Residência RP Pediátrica
Publicação Oficial da Sociedade Brasileira de Pediatria
ISSN-Online: 2236-6814

Submitted on: 11/09/2019
Approved on: 12/30/2019

ORIGINAL ARTICLE

Association between clinical and functional evaluation of children and teenagers

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Keywords:
Asthma,
Spirometry,
Pediatrics.

Abstract

Objectives: To describe the results of spirometry in children and adolescents with asthma, comparing these findings with the clinical classification. **Methods**: Retrospective, observational and descriptive study with asthma patients classified through the treatment STEPS suggested by the international guideline *Global Initiative for Asthma* (GINA) submitted to spirometry, followed by the Pediatric Pneumology Service in a quaternary hospital in a single health system network. **Results:** In 310 exams evaluated, the average age was 10 years old; 205/310 (66.1%) were male patients; 178/310 (57.4%) with mild obstructive ventilatory disorder, 10/310 (3.2%) with moderate obstructive ventilatory disorder ; 9/310 (2.9%) with severe obstructive ventilatory disorder and 113/310 (36.5%) exams were within the parameters of normality. The bronchodilator response was evaluated in 284/310 (91,6%) exams, obtaining a positive result in 32.7% (93/284). When analyzing the treatment STEP, 30.3% (94/310) of the patients were in STEP 1; 27.7% (86/310) in STEP 2; 32.6% (101/310) in STEP 3; 9.4% (29/310) in STEP 4. After analysis of the clinical-functional dates, the chi-square test showed a significant association between the following results: normal and mild obstructive ventilatory disorder spirometry and with patients in STEPS 1 and 2 ($p < 0.05$) and spirometry with moderate and severe with patients in STEP 3 and 4 ($p < 0.05$). **Conclusion:** The clinical classification of asthma through the treatment STEPS suggested by GINA was directly associated with the results obtained by spirometry in asthmatic children.

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DOI: 10.25060/residpediatr-2021.v11n3-225

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INTRODUCTION

Asthma is a chronic inflammatory disease of the airways, associated with hyperresponsiveness, recurrent episodes of cough, dyspnea, wheezing and chest tightness, in different degrees of intensity. These symptoms occur due to variable airflow obstruction, which may be spontaneously reversible. or with treatment[1]. In Brazil, a descriptive study of data extracted from a government database between 2008 and 2013 showed that the absolute numbers of deaths and hospitalizations due to asthma are still high, with high direct and indirect costs for society[2]. The clinical diagnosis of asthma is suggested by the presence of one or more of these respiratory symptoms, but should be complemented by objective methods, such as lung function assessment. Spirometry is one of the most used tests for this assessment[1,3,4]. Pulmonary function tests aim to identify and quantify the ventilatory disorder, estimate the severity of airway obstruction and allow the monitoring of clinical evolution and therapeutic response[5,6].

Spirometry is the most recommended method for the assessment of bronchial obstruction and reversibility (partial or complete) to the bronchodilator[7,8]. By means of standardized maneuvers, volumes and airflows are measured, obtaining the flow-volume and volume-time curves. The values found are compared to predicted values for gender and age. The bronchodilator test (PBD) corresponds to the use of a bronchodilator and subsequent spirometry to assess possible variation in ventilatory parameters[9].

The level of asthma control refers to the presence or absence of respiratory manifestations in response to the proposed treatment. The clinical steps recommended by the international guideline of the *Global Initiative for Asthma* (GINA) involve five categories that aim to establish the necessary treatment for the patient to obtain control of the disease[1].

Clinical reassessment of the patient to change the treatment stage, depending on asthma control, should preferably be performed every three months. However, before any change, good adherence to treatment, proper use of medication (including inhalation technique) and the presence of risk factors for exacerbations should be verified. Regular clinical evaluation and identification of patients predisposed to exacerbations are essential[1,3,10-13].

In children and adolescents, the assessment of clinical manifestations in asthma can be hampered by the difficulty in quantifying symptoms in this age group[14]. There are still doubts about the association between the data found by the clinical assessment of asthmatic children and adolescents through the GINA stages and spirometry[15]. The present study analyzed the association between these two forms of assessment.

