J Bras Pneumol. 2020;46(3):e20190102
http://dx.doi.org/10.36416/1806-3756/e20190102

ORIGINAL ARTICLE

Assessment of asthma control among different measures and evaluation of functional exercise capacity in children and adolescents with asthma

Natasha Yumi Matsunaga[1,2], Caio de Oliveira[2], Livea Gianfrancesco[1,2], Marina Simões Oliveira[1,2], Maria Cristina Ribeiro dos Santos Simões[2], André Moreno Morcillo[3], José Dirceu Ribeiro[2,3], Maria Angela Gonçalves de Oliveira Ribeiro[2,3], Adyléia Aparecida Dalbo Contrera Toro[2,3]

1. Programa de Pós-Graduação em Saúde da Criança e do Adolescente, Universidade Estadual de Campinas, Campinas (SP) Brasil.
2. Laboratório de Fisiologia Pulmonar, Universidade Estadual de Campinas, Campinas (SP) Brasil.
3. Departamento de Pediatria, Faculdade de Ciências Médicas, Universidade Estadual de Campinas, Campinas (SP) Brasil.

Submitted: 10 April 2019.
Accepted: 13 June 2019.

Study carried out in the Ambulatório de Pediatria, Setor de Pneumologia Pediátrica Hospital das Clinicas, Faculdade de Ciências Médicas, Universidade Estadual de Campinas e no Laboratório de Fisiologia Pulmonar, Centro de Investigação em Pediatria, Faculdade de Ciências Médicas, Universidade Estadual de Campinas, Campinas (SP) Brasil.

ABSTRACT

Objective: To assess the agreement among asthma control measures and functional exercise capacity in children and adolescents with uncontrolled and controlled asthma. **Methods:** Children and adolescents with asthma from 7-17 years old were selected, and they were attended in the "Pediatric Pulmonology Outpatient Clinic of State University of Campinas", in Brazil. All patients had asthma control level assessed by Global Initiative for Asthma questionnaire (GINAq), Asthma Control Test (ACT), spirometry and six-minute-walk-test (6MWT). Patients were classified as uncontrolled or controlled asthma in each test and agreement among measures was assessed by kappa statistics. The ROC curve was calculated for the 6MWT. The spirometric index obtained from spirometry was composed by FEV1, FEV1/FVC and FEF25-75%. Spirometry and 6MWT results were compared between uncontrolled and controlled asthma group by GINAq. **Results:** Of the 138 subjects included, 78 (56.5%) were male with median age of 11 (7-17) years old. GINAq detected 68.8% of patients with uncontrolled asthma. Moderate agreement ($p < 0.001$; $k = 0.56$) and high specificity (100%) was observed between GINAq and ACT. In 6MWT, the cut-off point of 82.03% of predicted distance was able to distinguish patients with controlled and uncontrolled asthma. Spirometric index presented 73.4% of sensitivity according to GINAq. The results for 6MWT in patients with uncontrolled asthma were the worst of all. **Conclusion:** This study highlights the importance of assessing more than one measure to differentiate asthma control level. GINAq identified more patients with uncontrolled asthma and presented moderate agreement with ACT. Spirometric index was associated with uncontrolled asthma according to GINAq. 6MWT was a suitable measure to distinguish patients with controlled and uncontrolled asthma.

Keywords: Asthma; Asthma control; Spirometry; Walk test; Children.

INTRODUCTION

Asthma control is defined by the extent to which the manifestations of asthma are reduced, decreased or removed with treatment.[1] It is determined by association among individual genetic factors, phenotypic expression, appropriate treatment, adherence, inhaler technique, response to therapy, environment control, trigger exposure, psychosocial and socioeconomic factors.[1-3]

The assessment of asthma control is important to guide the treatment, to provide information about the disease progression and its underestimation, seeing that it is a risk for increasing morbidity and mortality of asthmatic patients.[1,4,5] Asthma control level can be assessed by history of symptoms control by including the analysis of future risks of adverse outcome, physical examination and Pulmonary Function Tests (PFT) (spirometry measures).[1,5]

Studies have assessed asthma control according to the conventional clinical assessment by pediatrician, standardized questionnaires, lung function and inflammatory markers to establish the most appropriate measure for asthma evaluation, but there is a disagreement between these results.[5-8] Moreover, there is a lack of studies

