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The Role of Spirometry in the Diagnosis of Cough Variant Asthma in Children Aged 5 to 15 Years

Masoumeh Ghasempour[1], *Nemat Bilan[2, 3], Iman Vafaei[4]

[1]Fellowship of Pediatric Pulmonology, Pediatric Health Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.
[2]Pediatric Pulmonologist, Pediatric Health Research Center, Tabriz University of Medical Sciences, Tabriz, Iran. [3]Pediatrician, Medical Education Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.
[3]Resident of Pediatrics, Tabriz University of Medical Sciences, Tabriz, Iran.

Abstract

Background

Cough variant Asthma (CVA) is defined as chronic cough without wheezing, and may be precursor of typical asthma. Thus, the diagnosis of CVA and early intervention can partly inhibit asthma progression.This study aimed to evaluate the role of spirometry in diagniosis of Cough variant Asthma in Iranian Children.

Materials and Methods

This descriptive observational study included a total of 73 patients, who were referred to the specialized lung clinic of Tabriz Pediatric Center, Tabriz city, Iran. Patients were divided into two groups with classic asthma (n=37) and cough variant asthma (n=36) and basic spirometry parameters such as FEV1, FVC, FEV1/FVC, FEF 25-75% and PEF were measured, and the spirometry findings of each individual were measured based on the European Respiratory Society (ERS) criteria.

Results

The mean of FEV1 and FVC in the classic asthma group were 83.45 ± 20.49% and 86.45 ± 21.57%, respectively; and in the cough variant asthma group were 87.44 ± 13.99% and 86.8 ± 14.71%, respectively. There was no significant difference between the two groups for the basic spirometry parameters of FEV1 and FVC (p=0.343, P=0.916; respectively). The average FEV1/FVC parameter in the cough variant asthma group was 89.44±13.07, but it was 72.35±8.47 in the classic asthma group, with a significant difference between the two groups ($p<0.05$).

Conclusion

There was a significant difference in the FEV1 / FVC value between two groups of cough and classic asthma. Spirometry of patients with cough variant asthma showed the FEF values (25 -75%) were lower than expected; we suggest using spirometry in the diagnosis of cough variant asthma considering small airways changes.

Key Words: Classic Asthma, Children, Cough variant Asthma, Spirometry.

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Corresponding Author:

Prof. Nemat Bilan, Pediatric Pulmonologist, Pediatric Health Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.

Email: bilannemat@yahoo.co.uk

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1- INTRODUCTION

Classic asthma is defined as a triad of dyspnea, cough, and wheezing. A phenotypic variant of asthma is called cough variant asthma (CVA), and is described as chronic or recurrent cough without wheezing (1). CVA is a subset of asthma, with chronic symptoms such as chronic cough with bronchial hyper responsiveness and eosinophilic inflammation of the airway pathways (2). CVA was described for the first time in children (6-16 years old), in the first decade of 1980(3). Although there is no study showing the incidence of CVA; but, clinical studies have reported a lower incidence of CVA than classic asthma in children (4,5). Recent evidence has shown that children with only cough (without wheezing or dyspnea), usually do not have asthma (6). However, in specialized pediatric clinics, there are many children who develop cough in response to frequent asthma triggers and are likely to recover when they receive asthma medications (7).

In adults and children, CVA may be a pre-term trend for asthma. Adults lead to asthma after 1.5 to 9 years, and in long-term treatment with corticosteroids, this treatment reduces the risk of asthma. Progression towards typical asthma has been common in children population, and these patients are associated with excessive and severe response with bronchial hyper responsiveness (2). In a study of 28 patients with CVA that were followed for 5 years and treated with Theophylline and bronchodilators without inhaled corticosteroids; it was concluded that a long-term cough may be associated with a high risk of typical asthma (8). Therefore, the diagnosis of CVA in the early stages and interventions in these patients can contribute somewhat to reduce the progression of classic asthma. In adults and children who are able to co-operate and are over 6 years of age, response to stimuli such as Histamine or Methacholine is commonly associated with measuring lung function with spirometry tests (9). Spirometry is an objective method of measuring the air flow limitation that is possible in people over the age of 5 years and for the diagnosis and evaluation of the treatment of pulmonary diseases and the differentiation of obstructive pulmonary diseases (10-12). According to findings from the literature review, there were no adequate results on the role of spirometry in the evaluation and diagnosis of CVA, based on the fact that most recent studies were conducted on most adult ages and the number of subjects was limited. Therefore, the aim of this study was to evaluate the role of spirometry in the diagnosis of CVA.

