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Use of forced oscillometric technique for assessing bronchodilator responsiveness in adult patients of bronchial asthma

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ABSTRACT:
Objectives: Asthma and COPD are obstructive airway diseases, which lead to severe airway inflammation and restricted airflow. Forced oscillation technique (FOT) is a technique to evaluate the mechanics of the lungs that is noninvasive. Our aim was to assess the BDR by spirometry and FOT in adult asthma patients. **Methods:** Subjects used in the current study were bronchial asthma patients who were confirmed by expert respiratory doctors/physicians. The bronchodilator medicines were withheldin all patients for 8 hoursbefore the test. **Result:**150 subjects were recruited for the study who met inclusion criteria. A total of 56 **s**ubjects showed good control on current treatment, and there were around **50** ex-smokers and no current smokers. Majority of the subjects were administered with beta-agonists**Conclusions:** The outcome that published BDR cutoffs for FOT, using normative data, are useful in the assessment of asthma and relate to asthma symptom control. BDR measured by FOT is linked to poorly controlled symptoms is constant with parallel connotations with spirometry. Moreover, a connection amongst the scale of BDR and worst symptoms of asthma were detected. Per se, the results are applicable clinically and may advance results particularly in hard-to-treat patients unit with noteworthy symptom load.

Keywords: Chronic Obstructive Pulmonary Diseases, Asthma , FOT

I. INTRODUCTION

Obstructive airway diseases, such as asthma and chronic obstructive pulmonary disease (COPD), are common respiratory diseases that impair airflow and cause severe airway inflammation. These diseases can be distinguished by factors such as age of onset, clinical indicators, smoking history, among others. This discernment, however, can be challenging in elderly people as patients usually have symptoms of both diseases, leading to the development of the asthma-COPD overlap syndrome (ACOS) (1,2).

Asthma is a chronic inflammatory disease of the lungs that results in muscle tightening around the airways, leading to difficulty in breathing. Clinical indicators of asthma include coughing, wheezing, short breath, and chest tightness. The severity of symptoms varies and may be intermittent but can lead to acute exacerbations requiring emergency hospitalization. Management of asthma through effective treatment can help manage the condition. According to the World Health Organization (WHO), in 2019, asthma was responsible for approximately 262 million cases and 455,000 deaths globally.

Forced oscillation technique (FOT) is a technique to evaluate the mechanics of the lungs that is noninvasive (3). The technique involves the application of forced oscillations to the airway openings, resulting in the development of impedance of the respiratory system. The resistance of the respiratory system (Rrs) is the actual share of impedance, while the imaginary part is respiratory system reactance (Xrs). Several variants of the FOT have been developed since its first use with monofrequency in the 1950s. FOT, as a measure of lung function, has become more common in clinical settings, particularly for asthma and COPD. The FOT is advantageous because it does not require any distinctive breathing maneuver with normal breathing, unlike forced expiration spirometry. The FOT is particularly beneficial in older patients, where it is difficult to perform spirometry (3,4).

The assessment of bronchodilator response can aid in diagnosing asthma, but it may not necessarily guide asthma management. Bronchodilator response is linked to poorer

spirometry results and decreased asthma control, if anti-inflammatory medication is not used. However, a positive bronchodilator response is also indicative of better response to anti-inflammatory treatment in untreated asthma, according to Wells KE et al. (2016)(5).

There is growing recognition of the importance of traits, such as BDR. Studies have shown that despite anti-inflammatory treatment, persistent BDR is associated with higher doses of inhaled corticosteroids, less FEV1, poor asthma control, increased heart beat and higher death rates (6). These findings underscore the need to recognize ongoing BDR as a significant, yet often overlooked, therapeutic target in asthma management. As personalized medicine becomes an increasingly discussed topic in asthma management, it is important to consider the importance of treatable traits beyond just inflammatory phenotypes, such as BDR.Lung function monitoring is crucial for asthma management, but spirometry results may not always align with reported symptoms. Use of alternative methods like oscillometry can provide additional information on bronchodilator response. FOT measures respiratory impedance by overlaying pressure and flow waves during regular breathing. Research has revealed that BDR evaluated by FOT is linked to the finding of asthma in an autonomous manner compared to spirometry and is correlated with higher airway resistance, accompanied by decreased FEV1 (7). Additionally, FOT might be a more appropriate tool to gauge asthma control than spirometry, however, the association between FOT and BDR in this regard has yet to be explored.Impact of these thresholds on clinical relevance has yet to be assessed and in comparison to spirometry in cases of airway diseases. Commercial tools have made FOT more prevalent in clinical settings, which highlights the need for a greater grasp of how FOT, spirometry and symptom management relate in terms of asthma. Our hypothesis is that BDR cutoffs for FOT may be utilized for asthma as well as being an effective means of identifying cases of weak asthma control with sensitivity.