Correspondence to:
Adyléia Aparecida Dalbo Contrera Toro. Faculdade de Ciências Médicas, Universidade Estadual de Campinas, Rua Tessália Vieira de Camargo, 126, Cidade Universitária Zeferino Vaz, CEP 13083-887, Campinas, SP, Brasil.
Tel.: 55 19 3521-8983/55 19 3521-8958. E-mail: dalbotoro@terra.com.br
Financial support: Process nº 2016/22102-8, Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP).

which assessed asthma control using cardiorespiratory tests, such as six-minute walk test (6MWT) in pediatric age groups, and that evaluated differences in 6MWT between asthma control groups.

The objective of this study was to assess the agreement among asthma control measures, as GINAq, ACT, spirometry and 6MWT. Furthermore, it was also important to compare pulmonary lung function and functional exercise capacity between controlled and uncontrolled patients, classified by GINAq.

METHODS

Participants and study protocol

This was a prospective, observational, cross-sectional and analytical clinical study performed at the "Pulmonary Physiology Laboratory of the Pediatric Research Center" of the State University of Campinas – *Universidade Estadual de Campinas* (Unicamp).

Children and adolescents diagnosed with asthma from 7-17 years old were selected, and they were attended in the "Pediatric Pulmonology Outpatient Clinic" of Unicamp, in Brazil. The excluding criteria were: patients who presented cardiac comorbidities; other respiratory diseases; cognitive or motor limitations that could compromise their performance in any of the tests; who had exacerbated asthma on the day of test or those who could not perform all tests in the same day.

This study was approved by the "Research Ethics Committee" of the "Unicamp School of Medical Sciences" (Ruling no.438.481/2013). Parents or legal guardians of all children and adolescents signed a written informed consent (IC) document.

Measures of asthma control

In this study, asthma control was assessed through Global Initiative for Asthma questionnaire (GINAq), Asthma Control Test (ACT), spirometry and six-minute-walk-test (6MWT).

Step 1: GINAq is made by internationally renowned specialists to assess asthma control based on history of symptom control.[1] In this questionnaire, asthmatics must answer four questions about the past four weeks: a) presence of daytime asthma symptom more than twice a week; b) presence of any night waking due to asthma; c) needed to use relief medication for asthma symptoms more than twice a week; d) presence of any activity limitation due to asthma.[1] In this study, patients were classified as controlled asthma if they answered "no" to all questions and uncontrolled asthma when they answered "yes" to at least one question.[9]

Step 2: ACT consists in five questions regarding to daytime and nocturnal symptoms, presence of activity limitation, needed to use relief medication and self-evaluation of asthma control in the last four weeks.[10,11] The final score ranges from 5 to 25 points. Patients with 20 points or more were classified as controlled asthma and scores up to 19 points were considered uncontrolled asthma.[10]

Step 3: Spirometry was performed with spirometer CPFS/D model (Medical Graphics Corporation, St. Paul, MN, USA) according to the recommendations of European Respiratory Society (ERS) and American Thoracic Society (ATS).[11] Parameters were expressed as a percentage of predicted value reference and were evaluated before and after using four jets of 100 mcg each of salbutamol.[12]

For spirometry, patients were considered as controlled asthma if they presented: a) Tiffeneau index (FEV1/FVC) > 0.8 in adolescents with 12 years old or more and > 0.9 in children with 7-11 years old; b) forced expiratory volume in the first second (FEV1) pre-bronchodilator ≥ 80% of predicted; c) an increase on FEV1 post-bronchodilator < 12% and 200 mL from baseline in adolescents with 12 years old or more and < 12% in children with 7-11 years old; d) forced expiratory flow between 25% and 75% of Forced Vital Capacity (FEF 25-75%) pre-bronchodilator > 70% of predicted; e) an increase on FEF 25-75% post-bronchodilator < 30%;[1,13,14] f) normal spirometric index, which is developed from parameters of FEV1, FEV1/FVC and FEF25-75% regarding interpretation according to previously mentioned criteria. In spirometric index, the patient was classified as uncontrolled asthma if he/she had one altered parameter in spirometry.

