CAPÍTULO 10

LONGITUDINAL EVALUATION OF PULMONARY FUNCTION IN PRESCHOOL CHILDREN WITH ASTHMA USING OSCILLOMETRY

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ABSTRACT: Introduction: The Impulse Oscillometry System(IOS) is useful for evaluation of pulmonary function in children, since it does not require their active collaboration. **Objective:** to assess pulmonary function in preschool children diagnosed with asthma attending a specialized clinic and to re-evaluate them 12 months later. **Method:** The pulmonary function of children with asthma(aged 3 to 6 years) was evaluated using IOS at the admission of the study and after 12 months of follow-up. Total resistance at 5Hz(R5), central resistance at 20Hz(R20), the difference between these(R5-R20), reactance at 5Hz(X5) and the reactance area(AX) were measured before and after inhalation of bronchodilator. A reduction of 40%, 50% and 80% or greater for R5, X5 and AX respectively was deemed to constitute a positive response. **Results:** All the children(n=58) performed the pulmonary function evaluation correctly. There was no difference between R5 and X5(percentage of predicted) at the outset of the study and that registered at the end. In the first year, 24% and 36% of the children presented abnormal values of R5 and X5, respectively; and, in the second year, the figures were 29% and 53%. In six children R5 was increased on both visits and in 14 X5 was abnormal. Bronchodilator response was not frequent and changes were most observed in X5. **Conclusion:** Early abnormalities in pulmonary function can be observed in almost half preschoolers with asthma in spite of specialized care and treatment. This demonstrates the need for long-term specialized treatment, including monitoring of pulmonary function, and clinical follow-up in these patients.
KEYWORDS: Respiratory sounds, asthma, respiratory tests, oscillometry.

INTRODUCTION

Asthma is a chronic inflammatory disease of the airways associated with varying degrees of obstruction of airflow, presenting with recurrent episodes of wheezing, coughing, tightness of the chest and dyspnea[1]. Prospective investigations suggest that irreversible changes in lung function begin in infancy, before reaching school age[2,3]. One possible cause of this functional impairment may be late diagnosis and/or inadequate treatment of children with asthma, which may lead to progressive deterioration of pulmonary function extending into adulthood[2,3]. Pulmonary function follow-up in children with recurrent wheezing or asthma is important for confirmation of diagnosis, evaluation of the disease severity and monitoring of these patients over time[4].

Spirometry is a test that is widely used in diagnosis, follow-up and evaluation of the effectiveness of asthma treatment. However, the test is difficult to perform correctly in children aged six years or under, because it requires effort and cooperation of the patient in order to obtain acceptable and reproducible flow-volume curves[5]. Although IOS may correlate with spirometry, each is thought to measure different aspects of lung function, IOS assessing airway caliber, while spirometry reflects airflow characteristics[6].

For this reason, impulse oscillometry (IOS) is being introduced into clinical practice as an alternative to spirometry, since it requires minimal patient cooperation and can be successfully applied to preschool children[7].The advantage of IOS over spirometry is that measurements are carried out during tidal breathing and therefore can be performed in children from the age of two years onwards[8]. IOS assesses pulmonary function using frequency waves between 5 and 35 Hz. Low oscillation frequencies reach the distal airways and provide information of the whole lung. Thus, resistance at 5Hz (R5) may be heightened in the presence of proximal or distal obstruction[9].

IOS may be useful for evaluation of the pulmonary function of children and it is a auxiliary tool for the evaluation of disorders of the distal airways, especially in younger children, who often do not possess the degree of understanding or coordination required to undergo spirometry[10]. In asthma, it can be used to evaluate the bronchodilator response and contribute to the assessment of the disease control[10]. The aim of the present study was to assess pulmonary function in preschool children diagnosed with asthma attending a specialized clinic and to re-evaluate them 12 months later.

METHODS

The study covered children diagnosed with asthma[11] (aged 3 to 6 years, n=58) attending and regularly followed-up by the Allergy and Immunology Outpatients Clinic of the Federal University of Pernambuco's Clinical Hospital, in Recife, Brazil. The study was approved by the institution's Ethics Committee (protocol no. 2,361,934), and all parents / guardians signed a Term of Free Informed Consent.

