Prevalence of Celiac Disease Among Patients with Primary Sjögren's Syndrome

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A. Study Purpose and Rationale

Celiac disease is an inflammatory disorder affecting the small intestine in genetically susceptible individuals in response to gluten, a protein which is found in wheat, barley and rye. Histologically, it produces small intestinal villus blunting and increased lymphocytic infiltration. Clinically it can be seen in any age group with symptoms including weight loss, diarrhea, steatorrhea, and abdominal pain. Often these patients are increasingly susceptible to complications of malabsorption including osteoporosis, iron deficiency anemia and failure to thrive. Other complications can arise, however, involving oncologic, dermatologic, neurologic, immunologic and endocrine diseases. The mainstay of treatment is eliminating gluten from the diet. Traditionally, celiac disease has been diagnosed via small intestinal biopsy and is still the gold standard. More recently serologic tests have been introduced making screening easier and enabling a method for assessing response to treatment. IgA antigliadin antibody was one of the first tests available but has relatively poor sensitivity (80-90%) and specificity (85-95%). It is generally most useful in assessing response to therapy as levels decline in 3-6 months after instituting a gluten-free diet. IgA endomysial antibody has a sensitivity and specificity of 85-98% and 97-100%. IgA transg~utaminase antibody has a sensitivity and specificity of 90-98% and 95-97%. Using serologic screening of the general population, the prevalence of the disease has increased from I in 10,000 to as many as I in 250. The reason for this discrepancy is that many patients with celiac disease are asymptomatic and would not have traditionally been tested. "The potential advantages of screening for asymptomatic celiac disease include a reduction in risk for enteropathy-associated T-cell lymphoma, a reversal of unrecognized nutritional deficiency states, resolution of mild or ignored intestinal symptoms, avoidance of.other auto-immune disorders, and an improvement in general well-being."[1] Sj6gren's syndrome is among the autoimmune disorders thought to be related to celiac disease. It involves a complex of dry eyes and dry mouth with lymphocytic infiltration on salivary gland biopsy - associated with anti SS-A and SS-B (Ro and La). The first case report of this association appeared in 1965 at Columbia Presbyterian Medical Center.[2] More recently, an article appeared showing a prevalence of 15% of celiac disease in patients with primary Sj6gren's syndrome in Finland.[3] This study, however, did not have enough power to gain statistical significance. The purpose of our study is to examine if there is indeed an increased prevalence of celiac disease among patients with Sjögren's syndrome compared to the general population and compared to a population of patients with other rheumatologic conditions.

B. Study Design and Statistical Analysis

195 subjects will be enrolled. 65 subjects with the diagnosis of Sj6gren's syndrome, 65 matched controls taken from the general medical clinics, and 65 matched controls taken from the rheumatology -clinic. Sample size determined to be 65 in each group by chi square test with the prevalence of celiac disease in Sj6gren's syndrome estimated to be 14.7% (according to Itanen et al.). The prevalence of celiac disease will be determined in both study and control groups. The difference between the arms will be determined by a chi-square test.

C. Study Procedure

All subjects and controls will have their blood drawn and samples analyzed for antighadin, antiendomysial, and tissue transglutaminase antibodies. Those with a positive antibody test will be

advised to undergo upper gastrointestinal endoscopy for duodenal biopsy, the gold standard for diagnosing celiac disease. Patients with biopsyproven celiac disease will be advised to start a gluten-free diet and followed for 6 months to see if symptoms resolve. It is anticipated that the study will be completed within 2 years.

D. Medical Devices

Esophagogastroduodenoscopy (EGD) will be performed on patients suspected of having celiac disease based on positive serologies. Subjects will receive topical lidocaine applied to the oropharynx as well as light conscious sedation in the form of either midazolam or meperidine. Patients' vital signs will be continuously monitored throughout the entire procedure. Intestinal biopsies will be taken to document the presence of celiac disease.

E. Study Subjects

- Study Arm
  - Inclusion Criteria Patients must have the diagnosis of primary Sjögren's syndrome as defined by the San Diego Criteria which includes:
    - **Objective keratoconjunctivitis sicca and xerostomia**
    - **Characteristic minor salivary gland biopsy (≥2 foci of 50 or more lymphocytes) or evidence of a systemic autoimmune disease as manifested by characteristic antibodies [anti SSA (Ro) and anti SS-B (La)]**
    - **Absence of hepatitis C, lymphoma, sarcoidosis or other known causes of lymphocytic infiltrative disease**
  - Control Arms
    - Subjects will be matched to the study subjects in age (± 5 years) and gender
  - Exclusion Criteria
    - All subjects who started a gluten-free diet prior to study
    - Any history of Sj6gren's syndrome in the control groups

F. Recruitment of Subjects

Study Arm

All patients with the diagnosis of Sjbgren's syndrome at New York Presbyterian Hospital will be approached through their private physicians for participation in study.

Control Arms

Matched controls will be recruited through the physicians' offices as well as flyers. An additional control arm will be recruited from the rheurnatology clinic.

G. Confidentiality of Study Data

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

H. Potential Conflict of Interest

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

I. Location of the Study

Study will be conducted at New York Presbyterian Hospital. Locations include physicians' offices and the endoscopy suites.

J. Potential Risks

The risks involved with blood draws are minimal but include pain and risk of hematoma. EGD may be uncomfortable to some but is generally well tolerated using topical anesthetics and conscious light sedation. Light sedation may cause decreased respiratory rate but vitals and oxygen saturation will be closely monitored throughout the procedure. Intestinal biopsy may involve minimal risk of bleeding and infection.

K. Potential Benefits

Early diagnosis of celiac disease and institution of a gluten-free diet leads to early resolution of symptoms and will reduce the risk of nutritional deficiencies that often lead to anemia and osteoporosis. Gluten-free diet will also reduce the risk of other complications including lymphoma. It is unclear whether or not instituting a gluten-free diet in Sj6gren's patients will improve the symptoms of Sj6grens syndrome.

L. Compensation and Costs to Subjects

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

M. Referneces

1. Kelly, CP. Use of Serum Antibodies to Diagnose Celiac Disease. In: Up To Date, Rose, BD(Ed), Up To Date, Wellesely, MA, 2002.
2. Pittmqn FE. HoIub DA. Sjoögren's syndrome and celiac disease. Gastroenterology 1965; 48:869-76.
3. Itanen et al. Celiac Disease in Patients with Primary Sjoögrens. AM J Gastro 1999; 94:1042-1-46.