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Prevalence of Gastrointestinal Tract Lesions in Patients with Iron-Deficiency Anemia

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Abstract

Background: the Iron deficiency anemia (IDA) is a common cause of referral to medical departments. Chronic gastrointestinal (GI) blood loss is important cause of IDA and also an alarming sign of serious underlying disease. The information concerning ideal evaluation of the gastrointestinal tract in patients with the IDA is scant. We designed a prospective study to determine the frequency of GI tract lesions in patients with the IDA.

Methodology: This cross - sectional study was conducted since January 2006 to January 2008 at Imam Hospital, Urmia in the west of Iran. The study population was comprised of 227 patients including men over 40 years and post menopausal women with probable IDA. After identification of patients, we extracted detailed data via medical records, history taking, physical examination and laboratory. Data was analyzed by the chi square and student's t-test.

Results: the patients totally underwent 478 in : 214 upper GI endoscopies, 179 colonoscopies, and 85 bariumenema. The mean age of subjects was 61 years (SD±15), and 55% were women. Upper GI lesions (esophagitis, gastritis, peptic ulcer and gastric cancer) accounted 32.1 (73 case) percent of cases. Colonoscopy findings include: polyps of colon were found in 10 (4.4%) of cases and colon cancer in 15 (6.6%). Etiology of IDA was not detected in 126 (55.5%) of our patients.

Conclusion: We concluded despite relatively low rate of malignant gastrointestinal lesions that were found in our study, GI tract assessment is necessary in iron deficiency anemia, chiefly in the patients with symptoms related to upper or lower gastrointestinal tract.

Keywords: Iron deficiency anemia, colon cancer, gastrointestinal malignancy

Introduction

Anemia is common in the elderly and its prevalence increases with age [1, 2]. Using World Health Organization criteria for anemia (hemoglobin of less than 12 g per dL [120 g per L] in women and less than 13 g per dL [130 g per L] in men), the prevalence of anemia in the elderly has been found to range from 8 to 44 percent, with the highest prevalence in men with 85 years and more[3]. Anemia should not be accepted as an inevitable consequence of aging. A cause is found in approximately 80 percent of elderly patients. The most common causes of anemia in the elderly are chronic disease and iron deficiency[4].

The Iron deficiency anaemia (IDA) occurs in 2-5% of adult men and post-menopausal women in the developed world and is a common cause of referral to a gastroenterology clinic (4-13% of referrals)[5, 6]. Chronic gastrointestinal (GI) bleeding is leading cause of the IDA in men above age 50 and post-menopausal women[7].

Iron deficiency anaemia (IDA) resulting from gastrointestinal bleeding is a common feature of many gastrointestinal conditions, several of which may be asymptomatic, including tumours of the gastrointestinal tract [8]. In addition, the IDA is now one of the most common presenting features of coeliac disease[9]. It has thus become standard practice to recommend investigation of the IDA to

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establish a cause, although nearly a fifth of patients may not have an underlying cause found in spite of intensive investigation[10]. Investigations are often unpleasant and demanding on patients who therefore need to be persuaded of the reason for the tests.

Previous studies included heterogenous study groups, such as patients with and without GI symptoms, various ages, pre- and post-menopausal women and iron deficiency with or without anaemia[11-13]. There are only a few studies that specifically evaluated asymptomatic IDA[14, 15], but none of them addressed asymptomatic IDA in adult men or post-menopausal women. However, the aetiology and frequency of the GI tract lesions in this subset of patients may differ from those of other groups. Therefore, we designed a prospective study to determine the frequency and location of GI tract lesions in men older than 40 years and post-menopausal women with symptomatic and asymptomatic IDA.

Methodology

The study was designed as cross-sectional and was conducted since January 2006 to January 2008 at Immam Hospital, Urmia in the west of Iran. We investigated whether iron deficiency anemia, is associated with an increased likelihood of gastrointestinal malignancy. The study population comprised men over 40 years and post menopausal women with probable IDA.

Inclusion criteria

1- Age over 40 years for men and post menopausal women, 2- A haemoglobin concentration of 13 g/dl or less (men) or 12 g/dl or less (women), 3- A mean cell volume of less than 82 fl in district 1 or 78 fl in district 2 (the blood autoanalysers used by the two hospitals had different normal ranges), 4- Red cell count not exceeding 5.5 x 1012/l.

Exclusion criteria

1- Known haematological abnormalities such as haemoglobinopathy, 2- Known cause for blood loss such as recent surgery, trauma, or overt gastrointestinal haemorrhage, 3- having an established reason for anaemia such as renal failure.

