Serologic Markers for Celiac Disease in Young Children

Celiac disease (CD) is an autoimmune disease associated with small intestinal damage (villous atrophy and lymphocytic infiltration) in response to gluten ingestion. Although esophagogastroduodenoscopy (EGD) with duodenal biopsy is considered the "gold standard" test for confirming CD, the tissue transglutaminase IgA antibody titer (TTG IgA) is a highly sensitive and specific serum test for CD screening. National guidelines (such as from the Celiac Disease Foundation) do not recommend TTG IgA screening before 2 years of age because of concerns about testing sensitivity in that age group. The authors of this study tested this recommendation by reviewing medical records of children from 3 tertiary children's hospitals in the United States. Two of the hospitals had retrospective records reviewed as far back as 20 years while the third hospital utilized a prospective database of children with villous atrophy diagnosed by EGD. All included patients were evaluated for diagnostic criteria for CD (including serologic markers of disease and duodenal biopsy findings), resolution of gastrointestinal symptoms on a gluten-free diet, and normalization of serologic markers for CD while on a gluten-free diet. Thus, patients with CD associated with positive serologic markers and positive duodenal biopsy findings were compared to a control group of children with duodenal biopsies consistent with CD but who had negative serologic findings and no gluten exposure or no response to a gluten-free diet.

A total of 150 children were included in the study for which 127 had CD and 23 belonged to the control group. The median age at time of duodenal biopsy was 18 months (range 3 – 24 months) with most children having a diagnosis of failure to thrive. Biopsies demonstrated intraepithelial lymphocytosis in 3% of children, partial villous atrophy in 45% of children, and total villous atrophy in 52% of children. Various CD serologic markers were ordered for these patients with TTG IgA being the most common test although other testing types included endomysium IgA, anti-gliadin IgA with / without IgG, and deamidated gliadin protein IgA with / without IgG. Of the 127 children with CD, 115 underwent TTG IgA testing for which 112 patients (97.5%) had elevated TTG IgA titers with the remaining 3 patients having positive TTG IgG titers. IgA deficiency was present in 5.5% of patients with CD although all such children had some type of positive IgG testing (such as TTG, anti-gliadin, or deamidated gliadin protein). Alternatively, 19 of the 23 children in the control group had TTG IgA testing performed, and all tests were negative. The remaining 4 children in the control group consisted of one patient with negative endomysium IgA testing and 3 children with no other serologic testing performed. When all patients with TTG IgA testing were compared, patients with CD were significantly older (19 months versus 15 months, $P=0.001$) and had a higher TTG IgA level (7.4 times the upper limit of normal versus 0.3 times the upper limit of normal, $P<0.001$).

This study, based on retrospective data, seems to indicate that TTG IgA testing may be an appropriate screen for CD in children younger than 2 years of age. The authors point out that IgG antibody testing may be indicated for those young patients with negative TTG IgA testing but with symptoms of CD.

Khan M, Silvester J, Sparks B, Hintze Z, Ediger T, Larson J, Hill I, Absah I. The utility of IgA-based serologic markers in diagnosing celiac disease in children 24 months of age or younger. Journal of Pediatrics 2020; 224: 158-161.

Early Feeding in Acute Pancreatitis

Although acute pancreatitis (AP) in children typically is caused by different etiologies compared to adults, it still can be associated with severe disease complications, including the risk of mortality. There is evidence in the adult medical literature that early feeding in AP is safe and beneficial; however, no similar studies have been done in children. The authors of this study (from 3 tertiary children's hospitals in Australia and Israel) performed a randomized, controlled trial over 13 years looking at the efficacy and safety of early feeding for children with AP. AP was defined as consisting of abdominal pain consistent with AP, serum amylase and/or lipase ≥ 3 times the upper limit of normal, and abdominal imaging demonstrating AP. Patients

with AP associated with organ failure or AP due to biliary obstruction, autoimmune pancreatitis, or trauma were excluded from the study. These pediatric patients were prospectively divided into 2 groups: 1) patients with AP who were fed a low-fat diet only when their abdominal pain resolved (while kept on IV fluid initially), when their amylase and/or lipase levels declined, or per the discretion of the providing physician and 2) patients with AP who were given an unrestricted diet as soon as possible (less than 24 hours after presentation). Patients in the unrestricted diet group were given nasogastric or nasojejunal tube feeds if they could not eat orally in less than 24 hours. All patients underwent chart review as well as twice daily Wong-Baker Faces Pain Rating Scale scoring. Additionally, all patients were monitored in terms of analgesic use, weight, daily caloric intake, and estimated energy requirement (EER). The primary outcome of the study was time to hospital discharge based on no pain noted on the pain scale, no analgesic use, and the patient being able to reach 75–100% of EER.

In total, 33 children between 2 and 18 years of age were recruited into the study for which 15 patients (45%) were in the initial fasting group and 18 patients (55%) were in the early feeding group. No difference existed between the two groups in regards to age, weight, serum amylase and lipase levels, and pain scores at presentation. The median time to starting feeds was significantly shorter in the early feeding group (19.3 hours) compared to the fasting group (34.7 hours). Additionally, there was an earlier ability of the early feeding group to reach at least 50% of and greater than 75% of EER although the difference was not significant. Only one patient in the early feeding group required partial use of nasogastric feeds initially and no patients in either group required long term nasogastric or nasojejunal feeds. Both groups were similar in regards to the time required before being pain free, weight throughout hospital admission, and final amylase and/or lipase levels. Of note, two patients in the initial fasting group were re-admitted to the hospital for AP, and only one patient in the early feeding group was re-admitted to the hospital for diarrhea not related to AP. At follow up (median of 49 days), patients in the early feeding group had a significantly higher weight compared to the early fasting group which had a median loss of weight.

This study demonstrates that early feeding in uncomplicated pediatric AP is safe and effective and may have better long-term outcomes in regards to weight after hospital discharge. An early feeding regimen also requires less intervention and may reduce unnecessary healthcare costs.

Ledder O, Duvoisin G, Lekar M, Lopez R, Singh H, Dehlsen K, Lev-Tzion R, Orlanski-Meyer E, Shteyer E, Krisnan U, Gupta N, Lemberg D, Cohen S, Ooi C. Early feeding in acute pancreatitis in children: a randomized controlled trial. Pediatrics 2020; 146(3): e20201149.

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