

Retrospective Study

Under-diagnosing and under-treating iron deficiency in hospitalized patients with gastrointestinal bleeding

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Abstract

AIM: To determine whether patients hospitalized with gastrointestinal (GI) blood loss anemia are being checked and treated for iron deficiency.

METHODS: Retrospective chart review was conducted for all patients admitted to a single tertiary care hospital between 11/1/2011 and 1/31/2012 for any type of GI bleeding. The primary endpoint was the percentage of patients who had their iron studies checked during a hospitalization for GI blood loss anemia. Secondary outcomes included percentage of anemic GI bleeders who had adequate documentation of anemia and iron deficiency, and those who were treated for their iron deficiency. Then we tried to identify possible predictors of checking iron studies in an attempt to understand the thought process that physicians go through when managing these patients. Iron deficiency was defined as Iron saturation less than 15% or ferritin level less than 45 µg/L. Anemia was defined as hemoglobin level less than 13 g/dL for males and 12 g/dL for females.

RESULTS: Three hundred and seven GI bleeders were hospitalized during the study period, and 282 of those (91.9%) had anemia during their hospital stay. Ninety-five patients (30.9%) had iron studies performed during hospitalization, and 45 of those (47.4%) were actually found to be iron deficient. Only 29 of those 45 iron deficient patients were discharged home on iron supplements. Of the 282 patients that had anemia during hospitalization, 50 (17.7%) had no documentation of the anemia in their hospital chart. Of the 45 patients that had lab proven iron deficiency anemia (IDA), only 22 (48.5%) had documentation of IDA in at least one note in their chart. Predictors of checking iron studies in anemic GI bleeders were lower mean corpuscular volume, documentation of anemia, having fecal occult blood testing, not having hematemesis or past history of GI bleeding. There were no significant differences between the teaching and non-teaching services in any patient characteristics or outcomes.

CONCLUSION: Iron deficiency is under-diagnosed, under-recognized even when iron studies were checked, and under-treated in hospitalized patients with GI bleeding.

Key words: Gastrointestinal bleeding; Iron deficiency anemia; Acute blood loss anemia; Iron supplements; Documentation

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Core tip: Iron deficiency anemia (IDA) is under-diagnosed and under treated in hospitalized gastrointestinal (GI) bleeders. Less than a third of our patients had evaluation of their anemia to detect IDA. Around half of these investigated patients had lab proven IDA. Less than two thirds of those patients with proven IDA received iron supplementation, which means that IDA was either under-recognized or disregarded on purpose. In an attempt to understand the reasoning of physicians leading to this discrepancy, we analyzed predictors of checking iron studies on these hospitalized GI bleeders and the main predictors were lower mean corpuscular volume and early documentation of anemia in the chart.

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INTRODUCTION

Gastrointestinal (GI) bleeding is the cause of iron deficiency anemia (IDA) in the majority of men and post-menopausal women^[1-5]. However, in our

experience, only a small percentage of anemic patients admitted to the hospital with GI bleeding undergo appropriate evaluation to detect IDA and to treat it if present. This observation has also been documented in one observational and one retrospective study on hospitalized anemic patients without GI bleeding^[6,7] but such data on hospitalized GI bleeders is not available in the literature. Our observation was puzzling because tests to detect iron deficiency are noninvasive, readily available at the hospital, inexpensive, and finally highly reliable.

Patients admitted to the hospital for GI bleed and anemia have either been chronically losing small amounts of blood or had a severe acute loss of large amounts of blood. In both cases, being iron deficient because of blood loss is highly probable. Losing 4 units of blood, chronically or acutely, will deplete completely the body iron stores^[8]. However, losing much less than 4 units is enough to start depleting the iron stores and affect erythropoiesis. From here actually arises the necessity to test any GI bleeder with anemia for iron deficiency since anemia reflects a loss of significant amount of blood that would have probably affected iron stores. This concept was made even more plausible recently after a Danish group proved in a randomized controlled trial that iron supplementation significantly improved hemoglobin levels in GI bleeders over placebo^[9]. However, there have been no studies yet assessing the degree of compliance of physicians with investigating anemia looking for IDA in GI bleeders and then treating these patients with iron supplements.

Therefore, we designed this study to determine whether patients admitted to the hospital with acute blood loss anemia secondary to GI losses are being worked up for concomitant, highly prevalent, IDA and adequately treated for their iron deficiency prior to or at discharge. Then, we tried to find possible predictors that led physicians to evaluate for iron deficiency in our anemic GI bleeders in an effort to try to explain why physicians would check some GI bleeders for iron deficiency and not others in order to hopefully be able to raise physicians' awareness about the topic and ultimately affect patient outcomes.

