“Red Flag” Evaluation Yield in Irritable Bowel Syndrome

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Abstract

Background: The diagnosis of irritable bowel syndrome (IBS) is based on clinical criteria. Further diagnostic testing is advised for certain “red flag” alarm or warning signs. **Aim**: This investigation was designed to examine the yield of testing for “red flags”. **Methods**: Consecutive patients who were prospectively evaluated and met the ROME III criteria for IBS were reviewed for “red flags” which included: 1) rectal bleeding, 2) iron-deficiency anemia (IDA), 3) weight loss, 4) family history of colon cancer, 5) fever, and 6) age of onset after age 50. The evaluations were reviewed for type of testing and findings. Subjects with nocturnal symptoms and fecal soiling, although not traditional warning signs, were also reviewed. **Results**: There were 200 patients who met the IBS criteria; 139 (70%) had a “red flag” alarm symptom or sign. Diarrhea predominant-IBS (D-IBS) was seen in 105, constipation predominant-IBS (C-IBS) in 57, alternating, mixed, or pain predominant-IBS in 38. There were 30 men and 170 women. Testing was not often performed in this setting and, when done, the yield was low with few clinically significant diagnostic findings. **Conclusion**: There was a high prevalence of “red flag” symptoms or signs in the prospectively evaluated IBS cohort, but a low frequency of diagnostic testing directed at the investigation of these symptoms or signs. Further systematic study may show that the yield for testing in IBS is low even when “red flags” prompt diagnostic testing.

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Key words

Irritable bowel symptoms – alarm – diagnostic testing.

Introduction

Irritable bowel syndrome (IBS) is a functional bowel disorder characterized by abdominal discomfort/pain improved with defecation and associated with changes in stool consistency and frequency. IBS is one of the most common gastrointestinal disorders in the United States with an estimated prevalence of 14-24% in women and 5-19% in men [1]. It has been estimated that IBS accounts for 2.4-3.5 million physician visits per year and approximately 30% of all gastroenterology referrals [2]. The costs associated with IBS are significant with an estimated $30 billion spent per year in direct and indirect costs in the United States alone [3, 4]. The effect on employers and society is also significant with one study showing a 20% loss in work productivity among IBS patients [5].

The diagnosis of IBS is based on clinical symptoms and can be made using various criteria. The Rome III criteria are included in Table I and highlight the most recent consensus that diagnostic testing is not required to make the diagnosis. In patients with typical IBS symptoms and no alarm features, routine diagnostic testing is not recommended [6]. More extensive testing has been advocated, however, in patients exhibiting alarm features such as rectal bleeding, weight loss, anemia, fever, and family history of colon cancer [7, 8]. The utility of diagnostic testing among these patients has been called into question in recent years [9]. One large study by Whitehead et al showed that organic disease was identified in only 3% of patients with IBS and alarm features [10]. The present investigation was conducted to evaluate the real world” practice yield of diagnostic testing in patients meeting IBS symptom-based criteria and presenting with “red flag” alarm signs or symptoms. The objective was to measure the frequency of testing and the yield of that testing performed.

Methods

Study design

The study group was comprised of IBS patients prospectively evaluated in an academic health care sub-specialty gastroenterology setting from 2009 to 2011. This investigation was approved by the Institutional Review Board at the University of South Alabama College of Medicine on March 31, 2009.

Study subjects

Those identified in clinic visits with abdominal discomfort/pain, bloating and/or altered bowel habits were prospectively interviewed by physicians and asked to complete a written questionnaire or an online tool, www.ibsjennifer.com which refers to the various Rome criteria. Those who met Rome III for IBS criteria comprised the study group.

Table I. Rome III diagnostic criteria for irritable bowel syndrome

Recurrent abdominal pain or discomfort, 3 days per month in the last 3 months associated with two or more of the following:
1. Improvement with defecation
2. Onset associated with a change in frequency of stool
3. Associated with a change in form (appearance) of stool
Criteria fulfilled for the last 3 months with symptom onset 6 months prior to diagnosis

Demographics

Demographic data, including age and sex were collected. IBS subtypes were recorded based on the predominance of diarrhea, constipation, alternating bowel habits, and abdominal pain.

Alarm symptoms and signs

Patients who met IBS criteria were questioned to determine the presence of alarm symptoms and signs including rectal bleeding, weight loss, anemia, fever, family history of colon cancer, and onset of IBS symptoms after age 50. Although not traditional warning signs, patients were also asked about nocturnal symptoms and fecal soiling.

