout test performance. Raw and sGaw measurements were obtained while subjects were seated in a MEC-PFT Systems Body plethysmograph -MEC PFT BBox 100 system (Medical electronic construction-Pulmonary function test bodybox. Brussel, Belgium). The instrument was calibrated every morning for accuracy. After allowing adequate time for thermal stabilization of the cabin, and with mouthpiece and nose clips attached, subjects began a period of baseline tidal breathing. Once a stable tidal breathing was established, panting manoeuvres were performed. Following the initial plethysmographic measurements, subjects remained seated in the body plethysmograph, and standard spirometry was performed according to ATS standards.[14] Baseline testing was completed first as described above, and then repeated 20 minutes after administration of bronchodilator (Ipratropium bromide 500 mcg with Levosalbutamol 1.25mg) via a nebulizer.

The ATS/ERS defines a positive bronchodilator response as an increase in FEV_1 and/or FVC greater than or equal to 12% and 200 ml of the baseline value.[15] Reversibility criteria for sGaw is changes of $\geqslant$55 %.[6]

Ethical clearance was obtained. Written informed consent was taken from all the patients before the study.

Statistical Analysis

Descriptive statistical analysis has been carried out on the data obtained in the present study. Results on continuous measurements are presented on mean SD and results on categorical measurements are presented in number (%). Significance is assessed at 5 % level of significance. Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups. P value of <0.05 was considered as significant.

The statistical software SPSS version 15 was used for the analysis of the data. Microsoft word and excel have been used to generate graphs and tables.

RESULTS

Initial sample comprised of 40 patients (28 males and 12 females). Graph 1 shows the age distribution of the patients.

Out of total 40 patients, 33 met the FVC/FEV_1/sGaw criteria. Seven were excluded from the study as they did not show positive response to bronchoreversibilty criteria of FEV_1 or FVC or sGaw (Table 1). Mean values of FEV_1, FVC, PEF, $FEF_{25-75\%}$, Raw and sGaw increased significantly after bronchodilator in all the 33 patients who showed bronchoreversibilty (Table 2).

Out of 33 patients, 22 met the criteria of FEV_1 and / FVC criteria. In the remaining 11 who did not meet the flow criteria, met the sGaw criteria. Spirometry alone ($FEV_1$and FVC) identified bronchoreversibility in 66.7% of patients and sGaw identified remaining 33.3% (Table 3). Graph 2 explains the cumulative ability of parameters to assess bronchoreversibilty. It is found that percentage of patients who could be characterised as responsive differed depending on the criterion applied.

Graph 1: Bar diagram showing age distribution of patients

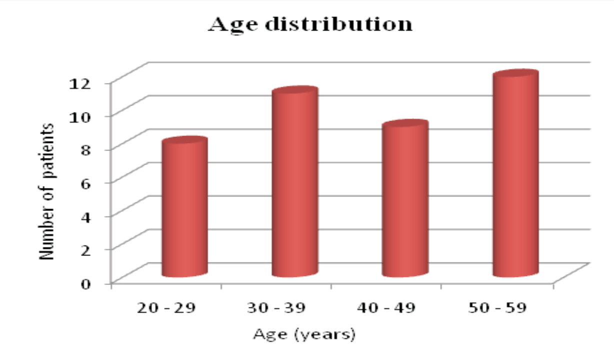

Table 1: Number of patients who met the bronchoreversibility criteria.

FVC /FEV1/sGaw	Patients	Percent
Bronchoreversibilty	33	82.5
No Bronchoreversibilty	7	17.5
Total	40	100

Graph 2: Percentage of patients recognised by spirometric or body plethysmographic parameter

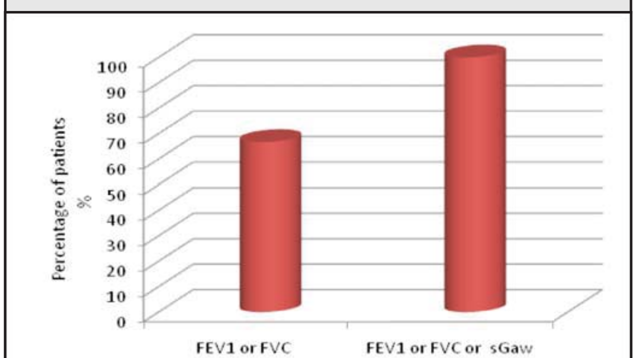

Table 2: Pulmonary function at baseline (pre) and after (post) bronchodilator administration