2- MATERIALS AND METHODS

2-1. Method

This is a descriptive observational study. A total of 73 patients from 5 to 15 years old with classic asthma and cough variant asthma who were referred to the specialized lung clinic of Tabriz Pediatric Center, Tabriz city, East Azarbaijan province, North West of Iran. This study was conducted in March 2015 to February 2016. The patients were divided into two groups with 37 (50.7%) cases of classic asthma, and 36 (49.3%) cases of cough variant asthma, and demographic characteristics such as age, gender, familial history of asthma, rhinitis, and sinusitis were recorded separately for each patient.

Basic spirometry parameters such as FEV1, FVC, and FEV1/FVC, FEF 25%, FEF 50%, FEF 75%, FEF 25-75%, and PEF were measured. Spirometry was performed again to evaluate the treatment outlines after one month of treatment (inhaled corticosteroids). The spirometry findings of each individual were measured based on the ERS criteria with the same age, gender, height and weight of each

patient. This method does not have a single each person based on age, sex, height and weight (32). This study was registered as a research project with ID- code: 11376/4/5, at the Pediatric Health Research Center. This study was approved by the Ethics Committee of the Tabriz University of Medical Sciences (with ethical code of TBZMED.REC.1394.856), and the parents of the patients completed the informed consent form for spirometry and interventions. CVA patients had a history of chronic dry cough for more than 8 weeks, non-sputum cough, mostly overnight, without wheezing and without dyspnea. Patients were excluded if they had coexistent heart, cardiopulmonary, and neuromuscular disease.

2-2. Statistical Analysis

The results are expressed as mean ± standard deviation (SD). The qualitative and quantitative variables were analyzed in gold standard, but is based on the ERS for two groups of classic asthma and cough variant asthma by independent t-test, and Chi -square test; respectively. A comparison of changes of the main variables in post-interventional spirometry (Salbutamol and exercise test) and basic spirometry were analyzed by paired t-test. Data analysis was performed using STATA 14 and SPSS version 16.0 software. A p-value of less than 0.05 was considered statistically significant.

3- RESULTS

In this study, 73 patients aged 5 to 15 years were studied, of which 36 (49.3%) patients had cough variant asthma, and 37 (50.7%) patients were with classic asthma. In total, the male patients were 48 (65.8%), while the female patients were 25 (34.2%). The patients' demographic characteristics are presented in **Table.1**.

Table-1: Demographic characteristics and predisposing factors of asthma,for each group of classic and cough variant asthma patients

Variables		Cough variant Asthma (n=36)	Classic Asthma (n=37)	P-value
Age(years)		7.14±1.79	7.92±2.84	0.165*
Gender	Male	27(75%)	21(56.8%)	0.101**
	Female	9(25%)	16(43.2%)	
Allergic rhinitis		9(25%)	6(16.2%)	0.353**
Sinusitis		2(5.6%)	3(8.1%)	1.00***
Family history of asthma		12(33.33%)	9(24.32%)	0.395**

*Independent Samples Test.
**Chi-Square Tests.
*** Fisher's Exact Test.

According to the Chi-square test, there was no significant difference between the classic asthma and the cough variant asthma in terms of gender (p=0.101). There was no significant difference in the family history (p=0.800), Sinusitis and Allergic rhinitis (p=0.730) of classic asthma and cough variant asthma. The mean of FEV1 and FVC in the classic asthma group were 83.45 ± 20.49% and 86.45 ± 21.57%, respectively; and in the cough variant asthma group were 87.44 ± 13.99% and 86.8 ± 14.71%, respectively. There was no significant difference between the two groups for the basic spirometry parameters of FEV1 and FVC (p=0.343, p=0.916; respectively) (**Table.2**).