Data collection

After identification of patients, we extracted detailed data from medical records, history taking, physical examination and laboratory. The data collected included: reason for initial full blood count request, signs and symptoms documented at the time, dates and results of laboratory and radiological investigations, dates and results of all hospital based investigations, previous medical history that might affect management, including previous anaemia, gastrointestinal complaints, and chronic comorbidity, dates and results of upper gastrointestinal endoscopy and colonoscopy.

Definition of iron deficiency anemia

A haemoglobin concentration of 13 g/dl or less (men) or 12 g/dl or less (women) accompanied by at least one of the following laboratory values consistent with iron deficiency: a serum iron concentration ≤45 µg per deciliter (8.1 µmol per liter; normal range, 50 to 150 [9.0 to 27.0]) with a transferrin saturation not higher than 10 percent (normal range, 16 to 60 percent), a serum ferritin concentration ≤20 µg per liter for men (normal range, 20 to 450) and ≤10 µg per liter for women (normal range, 10 to 250). Statistical methods: Data was collected in an Access database and analysed via SPSS (v10). Differences in the prevalence of upper and lower GI findings among subjects, as well as differences in haemoglobin levels, gender and age of patients with and without malignancy were assessed by the chi square test for categorical variables and the Student's t-test for continuous ones.

Results

During Over a 2-year period, the study population consisted of 98 outpatients and 129 in patients were referred to gastrointestinal department of our hospital to evaluate causes of the iron deficiency anemia. Totally underwent 475 individual investigatory methods: 214 upper GI endoscopies, 179 colonoscopies, and 85 bariumenemas.

The mean age of those undergoing our study protocol was 61 years (SD±15), and 55% were women. Nine women were menstruating; none had a history of unusual or heavy flow. All the patients were anemic, with serum ferritin levels or

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transferrin-saturation values that were consistent with iron deficiency.

The demographic parameters of the patients and the parameters of IDA are presented in Table 1. In table 2, frequency of presenting symptoms and in table 3, summary of laboratory data were noted.

According to the result of table 4, upper GI lesions accounted 32.1 (73 case) percent of causes for anemic patients.

Colonoscopy findings included: polyps of colon were found in 10 (4.4%) of cases and colon cancer in 15 (6.6%). Four of patients that were diagnosed as colon cancer, using barium enema fallowed by colonoscopy and tissue biopsy. In summary causes of iron deficiency anemia were found in 74 cases (32.6%) No complication of EGD, colonoscopy or barium enema was recorded.

Other investigations showed that 3 patients had celiac disease (2 male and 1 female). In table 5 etiologic causes of the IDA was summarized, according to this table etiology of the IDA was not detected in 126 (55.5%) of our patients.

This data confirmed that patients with upper GI symptoms and iron deficiency anemia were more likely to have causative lesions in endoscopy (P=0.0001, OR= 9.56, CI 4.83-19.18) and so for patients with lower GI symptoms more likely to have positive finding in colonoscopy or barium enema (P=0.001, OR= 4.02, CI 1.54 -10.47).

According to other result of this study no significant difference found between mean hemoglobin level (p=0.44), LDH (p=0.27) and serum ferritin (p=0.08) with GI malignancy in patients presented with the IDA.

***Table 1**: Demographic data of the patients with asymptomatic IDA*

Total number	227	
Mean age	61	SD ±15
Range of age	Female 44-86	Male 40-91
Sex	Female 119 (52.4%)	Male 108(47.6%)
Smoker	Female 11 (9.2%)	Male 32 (29.6%)
Alcohol	0 Female	7 (6.4%) Male
Urbane/Rural	Urban 147 (64.7%)	Rural 80 (35.2)

***Table 2**: Symptoms and clinical findings*

Symptoms	Frequency	%
Symptoms related to anemia	104	45.8
Upper GI complaints	81	35.6
Lower GI complaints	44	19.3
Upper and Lower GI complaints	18	7.9
Non specific complaints	25	12.7
Without GI symptoms	102	44.9

***Table 3**: Results of Laboratory Tests in Patients with Iron-Deficiency Anemia*

Laboratory Tests	Mean	SD
Hemoglobin in men (g/dl)	9.1	2.3
Hemoglobin in women (g/dl)	8.6	2.0
MCV (fl)	73	11.4
Serum Iron (µg/dl)	18.7	13.6
Serum Transferrin (µg/dl)	363	99.5
Transferrin Saturation %	6.1	2.8
Serum Ferritin (µg/Lit) in Men	11.7	10.1
Serum Ferritin (µg/Lit) in Women	9.3	8.9

Discussion

The Iron deficiency anemia (IDA) is a universal problem involving individuals of all ages and both sexes and is a common cause of referral to medical departments. This anemia is one of the most common types of anemia[16]. Recent evidence has suggested that gastrointestinal neoplasm may be missed in patients presenting with iron deficiency anemia unless investigations are performed. The information concerning ideal evaluation of the gastrointestinal tract and exact findings in patients with the IDA is scant[11]. However, there are no study-based guideline for efficienty management of this disorder[17]. The aim of this study was to evaluate patients with IDA for gastrointestinal lesions potentially causing the IDA.