If the patient does not fulfill any of the parameters from "a" to "f", he or she was classified as uncontrolled asthma. The classification in controlled and uncontrolled asthma was made in each parameter of spirometry. Spirometric parameters were also compared between groups of uncontrolled and controlled asthma classified by GINAq.

Six-Minute-Walk-Test (6MWT)

The 6MWT is a submaximal test, performed according recommendations of the American Thoracic Society (ATS).[15] The patient was asked to walk as far as possible in a flat floor, without running or jogging for 6 minutes.

The cardiorespiratory parameters were measured for heart rate, respiratory rate, systemic blood pressure, oxygen saturation and also for Borg scale for dyspnea and overall fatigue at baseline and immediately after the test.[15] During the test, standard phrases of encouragement were used and heart rate, oxygen saturation and Borg scale for dyspnea and overall fatigue were measured in 2, 4 and 6 minutes.[15] The 6MWT was immediately stopped if patient presented chest pain, intolerable dyspnea, leg cramps, staggering, diaphoresis, and pale or ashen appearance.[15]

To analyze the cardiorespiratory parameters in 6MWT, the variation between post-test and pre-test values were calculated. Total distance walked and percent of predicted distance was calculated in meters by using reference formulas for the Brazilian population.[16,17]

Patients with asthma were considered controlled if they: a) completed and finished the test regardless distance walked; b) presented values of percent-predicted distance above the cut-off point established by ROC curve. Otherwise, the patient was classified as uncontrolled asthma. The classification of controlled and uncontrolled asthma was made in both items of 6MWT.

6MWT variables were also compared between groups of uncontrolled and controlled asthma classified by GINAq.

Statistical analysis

The data were processed with the Statistical Package for Social Sciences for Windows, version 16.0 (SPSS Inc., Chicago, IL, USA).

Categorical variables were presented in a descriptive form and the differences were analyzed using the Chi-square test.

To calculate the cut-off point in 6MWT to classify in uncontrolled and controlled asthma, the classification by GINAq and created the ROC curve in MedCalc program were used, and the better value was defined by Youden index.

The outcome for each test was coded as uncontrolled (1) or controlled (2) asthma. Agreement among measures was assessed by cross-tabulation and kappa statistics (poor agreement ≤ 0.4; moderate agreement between 0.4 and 0.75; excellent agreement ≥ 0.75).[18]

GINAq was considered the gold-standard test, and affected by this disease (asthma) if the patient was classified as uncontrolled asthma. The sensitivity, specificity, positive and negative predictive values and accuracy with other measures were calculated by using the Openepi program version 3 - Diagnostic test.

To compare the distributions of nonparametric quantitative variables among two groups, the Mann-Whitney test was used. In all cases, the level of significance was set at 5%.

RESULTS

It could be evaluated all patients with asthma who were followed up in our Outpatient Clinic during the study period. Out of 261 patients selected based on inclusion criteria, 21 were excluded by presence of cardiac comorbidities, 63 for other respiratory diseases, 14 for cognitive limitations, three for motor limitations, nine by presence of immunodeficiency disease, three by presence of anaphylaxis history and 10 did not want to participate in this study.

Of the 138 children and adolescents included, 78 (56.5%) were male and the median age was 11 (7-17) years. According to GINAq, 43 (31.2%) children and adolescents were classified as controlled asthma, and 95 (68.8%) as uncontrolled asthma. The comparison of general characteristics of uncontrolled and controlled asthmatic patients are shown in Table 1.

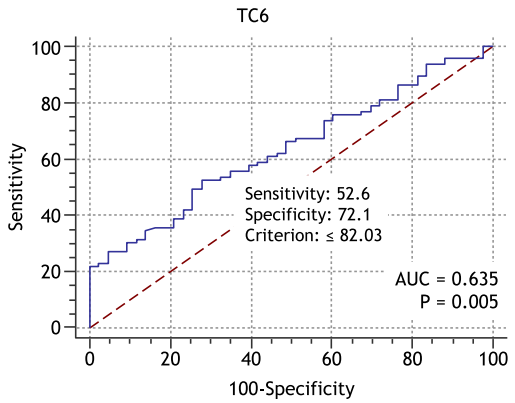

Figure 1. ROC-curve and cut-off point of controlled and uncontrolled asthma using percentage-predicted distance in 6MWT.

Table 1. General characteristics of asthmatic children and adolescents of this study.

