Automated Reminders for Celiac Disease Serologies in Patients with Iron Deficiency Anemia

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A. Study Purpose and Rationale:

Celiac disease, or gluten-sensitive enteropathy, is a relatively common chronic disorder of malabsorption due to an autoimmune reaction to gluten. Although patients with celiac disease have classically presented with diarrhea, it is increasingly common for patients to present with nonspecific gastrointestinal (GI) symptoms, bone disease, anemia, GI malignancy, or incidentally. Iron deficiency anemia, occurring due to the malabsorption of iron in the duodenum, was the presenting symptom in nearly 10% of patients.[1]

The development of sensitive and specific serologic assays for celiac disease has changed the diagnostic approach to the disease. Endomysial antibodies and anti-tissue transglutaminase (tTG) antibodies have been proven to be both extremely sensitive and specific for the diagnosis, and correlate well to duodenal biopsy findings.[2, 3] Although several other serologic markers have been identified, a recent study has shown that anti-tTG antibodies alone were sensitive enough marker for celiac disease.[4] The gold standard for diagnosis, however, remains duodenal biopsy showing histologic changes characteristic for the disease. There is ongoing debate as to the necessity of biopsy to confirm diagnosis; current recommendations are for patients with positive serologies to undergo endoscopy with 4 duodenal biopsies.[5]

While there is debate over the prevalence of celiac disease in the general population, a large US-based study has estimated rates of the disorder in asymptomatic individuals without familial risk factors at 1:133.[6] A large, population-based study in Italy that screened 69% of school-aged children revealing a prevalence of 1:184 and a ratio of known to undiagnosed celiac disease of 1:7.[7] These numbers suggest that a large proportion of patients with celiac disease remain undiagnosed. Patients with subclinical, undiagnosed celiac disease are at risk for developing nutritional deficiencies, have an increased risk of GI malignancies, and have a higher prevalence of other autoimmune disorders, making diagnosis a priority.[8]

Similar to celiac disease, iron deficiency anemia is common in the adult population and occurs in 2-5% of adult men and postmenopausal women.[9] Iron deficiency anemia is a common cause of referral to gastroenterologists, and loss from the GI tract is the most common cause of iron deficiency anemia.[10] Current recommendations for the GI workup of iron deficiency anemia include celiac disease screening for all patients and upper and lower endoscopies for all male patients and postmenopausal women.[11] Unfortunately, the recommendations for GI workup in patients with iron deficiency anemia are not always followed. Many patients receive incomplete endoscopic evaluation due to inadequate number of biopsies taken or simply because upper or lower endoscopy was not performed.[12, 13]

The rate of celiac disease screening via serologies for patients diagnosed with iron deficiency anemia is unknown. It is expected, however, that considering the noncompliance with recommendations for endoscopic procedures and the widespread under-diagnosis of celiac disease in the general population, the rate will be much lower than the recommended 100%. This study will examine patients diagnosed with iron deficiency anemia who are referred to gastroenterology for endoscopy by their primary care providers. The rates of ordering celiac serologies for these patients will be compared between those whose providers received an automated reminder upon GI referral to order celiac serologies before endoscopy and those whose provider did not receive a reminder.

B. Study Design and Statistical Analysis:

This study is a prospective, randomized, controlled, not masked trial to determine if adding a computer reminder to send celiac disease serologies upon referral to gastroenterology improves celiac disease screening in patients seen in the internal medicine resident clinic of New York-Presbyterian Hospital with iron deficiency anemia diagnosed by low serum ferritin.

All resident providers in the internal medicine (AIM) clinic will be randomly assigned to either receive the celiac disease screening reminder or not. Randomization will be stratified based on residency year (i.e. PGY1, PGY2, and PGY3) to ensure equal representation of all PGY groups in intervention and control arms.

If roughly 25% of patients sent for gastroenterology evaluation for iron deficiency anemia have been previously or currently sent for celiac serologies without a reminder, it is estimated that 50% will be sent in the group that is randomly assigned to receive a reminder upon gastroenterology referral. A chi-square test will be performed to compare the proportions of patients sent for celiac serologies in the two groups. With an effect size of 25%, power 80%, testing at p=0.05, the number needed in each arm is n=8(.25*.75+.5*.5)/.25^2+2/.25+2=66, for a total of 132 patients enrolled.

