Journal of Allergy & Therapy
ISSN: 2155-6121

Valadares et al., J Aller Ther 2013, S2
DOI: 10.4172/2155-6121.S2-006

Research Article Open Access

Spirometry with $FEV_{0.75}$ Increases the Sensitivity for the Diagnosis of Obstructive Disorder in Children of Asthmatic Mothers

Marco Antonio Valadares[1]*, Igor Neves Santos[1], Enaldo Vieira Melo[1], Ângela Maria da Silva[1], Priscila Teles Archanjo[1], Emilly Correia Nepomusceno[1], Roseane Lima Porto[1], Ricardo Queiroz Gurgel[1], Lucas Silva Brito[2] and Maria Luiza Doria Almeida[1]

[1]*Departamento de Medicina , Universidade Federal de Sergipe, Brazil*

[2]*União Metropolitana de Educação e Cultura, Brazil*

Abstract

Objective: To evaluate and compare the sensitivity of spirometry in children of asthmatic mothers by the parameters FEV_1 and $FEV_{0.75}$.

Methods: An observational cross-sectional analytical study nested in a cohort of 4,757 pregnant women. Clinical evaluation was performed for the diagnosis of asthma, besides the realization of spirometry in the children of asthmatic mothers, evaluating the following parameters and relationships: FEV_1, FVC, FEV_1/FVC, $FEV_{0.75}$ and $FEV_{0.75}$/FVC.

Results: A total of 86 children of asthmatic mothers were included in the study, with age mean of 79.8 ± 1.1 month old. Regarding the breathing pattern there was a predominance of normality. When using FEV_1, changes were observed in 26 children, representing 30.3% of the sample. Of these, 17 were classified as restrictive and nine as obstructive. Using the $FEV_{0.75}$ instead of the FEV_1 (and its consequent $FEV_{0.75}$/FVC) 29 ventilatory tests found changed, representing 33.7%. Of these, 27 were classified as obstructive and only two were restrictive. Of the 16 children diagnosed with asthma, only five had presented obstructive pattern when FEV_1 customization spirometry was used. In contrast, when we used $FEV_{0.75}$, 12 of these patients were considered obstructive. The sensitivity was higher in the spirometric test that used $FEV_{0.75}$, with even greater negative predictive value. On the other hand the test set for the parameter FEV_1 showed greater specificity and higher positive predictive value.

Conclusions: Spirometry, though with recognized value in the complementary diagnosis of obstructive disturbance, classically presents limitations in the pediatric population, especially in younger children. We observed a significantly higher sensitivity and negative predictive value when we used $FEV_{0.75}$ in substitution to the FEV_1. As a consequence, the parameter $FEV_{0.75}$ is probably more effective for the diagnosis of obstructive disorder in patients with clinical history or family history of asthma.

Keywords: Asthma; Child; Spirometry

Introduction

Asthma is a recognized multifactorial disease, resulting from the interaction between genetics and environment. However, heredity does not follow the classic Mendelian patterns and genetics of this disease is especially complicate because of its polygenic nature. The heritage transmitted by the mother seems to be more significant than the one transmitted by the father [1-3].

Over the past 30 years, the world population has seen a major technological breakthrough, which led to profound changes in the pattern of lifestyle and eating habits. However, parallel to this, an improvement in sanitary conditions and reduction of infectious diseases was noted. Nevertheless, asthma continues to impact on morbimortality in various age groups and all social groups [4,5].

The pulmonary function tests are usually performed with computerized systems that analyze the data and provide immediate results. Spirometry is one of these tests and it is recommended to clarify the diagnosis in patients with chronic cough (>3 weeks). Chronic cough is often an isolated manifestation of asthma. In asthma should be made in the following situations: in patients with wheezing or chest tightness applicant, to confirm the diagnosis, during the initial evaluation and after treatment with stabilization of symptoms and peak expiratory flow (PEF) to document the level of pulmonary function (normal or not), in patients with severe persistent asthma, when changes in maintenance treatment were done and the results achieved [6-8].

