Results of Gastrointestinal Evaluation in 90 Hospitalized Iron Deficiency Anemia Patients

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Abstract

Background: Chronic occult blood loss from the gastrointestinal tract is widely accepted as a major cause of iron deficiency anemia.

Objectives: To evaluate the diagnostic yield of gastroscopy, colonoscopy and fecal occult blood testing of hospitalized IDA patients, plus follow-up.

Methods: IDA was defined as hemoglobin <12.5 g/dl (men) and 11 g/dl (women), and serum iron <50 g/dl. The study group comprised 90 patients (42% male) with a mean age of 65±15 years and mean Hb 8.1 g/dl.

Results: Gastroscopy and colonoscopy revealed a bleeding source in 28.8% and 14.4% respectively. Gastrointestinal symptoms were found in 23% of patients with diseases of the upper gastrointestinal tract and in 15.3% of the lower. The sensitivity of fecal occult blood tests in detecting lesions in the lower and upper GI tracts was 100% and 30.7% respectively. Forty-four patients (48.9%) were discharged from the hospital with IDA of unknown origin. Over the following year, 20 of the 44 patients required further hospitalization, and of these, 13 were found to have anemia. Of the remaining 24 patients who were not hospitalized again, 15 had anemia. Four patients (9%) had significant gastrointestinal lesions and two died during the follow-up.

Conclusions: Fecal occult blood is a sensitive examination for lower but not for upper GI tract lesions

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Gastrointestinal bleeding can present as either gross bleeding (melena, hematemesis, rectal bleeding) or as occult bleeding. The most common cause of iron deficiency anemia in adults is assumed to be a result of occult bleeding from the gastrointestinal tract. Occult blood loss may be diagnosed through a positive guaiac test. Data from mass screening studies have shown an overall guaiac positivity rate for screened subjects of 2–6% for colon cancer [1,2]. However, these studies were primarily devoted to early detection of colon cancer in asymptomatic subjects. There are few prospective studies of endoscopic evaluation (upper endoscopy and colonoscopy) in patients presenting with IDA [3–6], and there are no guidelines for evaluating asymptomatic IDA patients.

This study was designed to examine the IDA patient referred to the gastroenterology unit for evaluation after all other possible sources had been excluded (hematological, nutritional, gynecological, etc.). It aimed to evaluate the diagnostic yield of the gastrointestinal studies, the divergent pathologies of the upper and lower GI tract, and the importance of symptomatology, as well as to measure the prevalence of non-steroidal anti-inflammatory drug usage and its contribution to IDA. Other goals included determining the predictive value of fecal occult blood examination and defining the optimal gastrointestinal evaluation for the IDA patient.

It appears that about half of the patients were discharged from hospital with no diagnosis as to the cause of the IDA [3–6], since conventional workup did not reveal the source of the bleeding. Dietary deficiency may be one explanation for this phenomenon, but a long-term follow-up of these patients is needed to preclude misdiagnosis.

There are also no guidelines for follow-up of patients with IDA. When we searched the literature after we had completed our study, we found only one published article on the subject, and it concluded that the prognosis for IDA patients is favorable [7]. The study group had undergone an extensive workup, including gastroscopy, total colonoscopy, fecal occult blood test, and small bowel X-ray in some of the patients, with no palpable results. We decided that it would be of value to examine and evaluate these patients 12–18 months after their discharge from the hospital.

Materials and Methods

Those eligible for inclusion in the first part of the study were IDA patients hospitalized at the Hillel Yaffe Medical Center, Hadera, from January 1994 through July 1995 and referred to the gastroenterology department for evaluation. Prior to the referral, each patient underwent a complete workup to exclude, among others, possible hematological, nutritional, or gynecological causes of IDA. Exclusion criteria were acute or recent overt GI tract bleeding or antithrombotic

IDA = iron deficiency anemia

therapy. All the anemic patients had microcytic anemia and 72% had a mean cell volume below 80.

Definition

Iron deficiency anemia was defined as hemoglobin level <12.5 g/dl for men and <11 g/dl for women, serum iron level <50 μg/dl, and total iron-binding capacity >300 μg/dl.

