Oral iron absorption test: myth or reality?

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ABSTRACT

Introduction: Anemia is a serious health problem affecting one-third of the world's population. The most common etiology is iron deficiency anemia (IDA). The oral iron absorption test (OIAT) is a method that has been used for a long time to demonstrate the level of iron absorption in patients, but it has not reached widespread use in clinical practice. The study aims to analyze predictive factors of iron absorption in patients with IDA.

Material and methods: A total of 108 patients between the ages of 18–65 who were diagnosed with IDA were included and patients with concomitant inflammatory bowel disease, celiac disease, history of gastrointestinal surgery, malignancy, using iron therapy, and patients with unavailable data were excluded from the study. OIAT applied to 108 patients.

Results: Female patients form the majority of the cohort (n = 100, 92.6%). OIAT was administered to 54 patients in tablet form and 54 patients in capsule form. The following study compared 88 patients with adequate oral iron absorption and 20 patients with insufficient oral iron absorption. Less iron absorption was found in male patients (p = 0.04) with increasing age, and it was statistically significant (p = 0.02).

Conclusion: The result of the current study demonstrated that male gender and older age have a significant impact on iron absorption. OIAT is recommended at the time of diagnosis in elderly patients and male patients so that the underlying cause can be identified without delay in the insufficient iron absorption group. Additionally, patients with oral iron absorption disorders can be diagnosed at an early stage by applying the OIAT.

Key words: anemia, iron, iron deficiency, tablet, capsule

INTRODUCTION

Anemia is a serious health problem affecting one-third of the world's population. The World Health Organization defines anemia as having a hemoglobin level below 12 g/dL for women, below 11 g/dL for pregnant women, and 13 g/dL for men. The most common etiology of anemia is iron deficiency anemia (IDA) and it is described as a ferritin level below 15 mg/dL and transferrin saturation below 16%. Since ferritin is an acute phase reactant, making a diagnosis entirely based on it could result in mistakes. IDA is an important public health problem affecting more than 1 billion people worldwide [1, 2]. In daily practice, patients may present with various signs of anemia. Symptoms are usually determined by the severity of anemia and any concomitant disorders [3, 4].

Laboratory assessment of iron parameters may guide clinicians in the differential diagnosis. In Table 1, the diagnostic approach is summarized according to laboratory values [5, 6].

The average person's body has 3 grams of iron for women and 4 grams of iron for men. Daily iron intake is between 10 and 20 mg, of which only 10% is absorbed, and most of which is utilized by hemoglobin [7]. Acute or chronic blood loss and poor dietary iron absorption are the two main causes of iron insufficiency. In developed countries, acute or ongoing blood loss is the most frequent cause. Decreased iron absorption is one of the rare causes of iron

Table 1. Laboratory assessment of iron parameters*

Variable	Normal values (adults)	Iron deficiency anemia	Functional iron deficiency	IRIDA	Anemia of chronic disease
Serum iron [µg/dL]	10–30	↓	N/↓	↓	↓
TSAT [%]	16–45	< 16	↓	< 10	N/↓
Serum ferritin [ng/mL]	20–200 (F) 40–300 (M)	↓	N	Variable	> 100
Hb [g/dL]	>12 (F) >13 (M)	↓	N	↓	↓
MCV [fL]	80–95	< 80	N	↓↓	N/↓
Serum hepcidin	**	↓↓	↓	N/↑	↑

*It is modified from reference [5] and [6]; **normal values are according to the method used; Hb — hemoglobin; F — female; IRIDA — iron-refractory iron deficiency anemia; M — male; MCV — mean corpuscular volume; N — normal; TSAT — transferrin saturation

deficiency, and absorption occurs mostly from the upper gastrointestinal tract, mostly in the duodenum. Atrophic gastritis, celiac disease, *Helicobacter pylori* infection, which affect the absorption ability of the gastric mucosa, and gastrectomy operations performed for various reasons, and the use of drugs that disrupt gastric pH such as proton pump inhibitors are important causes of iron deficiency due to malabsorption. The cause of the deficiency should be determined before beginning treatment for iron deficiency anemia to decide the form of replacement therapy, oral or intravenous. Ferric maltose, ferrous fumarate, ferrous gluconate, and ferrous sulfate are available in oral forms, while ferric carboxymaltose is commonly used intravenously [8–11].