In respiratory evaluation of children over six years old as well as in adults, spirometry has an important role because of its simplicity and its low cost, combined with good reproducibility. It also demonstrates the importance when the symptoms are not well characterized by the patients and their respective responsible, which may result in a ranking of asthma and thus inadequate treatment. Then we use spirometry as a resource to establish the most appropriate management of the patient. The spirometry is also used extensively in research, and the most common complementary outcome in studies of respiratory diseases [9,10].

Ideally, the interpretation of spirometry should be compared with reference values. There are dozens of reference equations in use today and many included in pulmonary function equipment. However,

***Corresponding author:** Marco Antonio Valadares, Universidade Federal de Sergipe, Departamento de Medicina, Rua Cláudio Batista, sem número, Bairro, Sanatório, Aracaju, Sergipe 49027000, Brazil, Tel: 55 79 98526203/55 79 3231 0547; E-mail: valadares-oliveira@uol.com.br

Received July 10, 2013; **Accepted** July 29, 2013; **Published** July 31, 2013

Citation: Valadares MA, Santos IN, Melo EV, da Silva ÂM, Archanjo PT, et al. (2013) Spirometry with $FEV_{0.75}$ Increases the Sensitivity for the Diagnosis of Obstructive Disorder in Children of Asthmatic Mothers. J Aller Ther S2: 006. doi:10.4172/2155-6121.S2-006

racial, socioeconomic, gender, equipment and application technique of spirometry affect the accuracy of interpretation, particularly when the results are compared with the predicted values of another ethnic group [9,11].

The "American Thoracic Society" suggests that in every place where tests of pulmonary function are performed their own reference values are produced from a random selection of individuals without lung disease [9,12].

One of the limiting factors that we can notice is the sudden interruption of expiration, which may interfere with the accuracy of spirometry. By submitting this expiratory maneuver usually shorter than that of an adult applying the criteria of acceptability of spirometry in adults is not indicated in children. This characteristic in children stimulated the formation of this study, which aims to compare the use of spirometry with FEV_1 and forced expiratory volume in time 75 hundredths of a second ($FEV_{0.75}$) [13,14] .

Materials and Methods

The method used was an analytical cross-sectional observational study nested in a cohort. In the original cohort (started in 2005) was applied a questionnaire to 4,757 pregnant women, with informed consent. Through this survey we identified 135 who reported physician-diagnosed asthma before pregnancy. Patients included in the study were children above cohort participants whose mothers had asthma since agreed to participate in the study signed by their parent or legal represent, the Term of Free and Informed Consent Form (ICF).

After about six years and eight months of the original work, were located and evaluated 86 children within the group of 135 mothers with a previous diagnosis of asthma. This number conforms to the expected sample size calculation; we estimated at least 82 at *n*. The conditions adopted for this calculation were as follows: frequency obstructive respiratory pattern for the study group equal to 15% (with an interval of 7 23%), the level of significance equal to 0.05, the test power equal to 0.80, the statistical test was used for a binomial proportion, the two-tailed test, and it was considered a waste sampling of 10%. It is a non-random sample, having children was consecutively selected.

There were no losses exclusion criteria. These were previously defined as birth weight <2500 g, gestational age <37 weeks, presence of respiratory distress at birth, abdominal surgery, thoracic or ophthalmic recent airway infections or wheezing in the previous two weeks and underlying diseases that could come interfering in ventilatory function test (heart disease, sickle cell anemia, cystic fibrosis, collagen diseases, neuromuscular diseases).