Table-2: Basic spirometry parameters for each group of classic and cough variant asthma patients

Spirometry Parameters	Mean ± SD		P-value
	Classic Asthma	Cough variant Asthma	
FEV1	83.45 ± 20.94	87.44 ± 13.9	0.342
FVC	86.45 ± 21.57	86 ± 14.71	0.918
FEV1/FVC	72.35±8.47	89.44±13.07	<0.001
FEF 25%	82.13 ± 23.70	74.64 ± 25.43	0.197
FEF 50%	81.16 ± 66.24	71.97 ± 27.13	0.443
FEF 75%	81.25 ± 27	70.45 ± 29.30	0.1058
PEF	83.86 ± 36.62	91.19 ± 31.50	0.363
FEF 25-75%	57.86±12.35	52.17±12.16	0.06

SD: Standard deviation; FEV1: Forced expiratory volume in 1 second; FVC: Forced vital capacity; FEV1/FVC: Forced expiratory volume in 1 second/ Forced vital capacity ratio; FEF25%: Forced expiratory flow at 25% of expired vital capacity; FEF50%: Forced expiratory flow at 50% of expired vital capacity; FEF75%: Forced expiratory flow at 75% of expired vital capacity; PEF: Peak expiratory flow; FEF(25-75%): Forced expiratory flow between 25% and 75% of expired vital capacity.

The average FEV1/FVC parameter in the cough variant asthma group was 89.44±13.07, but it was 72.35±8.47 in the classic asthma group, with a significant difference between the two groups ($p<0.001$). The FEF (25-75%) values were not significantly different in the two groups of cough and classic asthma ($p=0.06$).

A comparison of the spirometry parameters during diagnosis and post-treatment with corticosteroids in the cough variant asthma group and classic asthma group are shown in (**Tables 3 and 4**). After treatment in the two groups of patients (CVA and classic asthma), there was improvement in the pulmonary function tests.

Table-3: Comparison of spirometry parameters during diagnosis and post-treatment in cough variant asthma group

Parameter	Basic Mean ± SD	After Treatment Mean ± SD	P-value
FEV1	87.44 ± 13.9	99.61 ± 12.15	<0.001
FVC	86 ± 14.71	97.06 ± 12.60	<0.001
FEV1/FVC	89.44±13.07	99.68 ± 5.28	<0.001
FEF25%	74.64 ± 25.43	96.27 ± 20.26	<0.002
FEF50%	71.97 ± 27.13	96.40 ± 23.14	<0.001
FEF75%	68.45 ± 29.30	96.27 ± 26.95	<0.001
PEF	91.19 ± 31.50	107.13 ± 29.13	0.027

SD: Standard deviation; FEV1: Forced expiratory volume in 1 second; FVC: Forced vital capacity; FEV1/FVC: Forced expiratory volume in 1 second/ Forced vital capacity ratio; FEF25%: Forced expiratory flow at 25% of expired vital capacity; FEF50%: Forced expiratory flow at 50% of expired vital capacity; FEF75%: Forced expiratory flow at 75% of expired vital capacity; PEF: Peak expiratory flow; FEF(25-75%): Forced expiratory flow between 25% and 75% of expired vital capacity.

Table-4: Comparison of spirometry parameters during diagnosis and post-treatment in classic asthma group

Parameter	Basic Mean ± SD	After Treatment Mean ± SD	P-value
FEV1	83.45 ± 20.94	99.30 ± 15.05	<0.001
FVC	86.45 ± 21.57	98.02 ± 18.39	0.0015
FEV1/FVC	72.35±8.47	99.25 ± 5.96	<0.001
FEF 25%	82.13 ± 23.70	93.91 ± 28.28	<0.001
FEF 50%	81.16 ± 66.24	106.13 ± 29/13	0.039
FEF 75%	81.25 ± 27	98.90± 7/44	0.036
PEF	83.86 ± 36.62	110.08 ± 48.08	<0.007

SD: Standard deviation; FEV1: Forced expiratory volume in 1 second; FVC: Forced vital capacity; FEV1/FVC: Forced expiratory volume in 1 second/ Forced vital capacity ratio; FEF25%: Forced expiratory flow at 25% of expired vital capacity; FEF50%: Forced expiratory flow at 50% of expired vital capacity; FEF75%: Forced expiratory flow at 75% of expired vital capacity; PEF: Peak expiratory flow; FEF(25-75%): Forced expiratory flow between 25% and 75% of expired vital capacity.