METHODS

Retrospective, observational and descriptive study, carried out at the pediatric pulmonology outpatient clinic of a tertiary hospital in the public health system network. The study analyzed patients followed with asthma, aged 5 to 18 years, submitted to spirometry between January 2005 and December 2015, using a convenience sample. Spirometry was performed and reported by a pediatric pulmonologist. Spirometry and clinical data were analyzed from the spirometer database and the hospital's medical records. Patients with asthma associated with other pulmonary pathologies were excluded.

For clinical evaluation of asthma severity, the GINA classification by treatment steps from 1 to 5[1] was used. As for the functional assessment, the tests were performed according to national and international guidelines[5,7]. Forced vital capacity (FVC), forced expiratory volume in one second (FEV_1) and FEV_1/FVC ratio were analyzed. The theoretical references used were those of Mallozi[16], adopting the reduction of the FEV_1/FVC ratio below the lower limit of normality (LIN) as the cut-off point for defining obstruction[9]. The classification of severity followed the guidelines outlined by Pereira *et al*[5]. The disturbance was considered mild when the LIN values were up to 60% of the predicted value, moderate from 41-59% and severe ≤ 40%, in relation to FEV_1/FVC and FEV_1. When there was disagreement between the degrees, the disorder was classified by the most severe degree[6]. The spirometries analyzed were performed with a computerized spirometer Koko USB *Spirometer®*, model 2004k3231, in a closed circuit, with manual calibration always performed before the beginning of the exams and graphic recording of the volume-time curves and flow-volume. The recommendations of the 2005 international consensus were followed[7]. Baseline maneuvers were performed with the suspension of bronchodilator medications and repeated after 20 minutes of 400 micrograms of inhaled albuterol. PBD was considered positive when there was an increase in FEV1 of 12% and 200 ml in relation to the value of the initial test[9].

A descriptive analysis of the data obtained was performed, with measures of frequency and percentages of categorical variables. The association between the clinical stages by GINA and the spirometric patterns obtained was evaluated, using the chi - square test, with a significance level of p-value <0.05. The intensity of the association was assessed using the *odds ratio* (OR), with 95% confidence interval calculation (CI = 95%).

The project was approved by the Clinical Research Ethics Committee (CEP) of the hospital where the study was carried out, according to resolution 466/12 (CNS), under number 62339516.1.0000.5264, on 01/12/2017.

RESULTS

A total of 310 exams were studied, with acceptable and reproducible curves according to the criteria of the *American Thoracic Society / European Respiratory Society* (ATS/ERS)[7], making it possible to recover data on the regular treatment used. As requested, the patients were not on bronchodilators on the day of the exam. The population studied had a mean

age of 10 years (standard deviation = 2.96). More than half of the exams involved male children (66.1%; 205/310). There were 113/310 (36.5%) spirometric results within the normal range, 178/310 (57.4%) with mild obstructive respiratory disorder (OVD), 10/310 (3.2%) with moderate OVD and 9 /310 (2.9%) with severe OVD.

In 284/310 exams (91.6%) the bronchodilator response to albuterol was also evaluated , with positive results in 32.7% (93/284) of the exams and negative in 67.3% (191/284). After evaluating the stages of the GINA, it was found that 30.3% (94/310) of the patients received treatments from stage 1; 27.7% (86/310) from step 2; 32.6% (101/310) from step 3; 9.4% (29/310) from stage 4 and no patient received treatment from stage 5. The clinical and functional characteristics of the 310 patients are shown in Table 1.

Table 1. Clinical and functional characteristics of children and adolescents with asthma

Age group	N (310)	%
5-6 years	39	12,60%
7-9 years	105	33,90%
> 10 years	166	53,50%
Gender		
Female	105	33,90%
Male	205	66,10%
Spirometry results		
Normal	113	36,50%
Mild OVD	178	57,40%
Moderate or severe OVD	19	6,10%
Bronchodilator test (n=284)		
Positive	93	32,70%
Negative	191	67,30%
Treatment Steps		
Step 1 ou 2	180	58,10%
Step 3	101	32,60%
Step 4	29	9,30%
Step 5	0	0%

