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Fecal Elastase 1, Serum Amylase and Lipase Levels in Children with Cholestasis

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Key Words
Fecal elastase 1 · Amylase · Lipase · Biliary atresia · Progressive familial intrahepatic cholestasis · Byler disease · Alagille syndrome · Choledochal cyst · Exocrine pancreatic function

Abstract
Background/Aim: The pancreatic functions of children with cholestatic liver diseases were unclear. Due to anatomic vicinity and common ontogenic origin, hepatobiliary disorders of infancy may also affect pancreatic function. The aim of the study was to evaluate the exocrine pancreatic function and common pancreatic function tests in children with cholestatic disorders. ***Methods:*** In 40 children with cholestasis, fecal elastase 1 (FE1) concentrations were measured. Serum amylase and lipase values were tested. The diagnoses included 32 patients with extrahepatic cholestasis (biliary atresia (BA) and choledochal cyst), and 8 patients with intrahepatic cholestasis (progressive familial intrahepatic cholestasis and Alagille syndrome). None had renal insufficiency or clinical symptoms/signs of acute pancreatitis. ***Results:*** All the patients had normal FE1 (>200 μg/g). Nineteen percent (7/37) had elevated serum amylase levels (>100 U/l). Thirty-two percent (12/37) had elevated serum lipase levels above the normal (>120 U/l). Seventy-three percent (8/11) of BA patients with bilirubin >2 mg/dl had elevated serum lipase levels compared to 18% (3/17) with bilirubin ≤2 mg/dl ($p = 0.0036$). None had detectable pancreatic abnormality on ultrasonography and magnetic resonance images. ***Conclusions:*** None of the cholestatic children in this study had exocrine pancreatic insufficiency as detected by FE1. Hyperamylasemia and/or hyperlipasemia were frequently found. In children with BA, those with impaired biliary excretion tended to have elevated serum pancreatic enzymes as compared with those who had no jaundice. A decreased hepatic metabolism may be the cause.

Introduction

The causes of childhood cholestasis are diverse. Some result from pathological processes affecting the bile ducts, such as biliary atresia (BA) and choledochal cyst [1], and some are related to genetic mutations, such as progressive familial intrahepatic cholestasis (PFIC) and Alagille syndrome [2]. Since the pancreas is anatomically adjacent to and probably shares a common ontogenic origin with the hepatobiliary system [3, 4], children with these cholestatic diseases may have exocrine pancreatic insufficiency (EPI).

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Table 1. Clinical characteristics of the 40 children with cholestasis

Diagnosis	Number of cases				Serum total bilirubin (mg/dl) median (range)
	total	jaundice	failure to thrive	chronic diarrhea	
Extrahepatic disorders					
BA	31	11	5	1	1.0 (0.3–27.4)
Choledochal cyst	1	0	0	0	0.3
Intrahepatic disorders					
PFIC					
FIC1 gene defect	4	3	3	2	3.3 (0.8–11.9)
BSEP gene defect	1	1	1	1	2.2
MDR3 gene defect	1	1	0	0	3.1
No known gene defects identified	1	1	0	0	23.6
Alagille syndrome	1	1	0	0	4.0

Chronic diarrhea is frequently observed in cholestatic patients. A decreased bile acid excretion with subsequent fat malabsorption is a reasonable explanation [5], but EPI may also lead to chronic diarrhea. However, little was known about the exocrine pancreatic function in children with cholestatic disorders. This is likely caused by the fact that the direct pancreatic function tests, which are performed by duodenal intubation and stimulation with secretin-cholecystokinin or secretin-ceruletide [6], are time consuming, invasive and uncomfortable, especially in young children.

Elastase 1 is a pancreatic enzyme and it is not degraded during intestinal passage [7]. Measurement of fecal elastase 1 (FE1) concentration is relatively simple and noninvasive. It has been reported to be a sensitive screening test for severe EPI [8–10]. In addition, the adult reference value for FE1 of greater than 200 μg/g feces can be applied to infants older than 2 weeks [11]. The aim of the present study was to investigate the exocrine pancreatic function and common pancreatic function tests in children with different causes of cholestasis by measurements of FE1 and serum amylase and lipase levels.

Patients and Methods

A total of 40 children (17 boys, 23 girls) with cholestatic diseases were enrolled. Informed consents were obtained from their parents. The study has been approved by the Institutional Review Board. The ages of the subjects ranged from 4 months to 11.2 years (median, 2.4 years). The diagnoses included 32 patients with extrahepatic cholestasis: BA in 31 and choledochal cyst in 1; and 8 patients with intrahepatic cholestasis: PFIC in 7 and Alagille syndrome in 1. The clinical characteristics of these children are listed in table 1.

None of the subjects had clinical symptoms of acute pancreatitis, such as nausea, vomiting, or abdominal pain. None of them had renal insufficiency. All had received an abdominal ultrasonographic examination. Some patients, including 18 with BA, 5 with PFIC, and 1 with choledochal cyst, had received an abdominal magnetic resonance image examination.

Among the 31 children with BA, 30 had undergone hepatic portoenterostomy at an age ranging from 21 to 98 days, before this study. None had received liver transplantation. Eleven of the 31 with BA had jaundice (total bilirubin >2.0 mg/dl) at the time of the study. Among the 20 jaundice-free children, none had insufficient growth with a body weight below the 3rd percentile and none had chronic diarrhea.

Six of the 7 children with PFIC had gene defects described in our previous reports [12, 13]. Among them, 4 had a defective familial intrahepatic cholestasis 1 (FIC1) gene, 1 had a defective bile salt export pump (BSEP) gene, 1 had a defective MDR3 gene, and no known gene defects were identified in the remaining 1 case.

Among the 4 with FIC1 gene deficiency, 2 had received orthotonic liver transplantation and 1 had undergone biliary diversion before the study. In the child receiving biliary diversion, jaundice persisted after the operation. In the child with choledochal cyst, the study was performed before surgical resection of the cyst.

Samples of feces were collected from each patient and were stored at –40°C till analysis. All fecal samples were examined within 1 year after collection. Determination of FE1 was performed with an enzyme-linked immunosorbent assay, based on two monoclonal antibodies against human pancreatic elastase 1 (Schebo Biotech, Giessen, Germany). Samples of serum were also obtained from 37 of the 40 subjects for the detection of amylase and lipase, which were measured by an enzymatic method (Ortho-Clinical Diagnostics Inc., Rochester, N.Y., USA). Three children with BA had no result of serum amylase and lipase. Normal values are >200 μg/g for FE1 [8–11], <100 U/l for serum amylase, and <120 U/l for serum lipase [14].