Iron deficiency anaemia is a common condition that can be caused by low dietary intake of iron, reduced absorption, increased metabolic demand or blood loss. The mainstay of treatment is iron replacement

How to identify and treat adults with iron deficiency anaemia

By Deirdre Lynskey, BMBS, MRPharmS, and Stephanie Machin, MBBS

The term “anaemia” can describe either a reduced total number of red blood cells or a reduced level of haemoglobin within those cells. Haemoglobin is an oxygen-binding protein complex that carries oxygen to metabolically active cells. Without sufficient levels of haemoglobin the transport of oxygen throughout the body, together with many intracellular and enzymatic processes, is significantly impaired.

The World Health Organization defines anaemia as a haemoglobin level of less than 12g/dl for adult (non-pregnant) women and less than 13g/dl for adult men.1

There are different forms of anaemia but the most common affecting people in the developed world is iron deficiency anaemia (IDA).1 Iron is a dietary mineral that is an essential part of haemoglobin — it is necessary to maintain healthy bone marrow and a consistent turnover of red blood cells with their full quotient of haemoglobin.

The cause of anaemia must be investigated fully and appropriate management instigated when a diagnosis is made because anaemia has been associated with:2

- Increased mortality in the elderly
- An increased risk of falls
- Impaired cognition
- Reduced muscle strength and physical function
- Impaired quality of life

Causes of IDA
Deficiency of iron can be broadly classified as resulting from any of four causes: poor dietary intake (particularly among vegetarians); decreased absorption (eg, in Coeliac disease); increased metabolic demand (eg, in pregnancy); or excessive blood loss (acute or chronic).1

When a diagnosis of IDA is made it is important that the patient undergoes investigation for any sinister underlying cause. For premenopausal women IDA commonly occurs due to menstrual blood loss, pregnancy or lactation. In adult men and postmenopausal women, IDA may be the only indicator of occult blood loss from the gastrointestinal tract due to a colonic or gastric carcinoma.3

How IDA is diagnosed
A simple blood test looking at the characteristics of red blood cells can diagnose IDA. First, a low haemoglobin (Hb) level is necessary for a diagnosis of anaemia. Second, the mean corpuscular volume (MCV) — a measurement reflecting the
size of each red blood cell — will be low (hence IDA is described as a microcytic anaemia). Third, the mean corpuscular haemoglobin (MCH) — a measure of the amount of haemoglobin per red blood cell — must also be reduced (hence cells are “hypochromic”). These features, together with fewer immature red blood cells (reticulocytes) on a blood film, decreased serum iron and a low iron store (ferritin) are indicative of IDA (see Box 1).

Clinical signs and symptoms
Most patients with IDA are asymptomatic, with the diagnosis made only from an incidental finding on blood testing. Some patients, however, may experience increased fatigue or breathlessness. They may also exhibit clinical signs of anaemia, including pallor (best observed in the mucosa), painless glossitis of the tongue, ulceration in the corners of the mouth and characteristic spoon-shaped nails (termed “koilonychia”).

Pharmacological management

Oral iron
Once the underlying cause of IDA is identified (and treated where possible) the successful correction of the anaemia and replenishment of iron stores can be achieved with oral iron supplements. Additionally, iron-deficient patients should be advised to eat iron-rich foods such as red meats, legumes and green, leafy vegetables.

The British National Formulary contains a selection of oral iron preparations, each containing different amounts of ferrous iron, used for both treatment and prophylaxis of IDA. The first-line preparation is ferrous sulphate, which contains 65mg of ferrous iron in each 200mg anhydrous tablet. It is commonly used, is cost-effective and has a high bioavailability! An iron dose of 200mg (anhydrous) three times a day usually results in a rise of haemoglobin of 0.1g/dl per day from the 10th day of treatment (2g/dl in the first four weeks). Iron supplementation should be continued for about four to six months — a sufficient time to adequately replenish iron stores. After this period, 200mg once or twice a day should be prescribed until the underlying cause of the IDA has resolved.

There is little therapeutic advantage afforded by compound preparations of iron with ascorbic acid or B vitamins. The exception to this is preparations containing folie acid, which are beneficial during pregnancy or if a patient has a comorbid folate deficiency. Some patients will not respond to oral iron therapy and the reasons for this should be investigated before considering parenteral iron therapy (see Box 2, p57).

