Oral Iron Absorption Test: A Simple Test with Relevance in the Clinical Setting

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ABSTRACT **Background:** Iron deficiency anemia is a widespread problem. Although oral and intravenous therapy are available, iron malabsorption is a distinct possibility.

Objectives: To evaluate the applicability of the oral iron absorption test (OIAT) as a simple and effective means of determining the degree of oral iron absorption.

Methods: The study comprised 81 patients diagnosed with iron deficiency anemia who were referred to a hematology outpatient clinic. Participants were given two ferrous sulphate tablets. Iron levels in the blood were evaluated at intervals from 30 to 180 minutes after iron administration.

Results: We divided patients into three distinct groups. The first group consisted of patients with little iron absorption with a maximum iron increment (Cmax) in the blood of 0–49 ug/dl. The second group had a moderate maximum absorption of 50–100 ug/dl, while a third group had considerable absorption of with maximum iron increase of over 100 ug/dl.

Conclusions: The oral iron absorption test, although not clearly standardized, is easy to conduct in any outpatient clinic. This test can readily and clearly determine absorption or nonabsorption of iron. This test can have major implications on the need of oral or intravenous iron therapy and can also determine the need for further gastrointestinal evaluation of the small intestine, where iron absorption takes place and the success of therapy on subsequent iron absorption.

IMAJ 2021; 23: 662–664

KEY WORDS: hematology laboratory test, intravenous iron, iron deficiency anemia, iron malabsorption

Iron deficiency anemia (IDA) is a widespread problem. IDA is commonly treated with oral iron, which is convenient, inexpensive, and effective. Although many iron compounds exist, treatment with ferrous sulphate is the most common, although ferrous fumarate and ferrous gluconate are also effective.

There are several disorders that impair iron absorption [1]. To study iron absorption, the oral iron absorption test (OIAT) was introduced approximately 70 years ago. At first iron radioisotopes were used, but due to expense, radiation exposure, and technical difficulties an alternative method was developed. Usually ferrous sulphate was given and serial determination of sequential serum iron levels obtained over a period of several hours [2].

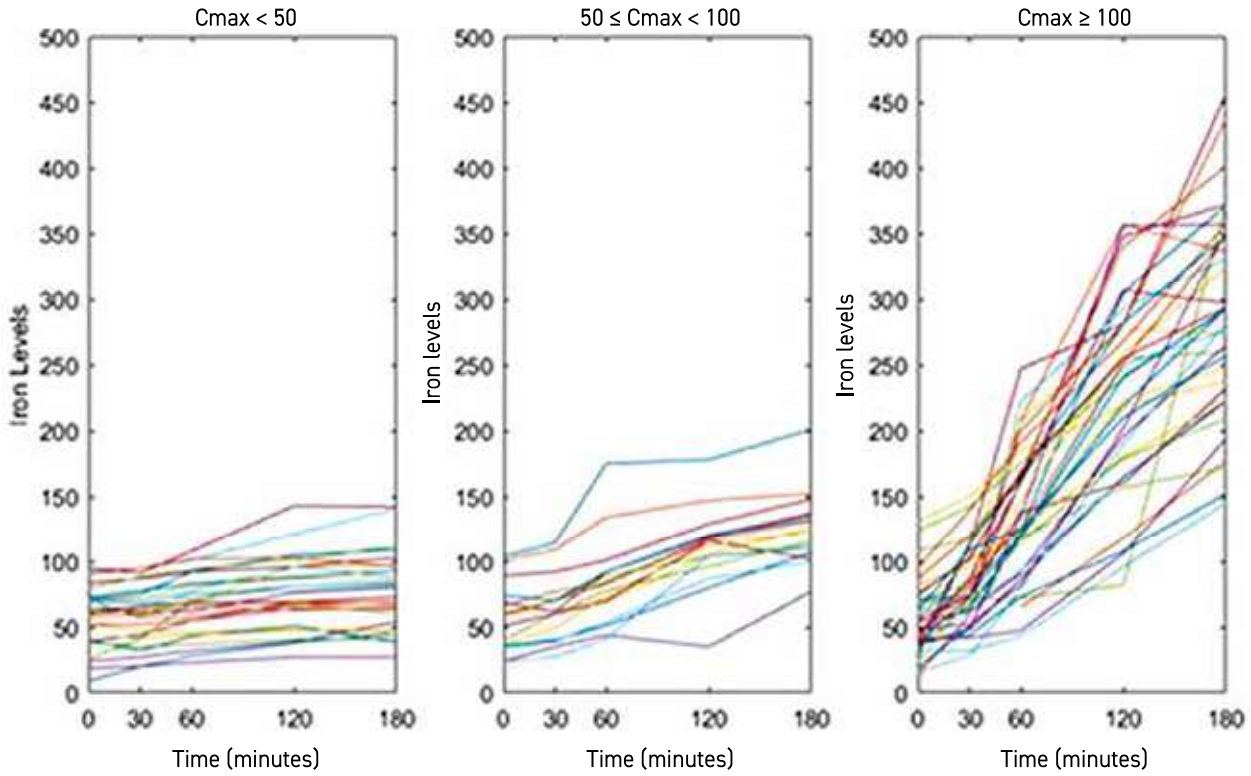
However, this test has not been used extensively in the clinical setting. Most recent reviews of IDA fail to mention or provide scant details of the OIAT. Camaschella [3] reported that the test is rarely used since it has not been extensively validated. She described the test as the administration of 60mg of iron and measurement of serum iron 1–2 hours later. Lopez et al. [4] stated that true malabsorption can be diagnosed by giving an oral dose of 50–60 mg of liquid ferrous sulphate and measuring serum iron concentration 1–2 hours later. In yet another review, Joosten [5] proposed that when iron malabsorption is suspected an OIAT can be conducted after an oral iron load, although adding that the test has not been validated, multiple iron doses are used and interpretation of the results is not standardized. However, it is a non-invasive test that can provide some limited additional information. In their flow chart for gastrointestinal investigation of elderly patients with IDA, an OIAT was recommended before iron treatment in those patients, in whom no clear diagnosis had been obtained after laboratory determination of IDA, serology to exclude celiac, or subsequent endoscopic or computed tomography evaluation of the gastrointestinal tract [5].