From the spontaneous demand of the service itself, patients of both sexes, aged between 3 and 6 years old, who had symptoms compatible with asthma, were inserted into the study continuously[11]. The exclusion criteria were prematurely-born children, as were those with low birth weight, those with recent respiratory infections (within the last 30 days), previous diagnosis of bronchitis or chronic lung disease other than asthma. The test was discontinued after six attempts or when the child did not achieve the coefficient or was not focused on the task. The children underwent skin prick test (Dermatophagoides pteronyssinus and Blomia tropicalis, dog epithelium, cockroach mix, cow's milk, egg, wheat, corn and soy)[12].

Anthropometric data were gathered using a duly calibrated pedestal scale (Filizola), attached to a stadiometer. For measurement the children removed their shoes and wore as little clothing as possible. The children then underwent a pulmonary function test using IOS and re-evaluate 12 months later.

IMPULSE OSCILLOMETRY

IOS was conducted employing a Masterscreen IOS (VIASYS Healthcare CmbH, Germany). Calibration was carried out with a 3.0L syringe, in accordance with the manufacturer's instructions. The position for the test was explained to the children using an illustration (a photo of a child in the correct position to begin the test), sitting comfortably in a chair with a backrest, both feet supported, chin and cheeks held in the hands to prevent air from escaping, and lips firmly closed around the disposable mouthpiece, using a nose clip to prevent air escaping through the nose, and breathing uninterruptedly through the mouthpiece to provide data for 40 seconds[13,14]. Three recordings of 40 seconds of tidal breathing were made at two distinct points in time: prior to and 15 minutes after inhalation of bronchodilator (salbutamol 200mcg with spacer and facemask)[15]. Standardization of the technique followed the guidelines of the American Thoracic Society/European Respiratory Society[16].

The parameters registered were: total resistance at 5Hz (R5), central resistance at 20Hz (R20), the difference between these two (R5-R20), which represents peripheral resistance; reactance at 5Hz (X5), and the reactance area (AX), all measured in kPas/L. The parameters were expressed as Z scores for reference values corrected for height and deemed to be indicative of altered pulmonary function if there was an increase of two standard deviations in R5, R5-R20 and AX and a decrease of two standard deviations in X5 in relation to the expected value[17].The response to bronchodilator was deemed positive, for R5, X5 and AX, when the parameter decreased, respectively by 40%, 50% and 80% or more, after use[18]. The results were considered reliable after correct application of the technique, with repeated measurements, when the acceptable coefficient was reached in R5 (0.8 cmH_2O) and R20 (0.9 to 1.0 cmH_2O)[19].

STATISTICAL ANALYSIS

Comparative analysis was carried out using SPSS 20.0 (*Statistical Package for the Social Sciences*). The Shapiro-Wilk test was used to test for normality. The means and standard deviations and derived parameters were calculated, along with the frequency percentages. Comparison of numerical parameters was carried out using the t test and the chi-squared test for qualitative parameters. A p value less than or equal to 0.05 was considered statistically significant.

RESULTS

Sixty-three patients were recruited and five were subsequently excluded for not completing the study protocol. The mean interval between the two evaluations was 12.9±1.6 months. All 58 participants performed the pulmonary function maneuvers correctly. More than 90% of patients were treated with inhaled corticosteroid, 90% had already used an bronchodilator prior to the initial visit, and over 80% had already received emergency care for wheezing exacerbations. Table 1 presents all the main characteristics of the population under study.

Variables	**N (%)**	
Sex (boys)	35 (60.3%)	
Time of return visit (months - mean ± sd)	12.9±1,6	
Wheezing in first year of life	50 (82.2%)	
Wheezing in the last 12 months	56 (90.5%)	
Use of IC during study period	53 (91.37%)	
Blood eosinophils >4%	18/36* (50%)	
Positive skin prick test †	23/37* (62.16%)	
Temporal Variables	**Initial Visit**	**Final Visit**
Age (years - mean ± sd)	4.08±0.8	5.22±0.95
Height (cm - mean ± sd)	105.7±7.1	113.6±7.8
Use of BD	56 (90.5%)	42 (72.4%)
Emergency visit prior to initial visit and during study period	48 (82.76%)	20 (34.5%)

IC = inhaled corticosteroid; * = Exams performed † = food and air allergens; BD = bronchodilator

Table 1 – Clinical Profile of Children included in Study (n = 58).