Variable	Uncontrolled asthma by GINAq	Controlled asthma by GINAq	p
Demographics characteristics			
Male gender	*55 (70.5)*	23 (29.5)	0.629*
Caucasian race	*48 (75.0)*	16 (25.0)	0.223*
Anthropometric characteristics			
Age (years)	10 (7-17)	11 (7-17)	0.256**
Weight (kg)	38.3 (20.9-91.6)	40.65 (22.3-79.3)	0.168**
Height (m)	1.42 (1.19-1.72)	1.44 (1.20-1.71)	0.346**
BMI	19.39 (13.6-35.96)	18.87 (15.04-33.64)	0.279**

GINAq: Global Initiative for Asthma questionnaire; kg: kilograms; m: meters; BMI: Body Mass Index; p≤0.005. Statistic test: *Chi-square Test; **Mann-Whitney Test.

In 6MWT, the better cut-off to distingue patients in controlled and uncontrolled asthma using the predicted distance was 82.03%, with 52% of sensitivity and 72.1% of specificity (Figure 1).

GINAq identified more patients with uncontrolled asthma (68.8%). In contrast, 6MWT analyzed when patients finished the test, in other words, the measure that detected the lowest number of patients with uncontrolled asthma, 13% of cases.

The number and percentage of cases with uncontrolled and controlled asthma based on cut-off points described in "Methods" section, as GINAq, ACT, spirometry and 6MWT are shown in Table 2.

Table 2. Number of cases with uncontrolled and controlled asthma among different measures in children and adolescents.

	Uncontrolled asthma N (%)	Controlled asthma N (%)
GINAq	95 (68.8)	43 (31.2)
ACT	64 (46.4)	74 (53.6)
FEV1/FVC	84 (60.9)	54 (39.1)
FEV1%	53 (38.4)	85 (61.6)
FEV1 BD	53 (38.4)	85 (61.6)
FEF 25-75%	65 (47.1)	73 (52.9)
FEF 25-75% BD	70 (50.7)	68 (49.3)
Spirometric index	94 (68.1)	44 (31.9)
Completed 6MWT	18 (13.0)	120 (86.9)
6MWT % ROC-curve	61 (44.2)	77 (55.8)

N: Number of cases; %: percentage of cases; GINAq: Global Initiative for Asthma questionnaire; ACT: Asthma Control Test; FEV1/FVC: Tiffennau index; FEV1%: Forced Expiratory Volume in the first second pre-bronchodilator; FEV1 BD: Increase in FEV1 post-bronchodilator; FEF25-75%: Forced Expiratory Flow between 25% and 75% of Forced Vital Capacity pre-bronchodilator; FEF25-75% BD: Increase in FEF25-75% post-bronchodilator; Spirometric index: composed by VEF1, VEF1/FVC and FEF25-75%; Completed 6MWT: Completed Six-minute-walk-test regardless of the distance walked; 6MWT % Receiver Operating Characteristic (ROC)-curve: classification based on ROC-curve values of percentage-predicted distance walked in 6MWT.

All tests were compared with each other and the proportion of agreement expressed by *k* statistic are shown in Table 3. A moderate agreement was observed between GINAq and ACT ($p < 0.001$; $k = 0.56$), both measures based on history of symptoms, however, it could be observed a poor agreement between GINAq and both measures of 6MWT. The spirometric index did not show any agreement with others measures of asthma control. Most of the spirometric parameters presented moderate agreement between their own parameters.

Considering GINAq as gold-standard test, the sensitivity, specificity, positive and negative predictive values and accuracy were calculated with ACT, spirometric parameters and 6MWT (Table 4).

When analyzing GINAq and ACT, which presented moderate agreement in kappa statistic, 100% of specificity and positive predictive value could be observed. All patients, being classified as uncontrolled asthma in ACT, were classified as uncontrolled asthma in GINAq.

Spirometric index presented higher sensitivity (72,6%) regarding GINAq. Of all patients, who presented altered spirometric index, 73.4% were classified with uncontrolled asthma by GINAq. Complete 6MWT presented 100% of specificity with GINAq. In 6MWT, 18 patients did not finish the test and all these cases were classified as uncontrolled asthma by GINAq (Table 4).