PATIENTS AND METHODS

To examine the relevance of the OIAT in the clinical setting we collected the results of this test in 81 patients referred to a hematology outpatient clinic for anemia for whom IDA had been diagnosed. Patients included 50 female and 31 male aged between 20 and 85 years. They had been requested to stop all iron therapy for 4 days prior to the test. They were also asked to abstain from dairy products, cereals, tea, and coffee on the day of the examination. An intravenous catheter was then placed and baseline serum iron levels taken. Empirically two ferrous sulphate tablets 325 mg each containing 105 mg of elemental iron (this dose had been the standard dose in the clinic) were then given. Serum iron levels were then obtained for 30, 60, 120, and 180 minutes after ingestion [Figure 1]. The maximum increase in serum iron from the baseline level (Cmax) was then calculated.

Figure 1. Serum iron levels at baseline and 30, 60, 120, and 180 minutes after oral iron had been given to each of the 81 patients from each of the three groups

[A] Cmax < 50 ug/dl **[B]** Cmax 50–100 ug/dl **[C]** Cmax > 100 ug/dl



RESULTS

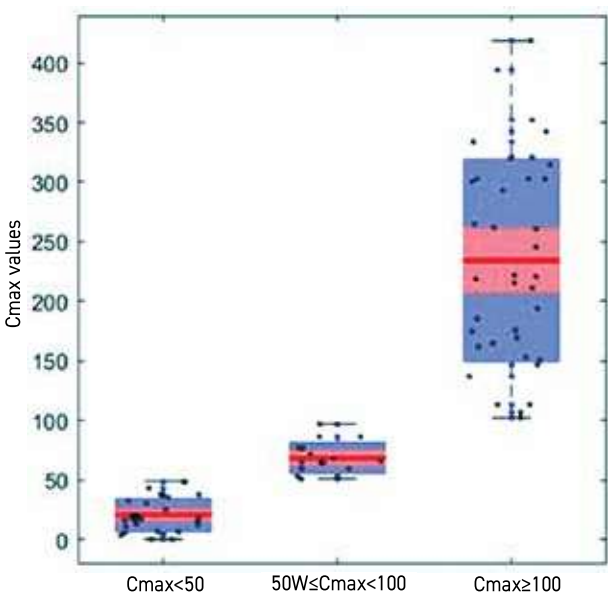
We managed to divide these 81 patients into three distinct groups according to the Cmax values obtained. Group 1 consisted of 27 patients (33%) with Cmax values of 0–49 microgram/deciliter (ug/dl). Group 2 included 16 patients (20%) with Cmax of 50–100 ug/dl, and group 3 comprised 38 patients (47%) with Cmax over 100 ug/dl [Figure 2].