Testing review

Diagnostic testing was performed at the discretion of the treating gastroenterology faculty and fellows at the University of South Alabama College of Medicine. Chart review was subsequently conducted in IBS patients who presented with alarm symptoms or signs. Information regarding diagnostic testing performed and findings were extracted and reviewed by the investigators. In particular, diagnostic testing results for celiac disease, colon cancer and polyps, inflammatory bowel disease (IBD), endocrinopathy, bacterial overgrowth, infectious etiologies, and carbohydrate malabsorption and maldigestion were recorded.

Results

Two hundred patients met IBS criteria and 139 (70%) had a "red flag" alarm symptom or sign. Diarrhea predominant-IBS was seen in 105, constipation predominant-IBS in 57, and mixed in 38. There were 30 men and 170 women. Table II lists the various alarm signs and symptoms found in our study group. There was a high prevalence of patients presenting with rectal bleeding (31%) and onset of symptoms after age 50 (28%). Weight loss and family history of colon cancer were also noted frequently. Seventy-five (38%) had nocturnal symptoms and 25 (13%) had fecal soiling. Fifty-eight subjects had multiple alarm symptoms.

Table II. "Red flag" alarm findings in 200 IBS Subjects

	Subjects Affected (#)	% (n=200)
Nocturnal symptoms*	75	38
Rectal bleeding	61	31
Onset after age 50	56	28
Weight loss	42	21
Family history of colon cancer	31	16
Fecal soiling*	13	7
Fever	12	6
Anemia	3	2

* Not considered traditional alarm findings.

Table III lists the results of diagnostic testing among patients presenting with alarm symptoms or signs. Sixty-four percent of the patients were evaluated with colonoscopy and nine patients (10%) were found to have non-advanced adenomas. One patient had non-specific, transient colitis that was not consistent with an inflammatory bowel disease. Seven patients were found to be anemic. Although a small percentage of patients had elevated values of inflammatory biomarkers such as ESR, CRP, fecal calprotectin or lactoferrin, there was no clinical evidence of inflammatory bowel disease in any patient. No subject had *Clostridium difficile* or other parasites. Seventy-five percent of the alarm symptom patients were tested for thyroid dysfunction, and no patient had clinically active thyroid disease. One patient had elevated lipase from an unrelated comorbidity that was not associated with IBS symptoms. Bacterial overgrowth and carbohydrate malabsorption and maldigestion were seen in 11/26 tested (61.1%) and 28/157 (17.8%), respectively (Table III). Among the 62 patients with rectal bleeding, 64% underwent colonoscopy and there were five abnormal results. All were adenomas and none explained the bleeding. Of the 31 patients with a family history of colon cancer, colonoscopy was performed in 61%. There were 3 abnormal findings. Sixty-two percent of the 42 patients with weight loss had colonoscopy with 3 abnormal findings (adenomas). No patients were found to have celiac disease tested by TTG-IgA and total IgA.

Discussion

This study is unique in that it examines the utility of diagnostic testing in IBS patients presenting with "red flag" alarm features [7, 14]. Previous studies have evaluated

Table III. Results of diagnostic testing in alarm feature patients.

Diagnostic modality	Number tested	% tested (n=144)	Abnormal result (number)
Lactose maldigestion	91	63	25
Lactulose (bacterial overgrowth)	26	18	11
Colonoscopy	92	64	10*
CRP	54	38	8**
Hb (anemia)	119	83	7
TSH (low or high)	103	72	6***
ESR	58	40	5**
Fructose malabsorption	66	46	3
Calprotectin	8	6	1**
Lactoferrin	4	3	1**
Lipase	20	14	1****
Ova and parasites	39	27	0
C difficile	53	37	0
TTG-IgA	69	48	0

*9 adenomas, 1 colitis; **No clinical evidence of inflammatory bowel disease in any of these subjects; ***All borderline, not clinically significant, unrelated; ****Unrelated comorbidity

diagnostic testing in IBS patients without alarm features. In general, it has been accepted that an exhaustive diagnostic evaluation for organic gastrointestinal disease in IBS is not indicated; however, further evaluation is recommended in patients presenting with alarm features [7, 8]. This is often considered a standard of care since the presence of alarm features is felt to identify a group of patients with a greater pretest probability of organic disease [11]. It is known that a low frequency of additional diagnostic testing to exclude organic disease contributes to the significant economic burden associated with IBS [12]. Our study highlights three important findings: 1) a high prevalence of "red flag" alarm features is seen among IBS patients (70% in our study), 2) additional diagnostic testing is routinely not performed among patients presenting with alarm features, and 3) even when performed because of the presence of alarm features, the yield of diagnostic testing is low.