Parameter		Mean	SD	SEM	% change	t value	p value
FVC (l)	Pre	2.59	0.81	0.14	10.39	-4.18	<0.0001*
	Post	2.84	0.89	0.15			
FEV_1 (l)	Pre	1.65	0.61	0.11	19.45	-7.99	<0.0001*
	Post	1.95	0.71	0.12			
PEF(l/s)	Pre	3.85	2.09	0.36	36.85	-6.48	<0.0001*
	Post	4.78	2.06	0.36			
$FEF_{25-75\%}$ (l/s)	Pre	1.51	0.86	0.15	28.48	-4.00	<0.0001*
	Post	1.87	1.07	0.18			
Raw kPa/(l/s)	Pre	0.45	0.28	0.04	-36.58	6.29	<0.0001*
	Post	0.24	0.13	0.02			
sGaw (1/kPa/s)	Pre	1.09	1.07	0.18	112.48	-2.65	<0.012*
	Post	2.45	3.88	0.67			

* Significant at 5% level
SD- Standard deviation
SEM- Standard error of Mean

Table 3: Recognition of bronchoreversibility by spirometric and body plethysmographic parameter

Bronchoreversibilty Criteria	Patients	Percent
FVC /FEV_1 with or without sGaw criteria	22	66.7
sGaw criteria without FEV_1 or FVC	11	33.3
Total	33	100

DISCUSSION

FEV_1 and FVC are traditional parameters used for detecting bronchoreversibility. However not all the obstructive lung disease patients showed bronchoreversibility (Table 1). Variation in $FEF_{25-75\%}$ as a parameter for bronchodilator response criterion is questionable and the ATS does not recommend its use.[6] Statistical significant improvement was seen all the parameters in patients who showed bronchoreversibilty (Table 2).

In this study spirometric parameters were a good indicator of bronchoreversibility however it still missed few cases. It was found that sGaw reversibility is seen in patients whom spirometric parameters do not show reversibility (Table 3, Graph 2). This is accordance with the study done by skinner et al who found that sGaw appears to be a more sensitive indicator than FEV_1 in assessing airway calibre after bronchodilator induction.[16] But skinner et al had considered only FEV_1 percentage change from baseline as criteria but not FVC percentage change and volume change which has been covered in this study.

Measurement of FEV_1 requires a deep inhalation manoeuvre which may alter airway calibre.[17] Airway dynamics measured during forced respiratory manoeuvres is associated with large transmural compressive pressures across the airways, maximal dynamic airway compression limiting airflow rates and possible alterations in airway smooth muscle tone.[1] This could be the reason why FEV_1 lacks to reveal significant response to bronchodilators in patients with chronic airflow obstruction. Similar observations were made by a study done by Pellegrino et al.[3]

Raw in a body plethysmography is more sensitive and more specific for airway tone, and usually easier for patient to perform than test that depend on deep inspiration to total lung capacity followed by forced exhalation, but this is dependent on lung volume.[1] sGaw is a test that measures lung function over tidal breathing range, is independent of the volume history effects of the deep breath, and is as sensitive to estimate airway patency.[10]

The clinical utility of acute bronchodilator testing is not well defined. Reversible airflow obstruction is the hallmark for asthma and FEV_1 reversibility criteria has been used in diagnosis asthma cases.[1,18] Number of patients classified as reversible is influenced by the parameter used. Failure to detect reversibility due to lack of parameters may result in misdiagnosis. Misdiagnosis of airflow obstruction not only results in misinforming and incorrectly educating the patients about their health, but can also lead to incorrect management.

However, both the GOLD and ATS/ERS guidelines indicate that lack of an acute bronchodilator response during reversibility testing does not preclude a clinical response to long-term bronchodilator treatment.[13,14]

Limitations: Information about subject relief as expressed by the patient and improvement in clinical signs after bronchodilatation should have been correlated with the post nebulisation data obtained. Long term treatment follow up studies are needed to know if laboratory results correlate with the clinical results.

CONCLUSION

Changes in spirometric parameters alone fail to detect significant bronchoreversibility in some obstructive patients. Specific airway conductance allows a broader evaluation of patients when included along with flows. Body plethysmography along with spirometry provide better opportunity for determining optimal bronchodilator responsiveness in obstructive airway disease patients. Hence body plethysmography must be included in knowing the real extent of bronchodilator response, deciding the therapeutic efficacy and in planning the treatment program for obstructive airway disease patients.

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