Role of Impulse Oscillometry in Assessing Asthma Control in Children

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Background: Impulse oscillometry is an effort-independent technique of assessment of airway resistance and reactance, and can be performed in children unable to complete spirometry.

Objective: To evaluate the utility of impulse oscillometry and spirometry for assessing asthma control in children.

Study design: Prospective cohort study.

Participants: Children aged 5-15 years, with mild to severe persistent asthma.

Intervention: On each 3-monthly follow-up visit, clinical assessment, classification of control of asthma, impulse oscillometry and spirometry were performed.

Outcome: Utility of impulse oscillometry parameters [impedance (Z5), resistance (R5), reactance (X5) at 5 Hz, and R5-20 (resistance at 20Hz -5Hz) (% predicted), and area of reactance (AX, actual values)] and FEV_1 (% predicted) to discriminate between controlled and uncontrolled asthma was assessed by receiver operating characteristic (ROC) curve. Association of FEV_1 and impulse oscillometry parameters over time with controlled asthma was evaluated by generalized estimating equation model.

Results: Number of visits in 256 children [mean (SD) age, 100 (41.6) mo; boys: 198 (77.3%)], where both impulse oscillometry and spirometry were performed was 2616; symptoms were controlled in 48.9% visits. Area under the curve for discrimination between controlled and uncontrolled asthma by FEV_1, AX, R5-20, Z5, R5, and X5 were 0.58, 0.55, 0.55, 0.52, 0.52 and 0.52, respectively. FEV_1 [OR (95% CI): 1.02 (1.01-1.03)] and AX [OR (95% CI): 0.88 (0.81-0.97)] measured over the duration of follow-up were significantly associated with controlled asthma.

Conclusion: Spirometry and impulse oscillometry parameters are comparable in ascertaining controlled asthma. Impulse oscillometry being less effort-dependent may be performed for monitoring control of childhood asthma, especially in younger children.

Key words: *Spirometry, impedance, resistance, reactance.*

Early diagnosis and good control of asthma is expected to improve the course of the disease, the most common chronic respiratory illness in children [1]. According to the current guidelines, treatment of asthma should aim at achieving and maintaining asthma control [2]. However, assessing control of childhood asthma is challenging and subjective as there is discordance in the perception of severity of symptoms between children and their parents. Various non-invasive techniques to objectively measure the lung functions in children have been developed which include spirometry, impulse oscillometry, body plethysmography, multiple breath washout test, forced oscillation techniques [3-6].

Conventional spirometry is considered as the gold standard test for assessment of airflow obstruction; however, it has certain shortcomings. Firstly, it is an effort-dependent test, younger children and those with acute exacerbation are generally unable to perform the test; hence, there is a poor correlation between symptoms and test results. Secondly, spirometry cannot properly differentiate between distal and peripheral airways. The forced expiratory volume in one second (FEV_1) and the mid-forced expiratory flow (FEF_{25-75}) mainly represents the large and small airways, respectively [7]. Thirdly, the effort dependent nature of the test interferes with the reproducibility of the test [8].

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Impulse oscillometry (IOS) is a much simpler, non-invasive technique of assessment of airway resistance and reactance in children. It is effort-independent, requires minimal patient cooperation, can be performed in tidal breathing, and can distinguish between the degree of obstruction in central and peripheral airways [4-6]. In young children where reliable spirometry is difficult to obtain, IOS allows for evaluation of lung function through measurement of both airway resistance and reactance [3]. There is limited number of studies on utility of IOS to assess asthma control, and there is no consensus on the cut-off values of IOS parameters to determine asthma control in children [5,9].

The aim of our study was to compare the utility of IOS and spirometry parameters for assessing asthma control in children 5-15 years of age.

METHODS

Children aged 5-15 years, attending Pediatric Chest Clinic and Pediatrics OPD of the All India Institute of Medical Sciences, New Delhi, between 2010 to 2016, were eligible for screening. Inclusion criteria were physician-diagnosed asthma and the ability to perform spirometry. Patients were excluded from the study if they had interstitial lung disease, congenital heart disease, tuberculosis, cystic fibrosis, bronchomalacia/laryngo-malacia, tracheaesophageal fistula, vocal cord dys-function, hypersensitivity pneumonitis, chronic liver/ renal disease, took medications that could induce chronic cough such as ACE inhibitors/α blockers, or residing outside Delhi or were unlikely to follow-up. Written informed consent was taken from the parent/guardian of the study participants. The study was approved by the Ethics Committee of the institution. Children were followed up regularly at an interval of three months.

Baseline spirometry and IOS were performed in all the children. At each three monthly visit, clinical assessment, IOS and spirometry were performed. After each visit, the symptom control was classified as controlled, partly controlled, uncontrolled or acute exacerbation according to the GINA guidelines and appropriate treatment were prescribed according to the control status of the patient [2]. To assess the symptoms in the interval between the visits, a symptom diary was provided, and medications (adherence and technique) were checked at each visit.

