Efficiency of pancreatic duct stenting therapy in children with chronic pancreatitis

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Background: Chronic pancreatitis (CP) is a rare disease in childhood. Although ERCP is commonly performed in children, the effect of pancreatic duct stenting therapy in children with CP is unknown.

Objective: To investigate the efficacy of pancreatic duct stenting in children with CP.

Design: Retrospective analysis.

Setting: National referral center.

Patients: A total of 208 children with CP hospitalized between 1988 and 2012.

Interventions: ERCP with pancreatic duct stenting.

Main Outcome Measurements: Results of endoscopic therapy and number of pancreatitis episodes per year before and after treatment.

Results: A total of 223 pancreatic duct stenting procedures were performed in 72 children. The median number of stent replacements was 3 (range 1-21). A statistically significant decrease in the number of pancreatitis episodes per year was observed: from 1.75 to 0.23 after endoscopic treatment ($P < .05$). Pancreatic duct stenting was performed more frequently in patients with hereditary pancreatitis (61.5%) and in children with CP and anatomic anomalies of the pancreatic duct (65%; $P < .05$).

Limitations: Retrospective analysis with the assessment of adverse events based on medical history.

Conclusion: Pancreatic duct stenting therapy is a safe and effective procedure in children with CP. This therapy should be recommended especially for children with hereditary pancreatitis and patients with anatomic anomalies of the pancreatic duct. (Gastrointest Endosc 2014;80:1022-9.)

Chronic pancreatitis (CP), characterized by inflammation-induced, continuous damage to the structure and/or function of the pancreas, is rare in childhood. In the adult population, the majority of patients have alcohol-induced CP. The prevalence of CP ranges from 20 to 200 per 100,000 in the general population and is increasing because of the influence of environmental factors.[1-3] Although the incidence of CP in the pediatric population is low, pancreatitis might cause significant morbidity, even mortality, in children.[4] The pathogenesis of CP in children is poorly understood. The etiology of CP in children is varied and includes gene mutations, anatomic anomalies, metabolic disorders, and others.[3,5-7]

Because of the infrequent occurrence of CP in childhood, the clinician may be unfamiliar with optimal diagnostic and management strategies. ERCP has been used

Abbreviations: AIP, autoimmune pancreatitis; ANCA, anti-neutrophil cytoplasmic antibodies; CFTR, cystic fibrosis transmembrane conductance regulator; CP, chronic pancreatitis; Ig, immunoglobulin; PRSS1, cationic trypsinogen/serine protease 1; SPINK1, serum protease inhibitor Kazal type 1.

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for many years in adults to investigate pancreaticobiliary diseases. At present, endoscopic drainage of pancreatic ducts is accepted as a viable option of pain management in severe CP and, in the majority of cases, precludes the need for surgery. The pancreatic ducts can be drained by introduction of a stent, which may help reduce pain and relieve obstructions. When a stricture of the pancreatic duct is present, long-term management is associated with the necessity of exchanging the stent. The indications for ERCP in children are similar to those in adults, but the relative frequency is different. Evaluation of CP is the most common indication for ERCP in children.[8,9]

Although experience with ERCP in children is growing, the effect of pancreatic duct stenting procedures in children with CP is unknown. There is a lack of well-documented safety information and accepted indications for ERCP in children.[10] Prior pediatric studies have shown the diagnostic and therapeutic significance of ERCP, but the effect of pancreatic duct stenting therapy in children with CP has not been systematically evaluated. Most of the information is found in individual case reports or small case studies.[4,10-13] To date, no study has assessed the long-term effect of stenting therapy in children.

The Children's Memorial Health Institute in Warsaw, a leading national pancreatic center, admits the majority of Polish children with CP. Our group of children with CP (over 200 patients) is one of the largest single-center groups in the world. Thus, investigations of endoscopic therapy in this group could deliver essential findings for medical practice.

In our retrospective review, we assessed the contribution of pancreatic duct stenting therapy to the subsequent management of children with CP. The aim of the study was to investigate the efficacy of endoscopic treatment (pancreatic duct stenting) in children with CP.

Take-home Message

- Pancreatic duct stenting therapy is a safe and effective procedure in children with chronic pancreatitis. The adverse event rates are similar to or lower than those observed in adults.
- We recommend this therapy especially for children with hereditary pancreatitis and patients with anatomic anomalies of the pancreatic duct.

METHODS

A total of 208 children with CP hospitalized at the Department of Gastroenterology, The Children's Memorial Health Institute (Warsaw, Poland) between 1988 and 2012 were enrolled in the study. The protocol of the study was approved by the local ethics committee (38/KBE/2012).

The inclusion criteria were as follows: age $\leq$18 years, diagnosis of CP verified by imaging methods (US scan, CT, MRCP, or ERCP), and observation $\geq$12 months from the time of the first visit. Children with acute pancreatitis, in whom CP was not confirmed according to the Cambridge classification system,[14] were excluded from the study.

All patients had prior radiographic studies, including abdominal US, CT, and/or MRCP. Clinical data were recorded and analyzed. Family history, laboratory test results, results of imaging studies, and results of surgical and endoscopic procedures were documented. All patients were monitored from their first pancreatitis attack. The first episode of acute pancreatitis, diagnosed on the basis of serum amylase activity $\geq$3 times over the upper normal range (normal 0-82 U/L), elevated urine amylase activity (0-380 U/L), and serum lipase activity $\geq$5 times over the upper normal range (0-210 U/L), was regarded as the onset of CP. Disease activity was established based on the following parameters: age at disease onset, number of pancreatitis episodes, changes found on imaging (US scan and/or MRCP), changes in ERCP according to the Cambridge scale,[14] results of endocrine and exocrine pancreatic function tests, nutrition status (body mass index, Cole Index), and endoscopic and surgical procedures. Additionally, all children were screened for post-ERCP pancreatitis.

Moreover, all participants were screened for gene mutations predisposing to CP: *CFTR* (cystic fibrosis transmembrane conductance regulator; OMIM (Online Mendelian Inheritance in Man) 602421; F508del, CFTRdele2.3, polyT variant, exons 9, 10, and 11 sequencing), *PRSS1* (cationic trypsinogen/serine protease 1; OMIM 276000; sequencing of all coding regions), and *SPINK1* (serum protease inhibitor Kazal type 1; OMIM 167790; N34S, IVS3+2T>c, exon 3 sequencing). Molecular analysis was performed at the Department of Medical Genetics of the Institute of Mother and Child, Warsaw, Poland (between 1988 and 2010) or Genomed S.A., Warsaw, Poland (2011-2012).

Additionally, 129 children were examined for the presence of autoimmune pancreatitis (AIP); the levels of immunoglobulin (Ig) G4 and gamma-globulins were determined, and the tests for anti-tissue antibodies: anti-nuclear antibodies, anti-smooth-muscle antibodies, anti-mitochondrial antibodies, anti-neutrophil cytoplasmic antibodies (ANCA, both p-ANCA and c-ANCA), and anti-histone antibodies were conducted. All tests were performed at the Department of Pathology of our institution. AIP was diagnosed according to the International Association of Pancreatology guidelines, that is, on the basis of immunologic criteria (presence of antibodies: IgG4 and autoantibodies), radiologic criteria (swelling of the pancreatic head and changes in the pancreatic duct), and response to corticosteroid therapy. However, we did not consider the morphologic criterion (inflammatory infiltration of biopsy specimen) because none of our patients had a pancreatic biopsy.

Patients were divided into 5 groups, depending on the etiologic factor: group 1, patients with hereditary pancreatitis (*PRSS1* gene mutation, n = 26); group 2, patients with