MATERIALS AND METHODS

This study was a retrospective chart review conducted at a single tertiary care hospital. Patients included in the study were all patients hospitalized with any kind of GI bleeding between 11/1/2011 and 1/31/2012. GI bleeding was not necessarily the primary reason for hospitalization. Excluded patients were those who were less than 18 years of age and those who were transferred from another hospital without complete medical records in the hospital electronic medical records system. The study was approved by our Institutional Review Board.

Table 1 Percentage of patients on iron supplements *n* (%)

	GI bleeders (<i>n</i> = 307)	GI bleeders with proven iron deficiency ¹ (<i>n</i> = 45)
Prior to hospitalization	44 (14.3)	7 (15.6)
During hospitalization	71 (23.1)	29 (64.4)
After hospitalization (discharge instructions)	68 (22.1)	29 (64.4)

¹Iron deficiency by laboratory results during the current hospitalization defined as either iron saturation < 15% or ferritin < 45 µg/L.

The primary endpoint of this study was the percentage of patients with iron studies performed in the hospital during a hospitalization for GI blood loss anemia. Secondary endpoints included prevalence of iron deficiency in acute GI bleeders, percentage of iron deficient patients that received treatment for their iron deficiency, percentage of anemic patients hospitalized for GI bleeding who had adequate documentation of anemia and iron deficiency in their charts. Secondary endpoints also included identifying possible predictors of checking iron studies or in other terms what were the patients' characteristics or laboratory or radiologic findings that made physicians check for iron deficiency in patients with acute blood loss anemia secondary to GI bleeding.

After identifying all ICD9 codes associated with any kind of GI bleeding, encounters that had any of these ICD9 codes within our study timeline were included in the review process. The authors then reviewed electronic medical records that were associated with these encounters. Each encounter represented one hospitalization.

Iron deficiency was defined as iron saturation less than 15% or ferritin level less than 45 µg/L. These cutoffs were used as criteria for iron deficiency in many studies in the literature^[3,6,10,11]. Serum ferritin level of less than 45 µg/L has been calculated to have a specificity of 92% and a positive likelihood ratio of 11 in diagnosing iron deficiency, and an iron saturation of less than 15% is around the 12th percentile of the iron saturation in the general population^[12,13]. Anemia was defined as hemoglobin level less than 13 g/dL for males and 12 g/dL for females as per the WHO definition of anemia^[14].

Variables obtained from the medical records for each patient included demographics like age, gender and race, and hospital team; medical history including history of anemia, transfusion, GI bleeds in the past, chronic diseases and GI diseases; medications including antiplatelets, anticoagulants and anti-acids; GI bleeding symptoms; complete blood count (CBC) result on hospital admission and lowest hemoglobin recorded in the chart during hospitalization; fecal occult blood testing (FOBT) result; iron panel including iron level, total iron binding capacity (TIBC), Transferrin, iron saturation, and ferritin; reticulocyte

count, peripheral blood smear results and bone marrow aspirate results if available; any radiology and endoscopy results; final diagnosis for the GI bleed; presence or absence and type of documentation of anemia and IDA in the electronic chart; iron treatment before, during or after hospitalization.

Statistical analysis was performed using SPSS 20.0 (SPSS, Chicago, IL, United States). Means and Frequencies were used to identify and summarize patients' characteristics and results for all continuous and categorical variables, respectively. To check for predictors of ordering iron studies in anemic patients with GI blood losses a univariate analysis was performed first comparing patients that had their iron studies done and those that did not have their iron studies done for each variable separately. Means and *t* tests were used to compare continuous variables. Crosstabs and χ^2 tests were used to compare categorical variables. All variables that were significantly different between the 2 groups on univariate analysis were included in the multivariable analysis. The multivariable analysis was performed using backward logistic regression model then confirmed with Forward and Enter models. *P*-value < 0.05 was considered to be significant.

RESULTS

Three hundred and seven charts of patients hospitalized with GI bleeding during the study period were identified and reviewed. Mean age was 66.2 ± 18.6 years. There was a slight female predominance with 177 (57.7%) females and 130 (42.3%) males. Two hundred and sixty one patients (85%) were Caucasians, 26 (8.5%) were African American or Black, and 14 (4.6%) were Hispanics. Of those 307 GI bleeders, 236 patients (76.9%) had anemia on admission to the hospital, while 282 (91.9%) had anemia at some point during their hospital stay.