Symptoms

Detailed clinical data were obtained for all the patients enrolled in the study with emphasis on gastrointestinal symptoms of the upper gastrointestinal tract (epigastric pain, dyspepsia, nausea, heartburn, vomiting, etc.) and the lower GI tract (abdominal pain, diarrhea, constipation, changed bowel habits, flatulence).

Fecal occult blood

Stool specimens were collected by digital rectal examination and tested on Hemoccult II slides (SKD, San Jose, CA, USA) without hydration. Each patient underwent three FOB tests.

Endoscopic criteria

A prerequisite for accepting the endoscopic findings as a source of occult gastrointestinal bleeding was any abnormality of the esophagus, stomach or duodenum. The criteria were unanimously accepted by all the participating gastroenterologists. The possible causes of upper lesions considered were: erosive esophagitis, esophageal ulcer, esophageal tumor, erosive/hemorrhagic gastritis, polyps (larger than 1 cm), gastric ulcer and gastric tumor. Lower GI tract lesions regarded as possible causes of IDA included colorectal cancer, angiodysplasia, colorectal polyp (larger than 1 cm) and colitis. Double (bi-directional) endoscopy was performed on each patient. The procedure was done routinely using Pentax EG 2901 video-endoscopy (Asahi Optical, Tokyo, Japan). Both procedures were carried out during the same hospital stay and usually on the same day. The sequence of procedure performance was arbitrary and the procedures were conducted by one of three gastroenterologists (Z.F., A.S., D.C.). Each upper panendoscopy included duodenal mucosal biopsy that was sent for histological examination to rule out celiac disease.

In patients whose evaluations (colonoscopy and upper panendoscopy) were found to be within normal limits and who had positive FOB test results, a barium meal and follow-through X-ray examination of the small bowel were administered.

The second part of the study comprised patients discharged from the hospital without diagnosis after an extensive workup. The patients and their family physicians were interviewed by phone 12–18 months later (July to August 1995). All clinical data were gathered from the non-hospitalized patients and their physicians via telephone by one of the authors (V.G.). The charts of patients rehospitalized during the study period were re-evaluated and clinical data and re-investigation results collected.

FOB = fecal occult blood

This study was approved by the Human Studies (Helsinki) Committee of the Hillel Yaffe Medical Center, Hadera. Informed consent, in compliance with Institutional Review Board requirements, was obtained from each patient.

Results

Our study initially enrolled 105 patients with iron deficiency anemia, but 15 did not meet the inclusion criteria. The hospitalized subjects included 38 men and 52 menopausal women with an average age of 65±15 (range 43–89 years). The average hemoglobin was 8.1 g/dl among the men and 8.4 g/dl among the women.

Following investigation, overall GI lesions were found in 66 patients and 24 of them were normal. Six patients had undergone partial gastrectomy, a recognized cause of IDA. In one patient, duodenal mucosal biopsy was compatible with celiac disease. Of 66 patients with GI tract lesions, only 39 were in accord with the predetermined possible causes of IDA. Twenty-six patients had upper GI lesions (28.8%) and 13 had lower GI lesions (14.4% of the entire study group). The specific lesions are shown in Table 1.

The importance of symptomatology was evaluated and correlated with pathological lesions [Table 1]. Only 8 of the 39 patients with GI lesions that could have contributed to the development of IDA were symptomatic. Thus, 31 patients with lesions were asymptomatic. Eighteen of the patients used NSAIDs, 15 of whom had lesions in the upper and lower gastrointestinal tract, 72.2% and 11.1% respectively [Table 2]. The remaining NSAID users (16.7%) were patients with normal gastrointestinal tracts. Exclusion of four patients with mild duodenitis/gastritis altered the percentages, i.e., abnormal upper GI tract patients 50%, abnormal lower GI tract 11.1%, and normal GI tract 38.9% [Table 2].