This study surveyed 227 patients referred to gastroenterology department of our hospital for investigation of the iron deficiency anemia to determine the diagnoses contributing to the anemia, the usefulness of certain clinical features, and the role of colonic and other investigations in obtaining the diagnosis.

Upper gastrointestinal lesions contributing to anemia were identified in 73 (32.1%) patients while colonic lesions were found in 25 (11.0%). Malignant lesions were found in 26 (11.4%) of total 227

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***Table 4**: Upper GI endoscopies findings*

Findings	frequency	%
Esophagitis	9	3.9
Erosive Gastritis	15	6.6
Gastric ulcer	17	7.4
Dudenal ulcer	21	9.2
Gastric cancer	11	4.8
Total	73	32.1

***Table 5**: Cause of iron deficiency anemia in our study population*

Findings	Frequency	%
Gastric ulcer	17	7.4
Dudenal ulcer	21	9.2
Gastric cancer	11	4.8
Esophagitis	9	3.9
Erosive Gastritis	15	6.6
Polyps	10	4.4
Colon Cancer	15	6.6
Celiac disease	3	1.32
Total determined causes	101	44.5
Undetermined causes	126	55.5
Total	227	100

patients that participated in our study. Only three patients had celiac disease and we did not find other lesion in the small bowel.

In western country GI sources for blood loss and iron deficiency have been frequently found and this was increased during recent decades. In 1965 Beveridge et al reported gastrointestinal neoplasms in only 2% of iron deficient patients[18], in 1986 Cook and collaborators found a potential cause for iron deficiency that was identified in 86 of 100 patients, and a specific gastrointestinal condition (previous gastric surgery excluded) capable to cause blood loss was identified in 70[18]. Furthermore, the widespread use of upper and lower gastrointestinal fibreoptic endoscopy accounts for-improved diagnosis of ulcerative oesophagitis, gastroduodenal ulceration, mucosal erosions, and gastrointestinal angiodysplasia.

The lower yield of our results, in comparison with some of other studies was significant and may have been due to special demographic and socioeconomic characteristics of our patients.

Previous heterogeneous studies [11, 19-23] have emphasized the importance of iron deficiency anemia as a marker for occult gastrointestinal malignancy. However, it is likely that these studies have highly variable results and we have overestimated the prevalence of these malignancies in persons with iron deficiency anemia [24] , because almost all of these studies recruited special high risk patients.

Annibale et al. found GI causes of the iron deficiency anemia in 85% of cases [25]. In another study that was published in 2005 and investigated risk factors for gastrointestinal malignancy in patients with the iron-deficiency anemia, malignancy was diagnosed in 91/695 (13.1%) and gastrointestinal malignancy in 78/91 (11.2%). The most frequently diagnosed cancers were colonic (n = 44, 6.3%), gastric (n = 25, 3.6%) and renal tract (n = 7, 1%). cases with usual non refractory IDA were studied [26]. One previous study found these lesions in 34% of iron deficient patients and approximately 10% were diagnosed with gastrointestinal malignancy as a cause for their anaemia and in 66% of patients no gastrointestinal cause was found.[27]

A study was conducted to determine the prevalence and locations of GI tract lesions in patients with asymptomatic IDA, the results showed that an anemia-causing lesion was found in 14 (29%) and 16 (33%) patients in the upper and lower GI tract, respectively. The prevalence of dual lesions (in both the upper and lower GI tract) was low (6%). In 14 (29%) patients, a malignancy, predominantly right-sided colon carcinoma, was responsible for the IDA. Only one patient had a lesion in the small bowel. In 14 (29%) patients, the work-up was negative [28]. It behooves us to regard that this high rate of GI tract malignancy was found in asymptomatic patients and it was inconsistent with other studies that we reviewed before.

There was no found cause for the IDA about 126 ones (55-5%) out of 227 patients, after upper and lower gastrointestinal investigations. The British Society of Gastroenterology (BSG) guidelines state that such patients should be monitored three monthly for one year with additional iron replacement to be given if the haemoglobin or mean cell volume falls below normal, with consideration of further investigations only if the haemoglobin concentration cannot be maintained. Reassuringly, follow up studies in patients with negative gastrointestinal investigations confirm that

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iron deficiency does not recrudesce and has a benign course in most patient [27].

Dietary insufficiency of iron causing anemia seems to be more prevalent in our region that study has been performed.

In conclusion, despite relatively low rate of malignant gastrointestinal malignant lesions that were found in our study population, GI tract assessment is necessary in patients with microcytic iron deficiency anemia specially in patients with symptoms related to the upper or lower gastrointestinal tract.

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