II. MATERIALS AND METHODS

Subject description

Subjects used in the current study were asthma patients who were confirmed by expert respiratory doctors/physicians. The criteria for inclusion of subjects are that all were asthma patients. Subjects who had other respiratory diseases, cognitive impairments, inadequate lung function measurements were excluded from the study. The history of subjects like smoking, demography was documented. Proper approval from the ethical committee was obtained before performing the study. Salbutamol at 400mcg was administered by inhaler and spacer and the tests were done 10 minutes before and after giving the bronchodilator.

Forced Oscillation Technique

Standard recommendations of ERS (European Respiratory Society) were followed for FOT and was done during tidal breathing, both pre and post bronchodilator administration immediately after spirometry. Mean of three measuremnets of 30 seconds were recorded before and after giving bronchodilator (Thremo-Flo; Thorasys Thoracic Medical Systems) and the results accepted were free from defect due to constriction, leakage or extreme or negative resistance (8).BDR cutoffs and reference values were taken from Oostveen et al.2003 (3)the definition of BDR stands as an absolute change in R5, X5, or AX afftergivingbronchodilator.

Spirometry

American Thoracic Society (ATS)/ERS guidelines were followed for the Spirometry (Mastrlab; Jeeger) which was executedinstantly after FOT, pre & post-bronchodilator giving(9) and the standard values were derivatives from the global lung initiative (10).As per the TAS/ERS guidelines BDR is taken as 12% and 200 ml enhancement in FEV1 and/or FVC after giving bronchodilator.

Asthma Control

The symptoms in subjects related to Asthma were evaluated with the ACT test and were taken as good control(ACT score - 20), not good control (ACT value= 16-19), or weakly controlled (ACT= 15) (Schatz M et al., 2006).

DataAnalysis

Statistical analysis was performed by SPSS 18 (IBM). For BDR assessment and agreement between FOT and spirometry Cohen's k was used. Cross- was performedfor comparing BDR as measured by FOT vs spirometry, and weak asthma control. C2 test was used for assessing the association between categorical variables and spearmans correlations were used to assess Univariate correlations and statistaical significance was considered at $p<0.05$.

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III. RESULTS

A total of 150subjects were involved in this study who met inclusion criteria. The subject data on lung function are shown in Table A and B. A total of 60 **s**ubjects showed good control on current treatment, and there were around 45 ex-smokers and no current smokers. Majority of the subjects were administered with inhaled ICS (81%) and a beta-agonist (77%).

Table 1. represents characteristics of subjects

s.no	Characteristics	value
1	Subjects (Number)	150
2	Gender (Male/female)	67/83
3	Age(years)	57±20
4	BMI	29.4±5.8
5	Smoking, pack-yrs	6±9
6	salbutamol (µg/d)	785
7	Long acting bronchodilator (LABA)%	78
8	Inhaled Corticosteroid (ICS)%	74
9	Score of ACT (5-25)	19±7
10	Number of subjects in terms of disease control (well/not well/poor control)	60/45/45

Data are presented as mean±SD. ACT is asthma control test

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Table 2. represents function of lungs and Brochodiatorreaction as per FOT and spirometry

	Before bronchodilator	After bronchodilator	Subjects with sig. BDR
FOT			
R5 cmH2O.s/l)	5.90±1.90	5.12±1.79	31(20%)
R5 (percentage predicted)	168±67	146±59	
X5 cmH2O.s/l)	-3.63±2.78	-2.82±2.18	68(45%)
X5 (percentage predicted)	268±178	199±123	
AX(cmH2O.s/l)	37.59±28.86	21.47±24.76	82(54%)
AX (percentage predicted)	968±977	657±835	
Spirometry			
FEV1, L	2.12±0.81	2.24±0.78	41(27%)
FEV1 (%)	72±20	78±22	
FVC, L	2.99±0.92	3.26±0.99	21(14%)
FVC (%)	83±18	93±20	
FEV1/FVC(%)	69±16	74±16	

Data are mean ±SD. AX- represents area belowthe reeactance curve between 5 hertz and the reesonantfrequecy. R5-resistance t 5HZ; X5-reectance at 5Hz;

FOT and Spirometry

Identification of BDR was done often by FOT (84 of 150 subjects, that means 56%) than spirometry (41 out of 150 subjcetsi.e, 30 %) (Table3 , Fig1). It was observed that in BDRpatients with spirometryBDRlargely had a bronchodilator retort in FEV1.Only few subjects were found to have spirometryBDRcentred on a

