THE VALUE OF SWEAT CHLORIDE TEST IN THE DIAGNOSIS OF CYSTIC FIBROSIS AMONG JORDANIAN CHILDREN

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ABSTRACT

Objective: To determine the frequency of cystic fibrosis by measurement of sweat chloride concentration among Jordanian children referred to Princess Iman Research and Laboratory Sciences Center, King Hussein Medical Center with a high index of suspicion of cystic fibrosis on clinical ground.

Methods: About 1565 patients highly suspected of having cystic fibrosis were tested for sweat chloride using the Wescor Macroduct collecting system and Sweat Chick 3100.

Results: One hundred fifty-three out of 1565 patients (9.8%) were found to have sweat chloride ≥ 60 mmol/l, 132 (8.4%) had sweat chloride 45-59 mmol/l. The false positive rate was 3% on test repetition and the false negative rate was 3.4%.
Thirty seven percent of our patients presented with failure to thrive, diarrhea and chronic chest infection, 26% presented with either failure to thrive or short stature and the rest of patients had a wide spectrum of clinical presentation.

Conclusion: Sweat chloride test is a very good screening and diagnostic tool. There is a high percentage of patients with intermediate sweat chloride concentration where the diagnosis is equivocal and thus a genetic study to establish the diagnosis should be carried out.

Key words: Cystic Fibrosis, Sweat Chloride, Sweat Check 3100.

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Introduction

Cystic fibrosis is the most common life threatening autosomal recessive disorder in Caucasians and it is believed to be rare in Arabs [(1)]. In most cases, the diagnosis is suggested by manifestations of chronic sino-pulmonary disease, exocrine pancreatic insufficiency, and abnormally high sweat electrolytes [(2, 3)].

Cystic fibrosis is a multisystemic disease with mortality mainly due to progressive respiratory disease. The spectrum of the disease has recently much expanded, the gene responsible have been identified, and its product is known as cystic fibrosis transmembrane conductance regulator, which is involved in the transport of chloride [(4)].

More than 1000 mutations have been identified which lead to different clinical presentations [(5)]. Normal sweat chloride values < 60 mmol/l are not always enough to exclude the diagnosis. Misdiagnosis is attributed mainly to sweat collection technique [(6)]. In this study, we tried to determine the frequency of cystic fibrosis by measurement of sweat chloride concentration among patients referred to KHMC with different clinical presentation.

Methods

During the period between April 1999 and June 2003, we received 1565 patients from six of the Royal Medical Services, hospitals for sweat chloride test. Those patients were highly suspected of having cystic fibrosis. The age ranged between 2 months to 18 years with a mean of 2.8 years.

Methods of measurement: Wescor Macroduct system (Wescor Inc. 459, South Main Street, Logan, Utah, 84321, USA) [(7-9)] was used for sweat collection. The forearm was cleaned with distilled water after drying, electrodes containing pilocarpine gel where applied 5-10 cm apart for 5 min. After that, the site was cleaned and dried, then the Macroduct was applied for sweat collection at positive electrode site, 30 µl or more of

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sweat was collected. The collection time was 15-40 min. and chloride was measured by Sweat Check 3100.

Results

Out of 1565 patients tested for cystic fibrosis, 153 patients (9.8%) were found to have elevated sweat chloride concentrations more than 60 meq/L. To confirm the result, the test was repeated twice in 121 out of 153 positive patients. Only 5 patients showed results less than 60meq/l. One hundred thirty-two patients (8.4%) had intermediate chloride concentration; 40-59meq/l [(9)]. Upon second repetition, only 4 patients (3%) were found to have sweat chloride concentration ≥ 60meq/l. The mean value of sweat chloride in all subjects with sweat chloride of ≤ 60meq/l was 34.8 ± 5.2meq/l. This value was found to be similar to what is considered as intermediate sweat chloride level for the Belgian population (35.2 ± 4.4meq/l) [(10)].

The presenting symptoms ranged from chronic respiratory symptoms, diarrhoea, failure to thrive, short stature, jaundice, gastroesophageal reflux symptoms, and prolapsed rectum. The number of patients and symptoms are illustrated in Table I and the sweat chloride values according to age distribution are shown in Table II.

Discussion

Sweat chloride is the corner stone for the diagnosis of cystic fibrosis [(9)]; it has a sensitivity of 90-99% when performed properly in duplicates. Sweat collection technique, inexperience of laboratory workers and lack of quality control were found to be the most common causes of errors [(9, 10)].

The results showed that the percentage of cystic fibrosis among those patients referred to our laboratory with a high index of suspicion for cystic fibrosis was 9.8%. The patients present with a combination of chronic respiratory chest infection, foul smelling diarrhea and failure to thrive constituted 37%, chronic respiratory chest infection 28.8%, failure to thrive 12%
and short stature 14%, which are almost comparable to the finding by Wesley and his colleagues in New Zealand [(11)]. Most of the children were referred for sweat chloride test after the first year of age, with a mean age of 2.8 years, which is a late presentation with increased complications. Also it was clear that around one quarter (26%) of patients presented with failure to thrive or short stature without any other symptoms, is a high percentage in comparison to other parts of the world.

In 8.4 % of patients, sweat chloride was 45-59 meq/l and those cases were repeated and only 4 turned to have sweat chloride >60 meq/l. Their sweat chloride was (49, 52, 55, 56meq/l) and their clinical presentations were wheezes, diarrhea, failure to thrive and prolapsed rectum, respectively.

The functional defect of cystic fibrosis was not understood until the gene responsible had been identified. This gene product protein is known as cystic fibrosis Transmembrane conductance regulator (CFTR), which is involved in the transport of chloride. Because of the multiple alleles at the cystic fibrosis gene, laboratory diagnosis still depends largely on demonstration of increased sodium and chloride concentration. A screening panel of the most frequent mutations [(12)] is required particularly in patients with intermediate sweat chloride levels (40 - 59 mmol/l).

Conclusion

In children, sweat chloride concentration over 60 mmol/l on at least two occasions are diagnostic. The mean value of sweat chloride is higher in Jordanian children and so the laboratory results interpretation should be revised all over the country. Cases with intermediate chloride levels should undergo genetic evaluation for CFTR mutations. The clinical presentations of a large number of cases were mild or non- specific, which could be due to different mutation types than what is commonly known in other parts of the world.

The identification of cystic fibrosis mutations in Jordan needs big efforts to be established.

Table I. The distribution of sweat chloride in patients with chloride concentration ≥ 60 meq/l according to clinical symptoms.

Presenting Symptoms	Number of patients	%
Chronic respiratory disease	44	28.3
Chronic respiratory disease Foul smelling diarrhoea, Failure to thrive	57	36.4
Failure to thrive	19	12.5
Short stature	23	14.9
Gastroesophageal reflux	4	2.6
Rectal prolapse	4	2.6
Pseudo-Bartter Syndrome	2	1.3
Jaundice with hepatomegaly	1	0.7
Sinusitis	1	0.7

Table II. The distribution of sweat chloride in the different age groups.

Age Group	Patients referred for sweat test	Patients with sweat chloride >60meq/L	% of patients with sweat chloride >60meq/L
2-4 months	36	4	11.1
4-12 months	264	18	6.5
1-2 years	571	52	9.1
2-3 years	175	26	14.8
3-5 years	166	16	9.6
5-7 years	175	18	10.4
7-10 years	138	15	10.8
10-12 years	35	4	11.4
12-18 years	05	3	60

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