The diagnostic yield of the FOB test was as follows: in the upper GI tract 8 patients tested true positive, 26 had GI lesions, and sensitivity was 30.7%. In the lower GI tract 12

Table 1. Correlation of lesion site with gastroenterology symptoms*

	GI symptoms	No GI symptoms	Total
UGI source of bleeding (Total)	6	20	26
Gastric cancer	1	1	
Gastric polyp	—	1	
Gastric ulcer	1	7	
Erosive gastritis	3	12	
Esophagitis	1	1	
LGI source of bleeding (Total)	2	11	13
Colorectal cancer	2	10	
Colonic polyp	—	1	
Total	8	31	39

* Not including 6 partial gastrectomy patients and one celiac disease patient.

Table 2. Correlation between NSAID users* and GI lesions

Upper GI lesions		Lower GI lesions		No GI lesions
Gastric ulcer	3	Colon cancer	2	3
Mild gastritis/duodenitis	4			
Erosive gastritis	5			
Ulcerative esophagitis	1			
Total	72.2%		11.2%	16.7%

* 18 patients used NSAIDs.

Table 3. State of IDA patients during the follow-up year

	Recurrent admission	No hospitalization
No. of patients	20	24
IDA	13	15
No anemia	7	9
Re-investigation	8	–
Upper GI lesions	2	–
Lower GI lesions	1	–
Death	2	–

tested true positive, 12 had GI lesions, and sensitivity was 100%. True FOB test results were found in 20 of the 90 patients.

Upon completion of the gastroenterological examination the patients returned to the hospital wards. Of the original 90 patients, 44 patients (not including the 6 patients with partial gastrectomy and one with celiac disease) were discharged from the hospital with no diagnosis as to the cause of iron deficiency anemia.

Forty-four patients participated in the second part of the study. The study group included 21 men and 23 women with an average age of 66±12 years. The most recent mean hemoglobin level was 8.9 g/dl among the men and 9.0 g/dl among the women. During the one year follow-up, 20 patients required hospitalization for a variety of reasons: 13 of them were found to be still anemic and 7 not. Eight of the 13 patients underwent gastrointestinal reinvestigation. Of the 24 patients not rehospitalized, 15 had anemia [Table 3]. Four patients (9%) had significant GI lesions: one had esophageal varices grade III, one had a severe erosive esophagitis, another had a suspected space-occupying lesion of the right colon (on standard barium enema, there was no further investigation), and the fourth patient died of liver metastasis from an unknown primary tumor. There were two deaths in the rehospitalized group: the patient with liver metastasis who was diagnosed by abdominal ultrasound, and the patient with the suspected colon cancer diagnosed by barium enema.

Discussion

Most previous data involving the yield of gastrointestinal investigations (carried out because of GI blood loss) refer to target variables such as incidence or prevalence of tumors (especially in the lower GI tract), or to the yield of different

Table 4. Summary of endoscopy evaluation studies in elderly patients with iron deficiency anemia

	Zukerman & Benitez [4]	Rockey & Cello [5]	Gordon et al. [6]	Present study
No. of patients	100	100	170	90
Hb (g/dl)	10.3	7.8	10.3	8.5
Lesions (%)	53	62	59	51
UGI (%)	36	37	41	33
Malignant (%)	1	1	0	2
LGI (%)	26	26	18	14
Malignant (%)	6	11	9	13
Both GI (%)	9	1	?	1.1
Discharged (%)	47	38	41	49
SB X-ray (%)	–	38	28	25
SB lesions (%)	–	0	3	1

SB = small bowel

therapeutic strategies or modalities [1,2]. Less research attention has been given to patients with anemia, even though they make up a large proportion of the patients referred to the endoscopy unit. Patients with IDA are regularly referred for endoscopic evaluation, a common practice that has not received the attention it merits until recently when three studies [4–6] explored the subject. These studies investigated the divergence of pathologies in gastrointestinal bleeding and suggested an optional investigation plan. The results of these studies are similar to, and agree with, our results [Table 4].

The recommendations emerging from our study refer only to the elderly (mean age 65 years) and not to studies of younger age groups from which we would expect different results. The results of the present study are completely irrelevant to other groups, e.g., patients with positive FOB test results as the sole presenting problem. Our study produced a number of interesting results, the most striking being that half of the patients were discharged from the hospital with no diagnosis as to the source or origin of the IDA in their gastrointestinal tract. Dietary deficiency could perhaps be one explanation for this phenomenon, but a long-term follow-up of these patients is needed to preclude misdiagnosis. Another interesting result is the diagnostic yield of endoscopy. In our study upper GI lesions provided a higher diagnostic yield in explaining IDA than did lower GI tract lesions. However, when the target variable is diagnosing and locating neoplasm, the diagnostic yield is higher for the lower GI tract than for upper GI tumors (13 cases as compared to 3).