Previous studies, including those by Hamm et al and Tolliver et al have shown the low yield of colonoscopy among IBS patients [13, 14]. Our results further validate these findings, but the distinction in our study is the low yield observed among patients with alarm symptoms. Chey et al [15] showed that common structural abnormalities were not more common in non-constipated IBS subjects than controls. They did find a small proportion of their patients to have microscopic colitis and advised that when colonoscopy is performed in D-IBS patients, random colonoscopic biopsies should be considered. The cost of colonoscopy is substantial and it is estimated that approximately 50% of IBS patients will undergo colonoscopy in the course of their diagnostic evaluation [16]. Although colonoscopy for colon cancer screening is generally recommended, when performed solely for alarm features associated with typical IBS symptoms, there is a low yield.

Routine laboratory tests including complete blood count, thyroid stimulating hormone, erythrocyte sedimentation rate, C-reactive protein, and stool analysis for ova and parasites are often included in the initial evaluation of IBS patients. These studies are often quick and inexpensive, yet little evidence exists to show that their routine use changes the management of suspected IBS. Recent studies by Sanders et al and Cash et al have found no significant differences in the results of routine laboratory tests which included complet blood count complete metabolic profile, ESR, CRP, thyroid testing, celiac antibodies, and IBD and lactose genomics among non-IBS and IBS patients [17, 18]. Our results show that even among those with alarm features, these routine tests are often of little value as no cases of inflammatory bowel disease, thyroid dysfunction, or infectious etiologies were identified through their use. The one case of "colitis" found on colonoscopy had a self-limited course without a substantiated diagnosis of IBD and no impact on the IBS course.

The American College of Gastroenterology IBS Task Force has recently recommended testing for celiac disease in patients presenting with non-constipated IBS symptoms. This recommendation was based on studies that suggested that serologic testing for celiac disease is cost effective when the pretest probability exceeds 1% [19]. A recent meta-analysis showed that the prevalence of celiac disease in individuals with suspected IBS may be four times greater than non-IBS controls [20], but many of the studies included in this analysis originated in Europe where the prevalence of celiac disease is different than in the United States. The British Society of Gastroenterology guideline advocates celiac screening [21]. Cash et al recently showed in a large, prospective US multicenter study that the prevalence of celiac disease in nonconstipated IBS subjects was similar to controls, approximately 0.4% [22]. Although only a small percentage of our patients were tested, no celiac disease was found in our patients with alarm features.

Lactose maldigestion has been reported in approximately 25% of IBS patients and fructose maldigestion in 10% [19]. Our study detected carbohydrate maldigestion when tested. These conditions may have symptoms independent of IBS but identification of carbohydrate maldigestion may not alter the course of IBS or its symptoms [23].

Recent studies have implicated bacterial overgrowth as a factor in IBS and the intestinal microbiota has been targeted for treatment opportunities [24], though the relationship between bacterial overgrowth and IBS symptoms remains controversial. Pimental et al have shown that antibiotic treatment provides significant relief of IBS symptoms of bloating, abdominal discomfort and diarrhea [24]. Additional work by Low et al discusses the potential role of antibiotic treatment of constipation-predominant IBS patients [25]. Among a small percentage (18%) of our IBS patients that were tested in our study, 42% of those tested had abnormal lactulose challenge breath test results suggesting bacterial

fermentation. Further investigation in this area evaluating improvement of symptoms after antibiotic therapy in IBS patients with bacterial overgrowth could encourage more frequent testing.

This study has several limitations. It is a single center study and is relatively small, introducing the possibility of a systematic bias that would prevent application of the findings to the larger IBS population. It is also limited in that the patients included in this study did not undergo a structured evaluation for alarm features and additional evaluation and treatment was at the discretion of the treating physician. It is possible that universal evaluation of all patients with alarm features could have yielded additional findings. The design of this study, however, better reflects the "real world" evaluation of IBS patients and sheds additional information on its yield. The rising costs of healthcare make the judicious use of diagnostic testing relevant. A positive diagnosis of IBS utilizing clinical criteria can avoid expensive, exhaustive diagnostic evaluations.

Conflicts of interests

There are no conflicts to disclose. This study was not funded by any entitiy and there was no support or assistance for writing.

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