The oral iron absorption test (OIAT) is a method that has been used for a long time to show the level of iron absorption in patients but has not reached widespread use in clinical practice. Identifying patients with OIAT absorption problems can guide us to prefer intravenous iron therapy instead of oral iron therapy [12, 13]. The current study aimed to analyze predictive factors of iron absorption in patients with IDA.

MATERIAL AND METHODS

The study was conducted in Ankara City Hospital Hematology outpatient clinic. The data of the patients were retrieved from retrospective records between 2018–2019. The local institutional review board approved this study. The study was performed under the ethical principles of the Declaration of Helsinki.

Patients between the ages of 18–65 who were diagnosed with IDA were included in the study. Patients with concomitant inflammatory bowel disease, celiac disease, history of gastrointestinal surgery, malignancy, using iron therapy, and patients with unavailable clinical and laboratory data were excluded from the study. Demographic data, a full blood count, and biochemistry test results were all recorded at the time of diagnosis. Arterial hypertension, diabetes mellitus, coronary artery disease, asthma, and thyroid diseases were recorded as comorbidities.

Oral iron absorption test: the iron level of the patients was measured initially in the morning on an empty stomach and two hours after taking the oral iron preparation. The iron level was measured two hours after taking a total of 540 mg (ferrous sulfate) of coated tablet form or 567.7 mg of capsule form together with water. An increase in serum iron of 100 mg/dL between two measurements was considered sufficient for oral iron absorption [14, 15].

The study compared the absorption levels of capsule and tablet forms of ferrous sulfate. In addition, the groups with adequate and insufficient absorption of iron and investigated the factors predicting absorption were compared.

The statistical analyses were performed with SPSS software (version 26, Armonk, NY). The data were summarized by presenting the continuous data as a median (range) and the categorical data as a ratio and percentage. To compare groups, the Mann-Whitney U test and chi-square tests were applied. A two-sided p value ≤ 0.05 was regarded as statically significant.

RESULTS

A total of 108 patients with a diagnosis of IDA were included in the study. 100 (92.6%) of the patients were female whereas 8 (7.4%) of them were male. At least one comorbidity was present in 25 individuals (23.1%). Demographic data and laboratory findings of the patients are summarized in Table 2.

An oral iron absorption test was performed on a total of 108 patients. It was administered to 54 patients in tablet form and the other 54 patients in capsule form. The two groups were similar in terms of age, sex, comorbidities, and baseline laboratory tests. While there was 89% adequate absorption in the group with tablet form, this rate was 74.1% in the group with capsule form ($p = 0.05$). The findings from the oral iron absorption test are summarized in Table 3.

The study compared 88 patients with adequate oral iron absorption and 20 patients with insufficient oral iron absorption. It was found that male patients ($p = 0.04$) and increased age ($p = 0.02$) were associated with poor iron absorption. In addition, although statistically different, the baseline laboratory test results for mean corpuscular volume (MCV), white blood cell (WBC), and thrombocytes were not considered clinically significant. The comparison between the two groups is summarized in Table 4.

Table 2. Demographic data and laboratory findings of the patients

Parameter	N, (%, range)
Age	39 (18–62)
Sex (female/male)	100/8 (92.6%/7.4%)
Comorbidity (yes)	25 (23.1%)
Basal laboratory	
Hb [g/dL]	11.0 (5.1–12.9)
HCT [%]	35.0 (24.5–38.4)
MCV [fL]	74.1 (19.9–92.7)
RDW [%]	15.8 (11.9–22.6)
WBC [× 10^3 cells/μL]	6.73 (3.23–12.17)
Thrombocyte [× 10^3 cells/μL]	284 (160–565)
Serum iron level [μg/dL]	28.5 (11–79)
Iron binding capacity [μg/dL]	425 (271–633)
Ferritin [ng/mL]	7.7 (2–100)
Vitamin B12 [ng/L]	336 (110–2000)
Folic acid [μg/L]	8.1 (2.0–100)