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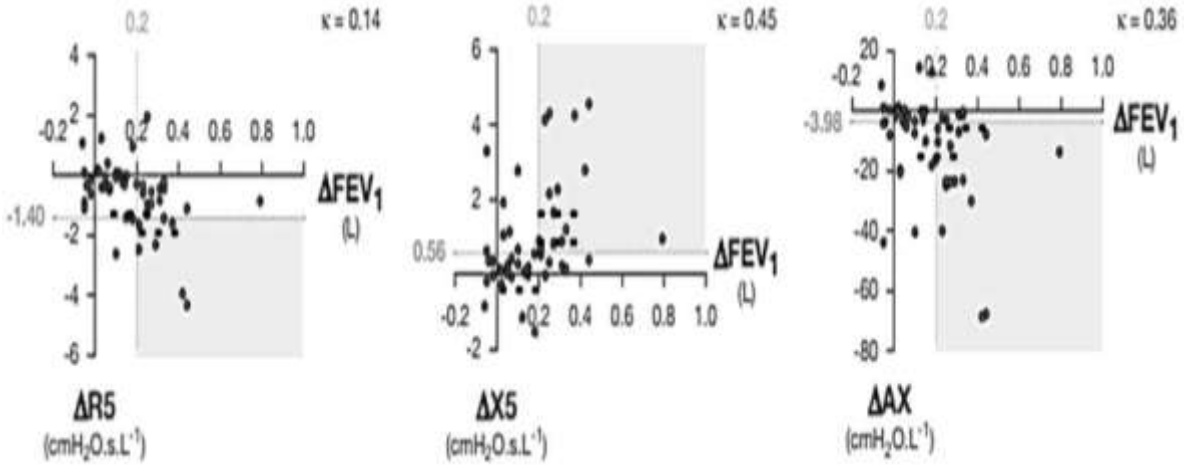
reaction in FVC alone. There were 68 subjectswho met BDRcuttoffsby X5 and AX and only 8 subjects were found to meet BDRstandards by spirometry.BDR as assessed by X5 (c2 ¼ 11.5, P ¼ .001) and AX (c2 ¼ 8.7, P ¼ .003) was associated with BDR on spirometry. A weak agreement was observed between BDRevaluated by spirometry vs X5 and AX (Fig1) and there was no covenant between BDRevaluatedby R5 and spirometry.

Table.3. BDR assessed by FOT in comparison with spirometry

		BDR by Spirometry Presnet	**Absent**
BDR by R5	Present Absent	12 30	18 96
BDR by X5	Present Absent	30 9	30 84
BDR by X5	Present Absent	32 6	42 58

The data here presents cross tabulation data on patients.

Fig.1. shows the comparison in BDR evaluated by FOT and spirometry.



Asthma andBDR

ACT valuelinkedtoBDRevaluated by X5and AX but not R5 or spirometry (Fig 2). There was weakcontrol of symptoms (ACT < 20) linked with BDRevaluated by spirometry (c2 ¼ 7.93, P ¼ .005), X5 (c2 ¼ 8.71, P < .003), and AX (c2 ¼ 9.45, P ¼ .002) but not R5 (P ¼ .272), when the categorization was done as per asthma control.

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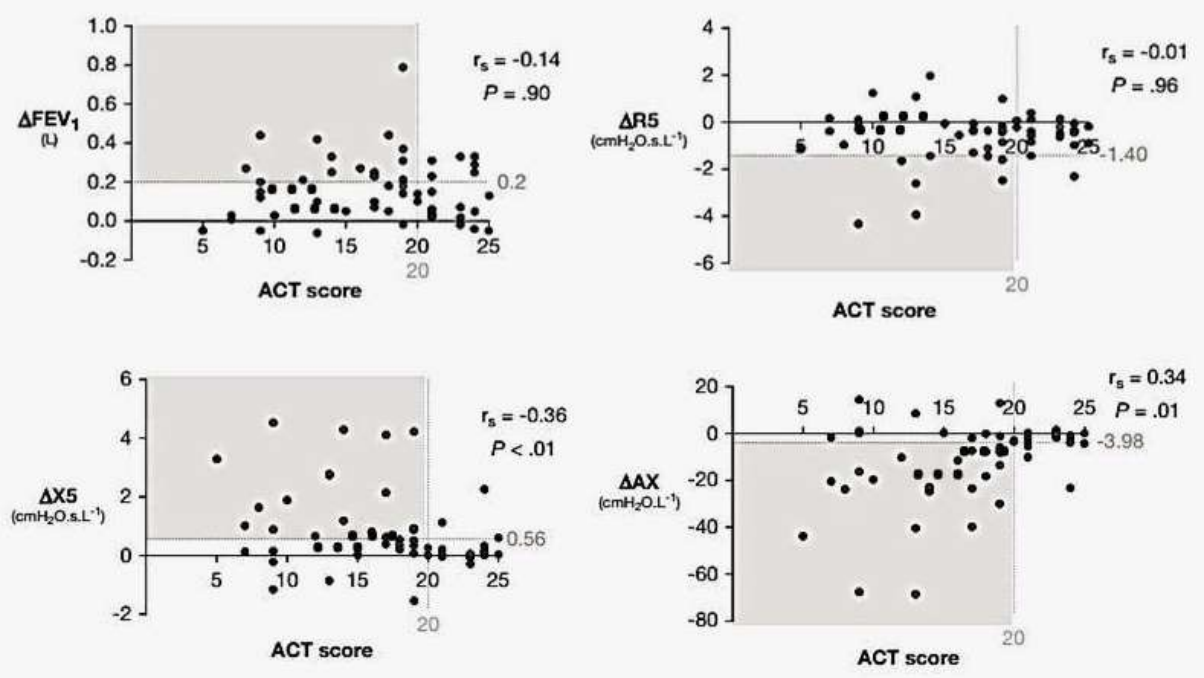
Further, a weak link between weak asthma control and BDRevaluated by spirometry but not R5 and it was found that BDR measured by X5 and AX recognizedmorepatients with poorly controlled asthma which were undientified by spirometry. Comparatively, spirometry found only 4 subjects with very weak asthma control which were undetected by FOT. It was found that BDRevaluated by AX have the utmost sensitivity to identifyweak asthma control.