All study procedures were performed using MasterScreen IOS (CareFusion, Germany 234 GmbH) and Spirolab III. Spirometry and IOS were performed and anthropometric measurements taken by trained research officer and technician at each visit. Patients were explained about the procedure and were then allowed to perform the test. The best among three readings was taken in spirometry to ensure reproducibility of the test. FEV_1 value was taken as a measure of airflow obstruction.

IOS was performed in the sitting position, with the child breathing at tidal volume through a mouthpiece with the nose-clip in place and head held in neutral position and the cheeks supported by hands to decrease the dead space. Readings for normal tidal breathing through the mouthpiece for 30 seconds were taken. The MasterScreen IOS was used to calculate the pulmonary impedance (Z) which compromises of pulmonary resistance (R) and reactance (X) and pressure-flow relationship of the respiratory system as a function of oscillation frequency. The IOS indices taken into consideration were R5 (resistance at 5 Hz), X5 (reactance at 5 Hz), Z5 (pulmonary impedance at 5 Hz) and AX (area of reactance). R5-20 were calculated by subtracting values of R20 (resistance at 20 Hz) from R5. IOS was performed before spirometry in each child.

Statistical analysis: All statistical analyses were performed using STATA version 13 (StataCorp, College Station, TX, US). IOS parameters (percentage predicted of Z5, R5, X5, R5-20, and actual values of AX) and FEV_1 (percentage predicted) were compared by Pearson correlation coefficient. The above mentioned parameters were individually compared in controlled and uncontrolled state of asthma by *t* test or rank-sum test as appropriate. The receiver operating characteristic (ROC) curves were used to evaluate the discriminatory powers of FEV_1 and the IOS parameters in assessing control of asthma. Generalized estimating equation (GEE) was used to evaluate the association between controlled state and FEV_1 and IOS parameters over time.

For the purpose of analysis, children with partly controlled or uncontrolled asthma were grouped together as uncontrolled asthma. Acute exacerbations were excluded from the analysis.

RESULTS

A cohort of 256 children with mild to severe persistent asthma was enrolled and followed up for a mean (SD) duration of 37.6 (13.1) months. The total number of follow-up visits (excluding the exacerbations) in 256 children were 3152 (range: 1-15 visits/child). Based on the treating physician's assessment, asthma was assessed to be controlled on 1542 (48.9%) and uncontrolled (partly controlled or uncontrolled) on 1610 (51.1%) visits. Demographic profile of all patients and airway indices are presented in ***Table* I**. Both IOS and spirometry were performed in 2616 visits and data from these visits were used for analysis. In 140 visits only IOS, but not spirometry could be performed, and only spirometry was performed in 396 visits because IOS was not available at that point of time.

FEV_1 and the IOS parameters Z5, R5, X5, R5-20 and AX were all significantly correlated with each other in both controlled and uncontrolled state (data not shown). FEV_1 and all the IOS parameters were significantly

TABLE I Baseline Demographics and Pulmonary Function Test of Children with Asthma (*N*=256)

Characteristics	*Values*
Age, mo	100 (41.6)
Boys, *n* (%)	198 (77.3)
FEV_1 (% predicted)	87.7 (17.9)
R5 (% predicted)	95.7 (28.3)
*R5-20, cm H_2O/L/s	5.02 (-5.9, 21.04)
Z5 (% predicted)	98.6 (28.6)
X5 (% predicted)	116.5 (55.3)
AX (kPa/L)	2.2 (1.8)

*Values are expressed as mean (standard deviation) or *median (IQR); FEV_1: Forced Expiratory Volume in the 1st second, R5 (resistance at 5 Hz), X5 (reactance at 5 Hz), Z5 (impedance at 5 Hz) and AX (area of reactance). R5-20 were calculated by subtracting values of R20 (resistance at 20 Hz) from R5.*

different in the controlled and uncontrolled state (***Table* II**). The areas under the ROC curve (95% CI) for discriminating the controlled and uncontrolled state were comparable (***Table* III**).

GEE showed a significant association of FEV_1 and AX measured over the duration of follow-up with the controlled state of asthma. For each unit change (increase) in FEV_1 over time, the odds of control of asthma was 1.02 (95% CI: 1.01-1.03). For each unit of increase of AX over time, the odds of control of asthma was 0.88 (95% CI: 0.81-0.97).