Hb — hemoglobin; HCT — hematocrit; MCV — mean corpuscular volume; RDW — red cell distribution width; WBC — white blood cell

DISCUSSION

IDA is an important problem, and patients resistant to oral iron therapy need further investigation. In the study by Hershko et al. [16], more than half of the patients with oral iron treatment resistance had celiac disease, autoimmune gastritis, or *Helicobacter pylori* infection. According to the study of Dahlerup et al. [17], gastrointestinal system cancer was the primary cause of up to 15% of the patient group with IDA.

OIAT is a method that has been used for a long time to show the level of iron absorption in patients. If OIAT can be practically performed on patients at the time of diagnosis, patients with insufficient oral iron absorption will not be given unnecessary oral iron therapy and the underlying cause will be investigated more quickly. OIAT still plays a crucial part in clinical practice. It can help guide future management by identifying patients with insufficient absorption as soon as possible. It may also help to choose patients for whom parenteral iron treatment should be considered. With these concerns, the authors performed OIAT in the study patients with IDA and analyzed the predictive and risk factors. It was found that about 20% of patients had insufficient absorption. Then were compared patients who had inadequate iron absorption with patients who had adequate iron absorption. An increased age and male gender were observed to be associated with worse oral iron absorption ($p < 0.05$)

In a study by Silay et al. [13], patients over 65 years of age were compared with patients under 65 years of age, and it was discovered that older patients absorbed less iron ($p = 0.01$), which is consistent with the present findings. In this study, although patients over the age of 65 were not included, it was found that iron absorption decreased with older age ($p = 0.02$). Patients with advanced age, male gender, and low hemoglobin levels were more likely to develop cancer, according to a study by Dahlerup et al. [17]. In the present study, it was found that worse iron absorption was associated with male patients and with increasing age. Patients, particularly men and the elderly, should be assessed for OIAT. Patients with poor absorption should not be treated with an oral iron formulation, and the underlying cause of inadequate iron absorption should be determined as soon as possible following intravenous iron therapy.

The test can be formed in either capsule or tablet forms. The present study examined OIAT in IDA patients and discovered that 48 (89%) of 54 patients who received OIAT in tablet form had sufficient absorption. It was also found that in the group where the absorption test was done using the capsule form, 40 (74.1%) of the 54 individuals had adequate absorption. It was determined that this difference was statistically significant. In the present research, it was

Table 3. Oral iron absorption test

Variable	Tablet form	Capsule form	p values
Age	35.5 (18–59)	40 (18–62)	
Sex (female/male)	52/2	48/6	0.14
Comorbidity (yes)	12 (22%)	13 (24%)	0.82
Basal laboratory			
Hb [g/dL]	10.9 (5.1–12.9)	11 (5.5–12.8)	0.77
HCT [%]	35.1 (21.5–38.4)	35 (21.8–38.3)	0.55
MCV [fL]	76.3 (53.6–92.7)	74.15 (57.4–88.4)	0.37
RDW [%]	15.5 (11.9–22.5)	16.3 (12.7–22.6)	0.41
WBC [× 10^3 cells/μL]	6.68 (3.43–12.17)	6.815 (3.23–9.73)	0.81
Thrombocyte [× 10^3 cells/μL]	272 (106–534)	303 (113–565)	0.10
Serum iron level [μg/dL]	29 (11–79)	28 (11–74)	0.56
Iron binding capacity [μg/dL]	413.9 (271–543)	432.8 (305–633)	0.08
Ferritin [ng/mL]	8.2 (2.9–100)	7.6 (2–55.7)	0.18
Vitamin B12 [ng/L]	353 (200–2000)	307 (110–1685)	0.08
Folic acid [μg/L]	7.8 (2.2–20)	8.3 (2.3–20)	0.49
Adequate iron absorption	48 (89%)	40 (74.1)	**0.05***