4- DISCUSSION

Cough variant Asthma is now considered to be an asthma precursor or an asymmetric predominance, with about 30% of patients progressing to have typical asthma, after some time (13-15). Therefore, the diagnosis and evaluation of cough variant asthma is very important. The goal of the clinical management of cough variant asthma is to control airways inflammation and improve bronchospasm (16). In both classic and cough variant asthma, coughing can be improved by treating with corticosteroids and bronchodilators. The Australian cough guidelines summary statement, recommended the use of bronchodilators and corticosteroids as the first line of treatment (17-21).

By the results of our study, there were no significant differences between the two groups regarding the FEV1, FVC and FEF values. However, the average FEV1/FVC parameter in the cough variant asthma group and in the classic asthma group had a significant difference between the two groups. In the study of classic asthma patients with episodes of attack in the stage of recovery and cough asthma, from 2010 to 2011,Yoo et al. found that the mean of the FEV1/FVC parameter in the classic asthma group with asthma attack was less than 80%, and FEF50%, FEF75% (maximal mid-expiratory flow), and MMEF(25-75) had clearly decreased. Also, in this study, in the CVA group, the mean of FEF75, and MMEF (25-75) was less than 80%. All the parameters of this study in classic asthma were lower than those of cough variant asthma and asthma that were recovering. There was no clear difference between the two groups of cough and the improved asthma group. Based on this study, it was found that in patients with classic asthma, there is a problem with the large and small airways, while in patients with coughing asthma, a dysfunction in the small airways is similar to those in the recovery stage (22).

In our study, there was no statistical difference among patients with classic and cough variant asthma in pulmonary function except FEV1/FVC. In another study by Chen et al. on 268 children with cough asthma, and 147 children with classic asthma, PEFR, FVC, and FEV1 were measured; but there was no significant difference between the two groups (p> 0.05), and this study was

similar to our study (23). In recent studies, the FEF (25-75%) parameter in children was more sensitive than the FEV1 and FEV1/FVC parameters for obstructive patients (24-27). In children, another benefit of the FEF (25-75%) parameter over the FEV1 parameter is that it depended less on the patients' efforts (30-31). Also, the FEV1/FVC parameter in children is more useful than FEV1. In our study, FEV1/FVC values were lower in the classic asthma group compared with the cough variant asthma group, but FEF(25-75%) values, although lower than expected, did not differ significantly between the two groups.

5- CONCLUSION

In this study, Lower FEV1/FVC values were found in the classic asthma group than in the cough variant asthma group. The FEF (25-75%) values were low in the two groups. It can be concluded that in patients with classic asthma, the problem was in the large and small airways; while in patients with cough variant asthma, there was a dysfunction in the small airways. In the spirometry of patients with a cough variant asthma, despite the normal values of FEV1/FVC, it was found that the FEF (25-75%) values can be lower than expected.

6- ABBREVIATION

FEV1: Forced expiratory volume in 1 second,

FVC: Forced vital capacity,

FEV1/FVC: Forced expiratory volume in 1 second/ Forced vital capacity ratio,

FEF 25%: Forced expiratory flow at 25% of expired vital capacity,

FEF 50%: Forced expiratory flow at 50% of expired vital capacity,

FEF 75%: Forced expiratory flow at 75% of expired vital capacity,

PEF: Peak expiratory flow,

ERS: European Respiratory Society,

FEF (25-75%): Forced expiratory flow between 25% and 75% of expired vital capacity.

7- CONFLICT OF INTEREST: None.

8- ACKNOWLEDMENTS

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