BRIEF COMUNICATION
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Sweat Test in Asthmatic Children; a Single Center Study

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ABSTRACT

Asthma and Cystic Fibrosis (CF) have some identical manifestations. In the present study, the frequency of positive sweat test was assessed in asthmatic children.

This cross-sectional study was performed in asthmatic children, who were referred to Bahrami Children Hospital, Tehran, during July 2003 to July 2005. Sweat test was performed for all children.

One hundred and thirty five (95 males and 40 females) asthmatic were studied. Sweat test was positive in 35 (26%) patients. Major signs and symptoms among these 35 patients were: Cough (35/35), Dyspnea (7/35), Chronic Diarrhea (6/35), and steatorrhea (1/35). Failure to thrive was found in 31 of 35 patients. The mean duration of asthma in patients with positive test was 49.3 months, which was significantly higher than 18.1 months in the group with negative test (P=0.001). Significant relations between recurrent respiratory tract infections (P=0.029), chronic diarrhea (P=0.001), failure to thrive (P=0.0001), and positive sweat test were found.

Sweat test should be recommended in asthmatic children with recurrent upper respiratory tract infections, long duration of asthma, chronic diarrhea, and failure to thrive.

Key words: Asthma; Cystic Fibrosis; Sweat test

INTRODUCTION

Asthma is a common reactive airway disorder, and its incidence has been increased during the recent years.[1,2] There are several diseases in the differential diagnosis list of asthma, in which Cystic Fibrosis (CF) is one of the most important one. CF is usually presented with respiratory and/or gastrointestinal symptoms or both.[2,3,4]

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A study on more than 11000 CF patients showed that delayed diagnosis was more common in CF cases with only respiratory symptoms and this is the major cause of malnutrition, respiratory problems and early death in these patients.[4] On the other hand it was not rare that CF children with only respiratory symptoms were treated as asthmatic patients until recognized as CF patients; therefore it is recommended that in children with chronic respiratory symptoms, sweat test should be considered as one of the diagnostic tests.[5] Although in some studies asthma was assessed in CF population, no study assessed the CF in asthmatic population in our country; so we conducted a study to find out the

frequency and association of positive sweat test and other manifestations of CF among asthmatic children.

PATIENTS AND METHODS

In this cross-sectional study, the asthmatic children (older than 2 years of age), who had been referred to Bahrami Children Hospital (Tehran, Iran) during July 2003 to July 2005, were investigated. Diagnosis of asthma was based on the positive history of symptoms and clinical signs as well as paraclinic tests in older children. A "positive history of symptoms" is considered as at least one positive answer to any of the following items:[6] cough for more than 10 days, exercise-induced cough, tormenting cough during sleep or wakefulness, recurrent dyspnea or wheezing, cough or dyspnea in a special season, cough or dyspnea which affected sleep, dyspnea or wheezing following contact with irritant materials, relief of symptoms after using bronchodilators. A "positive clinical sign" is defined as the existence of prolonged exhalation, with crepitation and wheezing. A positive paraclinic test is defined as a positive pulmonary function test in children above 6 years old.[1,2] Sweat test was considered positive, when sweat chloride was more than 60 mmol/lit.[3] Patients with at least two positive sweat tests were defined as a positive sweat test. All sweat tests were performed in an experienced laboratory by Pilocarpine Iontophoresis technique. Findings were recorded on data collection sheets and entered into a relational database; SPSS version 10.1; using chi-square and student *t*- test for analyzing data; p-value less than 0.05 was considered significant.

RESULTS

One hundred and thirty-five asthmatic children (90 males and 40 females), with mean age of 6 (range: 2-15) years, were studied. The history of recurrent respiratory infections and exacerbation of asthma symptoms during the course of these infections were found in 93 (69%) patients. Sixty-eight patients had a positive history of allergy in their first degree relatives. Positive sweat test was reported in 35 (26%) patients. There were not any significant relations between positive sweat test with age, sex and family history of allergy (P=0.15, P=0.77, P=0.30, respectively). The mean duration of asthma in patients with positive sweat test was 49.3 months, which was significantly higher than 18.1 months in those with negative sweat test (P=0.001). Major signs and symptoms of patients are depicted in Table 1. Significant associations were found between dyspnea, chronic diarrhea, wheezing and failure to thrive in patients with positive sweat test (P=0.001, 0.001, 0.036, 0.0001, respectively).

Table 1. Distribution of major signs and symptoms among the patients.

Symptoms/Signs	Positive Sweat Test – case (%)	Negative Sweat Test – case (%)	P-value
Cough	35 (100%)	100 (100%)	-
Dyspnea	7 (20%)	51 (51%)	0.001
Steatorrhea	1 (2%)	0	-
Chronic Diarrhea	6 (17%)	0	0.001
Wheeze	9 (25%)	46 (46%)	0.036
Rales	2 (5%)	9 (9%)	-
Failure to thrive	31 (88%)	15 (15%)	0.0001

DISCUSSION

Asthma is a common reactive airway disease in children; however the reactive airway disease is not synonymous with asthma, and it includes a broad differential diagnosis which asthma being the most common.[1,5] CF children may present with identical features of asthma; therefore diagnosis of asthma in children needs broad thinking and persistence and precision in ruling out other possible diagnoses.