The age was considered in full months, since all subjects included were born in the range of four months period of initial data collection of the original cohort. For a clinical evaluation, we used the criteria adopted in clinical severity (Global Initiative for Asthma-GINA, 2002), which includes research symptoms and their frequency, and the measurement of peak expiratory flow (PEF). Finally, we conducted the evaluation of lung function by spirometry based on all children participating in the study, the tests being performed by one of the study authors. For this study, we considered the following parameters and relationships: FEV_1, FVC, FEV_1/FVC, $FEV_{0.75}$ and $FEV_{0.75}$/FVC. The results were used as the criteria considered ATS/ERS ("American Thoracic Society" and "European Respiratory Society") and benchmarks modified by Pereira (1992) [7]. The same way, the criteria for the interpretation of values and $FEV_{0.75}$ $FEV_{0.75}$/FVC were those recommended by the same societies and cited by Aurora et al. (2004) and Burity et al. (2011) [12,14].

To start the tests we detected the beginning of the rapid peak flow and retro-extrapolation (VRE) ≤ 80 ml or 12.5% of CVF. Tests were suspended after 5 failures or before if the child shows to be fatigued. All tests were done by the same investigator (Valadares MA) [15].

The spirometer was used MicroloopR and SpidaR software. Five tests were conducted with each child, with the advantage of better results. Not used post-bronchodilator testing not append data to preconceived goals of the research, as well as after bronchial provocation test, for similar reasons, and because it was done at home. During the tests the children were helped to conduct the test in the most appropriate (standing and nose occluded). In addition, all children received a explanation of how to position the nozzle mouth and how to perform a forced expiration.

The results were tabulated in a spreadsheet program SPSSR version 17.0. It included means and standard deviations to describe quantitative variables, while simple frequencies and percentages were used for categorical variables. For calculation of sensitivity and specificity, as well as the positive and negative predictive values (and their respective confidence intervals for 95%) was applied EPIDATR (Program for Epidemiological Analysis of Tabulated Data) version 3.1 (January 2006). For the confidence interval (CI) calculation we used bootstrap technic, where estimation is done after "n" aleatory resampling. Receiver Operating Characteristic (ROC) curve was constructed to evaluate the relation of FEV_1/FVC e $FEV_{0.75}$/FVC variables with clinical diagnosis of asthma.

The study was approved by the Ethics Committee for Human Research of the Federal University of Sergipe (UFS-CEP), with approval number CAAE (Certificate of Appreciation Presentation for Ethics) 0104.0.107.000-11. Parents of all children included in the study signed consent form authorizing their participation in the research.

Results

The gender distribution showed 55.8% of boys and 44.2% girls, constituting the sample of 86 children with a mean age of 79.8 ± 1.1 months.

Being questioned about the presence of physician-diagnosed asthma for the child's study, 9.3% of mothers said yes (which represents eight patients). On the other hand, when responding to the minor symptoms, there was a percentage of 18.6% of asthma (16 patients). As intermittent asthma were classified eight patients. Of the other eight, six met criteria for persistent mild to moderate and two. No case of severe persistent found.

Spirometric parameters, described in their respective means and standard deviations, are shown in (Table 1).

Regarding the breathing pattern we obtained a distribution with a

Variable	Mean	Std deviation
FEV_1 (absolute)	1.18	0.24
FEV_1 (relative)	90.3	17.83
$FEV_{0.75}$ (absolute)	1.06	0.25
FVC (absolute)	1.28	0.25
FVC (relative)	92.44	17.86
PEF	2.16	0.73
FEV_1/FVC (absolute)	92.18	9.38
$FEV_{0.75}$/FVC (absolute)	83.43	12.6

FEV_1 (absolute) and FVC (absolute): expressed in liters; relative values described in percentages PEF expressed in liters/second

Table 1: Values obtained in spirometry base.

	N	%	95% CI
Normal	60	69.7	59.3–79.1
Restrictive	17	19.8	11.6–29.1
Obstructive	9	10.5	4.7–17.4

n: frequency
95% CI: confidence interval of 95% (bootstrap; based on 1000 bootstrap samples)
Classification according to reference standards of Polgar and Promadhat modified by Pereira, 1992
Confidence interval obtained through simulation with a thousand samples

Table 2: Frequency children's according to the ventilatory pattern observed spirometry base using FEV_1.

	n	%	95% CI
Normal	57	66.3	57-76.7
Restrictive	2	2.3	0-5.8
Obstructive	27	31.4	22.1-40.7

n: frequency
95% CI: confidence interval of 95% (bootstrap; based on 1000 bootstrap samples)
Classification according to reference standards of Polgar and Promadhat modified by Pereira, 1992 Confidence interval obtained through simulation with a thousand samples

Table 3: Children's frequency according to the ventilatory pattern observed spirometry base using $FEV_{0.75}$.