The pulmonary function parameters of the children are presented in Table 2. There was no difference between R5 and X5 at the baseline and at the end of the study. Even so, less than half of the patients presented abnormal values of R5 on the first and second visit and of X5 on the first visit. Persistent impaired pulmonary function (abnormal values in both visits) was observed in six children for R5 and in 14 for X5 (data not shown).

	Pulmonary Function Data		p value*
	1st year	2nd year	
R5			
Absolute value	1.03±0.24	0.91±0.26	-
% of expected	101.33±21.02	118.11±24.65	0.601
X5			
Absolute value	-0.34±0.18	-0.34±0.16	
% of expected	133.62±21.46	131.55±43.65	0.312
AX			
Absolute Value	3.78±1.66	3.19±1.45	-
R5-R20			
Absolute Value	0.35±0.15	0.30±0.16	-
Individuals with Alterations in Pulmonary Function			
	1st year	2nd year	
R5	14 (24%)	17 (29%)	0,529
X5	21(36%)	31(53%)	0,062

*T test and Chi-squared.

Table 2 – Pulmonary function parameters (IOS) for children studied (n = 58).

Only one child responded to bronchodilator in parameter R5, three in parameter X5 and none in AX. No children responded to bronchodilator in parameter R5, two children in X5 and one in AX. The difference between pre- and post-bronchodilator use was 40% for R5, 50% for X5 and 80% for AX (Table 3). X5 was the most heavily affected. Only some children who responded to the bronchodilator had presented altered pulmonary function on evaluation prior to the bronchodilator. The number of children with bronchodilator response in R5 was considerable increased when lower cut-offs (20% and 35%) were employed[20,21].

	Increase				
	20%	35%	40%	50%	80%
R5 1st visit	17/03*	06/02*	01/01*		
R5 2nd visit	15/07*	03/02*	00		
X5 1st visit				03/01*	
X5 2nd visit				02	
AX 1st visit					00
AX 2nd visit					01
R5-R20 1st visit	30	17	13		
R5-R20 2nd visit	37	20	14		

*Altered pulmonary function prior to bronchodilator.

Table 3 – Bronchodilator response: patients with bronchodilator response in this percentage/patients with abnormal lung function* (n = 58)

Mean response (%) in pulmonary function before and after use of bronchodilator are presented in Table 4.

Parameter	Visit		
	Initial (M±sd)	**Final** (M±sd)	*p-value
R5	17.95±11.89	17.28±10.44	0.683
X5	23.59±14.28	23.32±17.33	0.561
R5-R20	30.09±17.62	34.64±17.31	0.179
AX	30.03±20.83	34.00±19.44	0.686

*t test. M= mean, sd – standard deviation

Table 4 – Mean variation values (%) for parameters observed after inhalation of bronchodilator on initial and final visits.

DISCUSSION

The present study evaluated pulmonary function in preschoolers diagnosed with asthma undergoing regular follow-up and mostly using inhaled corticosteroid for a period of 12 months with IOS. Although no change in pulmonary function was observed in the study period, more than 24% of these children diagnosed with asthma and undergoing regular treatment presented altered pulmonary function for R5 and X5, indicating possible obstruction. These children deserve special attention because they have altered pulmonary function as well as symptoms.

A test was considered positive for abnormality prior to bronchodilator inhalation when

R5 was greater than twice the standard deviation compared to the predicted value for sex, age and height, and when X5 was two times lower[16,17]. In fact, R5 indicates resistance throughout the respiratory tract, including more distal airways[22]. Inflammation of the peripheral airways is an important component of the physiopathology of asthma[22]. It is estimated that the distal airways account for 15% to 24% of total resistance in healthy lungs and that this resistance is heightened in individuals with asthma[23] A comparative study found a significant increase in R5 prior to bronchodilator inhalation in children with uncontrolled asthma compared to those with controlled asthma and healthy individuals[10].

On the other hand, X5is related to the elasticity of the lung and obstruction of peripheral airways results in a loss of elastic recoil, demonstrated by more negative X5, as observed in diseases that reduce lung elasticity (such as fibrosis or hyperinsuflation)[15,24].

