Determination of the Frequency of Findings of Co-Morbidity in Pediatric Patients Undergoing Endoscopy for Diagnosis of Celiac Disease.

Thomas Wallach, MD, PGY2
CUMC, CHONY Pediatrics.

Introduction

The most recent meeting of the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) published new guidelines suggesting that endoscopic biopsy, previously the gold standard in diagnosing children with celiac disease, could be omitted given the appropriate clinical setting and serological results. This recommendation stands in opposition to the prevailing practice, based on the 1990 ESPGHAN guidelines, suggesting that a minimum of 3 small bowel biopsies (SBB) were necessary to confirm a diagnosis of celiac regardless of serologic markers or symptomatic presentation.[i]

The basis for this modification stems from several factors, the first being the increase in perceived prevalence of Celiac (initially thought to be a rare condition of people of Scandinavian descent, recent estimates suggest approximately 1%[ii] of the broader population suffers from the condition), and the second being the advancements in serologic diagnosis in the intervening 20 years. Most notable diagnostic tools including tissue trans-glutaminase (tTG) and anti-diamidated gliadin peptides (DGP), which have reported sensitivities and specificities >95%.[iii,iv] In addition, recent use of celiac-associated genotype markers such as HLA-DQ2 and/or HLA-DQ8 have provided sensitivities in excess of 96%.[v] In conjunction, the use of these tests allows for highly sensitive and specific diagnosis without the use of endoscopic or capsule investigation and SBB, and seemingly suggests that endoscopy and SBB are no longer necessary as the gold standard of Celiac diagnosis. Early studies in the wake of the 2012 ESPGHAN meeting have shown that the guidelines provide diagnostic accuracy of 97% or higher in symptomatic children using a "triple test" consisting of tTGA, anti-endoymsial antibody (EMA) and HLA-DQ2/DQ8 typing in opposition to the previous gold standard of SBB.[vi]

However, while the ESPGHAN guidelines may avoid invasive procedures in a subset of children who almost certainly have celiac disease, the drawbacks may be to miss other endoscopic findings such as Eosinophilic Esophagitis (EoE), gastritis, H. Pylori infection, reflux esophagitis, and rare lymphocytic gastritis. A recent preliminary study suggests that up to 10% of children undergoing endoscopy for diagnosis of Celiac Disease are found to have co-incident conditions.[vii] In particular, EoE has been shown to coexist in children with Celiac Disease in children with a diagnosis of Celiac disease increasing the likelihood of a diagnosis of EoE by nearly 50%.[viii] EoE is a diagnosis that can only be confirmed via endoscopy, with guidelines recommending 2-4 biopsies minimum[ix] (although some studies suggest 6-8 are necessary[x]). These biopsies must show one area of >15 eosinophils per HPF in order to confirm (along with symptoms) a

diagnosis of EoE. In the course of endoscopy for confirmation of Celiac Disease, these biopsies are typically taken, but in varying numbers due to some differences in the literature and practice variation.

Given the rapid increase in diagnosed cases of both Celiac Disease and EoE, faster, more accurate diagnosis is clearly a priority, however given the high frequency with which co-incident conditions are established by endoscopic evaluation and SBB, further investigation is required to determine what would be missed by adjusting to the 2012 ESPGHAN guidelines. The goal of our study is to assess the frequency with which co-morbid conditions (specifically EoE) are discovered in a large pathology series of SBB obtained from patients undergoing biopsy for Celiac Disease.

Methods:

We will undertake a retrospective analysis of a large database of pathology results collected by outpatient gastroenterologists and reviewed by a send-out pathology lab based in Texas. This database has been stripped of all patient-identifying information. The database comes with information of the state from which the sample came, age of the patient, presence of other conditions on review of pathology, and confirmation of celiac. This information will be used to determine the frequency with which co-morbidities, specifically EoE, occur with endoscopy for confirmation of Celiac Disease.

Data Analysis:

The core facet of our study will be to provide incidence rates of co-morbidities in the sub-population of children undergoing endoscopy for Celiac Disease, further broken down as well into the specific incidence of EoE. We will then use chi-square test on proportion to confirm true statistical variation from what is currently perceived to be the frequency of diagnosis of co-morbidity. Given that current estimates used to support the need for endoscopy suggest that 10% of endoscopy undertaken to confirm celiac finds co-morbid conditions, we believe that a frequency of less than 5% would suggest that implementation of the ESPGHAN guidelines will not result in the missed diagnosis of a significant quantity of disease. Seeing as our sample size is approximately 1000 pediatric patients, and given a power of 0.8 and a p value of 0.05, we will be able to determine a valid statistical effect if our frequency finding is less than 7.5%, allowing us to more than adequately show a frequency of 5% or lower.

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