Fig. 2 shows the link between BDR and asthma.



IV. DISCUSSION

In the present study we found that the BDR assessed by spirometry and FOT identified poor asthma control and is clinically applicable. It is reported that in subjects with asthma BDR cutoffs earlier used for FOT, using normative data. More importantly, it was found that BDR is linked with poorer asthma control. Comparatively, BDR determination by FOT can recognizeadditional subjects with very weakly controlled asthma than with spirometry. The outcome that that BDR measured by FOT is linked to poorly controlled symptoms is constant with parallelrelationsto spirometry.Moreover, a connectionamongst the scale of BDR and worst asthma symptoms weredetected.

It is essential to monitor BDR in the enduring sequel of patients with asthma where it is yet to be studied at length. The occurrence of BDR initially in asthma is a known feature, however persistant BDR inspite of treatment indicates more stark or sub-optimal treatment of the disease.

Ferrer Galvan et al., 2017(11) reported that reversibility in FEV1 is linked to poor asthma control in huge number of younger subjects and with more conserved spirometry. In the present study It was confirmed that there is strong link in asthma patients between BDR evaluated by spirometry and weak symptom control. It is suggested that the occurence of BDR can be additionalcurablepeculiarity in asthma. Further, reactance calculated by FOT is a clinically significant factor when evaluating BDR in asthma.Suggested BDR cutoffs and their normative data are already published (8). The results of the present study specify that opposition alone relates weakly to symptom control, is in agreement with the previous reports (12).

It is of outmost importance in clinical practice to identify patients with weak or poor asthma control in managing the disease of enhanced sensitivity is sensible and may be compensated by the mixed use of FOT and spirometry.Verbanck S, et al., 1999 (13) reported that many mechanisms like a decrease in bronchomotor tone, improved clearing of mucus, enhancement in the extent of ventilation etc., may be operative in lung function improvement after giving an inhaled bronchodilator. BDR assessment by spirometry or FOT were linked to weak asthma control.

Reactance measured by FOT is impacted by numerous intricate connections in the lungs, such as the qualities of the airways and volume of lungs as well as ventilation heterogeneity. It serves as a representation of the delivery of lung units that are present to the signals of oscillation.The spirometric BDR is evident of these same mechanistic revisions to the degree that they impact the flow in the large airways (14,15).

However, the percentage of patients with BDR was alike to that reported previously in the research. More research needs to be carried out in this to toexplain if these outcomes translate to patients with less sever disease, those who don't receive ICS, or subjects having asthma and are also smokers.The relation between BDR and symptoms is of clinical significance.

Ours is the first such well characterized study with this sample size, which included a variety of asthma ruthlessness and symptom load, which describes the report on adult samples BDR evaluated by FOT in amalgamation with symptom values in a good population.

Per se, the results are applicableclinically and may advanceresultsparticularly in a hard-to-cure subjects with noteworthy symptom load.

V. CONCLUSION

The outcome that BDR measured by FOT is linked to poorly controlled symptoms is constant with spirometry. Moreover, a connection between the scale of BDR and worst asthma symptoms were detected. Per se, the results are applicable clinically and may advance results particularly in a hard-to-cure patient unit with noteworthy symptom load.

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