Genotype–phenotype correlation of pancreatic function in children with cystic fibrosis

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Objective: To assess the level of fecal elastase-1 (FE-1) in relation to CFTR gene mutations in patients with cystic fibrosis (CF).

Materials and Methods: This study included 49 patients (23 boys) with CF, mean age 8.43±0.99 years. CF was established on the basis of a positive sweat test (Macroduct, Wescor USA) and the results of molecular genetic analysis. Genetic diagnosis was realized for 46 CFTR mutations in genetic laboratories from Germany and France. To detect pancreatic insufficiency (PI) was defined FE-1 (Schell Biotech, Germany). The values of FE-1 in the range 0–100 μg/g, are characteristic for severe exocrine PI, 100–200 μg/g for moderate exocrine PI, and >200 μg/g for pancreatic sufficiency.

Results: F508del mutation was revealed in 73.33% cases (40.0% – homozygotes), known genotype with other mutations was found in 18.26% cases. Low values of FE-1 (7.89±3.70 μg/g) confirmed exocrine PI in 81.64% patients with CF. PI with FE-1 of 2.90±0.78 μg/g was confirmed in 100% children with homozygous state of F508del mutation. F508del mutation in heterozygous state caused decreased levels of FE-1 (33.69±19.34 μg/g). Only 5.88% patients with CF F508del heterozygous were pancreatic sufficient and other 11.7% cases were moderate PI. Non-F508del CFTR mutations determined FE-1 levels of 218.64±64.87 μg/g, with PI in 57.89% patients.

Conclusion: The F508del mutations in homozygous state were associated with severe pancreatic exocrine insufficiency in all patients. Heterozygous state of mutation F508del requires association with another mutation and in most cases led to pancreatic enzyme deficiency. Non-F508del CFTR mutations are not obligatory associated with PI.

Intestinal inflammation is present, in varying degrees, in cystic fibrosis (CF).

The cause of inflammation is unclear but likely multi-factorial. The primary aim was to define the stool calprotectin and S100A12 levels as markers for intestinal inflammation in CF. The secondary aim was to define the relationship between intestinal inflammation and pancreatic enzyme therapy (PERT).

Methods: Stools were collected in children with CF for calprotectin and S100A12 measurement. Comparisons were made to levels in healthy children (HC) and children with active inflammatory bowel disease (IBD). Pancreatic function status (sufficient [PS] or insufficient [PI]) and PERT dose were determined.

Results: 39 CF patients (median [range] yrs: 3.5 [4–18]), 31 IBD patients (3.3yrs [2.4–16]) and 30 HC (3.6yrs [2.2–15.5]) were recruited. CF patients had significantly higher stool calprotectin levels compared with HC (median = 71.9 μg/g; 30.5 mg/kg; p<0.005), but lower than in IBD (median = 1265 mg/kg; p<0.0001). Higher stool calprotectin levels were seen in those with PI (n=35) than in those with PS (n=4) (median = 92.2 μg/g; p=0.037). There was no significant difference in stool S100A12 levels between CF and HC (median = 0.4 μg 1.2 mg/kg; p>0.05) but stool S100A12 was significantly raised in IBD (median = 55.2 mg/kg; p<0.05) compared to both CF and HC. There was no correlation between stool calprotectin levels and PERT dose (r=−0.08; p=0.6).

Conclusion: Stool calprotectin but not S100A12 levels were raised in CF, especially PI patients. There was no association between PERT dose and intestinal inflammation. These data may provide insight into the intestinal inflammatory pathways involved in CF.

Intestinal inflammation in CF: stool markers and correlation with pancreatic enzymes

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Plasma citrulline levels in cystic fibrosis patients

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Background and Objective: The small intestine is one of the main sites of cystic fibrosis (CF) manifestations and non-pancreatic intestinal factors are suggested to contribute to fat malabsorption. Recent findings suggest that the small bowel mucosa of CF patients frequently demonstrates inflammatory changes. Citrulline is a non-protein amino acid synthesized in the small intestine and its plasma levels have been proposed as a reliable intestinal marker in various conditions. The objective of the present study was to investigate the value of plasma citrulline levels as a marker of intestinal inflammation in cystic fibrosis (CF) patients.

Methods: Thirty-six stable CF patients (age range 13 to 28 years) without overt gastrointestinal symptoms and 36 age-matched controls were included in the study. Plasma citrulline levels were measured by ion-exchange high performance liquid chromatography. Possible relationship of plasma citrulline levels to the nutritional status of CF patients was also studied.

Results: Plasma citrulline levels did not statistically differ between CF patients and age-matched controls (38±7 μmol/L and 39±11 μmol/L respectively). Nine patients were malnourished while 27 patients had normal nutrition. Comparison of plasma citrulline levels between patients with malnutrition and patients with normal nutrition did not reveal any differences, either (37±7 and 38±8 μmol/L respectively).

Conclusion: Plasma citrulline did not appear to be a sensitive marker of intestinal inflammation in stable CF patients. The presence of malnutrition did not affect plasma citrulline levels and our results agree with previous reports in conditions other than cystic fibrosis.