The gold standard for celiac disease diagnosis is duodenal biopsy, and 4 are generally recommended to definitely rule out the diagnosis. Patients who are not screened for celiac disease prior to endoscopy may need a repeat endoscopy in order to obtain adequate duodenal tissue samples. Given the risk associated with endoscopic intervention, from initiation of the study only the first patient seen with iron deficiency anemia by each individual provider will be included in the study. For providers in the intervention arm, no further action will take place and reminders will continue to occur for the rest of the study. For providers in the control arm, after their first iron deficiency anemia patient that is referred to GI, an automated message will be sent reminding them that celiac serologies should be ordered before that patient is seen by the gastroenterologist and endoscopy is performed. The providers in the control arm will receive automated reminders to send celiac serologies for all subsequent patients, and subsequent patients will not be included in the study.

There are currently 132 residents in the internal medicine program, 44 in each PGY group. Each resident sees an average of 80 patients per year. Given that the prevalence of iron deficiency anemia in adults is conservatively 2%, over the course of one year it is reasonable to expect that each resident will encounter a patient with iron deficiency anemia.

C. Study Procedure:

Data obtained from the electronic medical record (Eclipsys) at New York-Presbyterian Hospital will include: age, gender, ethnicity, serum ferritin, serum iron, serum transferrin, IgA anti-tissue transglutaminase antibodies, IgA endomysial antibodies, IgA anti-gliadin peptide antibodies, date of gastroenterology referral, reports from endoscopy, endoscopic tissue biopsy findings, all past medical diagnoses. No procedures will be performed solely for the purposes of this study. As stated previously, the study will continue for approximately one year until a sufficient number of patients have been enrolled.

D. Study Drugs: NA

E. Medical device: NA

F. Study Questionnaires: NA

G. Study Subjects:

All subjects will be patients seen by internal medicine residents at the New York-Presbyterian Hospital internal medicine clinic. Inclusion criteria for the study are a diagnosis of iron deficiency anemia based on serum ferritin levels and referral to gastroenterology for evaluation. Exclusion criteria are recent gastroenterology evaluation within 1 year, recent esophagogastroduodenoscopy within 1 year, and known etiology of iron deficiency anemia including active blood loss and former diagnosis of celiac disease.

H. Recruitment of Subjects:

The first patient seen by each individual resident provider in the internal medicine clinic with a diagnosis of iron deficiency anemia and referred to gastroenterology will be automatically enrolled in the study. There will be no active recruitment of patients. A waiver of documentation is requested as this study does not require any additional procedures or interventions.

I. Confidentiality:

All patient data will be maintained on password-protected computers accessible only to the study's primary investigators. All patients will be given a unique study identification number and will remain de-identified for the duration of the study.

J. Potential Conflict of Interest: There are no potential conflicts of interest.

K. Location of the Study:

The study will take place within the internal medicine resident clinic at New York-Presbyterian Hospital.

L. Potential risks:

A potential risk of the study is that the patients of a provider assigned to the control arm could remain with undiagnosed celiac disease or would have to undergo unnecessary additional endoscopic procedures in order to diagnose celiac disease. In order to minimize this risk, in the control arm each provider will receive a message the following day that patients referred to GI for iron deficiency anemia should have celiac serologies sent before endoscopy. After the first patient, all providers will receive the automated instant message to send for celiac serologies during active GI referral.

M. Potential benefits:

Patients who would have remained previously undiagnosed with celiac disease may be identified and treated, leading to less symptoms and complications from celiac disease including malabsorption, diarrhea, abdominal pain, weight loss, vitamin deficiencies, and adenocarcinoma and lymphoma of the small bowel. The potential benefits to society include improved rates of celiac disease diagnosis and more effective screening.

N. Alternative therapies: NA

O. Compensation to Subjects: None.

P. Costs to Subjects: None.

Q. Minors as Research Subjects: NA

R: Radiation or Radioactive Substances: NA

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