Regarding asthma control assessed by GINAq and 6MWT, it could be observed statistically a significant increase of dyspnea evaluated by Borg scale in patients with uncontrolled asthma after test ($p = 0.001$). In addition, patients with uncontrolled asthma presented a lower distance walked ($p = 0.001$) and percent of predicted distance ($p = 0.014$) when compared to children and adolescents with controlled asthma. No differences between spirometric parameters and groups of asthma control were observed.

The 6MWT measures and variation of cardiorespiratory parameters between baseline and post-test and spirometric parameters are shown in Table 5.

Table 3. Proportion of agreement, expressed by *k* statistic different measures of asthma control in children and adolescents.

	ACT	Spirometric index	Completed 6MWT	6MWT%ROC-curve
GINA	k= 0.563	k= 0.144	k= 0.127	k= 0.67
	p<0.001	p= 0.091	p= 0.002	p= 0.026
	ACT	k= 0.096	k= 0.234	k= 0.196
		p= 0.212	p<0.001	p= 0.021
		Spirometric index	k= 0.017	k= 0.015
			p= 0.689	p= 0.839
			Completed 6MWT	k= 0.318
				p<0.001

GINA: Global Initiative for Asthma questionnaire; ACT: Asthma Control Test; Spirometric index: composed by VEF1, VEF1/FVC and FEF25-75%; Completed 6MWT: Completed Six-minute-walk-test regardless of the distance walked; 6MWT % Receiver Operating Characteristic (ROC)- curve: classification based on ROC-curve values of percentage-predicted distance walked in 6MWT.

Table 4. Sensitivity, specificity, positive and negative predictive values and accuracy between GINA questionnaire (GINAq) and others measures of asthma control.

	Sensitivity	Specificity	Positive PV	Negative PV	Accuracy
ACT	67.4%	100%	100%	58.1%	77.5%
FEV1/FVC	66.3%	51.2%	75.0%	40.7%	61.6%
FEV1%	36.8%	58.1%	66.0%	29.4%	43.5%
FEV1 BD increase	38.9%	62.8%	69.8%	31.8%	46.4%
FEF25-75%	49.5%	58.1%	72.3%	34.2%	52.2%
FEF25-75% BD increase	51.6%	51.2%	70.0%	32.3%	51.4%
Spirometric index	72.6%	41.9%	73.4%	40.9%	63.0%
Completed 6MWT	18.9%	100%	100%	35.8%	44.2%
6MWT %ROC-curve	50.5%	69.8%	78.7%	39.0%	56.5%

PV: Predicted values; GINAq: Global Initiative for Asthma questionnaire; ACT: Asthma Control Test; FEV1/FVC: Tifennau index; FEV1%: Forced Expiratory Volume in the First Second pre-bronchodilator; FEV1 BD increase: Increase in FEV1 post-bronchodilator; FEF25-75%: Forced Expiratory Flow between 25% and 75% of Forced Vital Capacity pre-bronchodilator; FEF25-75% BD increase: Increase in FEF25-75% post-bronchodilator; Spirometric index: composed by VEF1, VEF1/FVC and FEF25-75%; Completed 6MWT: Completed Six-minute walk test regardless of the distance walked; 6MWT % Receiver Operating Characteristic (ROC)-curve: classification based on ROC-curve values of percentage-predicted distance walked in 6MWT.

Table 5. Comparison of 6MWT results and spirometric parameters between groups of uncontrolled and controlled asthma by GINA questionnaire (GINAq).

Variable	Uncontrolled asthma by GINAq	Controlled asthma by GINAq	p
6MWT			
Total distance walked (m)	481.0 (40.0 - 625.8)	520.0 (362.7 - 700.0)	0.001
Predicted distance (%)	81.6 (7.0 - 106.1)	85.5 (65.5 - 107.2)	0.014
Δ Heart rate	45 (9 - 92)	36 (4 - 121)	0.517
Δ Respiratory rate	5 (-8 - +19)	3 (-7 - +17)	0.099
Δ Oxygen saturation	-2 (-15 - +2)	-1 (-6 - +1)	0.216
Δ Systolic blood pressure	5 (-10 - +26)	5 (-5 - +30)	0.732
Δ Diastolic blood pressure	5 (-10 - +30)	5 (-10 - +30)	0.857
Δ Borg scale for dyspnea	1 (-0.5 - +10)	0 (0 - 6)	0.001
Δ Borg scale for overall fatigue	0.5 (-0.5 - +8)	0 (0 - 8)	0.070
Spirometric parameters			
FEV1/FVC	81 (49 - 100)	82 (59 - 96)	0.256
FEV1%	84 (45 - 116)	83 (60 - 112)	0.966
FEV1 BD increase	7 (-11 - +51)	7 (-19 - +51)	0.439
FEF 25-75%	70 (20 - 131)	71 (27 - 124)	0.490
FEF 25-75% BD increase	30 (-39 - +109)	29 (-46 - +72)	0.290