Variable	T1	T2
Sensitivity	31.25 (5.41-57.09)	75 (50.66-99.34)
Specificity	94.29 (88.13-100)	78.57 (68.24-88.9)
Positive predictive value	55.56 (17.54-93.57)	44.44 (23.85-65.04)
Negative predictive value	85.71 (77.25-94.18)	93.22 (85.96-100)

T1: spirometry with FEV_1
T2: spirometry with $FEV_{0.75}$
Values expressed in % (95% CI)
Prevalence of asthma in the sample: 18.6%

Table 4: Comparison of spirometric tests using FEV_1 and $FEV_{0.75}$.

predominance of normality. When using FEV_1 changes were observed at a frequency of 26, representing 30.3% of the sample. Of these, 17 were classified as restrictive as obstructive while nine (Table 2).

TEF median was 1.4seg, with 25 and 75 percentiles of 0.9 and 2.6 seg. A total of 29 patients (33.7%) had TEF below 1 second. Of these, 23 (26.7%) presented this time superior to 0.75 seconds.

Using the $FEV_{0.75}$ in the place of the FEV_1 (and its consequent relative to the FVC) 29 ventilatory tests found changed, representing 33.7%. Of these, 27 were classified as obstructive and restrictive as only two (Table 3).

Of the 27 patients who demonstrated obstructive lung disease using the $FEV_{0.75}$ as observed spirometric parameter 23 as mild, two as moderate and two as severe. When using FEV_1, the nine appointed as having obstructive, seven were characterized as mild and two moderate, none severe was found.

Of the 16 children diagnosed with asthma, only five had presented obstructive pattern when used in FEV_1 customization spirometry. In contrast, when used $FEV_{0.75}$, 12 of these patients proved to have obstructive. This difference in sensitivity can be seen in the results shown in Table 4.

By analyzing the sensitivity and specificity of spirometric tests using either forced expiratory volume (FEV_1 and $FEV_{0.75}$) met the above in Table 4. The sensitivity was higher in the spirometric test that used $FEV_{0.75}$, with even greater negative predictive value. On the other hand the test set for the parameter FEV_1 showed greater specificity and higher positive predictive value.

When we associated clinical diagnose of asthma to the FEV_1/FVC relation using ROC curve we found 0.632 ± 0.087 (95% CI: 0.461-0.804; p=0.10) under the curve (Figure 1). Inversely when clinical diagnosis of asthmas was associated to $FEV_{0.75}$/FVC relation, the area under the curve was 0.860 ± 0.440 (CI 95%: 0.775-0.948; p<0.0001) (Figure 2).

Discussion

The studied population had a previous diagnosis of asthma in the frequency of 9.3%. When subjected to critical evaluation, there was an increase that rate to 18.6%, which clearly indicates a possible under diagnosis of this disease in our country. Asthma is recognized as the most common chronic illness in children, affecting about 15% of the

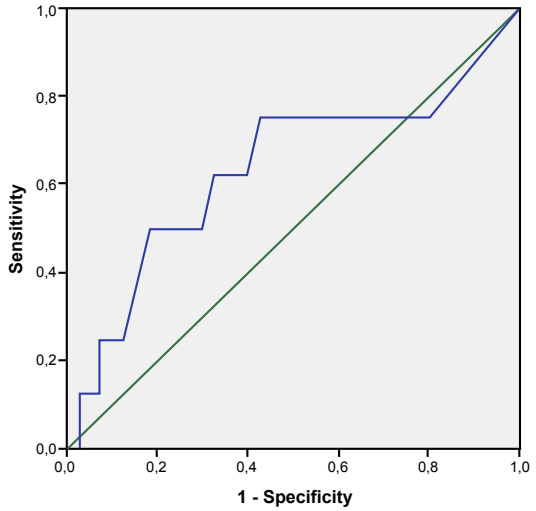

Figure 1: ROC Curve FEV_1/FVC.
Area under the curve: 0.632 ± 0.087 (95% CI: 0.461-0.804).