Based on these results, we ascertained that serum levels must be taken for at least 180 minutes, as in many cases (80% of patients) the maximum level Cmax was obtained only after 180 minutes.

DISCUSSION

We believe the OIAT remains relevant today both to pursue further examination for malabsorption in the small intestine as outlined [1] and also to determine which patients to refer for intravascular (IV) iron therapy. Most recommendations still prefer initiation with oral iron, which is still considered the mainstay of therapy, although IV therapy has become more widespread and preferred when severe side effects with oral

Figure 2. Values of Cmax for each patient and of all three groups. Each circle represents the Cmax value of an individual patient



compounds, malabsorption, persistent or heavy blood loss, or low levels of hemoglobin below 8 gm/dl are found [6]. Although IV iron was shown to be relatively safe by a meta-analysis [7], until recently the United States Food and Drug Administration still expressed concern over safety issues with IV iron [8]. Therefore, a simple test, which clearly differentiates between patients who will readily absorb iron and those with difficulties, would clearly be most beneficial and could help decide which treatment should be given.

We concur with several authors that a Cmax level of 100 mg/dl is indicative of adequate absorption [4,9]. We nonetheless divided our patients into three groups, including a group with a Cmax of 50–100 ul/dl, as we believe, at the moment arbitrarily, that patients with Cmax of 50–100 ul/dl should be offered a trial of oral iron until further validation. However, we found that measurement of iron must also be conducted at 180 minutes as the Cmax of 80% of our patients was only obtained at this time.

CONCLUSIONS

We found the OIAT to be very reliable and of great use in the daily clinical setting. Successful treatment for iron malabsorption can be ascertained by repeating the OIAT after establishing factors causing malabsorbtion and determining whether Cmax values had improved. Recent studies have noted that alternate day oral iron therapy is preferable to daily therapy, which can also be verified with the OIAT. The question whether certain iron medications are better than others can also be determined by this test. We believe that this fairly neglected yet simple test has a definite place in the management of iron deficiency anemia.

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Capsule

Coronavirus targeting a range of betacoranaviruses

In the past 20 years, three highly pathogenic β-coronaviruses have crossed from animals to humans, including the most recent: severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). A spike protein that decorates these viruses has an S1 domain that binds host cell receptors and an S2 domain that fuses the viral and cell membranes to allow cell entry. The S1 domain is the target of many neutralizing antibodies but is more genetically variable than S2, and antibodies can exert selective pressure, leading to resistant variants. **Pinto** and colleagues identified five monoclonal antibodies that interact with a helix in the S2 domain. The most broadly neutralizing antibody inhibited all β-coronavirus subgenera and reduced viral burden in hamsters infected with SARS-CoV-2.

Science 2021; 373: abj3321
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Capsule

T Cells T_{regs} potentiate skin inflammation

Regulatory T cells (T_{regs}) regulate various immune responses all over the body, with their specific roles differing between anatomical locations. In the skin, T_{regs} help to control wound healing, but the details of their role in this process are unclear. **Moreau** and colleagues used transcriptomics and engineered mouse models to show that T_{regs} in the skin have heightened transforming growth factor-β (TGF-β) signaling and αvβ8 integrin expression, which contributes to delayed epidermal repair after inducing skin injury. Specifically, αvβ8 expression in skin T_{regs} helps to activate TGF-β in neighboring keratinocytes, leading to innate immune influx and protection from *Staphylococcus aureus* infection. These data provide a better understanding of the interactions between T_{regs} and epithelial cells in the skin during skin injury and bacterial infection.

Sci Immunol 2021; 6: abg2329
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