GINAq: Global Initiative for Asthma questionnaire; 6MWT: Six-minute-walk-test; m: meters; Δ: Variation (final value – baseline value); FEV1/FVC: Tifennau index; FEV1%: Forced Expiratory Volume in the First Second pre-bronchodilator; FEV1 BD increase: Increase in FEV1 post-bronchodilator; FEF25-75%: Forced Expiratory Flow between 25% and 75% of Forced Vital Capacity pre-bronchodilator; FEF25-75% BD increase: Increase in FEF25-75% post-bronchodilator.

DISCUSSION

All asthma guidelines suggest that asthma control should be assessed, whenever possible, to verify and guide the disease management and adequate treatment.[1,19] However, there are many measures available to assess asthma control and each of them analyze different aspects regarding the asthmatic patient. In the current study, it could be assessed the history of symptoms by GINAq and ACT, lung function by spirometry and functional exercise capacity by 6MWT.

As well as in other studies, GINAq as gold-standard test was used.[20] In this study, GINAq was able to identify more patients with uncontrolled asthma and presented moderate agreement, and 100% of specificity with ACT. Although GINAq uses a categorical scale for classification and ACT uses multiple choice, both questionnaires are based on history of symptoms.[1,21]

According to our study, Koolen et al.[22] showed that c-ACT or ACT demonstrated good agreement with GINAq in children and adolescents and demonstrated the use of "19" as a cut-off point for ACT results in 66% of sensitivity and 100% of specificity. Waibel et al.[7] also verified a moderate agreement between GINAq and c-ACT and concluded that c-ACT was useful for monitoring children with asthma. In adults with asthma, Vermeulen et al.,[8] studied five measures of asthma

control assessment and found moderate agreement between GINAq and ACT, with higher percentage of patients with uncontrolled asthma classified by GINAq.

In contrast, other authors found a significant disagreement between c-ACT and GINAq and between c-ACT and pediatrician's assessment.[23,24] They concluded that the use of only one measure for determining asthma control level does not seem to be consistent and accurate and the assessment of asthma control should include analysis of symptoms and lung function.[23,24]

The GINA guideline emphasizes the importance of development of other asthma control measures to help in clinical practice, to distinguish levels of symptoms control and to provide more information on disease progress.[1,25]

The assessment of spirometry should be included on evaluation of children with asthma at least once a year for a better measure on lung function and asthma control and progression.[1,11,13,25] Many authors corroborated our results and related a disagreement between asthma control level evaluated by symptoms and spirometric parameters analyzed individually.[5,25,26] However, we found that spirometric index presented higher sensitivity with GINAq, therefore, presence of at least one alteration in spirometry is associated with classification as uncontrolled asthma by GINAq.

Salviano et al., assessed Brazilian asthmatic children and adolescents and found an association between FEV1 and asthma control level according to GINAq, reinforcing the importance of spirometry in clinical follow-up of these patients.[27] Some authors highlighted that VEF1 should be used as a risk factor for the worst asthma outcome, and failure to include spirometry a measure of asthma control index can underestimate future risk of exacerbations.[28,29]

Then again, some studies demonstrated that despite asthmatic children were classified as controlled by GINAq or c-ACT, their lung function might not be normal, and they may have persistent abnormal lung function or airway reversibility.[25,26]

We found a moderate agreement between spirometric parameters such as FEV1 and FEF25-75%. Green et al. also found an agreement when comparing spirometric parameters, however, they found a poor agreement between FEV1 and FEF25-75%.[5] Some authors have shown that altered FEF25-75% values are associated with worse asthma control, increase of severity, exacerbations, morbidity and use of systemic corticosteroids.[15,30,31] In contrast, other study reported that FEF25-75% is not a good parameter to be used in the evaluation of spirometry in children and adults.[32]