n= number; () = total number. % =percentage

Despite the prevalence of less severe patients (stages 1 and 2), corresponding to 58.1% (180/310) of the total, it was observed that 41.9% (130/310) received treatment corresponding to clinical situations of asthma of greater severity (steps 3 and 4). Of the 113 patients with a NORMAL spirometry result, 52 (46%) did not receive prophylactic treatment, only medication for crisis (step 1), 32 (28.3%) received low dose inhaled corticosteroids (IC) between crises (step 2), 22 (19.5%) received moderate-dose or low-dose IC associated with a long-acting bronchodilator (LABA) (stage 3) and 7 (6.2%) received high-dose or moderate-dose IC associated with LABA (stage 4). No patient with normal spirometry received GINA step 5 treatment. Of the 178 patients with mild OVD, 42 (23.6%) were in stage 1 of treatment, 50 (28.1%) in stage 2, 66 (37.1%) in stage 3 and 20 (11.2%) in step 4.-Of the 10 patients with moderate OVD, 4 (40%) were in stage 2, 4 (40%) in stage 3 and 2 (20%) in stage 4. No patient with moderate OVD received treatment from stage 1 of the GINA. Of the 9 patients with severe OVD, all (100%) received moderate or low dose IC associated with LABA in stage 3 (Figure 1). Comparing the tests with normal spirometric results and those with mild OVD, we found that 60.5% (176/291) of them received treatment from stages 1 and 2 of the GINA, while in those with moderate or severe OVD, 78.9% (15 /19) received GINA step 3 and 4 treatment. There was an association between normal spirometry and mild OVD and stages 1 and 2 and between moderate-severe OVD and stages 3 and 4 (OR = 5.74; 95% CI = 1.858-17.72; *p* -value = 0.0008606) (Table 2).

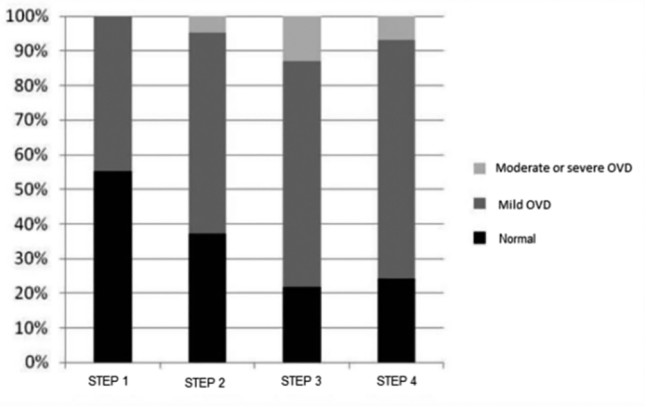

Figure 1. Percentage of patients in the GINA treatment stages in relation to spirometry OVD = obstructive ventilatory disorder. Mod = moderate.

DISCUSSION

The present study carried out in a pediatric referral center showed a positive association between the GINA classification of asthma in treatment stages and spirometry. The severity of asthma can be evidenced in the spirometry result.

Given the high prevalence of pediatric asthma, it has been the subject of numerous studies. Deschildre *et al*[17] , studied 525 children with asthma, followed up in four tertiary-level pediatric pulmonology centers in France, with the objective of describing the control of asthma through different methods. They concluded that, although the clinical assessment of *Asthma Clinical Control* (ACT) proves to be a useful complementary method, it does not include functional assessment, which is regularly recommended by several guidelines. Our study included 310 exams, with a mean age of 10 years of analyzed patients, which contributed to the large number of adequate exams, since younger children perform acceptable and reproducible exams with more difficulty. Comparing preschoolers with older children, the studies concluded

Table 2. Association between GINA treatment steps and spirometry results.

	STEP 1-2		STEP 3-4		Total				
	n	%	n	%	n	%	OR	IC 95%	p
Normal - Mild OVD	176	60,5	115	39,5	291	93,9			
							5,74	1,858-17,72	0,000086
Moderate or severe OVD	4	21,1	15	78,9	19	6,1			
Total	180	58,1	130	41,9	310	100			

OD = obstructive ventilation disorder; mod = moderate; n = number of exams; % = percentage; OR = odds ratio; CI = confidence interval; p = chi-square test; P value considered significant below 0.05.

that, although they are feasible in daily clinical practice, there is an increase in the success rate in older children[18-19].