As for our primary outcome, only 95 patients (30.9%) had iron studies performed during hospitalization. Additionally, 4 patients (1.3%) were discharged home with recommendations to their primary care physician to check iron studies.

We also had many secondary outcomes. Of the 95 patients that had iron studies performed, 45 were actually found to be iron deficient (47.4%). However, only 29 of those 45 iron deficient patients were discharged home on iron supplements. Iron supplementation data is summarized in Table 1.

Ninety patients (29.3%) were admitted to a residency teaching service and 217 (70.7%) to a hospitalist non-teaching service. There were no significant differences between the 2 services in any patient characteristics or outcomes.

Of the 282 patients that had anemia during hospitalization, 50 (17.7%) had no formal documentation of the anemia diagnosis on their discharge summary, 30 (9.8%) had a documented IDA, and 202 (71.6%) had a documented anemia diagnosis

Table 2 Predictors of iron deficiency anemia investigation *n* (%)

Variable	Univariate analysis ¹		Multivariate analysis	
	No iron studies (<i>n</i> = 188)	Iron studies (<i>n</i> = 94)	<i>P</i> value	OR (95%CI)
Anemia documentation ²	None	35 (92.1)		Reference
	Before discharge summary	153 (62.7)	0.001	8.45 (2.35-30.33)
History of GI bleed	None	150 (63.0)		Reference
	Yes	38 (86.4)	0.001	0.19 (0.07-0.50)
Hematemesis	None	130 (61.6)		Reference
	Yes	58 (81.7)	0.003	0.32 (0.15-0.68)
FOBT	Negative	56 (62.9)	< 0.001 ³	Reference
	Positive	59 (55.7)	0.07	1.87 (0.95-3.69)
	Not performed	73 (83.9)	0.005	0.32 (0.14-0.71)
MCV ⁴		90.5 ± 9.4 fL	< 0.001	0.95 (0.93-0.98)

¹All variables included in multivariable analysis were statistically significant on univariate analysis, including all the variables shown in this table;

²Anemia documentation on any note including admission, consultation or progress notes but excluding discharge summary; ³*P* value for trend; ⁴MCV is a continuous variable, so a OR < 1 means that higher MCV was inversely associated with iron deficiency investigation (with every 1 fL increase in MCV there was a 5% decrease in probability of getting iron studies). GI: Gastrointestinal; IDA: Iron deficiency anemia; FOBT: Fecal occult blood testing; MCV: Mean corpuscular volume. Variables included in the multivariable logistic regression but excluded from the table above for being not statistically significant are: Iron supplements on admission, occult bleeding, and lowest hemoglobin. All patients' characteristics that were not included in the multivariate regression were not significantly different on univariate analysis.

without specification whether it was iron deficient or not. Of the 45 patients that had lab proven IDA, only 22 (48.5%) had documentation of IDA in at least one note in their chart.

On multivariable analysis, using logistic regression modeling, predictors of checking iron studies in anemic patients with GI blood losses are presented in Table 2.

DISCUSSION

Our results confirmed our original hypothesis. IDA is under-diagnosed and under treated in hospitalized GI bleeders. Less than a third of our patients had evaluation of their anemia to detect IDA. Around half of them had lab proven IDA and less than two thirds of those patients with proven IDA received iron supplementation.

In an attempt to understand the reasoning that was leading physicians not to check iron studies and then sometimes to not prescribe iron supplements for patients that did turn out to have IDA, we designed the study with our secondary outcomes in mind, too. These results we think were able to explain this problem partially but not completely by any means.

According to our results, lower mean corpuscular volume (MCV) was associated with higher probability of checking iron studies. This reflects the current teaching that IDA is a microcytic anemia. However, this finding also means that physicians might be getting deterred from checking iron studies when there is no microcytosis and forgetting or dismissing the fact that there might be an overlap with another kind of anemia like anemia of chronic disease or B12 deficiency that keeps the MCV within normal range.

Documenting anemia as a diagnosis on any note including History and Physical, consult note, or

progress note, but excluding discharge summary note, was also associated with ordering iron studies. This finding reflects the fact that when physicians were aware of the anemia and hence documented it in their notes they were more likely to investigate it. This reasoning might lead us to say that in the cases where patients did not get their iron studies checked, physicians in some of these instances, at least, might have been unaware of a mild anemia or did not consider that it was important or worthy enough to spend time documenting it or working it up, especially when patients had many other comorbidities. The documentation of anemia or IDA on the discharge summary note was not part of that variable because it would be more of a consequence rather than a predictor of IDA since discharge summaries are generally written after discharge.