TABLE II Comparison of Impulse Oscillometry and Spirometry Parameters in Controlled *vs* Uncontrolled Asthma

Parameters	*Controlled (n= 1315)*	*Uncontrolled (n=1301)*	*P value*
Spirometry parameter			
FEV_1 (% predicted)	91.3 (15.3)	86.0 (18.1)	<0.001
IOS parameters			
R5 (% predicted)	98.1 (31.8)	101.3 (32.9)	0.01
Z5 (% predicted)	103.9 (38.9)	107.7 (41.7)	0.01
X5 (% predicted)	147.9 (79.2)	157.4 (87.9)	0.003
AX (kPa/L)	1.9 (1.8)	2.2 (2.09)	<0.001
*R5-20, cm H_2O/L/s	1.9 (-9.5, 14)	3.3 (-7.3, 17.9)	<0.0012

*Values are expressed as mean (standard deviation) or *median (IQR); FEV_1: Forced Expiratory Volume in the 1st second, R5 (resistance at 5 Hz), X5 (reactance at 5 Hz), Z5 (impedance at 5 Hz) and AX (area of reactance). R5-20 were calculated by subtracting values of R20 (resistance at 20 Hz) from R5.*

TABLE III IOS and Spirometry Parameters in Assessing Control of Asthma

Parameters	*AUC of ROC (95% CI)*
FEV_1 (% predicted)	0.58 (0.56-0.60)
AX (kPa/L)	0.55 (0.52-0.56)
R5-20, cm H_2O/L/s	0.54 (0.52-0.56)
Z5 (% predicted)	0.52 (0.5-0.55)
R5 (% predicted)	0.52 (0.5-0.55)
X5 (% predicted)	0.52 (0.5-0.55)

Total numbers of episodes = 2616; FEV_1: Forced Expiratory Volume in the 1st second, R5 (resistance at 5 Hz), X5 (reactance at 5 Hz), Z5 (impedance at 5 Hz) and AX (area of reactance). R5-20 were calculated by subtracting values of R20 (resistance at 20 Hz) from R5.

DISCUSSION

Our study demonstrated that IOS and spirometry have comparable ability to detect the control state of asthma in children. Both IOS and spirometry yielded similar results in differentiating children with controlled and uncontrolled state of asthma. There was a significant association of increase in FEV_1 and AX measured over the duration of follow-up, with the controlled and uncontrolled state of asthma, respectively. The FEV1 values were statistically different in the controlled *versus* uncontrolled groups; however, the uncontrolled group too had a fairly good lung function.

IOS is a form of forced oscillation technique which is based on the physiologic concepts originally described in 1956 [10], and can measure the mechanical properties of lung [11-13]. Spirometry, being effort dependent is difficult to perform in younger children, particularly those who present with uncontrolled or acute exacerbation of asthma. There are limited numbers of studies in children which have observed the utility of IOS in assessing long term control of asthmatic children [5,9]. IOS is especially important in determining the status of smaller airways and studies have also inferred that AX, which is a parameter representing the smaller airways, is the best indicator of long-term control and treatment response in childhood asthma [4,9,14]. A recent trial found that assessment of pulmonary function over time with IOS might offer additional insights into the response of asthmatic patients to therapy, and might detect alterations in airway mechanics not reflected by spirometry [4]. Over a prolonged period in their study, the area of reactance (AX) showed continued improvement compared to spirometry parameters [4].

In our study, a significant difference in R5-20 and AX in controlled and uncontrolled state was observed.

What is Already Known?

- Assessment of control of asthma is presently done primarily by clinical scores and spirometry in case of older children.

What This Study Adds?

- Spirometry and Impulse oscillometry are comparable in assessing control in children with asthma.
- Impulse oscillometry may be used in place of spirometry in children who are unable to perform spirometry.

Similar findings were demonstrated prior to bronchodilator therapy in asthmatic children where both IOS and spirometry were performed, and small airway measurements by IOS in uncontrolled asthma were significantly different from those of controlled asthma [14]. IOS parameters that reflect smaller airways like the difference in resistance between 5 Hz and 20 Hz (R5-R20) and the area under the reactance curve (AX), are more closely related to asthma control [15]. The assessment of asthma control over a period of time in our cohort showed that both IOS and spirometry measurements were equally useful in the assessment of asthma control, as concluded in a study in adults with persistent asthma [16].

The strength of our study is that it is one of the few studies in children with prospectively collected data on long term follow-up of children with asthma. However, limitation of our study is that we were unable to comment on the utility of IOS in preschool children from this study; preschool children being a group who would benefit the most from an effort independent test like IOS. The assessment was done clinically, and children were labelled as controlled or uncontrolled depending on the symptom diary and feedback of the caregiver's version during the follow up visits. Uncontrolled group consisted of both partly controlled and uncontrolled cases. Both these features might have led to overestimation of the uncontrolled state.

As the GINA 2019 guidelines [17] recommend monitoring of lung function at baseline and during follow-up, it will be desirable to determine the cut-offs of various parameters of IOS which could be used instead of spirometry, particularly in young children. AX is a particularly important IOS parameter associated with the controlled state of asthma. IOS being less effort dependent can be performed for monitoring control in childhood asthma, especially in younger children and in sicker children who are unable to perform spirometry. Thus, IOS may be a good alternative for evaluation of asthma in children.

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