Population Screening for Biliary Atresia

Biliary atresia (BA) is a progressive, obstructive cholangiopathy which is the leading cause of liver transplantation in children. Early detection of BA is essential as a Kasai hepatoportoenterostomy ("Kasai procedure") can slow progression of hepatic fibrosis associated with BA which potentially allows a patient to be older when liver transplantation is needed. The Kasai procedure is most beneficial when performed before 45 days of age. Thus, it should be of utmost importance to develop accurate population screening methods allowing for the early diagnosis of BA. The authors of this study evaluated the feasibility of a BA screening program at a large United States Intermountain West healthcare system.

The authors utilized data from 4 of the 33 included healthcare system hospitals over a 15-month period. Newborns born 35 weeks or older and who were admitted to the newborn nursery were included, and all infants admitted to the newborn intensive care unit (NICU) were excluded. Infants who were supposed to undergo total bilirubin level serum testing had their orders modified to include a fractionated bilirubin level which included a direct bilirubin level. Any infant with an elevated direct bilirubin level was identified, and the parents or the child's primary care provider subsequently was contacted so that consent could be obtained to check a second fractionated bilirubin level. All infants with a second elevation of the direct bilirubin level were then referred to the pediatric hepatology clinic at the tertiary children's hospital involved in this study. A direct bilirubin level was considered elevated if it was ≥ 0.6 mg/dL.

In total, 12,276 newborns were eligible for this study, and 98.2% of these infants (12,055) underwent direct bilirubin testing. An elevated direct bilirubin level was identified in 100 infants for which 6 were excluded due to either underlying medical or social issues. Another 4 infants were lost to follow up. The remaining 90 infants were available to be screened with a second fractionated bilirubin level. The families of 70 infants could not be contacted or declined study participation. The primary care physicians of these infants were contacted so that follow-up fractionation of the total bilirubin level could be recommended. Only 20 infants underwent actual second screening of their direct bilirubin level for which an elevated direct bilirubin level was still present in 15 infants. Those 15 infants were evaluated by pediatric hepatology, and no BA cases were identified.

There was no statistically significant difference in sex or birthweight between infants with normal and elevated direct bilirubin levels although infants with an estimated gestational age greater than 39 weeks were significantly more likely to have an elevated direct bilirubin level. The authors note that during the study period, two newborns born at participating study hospitals were eventually diagnosed with BA. However, both infants had been admitted to the NICU and initially were excluded from study participation.

Although this feasibility study did not identify any newborn infants with BA, it did demonstrate the potential for BA screening in a large healthcare system. The study process used to screen for BA has the potential to be applied in other healthcare systems as well as with state newborn screening.

Guthery S, Jensen M, Esplin M, O'Brien E, Krong J, Srivastava R. Feasibility of biliary atresia newborn screening in an integrated health network. Journal of Pediatric Gastroenterology and Nutrition 2024; 79: 954-961.

Long-Term Outcomes in Pediatric Ulcerative Proctitis

Ulcerative proctitis in children is a variant of ulcerative colitis, but unlike the adult population, treatment guidelines for pediatric ulcerative proctitis are not clear. The authors of this study performed a retrospective study to determine the disease course and treatment outcomes for pediatric patients with ulcerative proctitis.

Data from this study came from 10 pediatric treatment centers throughout Japan during the period between 2013 and 2022. All included

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patients were under 18 years of age and had a diagnosis of ulcerative colitis. Patients with inflammatory bowel disease (IBD) unclassified, monogenic IBD, and no IBD follow up were excluded. Patient demographics, clinical course, laboratory testing, and treatments for ulcerative proctitis were determined. The Pediatric Ulcerative Colitis Activity Index (PUCAI) and the partial Mayo Endoscopic Score were utilized to assess disease. Ulcerative colitis was diagnosed per the Revised Porto Criteria, and ulcerative proctitis was defined as inflammation present from the rectosigmoid region extending to the anorectal junction.

A total of 54 patients were included in the study. The median age at diagnosis was 12 years, and 44% of patients were male. Median PUCAI at time of diagnosis was 20 (remission score was considered less than 10) with 62% of patients having a partial Mayo Endoscopic Score of 2 at diagnosis. The authors noted that C-reactive protein and albumin levels were typically normal at time of ulcerative proctitis diagnosis. The most common treatment after initial diagnosis was 5-aminosalicylic acid therapy (5-ASA) given as a suppository (40%). Oral 5-ASA therapy was used in 20% of patients while a combination of oral 5-ASA and topical 5-ASA therapy (suppository or enema) was used in 25% of patients. Long-term disease remission occurred in 95% of patients (62% during initial therapy) although 93% of patients required modification of therapy. Nonadherence to therapy occurred in 39% of patients.

Control of ulcerative proctitis symptoms using 5-ASA therapy monotherapy occurred in 63% of cases while 30% of patients had disease remission followed by symptom breakthrough requiring immunosuppression therapy. No initial disease remission with a subsequent need for immunosuppression occurred in 7% of cases. Patients requiring immunosuppression were statistically more likely to require more colonoscopies, have inflammation extending above the peritoneal reflection or rectosigmoid region, or have inflammation eventually extending past the left side of the colon compared to patients who responded to 5-ASA monotherapy. Patients who were unable to achieve disease remission after 3 months were more likely to require biologic therapy.

This study demonstrates that 5-ASA therapy appears to control ulcerative proctitis in most pediatric patients. However, disease extension, need for frequent diagnostic colonoscopies, and prolonged time to disease remission appear to be risk factors for requiring a step up in medical therapy. This study occurred in Japan, and similar studies are needed in other countries to see if similar outcomes to therapy exist in pediatric patients with ulcerative proctitis internationally.

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