Although there are no recommendations in current guidelines about the usefulness of FEF 25-75% for asthma diagnosis and management, we suggest the use of this parameter in association with FEV1 and FEV1/FVC in evaluation of children and adolescents with asthma, once it may provide important information regarding changes and presence of hyperresponsiveness in small airways.[14,33,34]

In order to classify patients with controlled and uncontrolled asthma according to predicted distance in 6MWT, we need to calculate the cut-off point, since there are no studies with this information on asthmatic children and adolescents. The cut-off point of 82,03% was able to differentiate patients with controlled and uncontrolled asthma.

Despite being a simple and highly applicable test, there are few studies that uses 6MWT in children and adolescents with asthma and none of them associated this test and asthma control level.[15,35-37] In our study, subjects with uncontrolled asthma presented higher presence of dyspnea, lower total distance walked and percent of predicted distance in 6MWT. Andrade et al., assessed physical performance and cardiorespiratory responses in asthmatic children using 6MWT and concluded that the distance walked is significantly lower than the predicted values for healthy children, and it is directly influenced by sedentary lifestyle.[35] Basso et al., compared physical performance in 6MWT between asthmatic and healthy adolescents and verify that asthmatic adolescents had positive correlations between walked distance and duration of intense activity.[36] Gonzalez-Dias et al., compared children with and without asthma and found no significant difference in distance walked between two groups.[37]

The 6MWT is a submaximal test, used to assess presence of dyspnea and desaturation during physical activity, to evaluate the aerobic capacity for practicing exercises, to verify response to therapeutic or rehabilitation programs and to assess the disease evaluation.[15] In addition, a review that studied the 6MWT as a tool for assessing pulmonary impairment concluded that the application of this test was recommended as a complementary exam in evaluation of patients with pulmonary and cardiovascular diseases.[38] Therefore, we emphasize the importance of this study, once it was able to establish a cut-off point to distinguish controlled and uncontrolled asthma in children and adolescents using predicted distance in 6MWT and demonstrate a correlation between asthma control level and application of this test in clinical practice. Furthermore, most activities done by children and adolescents with asthma in daily living are performed at submaximal levels, nevertheless, the 6MWT may reflect the functional exercise level required for these activities.[15]

The whole evaluation of history of symptoms, cardiopulmonary function, aerobic capacity and analysis of inflammatory biomarkers to assess asthma control would be ideal, but unfortunately this does not happen nowadays in all healthcare centers of asthma management.[39,40] In many cases, measures such as spirometry or 6MWT are not available or the healthcare center does not have trained professionals to do it. In this

situation, GINAq can be a good measure to use, since it is a simple and standardized questionnaire, which does not require special equipment to be applied.[1,21] Besides this, our study demonstrated that GINAq was able to distinguish more patients with uncontrolled asthma when compared to other measures.

We consider that a measure which assess asthma phenotypes by inflammatory markers would contribute even more to our findings, therefore its absence is a limitation of our study.

In conclusion, GINAq was the measure that identified more patients with uncontrolled asthma and presented moderate agreement with ACT. A disagreement was found between GINAq, spirometry and 6MWT. In spirometry assessment, the spirometric index did not show agreement with GINAq and ACT. However, there was a 72.6% sensitivity between spirometric index and GINAq. Regarding 6MWT and asthma control, we established a cut-off point to distinguish controlled and uncontrolled asthma in children and adolescents using predicted distance. In addition, we highlight the importance of 6MWT in the assessment of daily living activities, cardiorespiratory parameters and aerobic capacity in this population.

Therefore, to avoid the indiscriminate use of medications and underestimate asthma severity, we emphasize that the assessment of asthma control should be done with caution, regardless of the measure used in, physician evaluation, questionnaires, lung function measures, cardiorespiratory parameters or biormarkers.[4,5] It is important to state that the use of more than one measure to assess asthma control will provide the healthcare team a better information regarding the disease control and progression and therefore enable a better management of treatment.[23] It is important to notice that before changing medication, the physician must evaluate the diagnosis, adherence to treatment and adequate inhalation technique.[1]

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