For a better clinical-functional assessment, we chose to follow the GINA guidelines, which, since 2006, have simplified the way of evaluating the initial treatment and in subsequent consultations. Instead of using tables to classify severity, simplified assessment of asthma control is recommended and treatment can be changed according to the control state[20]. Our sample showed a distribution of patients in the different treatment steps of 58.1% (180/310) of cases in steps 1 and 2 and 41.9% (130/310) in steps 3 and 4. No patient was classified in step 5. In our outpatient clinic, we complemented the initial spirometry with the PBD in order to identify whether there is a variation in FEV 1 of 12% and 200ml in relation to the initial value. The literature suggests applying it systematically[6]. Thus, in 91.6% (284/310) of the tests performed, the PBD was performed, only 32.7% (93/284) responded to the test. We can infer that this is due to the fact that we are a tertiary service, receiving patients who have already started prophylactic medication and are in full or partial control of the disease [21]. In addition, we must remember that spirometry also has limitations, indirectly assessing larger airways, and that small airway involvement is also an important component, especially in patients with longer disease duration[22-23]. Cordina *et al*[24] studying adults *asthmatics* in Malta, analyzed the influence of anxiety in the treatment of asthma and found that, despite the fact that most patients (58%) had spirometric indices considered normal (with FEV_1 greater than 80% of the predicted), 58.7% received treatment for asthma. more advanced steps of GINA (steps 4 and 5). In our study, 93.9% of the exams showed either normal spirometry or mild OVD (291/310), and 60.5% (176/291) of this group received drugs from stages 1 and 2, reflecting a sample of patients already undergoing treatment, with their disease controlled or partially controlled. On the other hand, similarly to the study by Cordina *et al* [24], a significant portion of our patients (41.9%;130/310) in the current study received treatment at stages 3 or 4, with only 11.5% (15/130) of these had moderate or severe OVD. This apparent clinical-functional disagreement, found both in the literature and in the present study, may be due to the exacerbated perception of symptoms by patients or their caregivers, leading to the prescription of high doses of corticosteroids and/or association with LABA, often not necessary for the control of the patient in question[25]. On the other hand, we have to be careful because spirometry is not the only pulmonary function test, and in these patients with apparent disagreement, other methods should be performed to identify and quantify small airway disease. A recent study, using plethysmography and the forced oscillation technique and other methods, in 100 children, demonstrated small airway disease, even in patients with moderate to severe asthma, with normal FEV1 spirometry[26]. In addition to forced oscillometry, the nitrogen wash test has been shown to be promising in the evaluation of smaller-caliber portions[27]. According to other authors, we can infer a probable portion of the underestimation of the severity of the disease in the present study, since nine patients classified as severe OVD by spirometry received treatment in stage 3, which, according to the GINA, would be consistent with moderate OVD. Silva and Barros [25] in two pediatric allergology services in Portugal also found this disagreement. They showed the tendency of parents to underestimate the severity of the disease and underreport asthma symptoms, especially in patients who had already received this diagnosis a long time ago. By underestimating the patient's symptoms, there is an imminent risk of increased asthma morbidity, in addition to hindering adequate therapy to achieve better control of the disease[24-25]. Some studies report the influence of spirometry on patient management. Nair *et* al[22], in primary treatment centers in Pennsylvania, reported that health professionals tended to underestimate the degree of airway obstruction in asthmatic children and often changed treatment based on spirometric results, despite the initial clinical assessment. In the absence of spirometry, physicians tended to overestimate asthma control by prescribing less than necessary therapy.

One of the limitations of our study was that it was not possible to assess whether the spirometry results interfered with the patient's sequential treatment or whether, even in the face of a test with out-of-expected results, the physician maintained the therapy, taking into account, mainly, the the patient's clinical picture. The use of a convenience sample, since not all medical records could be retrieved, also limits the generalizability of the results. Another limitation was that we were unable to use imaging methods or other more complex functional tests in patients with disagreement between clinical assessment and spirometry. Thus, our study corroborates others who state that no single assessment measure can cover

all aspects of asthma. Its remarkable variability in severity between individuals and in the same patient over time, as well as the change in the presentation of the disease under the administration of drugs, forces the use of different forms of evaluation of control and severity of the disease, based on symptoms, treatment levels and in various pulmonary function tests[14,23].

FINANCING

The study received no funding.

INTEREST CONFLICTS

The authors declare no conflicts of interest.

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