Prevalence of Celiac Disease in Patients with Irritable Bowel Syndrome

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A. Study Purpose and Rationale

Celiac disease is a syndrome characterized by small intestinal mucosal damage caused by gluten in wheat, barley, and rye in genetically susceptible individuals. The presence of gluten leads to self-perpetuating mucosal damage, where as the elimination of gluten results in full mucosal recovery. It can manifest as chronic diarrhea, abdominal pain, fat malabsorption (the so called classical presentation) as well as a spectrum of hematologic, immunologic, endocrine, dermatologic, neurologic, and musculoskeleal diseases. CD is considered a rare disease in the U.S. with the diagnosis made in one out of every 10,000 people. However, screening based on serology has revealed a prevalence rate as high as I in I 11. Such discrepancy is attributed to the lack of physician awareness and more occult, non-classical presentations. Early diagnosis of CD is important in preventing GI malignancies, lymphoma, and other autoimmune diseases. Our prior study on gender difference in celiac disease found women had longer duration of symptoms and often carried the diagnosis of irritable bowel disease (IBS) prior to diagnosis of CD. The question arises whether patients with CD are under-diagnosed partially because of being mislabeled as irritable bowel syndrome. Two studies from the UK on prevalence of CD in IBS have shown conflicting results in respect to this question. We are interested in studying the prevalence of CD in the IIBS population in US.

B. Study Design and Statistical Analysis

800 subjects will be enrolled. 400 subjects with diagnosis of IBS in the study arm and 400 matched controls without IEBS. The sample size is determined to be 352 (in each group) by chisquare test with the prevalence of CD in IBS as 4.7% (according to Sanders et al.) and an oc error of 5% and 0 of 10%. The prevalence of CD will be determined in both study and control groups. The difference between the two arms will be determined by a chi-square test.

C. Recruitment of Subjects

a. Study Arm

All patients with the diagnosis of irritable bowel syndrome at New York Presbyterian Hospital will be approached through their private physicians. Once patients have expressed interest in the study, they will be contacted by study investigators.

b. Control Arm

Matched controls will be recruited through physicians' offices as well as flyers distributed in New York Presbyterian Hospital.

c. Inclusion Criteria

i. Study Arm

Patients must have the diagnosis of IIBS satisfying the ROME criteria: at least 12 weeks (not necessarily consecutive) of symptom in the preceding 12 months satisfying 2 of the following:

- Pain is relieved with defecation
- Change in stool form (loose, watery, or pellet-like)
- Change in bowel frequency (diarrhea or constipation)

Other biochemical and structural diseases have been ruled out before diagnosis of IBS by completing a full physical exam, labs (CBC, chem -7, LIFT, TSH), flexible sigmoidoscopy for those age <50 and colonoscopy (flex sig + barium enema) for those >50.

ii. Control Arm

Subjects will be matched to the study subjects in age (± 5 years), gender, and race.

d. Exclusion Criteria

All subjects who started gluten free diet prior to study. Any possible history of IBS will be excluded from the control group.

D. Study Procedures

All subjects will have their blood drawn and samples analyzed for antigliadin antibody, antiendomesial antibody, and tissue transglutaminase antibody. Those with positive antibodies will be advised to undergo upper gastrointestinal endoscopy for intestinal biopsy, which is the gold standard of diagnosis of CD. Once celiac disease is proven by biopsy, patients will start on a gluten free diet which implies avoidance of wheat, rye, and barley. Patients will be monitored for 6 months for resolution of symptoms. The entire study is expected to complete within 2 years.

E. Medical Device

Esophagogastroduodenoscopy (EGD) will be performed on selected patients using the routine EGD endoscope. Subjects will receive light conscious sedation using either midazolam (versed) or meperidine (demerol). Patients' vital signs will be continuously monitored during the entire procedure. The oropharynx will also be numbed with a spray of topical anesthetics using lidocaine. Intestinal biopsies will be taken to document the presence of celiac disease.

F. Confidentiality

All study data will-be coded by a unique coding system. All data will be stored in a secure and locked location only accessible by the investigators.

G. Potential Conflict of Interest

The investigators of the study have no financial interest in the result of the study.

H. Locations of the Study

Study will be conducted at New York Presbyterian Hospital at both Columbia and Cornell campuses, Locations include doctors' offices and the endoscopy suites.

I. Potential Risks

The risks involved with blood draws include pain and extremely small risks of hematomas. Esophagogastroduodenoscopy (EGD) may be uncomfortable to some patients due to the natural gag reflex, however most tolerate it well using light conscious sedation and topical anesthetics. Conscious sedation may occasionally cause decreased respiratory rate. However, patients' vital signs and oxygen saturation will be closely monitored throughout the procedure. Intestinal biopsies may involve minimal risks of bleeding and infection.

J. Potential Benefits

The correct early diagnosis of celiac disease will lead to early resolution of symptoms by simply adhering to a gluten free diet. This will help the decrease the $8-25 millions annual health care cost incurred by IIBS. It will prevent long term complications of cancers, lymphoma, and possibly other autoimrnune diseases.

K. Compensation and Costs to Subjects

Subjects will be reimbursed costs due to the study such as parking fees, transportation costs, etc.