Parenteral iron
Parenteral iron is indicated when:

- There is a clinical need to replenish iron stores rapidly
- The patient is intolerant of oral iron therapy
- Oral iron is deemed ineffective or impractical due to active inflammatory bowel disease or severe malabsorption

<table>
<thead>
<tr>
<th>Box 1: Test results indicating iron deficiency anaemia</th>
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<tr>
<td><strong>BLOOD MARKER</strong></td>
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<tr>
<td>Haemoglobin (Hb)</td>
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<tr>
<td>Mean corpuscular volume (MCV) and mean corpuscular haemoglobin (MCH)</td>
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<tr>
<td>Serum ferritin</td>
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<td>Reticulocytes</td>
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<td>Transferrin or total iron binding capacity (TIBC)</td>
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There are currently four parenteral iron products available in the UK: iron dextran (Cosmofer); iron sucrose (Venofer); ferric carboxymaltose (Ferinject); and iron isomaltoside 1000 (Monofer). Parenteral iron doses are calculated according to a patient’s body weight, haemoglobin level and total iron deficit. Dosage tables and formulae for calculating a patient’s dose based on these parameters are available in prescribing information for the individual products.

Intravenous iron dextran can cause serious adverse reactions (hypersensitivity or anaphylaxis in 0.7% of cases) and has been associated with 31 fatalities (between 1976 and 1996). Owing to the risk of hypersensitivity and anaphylaxis a test dose should be given under the supervision of a doctor before administering the first dose of iron dextran or iron sucrose to a new patient.

One advantage of the newer preparations (ferric carboxymaltose and
iron isomaltoside) is that they do not require administration of a test dose — close observation for anaphylactic reactions and the availability of resuscitation facilities in the event of a medical emergency are sufficient.

Another advantage of the newer preparations is that their infusion time is shorter. This, alongside the avoidance of test doses, can reduce the length of time patients need to spend in hospital. It is not clear whether or not this results in an overall reduction in the cost of care, taking into account the higher cost of these newer preparations.

If oral iron therapy is required after parenteral iron administration, it should not be started until at least five days after the last parenteral dose. This is because parenteral iron preparations reduce the absorption of oral iron when administered in close succession. Parenteral iron therapies will produce an initial rapid rise in Hb but studies have shown that the Hb level at 12 weeks would be similar to that had the clinician prescribed oral iron therapy.

Blood transfusion
Red blood cell transfusions are reserved for patients with severe symptomatic anaemia. Currently, the widely accepted “transfusion trigger” (the Hb level at which a transfusion is indicated) is Hb <8g/dl, however, hospital transfusion guidelines do vary. Patients with IDA requiring transfusion will go on to have endoscopic investigations (unless contraindicated) to ascertain the underlying cause of the condition. Iron therapy should be started after transfusion to replenish iron stores.

Drug interactions
Oral iron therapy can reduce the absorption of medicines such as tetracyclines, quinolones and bisphosphonates. Tetracyclines can also reduce the absorption of oral iron preparations.

Likewise an increase in gastric pH can reduce the absorption of oral iron and this must be considered when giving proton pump inhibitors and antacids. Oral iron and zinc products can each reduce the other’s bioavailability.

Ascorbic acid has been found to enhance iron absorption and it may be helpful to encourage patients to take their tablets with a glass of orange juice.

Side effects
Iron is absorbed in the duodenum and is best given on an empty stomach. However, it can be taken after food to reduce the incidence of gastrointestinal side effects. Some patients will experience nausea or epigastric pain. These effects can be lessened or resolved by switching to an alternative preparation that contains less elemental iron. Patients taking iron should be warned to expect dark discoloration of their stools and a change in bowel habit, leading to either constipation or diarrhoea.

References

Finally, caution should be exercised when prescribing oral iron for patients with inflammatory bowel disease (because it may exacerbate diarrhoea) and for patients with intestinal strictures or diverticular disease (due to an increased risk of faecal impaction).

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Box 2: Possible causes of non-response to oral iron

Some patients with iron-deficiency anaemia will not respond to treatment with oral iron supplements. Reasons for this include:

- Mixed deficiencies (eg, folate, vitamin B12 deficiency)
- Continuing blood loss
- Alternative condition undiagnosed (eg, thalassaemia)
- Malabsorption (eg, Coeliac disease)
- Non-adherence with treatment

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