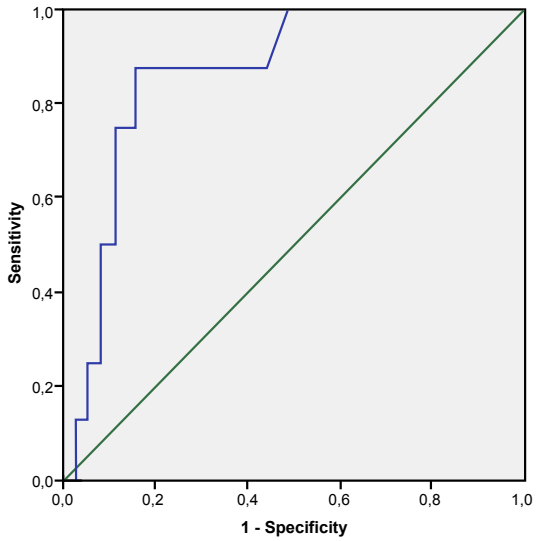

Figure 2: ROC Curve $FEV_{0.75}$/FVC.
Area under the curve: 0.860 ± 0.440 (95% CI: 0.775-0.948).

pediatric population. However, it is estimated that the prevalence of symptoms associated with asthma is higher than 20% [13].

Spirometry, though with recognized value in the diagnosis of obstructive supplement, classically presents limitations in the pediatric population, especially in younger children. The obstructive pattern expected to be observed in a population with a clinical diagnosis of asthma may sometimes not be evidenced by the technical implementation of spirometry, which requires patient cooperation. The expiratory time limited, characterizing the so-called "short breath" is the largest of these limitations. This limitation was describe in the research of Veras and Pinto [16].

In the present study, we used the traditional FEV_1 and its correspondent relationship with FVC, met only nine children with obstructive pattern. That number rose to 27 when used $FEV_{0.75}$ and their corresponding relationships. In 2007, as the studies of Piccioni et al., involving children younger than 6 years old proposed equations with parameter in 0.75 s FEV ($FEV_{0.75}$), this is perhaps the most appropriate parameter for this age group. This follows from the fact that children have smaller airways proportionally greater than their lung volumes, which enables them to perform forced expiration in less than 1 second, as cited Stanojevic et al. (2009) [15,17].

In our sample 33.7% of the patients could not execute TEF superior or equal to 1 second. This justifies the high inadequacy level when using VEF1. Restrictive disturbs moderate to severe full CVF can be expired within the first second and VEF1=CVF (relation VEF1/CVF%=100%). This can explain the high number of restrictive disturbs found when VEF1 and its relation to CVF was used. Although several VEF1 may be obtained, its value for young children is questioned, because of the airway size is bigger than pulmonary volume and this volume is expulsed faster, showing VEF1/CVF relation >90%, which may underestimate obstructive pulmonary pathology [14].

By using FEV_1, struck by the large number of tests that accused restrictive disorder (27 in total) that number dropped to just two when used $FEV_{0.75}$, which leads invariably to think that many of those with restrictive pattern initially were by the technical limitation (short breath).

A limitation of this study is the absence of repeating the test after bronchodilator, which may explain the lower specificity of the test when using $FEV_{0.75}$ and its corresponding lower positive predictive value. Other limitation is that, with the general agreement that asthma obstruction is a reversible condition, we can expect several patients with normal spirometric results in some moments. Consequently a single evaluation may underestimate diagnosis accuracy.