Bisgard et al[25], studied children aged 4 to 6 years and found that R5 and X5 showed a heightened response to the metacholine challenge test, suggesting that there is a relation between these two parameters and indicating that X5-confirmed hyperinsufflation increase in proportion to increased R5 resistance.

It is acknowledged that there is a correlation between R5 and X5 with the degree of airway obstruction or restriction, helping the clinic to detect respiratory symptoms. These parameters are thus recommended for clinical detection of respiratory symptoms[13,21]. It would seem, therefore, that the reduction in pulmonary function in preschoolers observed using IOS can be used to identify a subgroup of children with asthma with persistent morbidity, indicating the possible need for more careful follow-up during childhood[26].

The findings of the present study may be attributed to the fact that, in the age group under study, respiratory symptoms may be milder and develop later[27]. The increase in the number of tests showing abnormalities on second visit, as shown by these two parameters, may be associated with the reports of attacks of wheezing during the follow-up period in over 90% of children, and consequent use of a bronchodilator to alleviate symptoms in more than half of them. However, as no instrument, such as GINA[11] or the *Test for Respiratory and Asthma Control in Kids* (TRACK)[28], was included to measure symptoms control it is not possible to make such an inference.

The bronchodilator response was infrequent, considering the new ERS guidelines of a level of reduction in R5, X5 and AX of 40%, 50% and 80% respectively compared to the figures prior to bronchodilator use[18]. The exact cut-off point for bronchodilator response is a matter of some controversy. Some authors suggest a cut-off point of 40% for R5 in children aged between 3 and 6.5 years[14,15]. In preschoolers and school-aged children, it is suggested that a positive response to the bronchodilator has occurred if the reduction is greater than 40%, signifying reversibility in the airways of these children. However, this cut-off point is unable to differentiate between asthmatics and non-asthmatics[24].

Nevertheless, some authors believe that IOS outperforms spirometry in distinguishing preschoolers with asthma from normal cohorts, especially when using the bronchodilator response at R5 or R10 of 20% (20,21). It is possible that, when adopting a higher cut-off point, some children with abnormal pulmonary function may fail to receive adequate follow-up[27]. The diminished pulmonary function in preschoolers observed using IOS may be able to identify a subgroup of children with asthma with persistent morbidity, indicating the need for more careful follow-up during childhood.

Some authors believe the R5-R20 parameter to be associated with greater specificity for the peripheral airways in patients with asthma[24,26]. One study evaluated the inflammatory and obstructive processes of asthma using IOS and confirmed that the peripheral airways (R5-R20) are useful for addressing the issue of asthma in children and may help to confirm the response to treatment[22]. In our study, the response to the bronchodilator was low compared to parameters R5 and X5. However, the lack of information on local patterns of normality prevents firmer conclusions from being drawn for the purpose of comparison[25,29].

The clinical data, along with the use of medication during the study, were not strongly associated with pulmonary function. Clinical indicators based on symptoms may thus lead to false-positive or false-negative diagnoses, and the use of objective methods, such as IOS, to back up diagnosis, should be encouraged in preschoolers with a diagnosis of suspected asthma[30].

The present study included only children diagnosed with asthma. This may more accurately reflect the situation in the real world, where pulmonary function is tested using IOS only in children displaying symptoms. Clinical evaluation was carried out using data on symptoms reported by the child's parent/guardian during follow-up visits and we did not use any other instrument to evaluate the control or not of symptoms[12,29]. This may have led to under- or overestimation of the clinical status at the time of evaluation. Even so, some children were identified as having early onset altered pulmonary function that went unnoticed during spirometry or clinical evaluation and, in this case, all would be treated without the follow-up necessary for children whose symptoms may persist.

The sample size ruled out extensive multifactorial analysis and a longer follow-up period might have provided a more accurate picture of the development of pulmonary function in these children over time. Finally, there are no benchmark values for healthy children for the age group covered by our study (brazilian children) and it was therefore necessary to use data from similar populations.

CONCLUSION

This study showed altered pulmonary function in children aged 3 to 6 years with asthma, who, despite receiving specialized care and treatment, showed no change over a twelve-month period. This shows the need for long-term specialized care, including evaluation of pulmonary function, to follow up the evolution of asthma in these patients.

Our findings suggest that IOS may improve evaluation of asthma and increase the likelihood of early more accurate diagnosis and adequate treatment in preschool children.

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