Characterizing EGD biopsies of pediatric patients with celiac disease
IRB Protocol

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A. Study Purpose and Rationale

Celiac disease, a genetically determined immune-mediated enteropathy that often presents in childhood, affects roughly 1% of the population. However its prevalence has been increasing over the last couple of decades, attributable to both increased awareness of the disease and improvements in diagnostic methods. Last year, the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) published new guidelines for diagnosing celiac disease in children. Whereas endoscopic biopsy had previously been the gold standard (and currently remains so in the United States), the new guidelines obviate the need for endoscopic diagnosis if certain criteria are met. More specifically, if a patient has symptoms consistent with celiac disease (such as abdominal pain, diarrhea, , failure to thrive, and anemia, among many others), and has a positive tissue transglutaminase antibody titer > 10 times the upper limit of normal (in the setting of IgA immunocompetence), as well as a positive endomysial antibody test and positive haplotype associated with celiac disease (HLA DQ2 or DQ8), then the diagnosis of celiac disease can be made without a confirmatory biopsy.[1] These serological markers, if positive in aggregate, increase the sensitivity and specificity of diagnosing celiac disease to >98% and >96% respectively.[2]

These guidelines are a big step in avoiding endoscopies, which are invasive procedures and require sedation, in children who most likely have celiac disease. However, endoscopy may lead to findings that suggest an alternative diagnosis or additional diagnoses. Mucosal abnormalities in the upper gastrointestinal tracts of children with celiac disease have been described, though not extensively characterized. There are relatively small case series of children with celiac disease which have been shown to have lymphocytic gastritis[3,4] and superficial chronic gastritis.[5-7] Eosinophilic esophagitis and peptic ulcer disease have also been documented in children and young adults with celiac disease.[8,9] In a preliminary multicenter study, almost one quarter of patients diagnosed with celiac disease via EGD had additional, unexpected pathology, of which half were diagnoses that have known treatment that differs from celiac disease treatment.[10] Thus, this study suggests that about 12% of patients with celiac disease may have a co-morbid condition that requires additional treatment.

It is recommended that 4-6 biopsies of the descending duodenum are done to establish a diagnosis of celiac disease, and many pediatric gastroenterologists routinely do biopsies on all portions of the upper GI tract. Thus, we are in a unique position to better characterize the nature of upper GI inflammation in children with celiac disease, in comparison to children without celiac disease who have undergone biopsy for other reasons. Research in this area will help guide pediatric gastroenterologists to decide if endoscopy is indicated in children with suspected or established celiac disease.

References:

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B. Study Design and Statistical Analysis

This is a retrospective study of clinically symptomatic subjects who have undergone EGD for various reasons. Subjects will be divided into two groups: One group composed of subjects with newly diagnosed with celiac disease via EGD biopsy results, and a second group of subjects without celiac disease (based on their past medical history or their EGD results). In both groups, the prevalence of other diagnoses will be calculated. These alternate diagnoses are either concurrently made along with a diagnosis of celiac disease (in the first group) or as a stand alone diagnosis (in the second, or control, group).

Each diagnosis will be analyzed via chi-square analysis for two groups (celiac vs. control). Effect size will be calculated for each diagnosis in both groups, as well as for aggregates of diagnoses in both groups. Types of diagnoses will also be analyzed together; for example diagnoses with known treatment that differs from celiac disease treatment will be considered "major alternate diagnoses" and be analyzed together in the celiac vs. control group. The prevalence of each diagnosis in the celiac group will be compared to epidemiologic data of that diagnosis in the general population, when known. Also, from data drawn from the literature and careful consideration of risk/benefit ratio of undergoing an EGD, a prevalence increase of at least 6% in the celiac group, compared to the control group, will be used in this study to determine if a given diagnosis is worth undergoing EGD for all patients presenting with initial symptoms and serology consistent with celiac disease.

C. Study Procedure.

There are no procedures associated with this study.

D. Study Drugs.

There are no drugs associated with this study.

E. Medical Device.

There are no medical devices associated with this study.

F. Study Questionnaires.
There are no questionnaires associated with this study.

G. Study Subjects
Study subjects include all children 0-18 years of age who have presented with symptoms of abdominal pain warranting an EGD, at the discretion of the practicing pediatric GI physician. Subjects include patients who have a history of celiac disease and have had a repeat EGD. Subjects are from the United States only and who have had EGD performed from 2001 to 2013.

H. Recruitment of Subjects
Subjects are identified retrospectively from a specific pathology laboratory company that analyzes biopsies from all over the country. Any subject who has had EGD biopsies analyzed through this laboratory, and is within the correct age range is pulled into the data set. Subject data includes their age, the state the procedure was performed in, the date of the procedure, presenting symptoms that led to the EGD, the anatomical location of the biopsies done, biopsy diagnoses, and if the patients had a past history of celiac disease.

I. Confidentiality of Study Data
The data is completely de-identified, and subjects do not have associated names or initials, birthday, or city that the procedure was performed in. The code number key is held by a researcher in Texas, and not by the researchers at Columbia who are analyzing the data set. The data is securely stored on Columbia University Medical Center computers and/or encrypted, pass-coded flash drives.

J. Potential Conflict of Interest
There is no conflict of interest in this study.

K. Location of the Study
The subjects come from all over the United States. The data analysis is done at CUMC, through the pediatric GI department.