Our study did not examine the question as to which examination should be performed first. Rockey and Cello [5] recommended that the initial examination be directed by site-specific symptoms. Most of our patients were asymptomatic, and the few symptoms that were presented had no correlation with the final endoscopic results. It is our opinion that special attention should be paid when symptoms are present, as lesions were discovered in all symptomatic patients in our study. As to the necessity of bi-directional endoscopies, even when one lesion is found we recommend

completing both studies since about 1% of the patients had lesions in both upper and lower GI tracts. Even though only one patient was diagnosed as having asymptomatic celiac disease, we recommend doing a routine small bowel biopsy. In fact, the literature shows that among elderly IDA patients the incidence of celiac disease is as high as 3%. The cost-effectiveness was not examined.

Regarding diagnostic expectations and recommendations, we may expect to find that the most common origin of occult blood loss is in the upper GI tract, that even after a full investigation 48.9% of patients are discharged from hospital with no diagnosis as to the probable origin of IDA, and that FOB is a sensitive test for lower GI lesions in IDA patients but not for upper GI lesions. Previously, little attention had been given to follow-up of these patients. In half of them, even after an extensive workup, there is no explanation for IDA [4–6]. They are usually referred to family physicians and some undergo repeated gastrointestinal evaluation. A recent follow-up study by Shay and Scott [7] suggests that in two-thirds of these patients the anemia resolves and does not recur. Gordon et al. [8] recently described their experience in following 69 elderly IDA patients over an average period of 39 months. The anemia was resolved in 71% of the patients but persisted in the rest. This study showed that two-thirds of the patients had persistent anemia, but only 4 (9%) had significant, possibly bleeding, gastrointestinal lesions. The mortality (two patients) was probably due to malignant disease; one patient had liver metastasis and the other had a suspected tumor of the right colon that had been missed a year earlier. On the other hand, in 36% of the patients discharged without an identifiable cause of IDA, the anemia disappeared.

Our recommendation to IDA patients who have undergone gastroscopy, total colonoscopy and FOB testing with no pathological finding, is long-term follow-up that includes repeated complete blood count *and* ongoing consultation with a dietitian. Our experience shows that "misdiagnosis" is the exception rather than the rule in IDA of unknown etiology. There were only two deaths among our 44 patients, which is not above the average mortality rate in populations of that age; and changes of medical diagnosis and treatment were achieved during the follow-up in two cases. In this study enteroscopies were not performed and therefore not evaluated. We believe that enteroscopy should be part of the workup of IDA patients, along with X-ray studies, especially in patients with negative endoscopic studies of the upper and lower gastrointestinal tracts. The recommendations resulting from this study refer only to the elderly (mean age 65 years).

As there are no guidelines in the literature for following patients with IDA of unknown origin [9], we summarize our experience here. Additional causes were identified in the course of the follow-up (1–1.5 years) in about 9% of patients. For most of the patients, follow-up did not change the medical approach. In about one-third of the patients the anemia regressed or disappeared. There is no evidence that contrasting small bowel studies are necessary to finalize the evaluation, a conclusion supported by the results of other studies [5,9,10]. New procedures, such as enteroscopies, may alter these recommendations but were not evaluated.

We recommend that patients with iron deficiency anemia be closely watched by the family physician, who should order blood tests at regular intervals, including blood count, iron, and fecal occult blood. If, in spite of iron salt supplement, there is a reduction in hemoglobin, a repeat endoscopic evaluation should be performed.

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Erratum

In the article "Perforated appendicitis in shigellosis" that appeared in the October issue (vol 1, no. 2, page 124), the names of the second and third authors were wrongly placed. The correct order is: I. Sukhotnik, D. Miron, B. Kawar, D. Yardeni and L Siplovich.