*$p \leq 0.05$ was assessed as statistically significant; Hb — hemoglobin; HCT — hematocrit; MCV — mean corpuscular volume; RDW — red cell distribution width; WBC — white blood cell

Table 4. Iron absorption groups

Parameters	Adequate iron absorption		p values
	Yes (n = 88)	No (n = 20)	
Age	37 (18–59)	43.5 (25–62)	**0.02***
Sex (female/male)	84/4	16/4	**0.04***
Comorbidity (yes)	22 (25%)	3 (15%)	0.34
Basal laboratory			
Hb [g/dL]	11 (5.1–12.9)	10.2 (5.5–12.8)	0.32
HCT [%]	35.3 (21.5–38.4)	32.2 (21.8–38.3)	0.3
MCV [fL]	76.4 (53.6–92.7)	69.8 (57.4–85.5)	**0.02***
RDW [%]	15.5 (11.9–22.5)	16.8 (13.1–22.6)	0.25
WBC [× 10^3 cells/μL]	7 (3.43–12.17)	6.03 (3.23–9.93)	**0.05***
Thrombocyte [× 10^3 cells/μL]	298 (123–565)	235 (106–387)	**0.001***
Serum iron level [μg/dL]	28.5 (11–202)	28.5 (11–310)	0.94
Iron binding capacity [μg/dL]	432 (271–543)	417 (274–633)	0.19
Ferritin [ng/mL]	7.6 (2.8–67.6)	8.7 (2–100)	0.55
Vitamin B12 [ng/L]	346 (147–1685)	343 (110–2000)	0.57
Folic acid [μg/L]	8.1 (2.1–20)	8 (3–20)	0.63

*p ≤ 0.05 was assessed as statistically significant; Hb — hemoglobin; HCT — hematocrit; MCV — mean corpuscular volume; RDW — red cell distribution width; WBC — white blood cell

discovered that OIAT in tablet form was more effective. This may be due to the late opening of the capsule form from the gastrointestinal tract. Therefore, when OIAT will be done in daily practice, it may be more appropriate to do it in tablet form. However, both oral agents can be preferred for treatment [18].

As a result of the present study, the authors have advised that the OIAT test be performed on a subset of patients as performing it on every patient will result in higher expenses. On the other hand, starting parenteral therapy early stages as a result of the OIAT test may also benefit clinicians' time and cost.

The limitation of this study is that it is a retrospective study. The investigation revealed significantly lower absorption in male patients, but because there are fewer male patients than female patients in this study, this conclusion needs to be confirmed by studies that include a larger population. Another limitation is the lack of data on the causes of iron deficiency. The positive aspect of this research is that, to the authors' knowledge, it is the first study in the literature to compare tablet form and capsule form for OIAT.

CONCLUSION

In conclusion, for daily practice, oral iron absorption testing in tablet form is more convenient than in capsule form. If possible, the authors recommend OIAT at the time of diagnosis to all patients with IDA. Particularly, it is suggested that OIAT should be performed in elderly patients and male patients so that the underlying cause can be identified without delay in the insufficient iron absorption group. Additionally, patients with oral iron absorption disorders can be diagnosed at an early stage by applying the OIAT and these patients can start parenteral therapy earlier. Prospective investigations are needed for OIAT.