An important correspondence indicated by this study was the high sensitivity of the test using the $FEV_{0.75}$ to diagnose obstructive pattern within the group of patients with asthma. Associated with this, we must reveal a high negative predictive value for this reference because of the reduced forced expiratory volume. Spirometry, though with recognized value in the diagnosis of obstructive supplement, classically presents limitations in the pediatric population, especially in younger children. We observed a significantly higher sensitivity and negative predictive value when we used $FEV_{0.75}$ in substitution to the FEV_1. As a consequence, the parameter $FEV_{0.75}$ is probably more effective for the diagnosis of obstructive disorder in patients with clinical history or family history of asthma.

References

1. von Mutius E, Nicolai T (1996) Familial aggregation of asthma in a South Bavarian population. Am J Respir Crit Care Med 153: 1266-1272.
2. Warner JA, Jones CA, Jones AC, Warner JO (2000) Prenatal origins of allergic disease. J Allergy Clin Immunol 105: S493-S498.
3. Vidal PC, Jones MH (2010) Spirometry reference values for Brazilian children Paper presented at the V Mostra de Pesquisa da Pós-Graduação.
4. Fontes MJ, Affonso AG, Calazans GM, de Andrade CR, Lasmar LM, et al. (2011) Impact of an asthma management program on hospitalizations and emergency department visits. J Pediatr (Rio J) 87: 412-418.
5. Bierbaum S, Heinzmann A (2007) The genetics of bronchial asthma in children. Respir Med 101: 1369-1375.
6. Pereira (2001) Pulmonary function tests: Guidelines Project. Brazilian Society of Pneumology and Tisiology: 1-12.
7. Pereira CAC (2002) Spirometry. J pneumology 28: 1-82.
8. Monteiro CA, Conde WL (2000) [Secular trends in malnutrition and obesity among children in the city of São Paulo, Brazil (1974-1996)]. Rev Saude Publica 34: 52-61.
9. Malucelli M, Rosário NA, Riedi C, Kovalhuk L, Barros JA (2007) Accuracy of pulmonary function test in pediatric and adolescent asthma classification. Rev Bras alerg imunopatol 30: 27-31.
10. Subbarao P, Lebecque P, Corey M, Coates AL (2004) Comparison of spirometric reference values. Pediatr Pulmonol 37: 515-522.
11. Ladosky W, Andrade RT, Loureiro NG, Gandar JM, Botelho MM (2001) Comparing reference spirometric values obtained from Knudson and Pereira equations–Adults. J Pneumol 27: 315-320.
12. Burity EF, Pereira CA, Rizzo JÂ, Sarinho ES, Jones MH (2011) Early termination of exhalation: effect on spirometric parameters in healthy preschool children. J Bras Pneumol 37: 464-470.
13. Mallol J, Solé D, Asher I, Clayton T, Stein R, et al. (2000) Prevalence of asthma symptoms in Latin America: the International Study of Asthma and Allergies in Childhood (ISAAC). Pediatr Pulmonol 30: 439-444.
14. Aurora P, Stocks J, Oliver C, Saunders C, Castle R, et al. (2004) Quality control for spirometry in preschool children with and without lung disease. Am J Respir Crit Care Med 169: 1152-1159.
15. Piccioni P, Borraccino A, Forneris MP, Migliore E, Carena C, et al. (2007) Reference values of forced expiratory volumes and pulmonary flows in 3-6 year children: a cross-sectional study. Respir Res 8: 14.
16. Veras TN, Pinto LA (2011) Feasibility of spirometry in preschool children. J Bras Pneumol 37: 69-74.
17. Stanojevic S, Wade A, Cole TJ, Lum S, Custovic A, et al. (2009) Spirometry centile charts for young Caucasian children: the Asthma UK Collaborative Initiative. Am J Respir Crit Care Med 180: 547-552.

This article was originally published in a special issue, **COPD: Epidemiology and New Therapeutics** handled by Editor(s). Dr. A.B.Raja Chatterjee, Wake Forest University, USA