Our search for iron deficiency investigation predictors also resulted in 3 other predictors that were all inversely associated with ordering iron studies: Past history of GI bleeding, hematemesis as one of the symptoms of the current GI bleeding episode, and not having a FOBT done during this current hospitalization.

It was especially surprising to find that having a past history of GI bleeding was a deterrent for physicians to check their patients iron storage levels since these patients were probably even more iron deficient than others since they have lost at least part of their iron stores in the previous bleeding event. A possible explanation for this finding could be that physicians consider patients presenting with anemia in the setting of a GI bleed, especially recurrent GI bleed, to have an explained anemia that does not need further workup and forget about the iron losses that accompany the blood losses which require replacement for a quicker hemoglobin recovery.

Hematemesis was the only symptom that was associated in any way with predicting iron level evaluations. It was most likely a confounding variable for something else that we did not assess in our multivariate analysis because there is no clear clinical reasoning that might explain why hematemesis would be associated with iron stores evaluation while melena, for example, was not evaluated.

Like any retrospective study, our study has its own limitations. We could not follow up patients after their discharge from the hospital. We could not contact them or check their outpatient records. However, we checked discharge summaries for any recommendations from the hospitalist to the patient's primary care physician regarding anything related to anemia or IDA in an attempt to try to minimize this specific limitation in the study design that could not have been otherwise overcome given that it is a retrospective chart review study. In the absence of a prospective randomized trial on the subject, our study is still the best evidence on the topic so far.

Our study had a good representative sample of GI bleeders that get admitted to our hospital. It included all patients hospitalized with any GI bleed as a primary or a secondary diagnosis for a whole 3 mo period. We believe that 3 mo is a long enough period to represent the usual population and be able to capture the usual practices of our physicians. Our study also included patients on 2 different types of services, the residency teaching services and the hospitalist non-teaching service. All patients' characteristics were the same between the 2 services, which was expected since patients were admitted usually randomly to either the residency team or the hospitalist team. However, patient outcomes were also not different and being on one team instead of the other was not a predictor of a different outcome regarding iron studies or iron supplementation.

In conclusion, Iron deficiency was under-diagnosed and under-treated in hospitalized GI bleeders. Possible reasons could be that physicians are dismissing iron deficiency when there is no microcytosis, forgetting about the possibility of overlap with another type of anemia, or when anemia is not very severe they might be deeming it unimportant or unworthy of investigation in a sick patient.

We believe that investigating GI bleeders for iron deficiency is important, especially that there is evidence in the literature that upper GI bleeders treated with iron had significantly higher hemoglobin with 2.0 g/dL difference on average compared to placebo as early as 4 wk from hospital discharge^[9]. Therefore, we believe that physicians need to be made aware of our results and about that topic in general for better patient care and outcomes. We understand that our study is a retrospective study and that it has its limitations, therefore a future prospective trial might add strength to the evidence.

COMMENTS

Background

From the authors' experience, only a small percentage of anemic patients admitted to the hospital with gastrointestinal (GI) bleeding undergo appropriate evaluation to detect iron deficiency anemia (IDA) and to treat it if present. This observation has also been documented in two other studies on hospitalized anemic patients without GI bleeding but such data on hospitalized GI bleeders is not available in the literature.

Research frontiers

One recent randomized controlled trial proved that iron supplementation significantly improved hemoglobin levels in GI bleeders over placebo. However, there have been no studies yet assessing the degree of compliance of physicians with investigating anemia looking for IDA in GI bleeders and then treating these patients with iron supplements.

Innovations and breakthroughs

This is the first study to address this specific question. The authors designed this study to determine whether patients admitted to the hospital with acute blood loss anemia secondary to gastrointestinal losses are being worked up for concomitant, highly prevalent, IDA and adequately treated for their iron deficiency prior to or at discharge. The results indicated that IDA was under-diagnosed and under-treated in this group of patients.

Applications

The authors hope that our study will help in raising physicians' awareness about this topic of IDA in GI bleeders for a better recognition and treatment of IDA and ultimately affect patient outcomes.

Terminology

IDA was defined as hemoglobin less than 13 g/dL in males and 12 g/dL in females with iron saturation less than 15% or ferritin level less than 45 µg/L.

Peer-review

The paper is very interesting and important because it highlights the fact that IDA is underestimated even in the United States.

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