Article information

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REFERENCES

1. Camaschella C. Iron deficiency. Blood. 2019; 133(1): 30–39, doi: 10.1182/blood-2018-05-815944, indexed in Pubmed: 30401704.
2. Chaparro CM, Suchdev PS. Anemia epidemiology, pathophysiology, and etiology in low- and middle-income countries. Ann NY Acad Sci. 2019; 1450(1): 15–31, doi: 10.1111/nyas.14092, indexed in Pubmed: 31008520.
3. Lopez A, Cacoub P, Macdougall IC, et al. Iron deficiency anaemia. Lancet. 2016; 387(10021): 907–916, doi: 10.1016/S0140-6736(15)60865-0, indexed in Pubmed: 26314490.
4. Bager P. Fatigue and acute/chronic anaemia. Dan Med J. 2014; 61(4): B4824, indexed in Pubmed: 24814598.
5. Elstrott B, Khan L, Olson S, et al. The role of iron repletion in adult iron deficiency anemia and other diseases. Eur J Haematol. 2020; 104(3): 153–161, doi: 10.1111/ejh.13345, indexed in Pubmed: 31715055.
6. Camaschella C. Iron deficiency: new insights into diagnosis and treatment. Hematology Am Soc Hematol Educ Program. 2015; 2015: 8–13, doi: 10.1182/asheducation-2015.1.8, indexed in Pubmed: 26637694.
7. Santiago P. Ferrous versus ferric oral iron formulations for the treatment of iron deficiency: a clinical overview. ScientificWorldJournal. 2012; 2012: 846824, doi: 10.1100/2012/846824, indexed in Pubmed: 22654638.
8. Camaschella C. Iron deficiency: new insights into diagnosis and treatment. Hematology Am Soc Hematol Educ Program. 2015; 2015: 8–13, doi: 10.1182/asheducation-2015.1.8, indexed in Pubmed: 26637694.
9. Stoffel NU, von Siebenthal HK, Moretti D, et al. Oral iron supplementation in iron-deficient women: How much and how often? Mol Aspects Med. 2020; 75: 100865, doi: 10.1016/j.mam.2020.100865, indexed in Pubmed: 32650997.
10. Li N, Zhao G, Wu W, et al. The efficacy and safety of vitamin C for iron supplementation in adult patients with iron deficiency anemia:

a randomized clinical trial. JAMA Netw Open. 2020; 3(11): e2023644, doi: 10.1001/jamanetworkopen.2020.23644, indexed in Pubmed: 33136134.
11. Lichtenstein GR, Onken JE. Improved hemoglobin response with ferric carboxymaltose in patients with gastrointestinal-related iron--deficiency anemia versus oral iron. Dig Dis Sci. 2018; 63(11): 3009–3019, doi: 10.1007/s10620-018-5204-3, indexed in Pubmed: 30056562.
12. Gardyn J, Chapal N, Floru S. Oral iron absorption test: a simple test with relevance in the clinical setting. Isr Med Assoc J. 2021; 23(10): 662–664, indexed in Pubmed: 34672450.
13. Silay K, Akinci S, Yalcin A, et al. The status of iron absorption in older patients with iron deficiency anemia. Eur Rev Med Pharmacol Sci. 2015; 19(17): 3142–3145, indexed in Pubmed: 26400514.
14. Hacibekiroglu T, Akinci S, Basturk AR, et al. et al.. A forgotten screening test for iron deficiency anemia: oral iron absorption test. Clin Ter. 2013; 164(6): 495–497, doi: 10.7417/CT.2013.1627, indexed in Pubmed: 24424212.
15. Alleyne M, Horne MK, Miller JL. Individualized treatment for iron-deficiency anemia in adults. Am J Med. 2008; 121(11): 943–948, doi: 10.1016/j.amjmed.2008.07.012, indexed in Pubmed: 18954837.
16. Hershko C, Hoffbrand AV, Keret D, et al. Role of autoimmune gastritis, Helicobacter pylori and celiac disease in refractory or unexplained iron deficiency anemia. Haematologica. 2005; 90(5): 585–595, indexed in Pubmed: 15921373.
17. Dahlerup JF, Eivindson M, Jacobsen BA, et al. Diagnosis and treatment of unexplained anemia with iron deficiency without overt bleeding. Dan Med J . 2015; 62(4): C5072, indexed in Pubmed: 25872536.
18. Auerbach M, Adamson JW. How we diagnose and treat iron deficiency anemia. Am J Hematol. 2016; 91(1): 31–38, doi: 10.1002/ajh.24201, indexed in Pubmed: 26408108.