CF is an autosomal recessive genetic disorder, which affects various organ systems and leads to obstructive lung disease, pancreatic insufficiency and abnormal sweat electrolytes.[3,7] CF is the most common respiratory single gene disorder and 4% of the caucasoid populations are asymptomatic carriers of mutations in CF gene.[3] Nowadays the survival of CF patients has reached over 30 years, so it is not rare to visit a CF patient in an outpatient clinic.[7] CF has a wide spectrum of clinical manifestations. In mild CF the respiratory symptoms are similar to asthmatic patients and if these patients do not show gastrointestinal symptoms, they might be diagnosed as asthmatic patients and this process can lead to unnecessary treatment or under treatment and consequential morbidity.[8]

In our present study, 35 patients with primary diagnosis of asthma had positive sweat test. On the other hand although we did not perform genetic studies,

these patients may be the undiagnosed CF cases. Although this frequency of CF among asthmatic children is high, we would not like to consider this frequency as a normal frequency of CF in asthmatic population because our sample size was not enough and there is a bias due to referring or presenting patients to a subspecialty hospital. It should be noticed that the recurrent respiratory tract infections and long duration of asthma symptoms were more common in patients with positive sweat test; and these factors were helpful in diagnosing of concomitant CF in asthmatic patients (P=0.029, P=0.001, respectively).

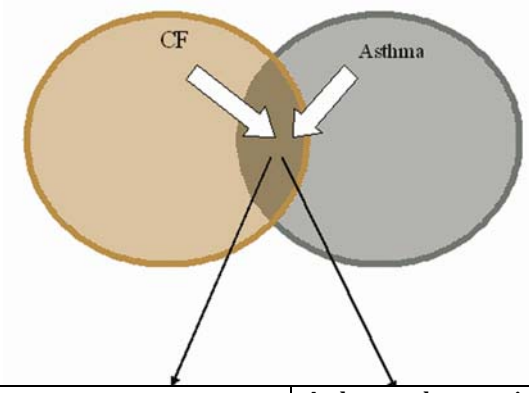
Data collected from teenage children around the world, based on the international study of asthma and allergies in childhood (ISAAC) indicated the prevalence of asthma symptoms ranging from 2% to 37%, depending on country;[6] so in theory it is estimated that this proportion of CF patients would be expected to have concomitant asthma. On the other hand, the asthma like symptoms in CF cases reported by The North American Epidemiologic Study of Cystic Fibrosis (ESCF) and The European Epidemiologic Registry of Cystic Fibrosis (ERCF) were 19% and 17%, respectively.[9,10]

In both studies the same proportions were found in children and adults. These data showed that the CF gene defect had no influence on the development of asthma.[8]

In clinical practice, diagnosis of CF is generally straightforward but diagnosis of asthma can be difficult, especially in children. There is no dispute that many CF cases have wheeze, but it is difficult to determine which patient has concomitant asthma and in which case it is the result of the underlying disease.

Therefore we are confronted to 3 groups of patients (Figure 1): 1. A group of asthma patients without CF; 2. A group of CF patients with some respiratory problems, but not asthma; and 3. A group of patients with CF and concomitant asthma.

It seems that clinical diagnosis of concomitant asthma in a CF child, especially mild CF, is as complex as the diagnosis of CF in an asthmatic child; however both require clinical experience, suspicion and precision. Based on typical clinical pictures of CF patients, some authors suggested the following clinical manifestations as discriminative pictures of CF in asthmatic patients:[11] Early life asthma, recurrent lower respiratory infections, bronchiectasis, pansinusitis and diabetes mellitus, a poor response to bronchodilators, pulmonary radiological abnormalities, pancreatic insufficiency and recurrent pancreatitis. Virtually in routine clinical practice these manifestations often are attributed to severe or typical cases of CF and are not common in mild CF with only respiratory symptoms.



CF and concomitant asthma	**Asthma and concomitant CF**
Major differentiate features of asthma in CF patients: [8] 1- History of atopy (Eczema, Rhinitis allergic) in patients 2- History of atopy (Eczema, Allergic Rhinitis and Asthma) in first degree relatives 3- Wheeze	Major differentiate features of CF in asthmatic patients in our study: 1- Recurrent respiratory tract infections 2- Long duration asthma > 18.1 months 3-Chronic diarrhea > 2 weeks 4- FTT 5-Wheeze 6-Dyspnea

Figure 1. Major features of concomitant asthma in CF patients and concomitant CF in asthmatic patients.

In the present study in asthmatic patients' population, we found that; long duration of asthma (more than 18.1 months), recurrent respiratory tract infections, chronic diarrhea (more than 2 weeks) and failure to thrive are good pictures in suspecting CF in asthmatic children. We also found that dyspnea, wheeze and normal auscultation of lungs are helpful diagnostic features of CF in our asthmatic patients. However, we did not find any relation between the early life asthma and CF, which is not consistent with previous reports.[11] It may be due to the severity of cases in previous studies and the range of age in our subjects.

Studies assessing asthma in CF population concluded that the diagnosis of asthma in patients with CF was predominantly based on the patients' history; the presence of cough was irrelevant but recurrent wheezing was a cardinal symptom and the diagnosis was strengthened by a strong family and personal history of atopy.[8]

Although the two types of the aforementioned studies were performed in two different populations and comparing them dose not seem logical but it is interesting to notice that wheeze was a common manifestation in both groups (Figure 1).

Other studies that assessed persistent wheeze in asthmatic children recommended that sweat test, chest radiography and allergy skin testing should be performed for these children to rule out foreign body aspiration or tuberculosis.[5] In our study we performed chest radiography and allergy skin test for selected patients but we did not find any abnormality.

In conclusion, it could be suggested that sweat test should be performed for asthmatic children with long duration asthma (>18.1 months), recurrent respiratory tract infections, chronic diarrhea (>2 weeks), and failure to thrive.

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EDITORIAL COMMENT

The Editorial Board of Iranian Journal of Allergy, Asthma and Immunology would like to emphasize the fact that the results of studies, which have been done in a specialized referral center, unless supported by complementary studies, can not be considered solely to attain the prevalence ratio in the community at large.