Iron deficiency anaemia

The disease belongs to the microcytic hypochromic anaemias. The primary cause has to be identified first, and then corrected. Oral ferrous iron is the standard replacement treatment; and could be dispensed OTC in case of heavy or prolonged menstruation. Iron salts may be harmful and result in iron overload if given alone to patients with anaemias other than those due to iron deficiency.

Etiology and risk factors

Inadequate iron absorption: Parasitic infestations, dietary iron deficiency (poor diet or - strict vegetarians), and malabsorption states (e.g. Coeliac disease).

Increased physiological demand: Multiple pregnancies.

Loss through bleeding: Premenopausal women due to menstrual loss, G.I. bleeding - {Peptic ulcer disease (PUD), reflux oesophagitis, colon cancer...others}, parasitic worms, postpartum haemorrhage and haemorrhoids. In addition, chronic use of drugs such as salicylates, NSAIDs, anticoagulants, or corticosteroids which may cause drug-induced blood loss.

Clinical manifestations

Non-specific signs and symptoms normally associated with anaemias (fatigue, pallor of skin or mucous membranes, fainting, exertional dyspnoea and palpitations.

Investigations

A CBC is an essential screening test. The blood film shows microcytic hypochromic cells. Thrombocytosis is consistent even if there is no blood loss.

Confirmatory tests reveal elevation of serum transferrin, while serum ferritin level is reduced.

The underlying cause should be identified before giving iron replacement. Since G.I. blood loss is a common cause, investigations could include gastric endoscopy.

Oral iron therapy

Prophylactic doses may be used in conditions like poor diet, pregnancy, haemodialysis patients, menorrhagia, after partial gastrectomy and in some low birth weight infants, e.g. premature twins.

An oral dosage form (capsules, chewable tablets, syrups, and oral drops) of iron in the ferrous state is a cheap, effective and safe replacement therapy to correct anaemia.
Patient counseling tips

Faeces may become darker and that this is nothing to worry about -

After the haemoglobin level reaches the reference range, treatment should be continued for a further 3 months to replenish depleted iron stores. This should be explained to the patient upon dispensing to avoid non compliance.

Salt forms in oral dosage forms include: sulphate, gluconate and fumarate salts. They differ in the "equivalent elemental iron" content (e.g. in the case of sulphate salt, (one 200 mg ferrous sulphate tablet is equivalent to only 65 mg of elemental iron).

The standard replacement regimen is 100 to 200 mg daily of elemental iron; i.e. ferrous sulphate 200 mg 2-3 times a day.

Adverse effects

Nausea, abdominal pain, constipation, and diarrhea may trouble some patients, especially pregnant women; the first two effects appear to be related to the dose of elemental iron given; and in this case the following counseling points may result in better tolerance by patients:

- Giving iron with food -
- "Trying alternative salt forms containing less "equivalent elemental iron -
- Also taking fewer ferrous sulphate tablets each day, while sticking to the recommended dosage range

Drug Interactions

Despite being non-significant interactions; iron should not be administered concomitantly with drug classes like: Bisphosphonates, Tetracyclines, most of Quinolones, Zinc, Calcium and Magnesium salts. (Determine 2 examples for each of these classes). Dose spacing should be an appropriate intervention during patient counseling.

(Parenteral iron (prescription only medicine)

For most patients, when equivalent doses of oral and parenteral iron are used there is no difference in the rate of rise of the Hb level; so parenteral iron should be reserved only for patients who fail on oral therapy usually because of poor compliance, intolerable side effects, malabsorption states, or continuing blood loss.

Patients with chronic renal failure who are receiving haemodialysis also require iron by the intravenous route on a regular basis. Parenteral iron complexes (e.g. iron dextran or iron sucrose) vary in the routes of administration which could be slow I.V injection, I.V infusion, or deep I.M injection. Oral iron therapy should not be given until .5 days after last injection.

Patients who are prescribed some of these parenteral products should be given a test dose first due to a risk of anaphylactoid reactions upon I.V or even I.M. administration, so the patient should not administer them in the pharmacy.
Monitoring tests

It typically takes between 1 and 2 weeks for the **Hb level** to rise 1 g/dL. Repeating the test after 2–4 months would confirm replenishment of iron stores. An early indication of the patient's response can be seen by looking at the reticulocyte count, which should .start to rise 2-3 days after starting effective treatment

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**Megaloblastic anaemias**

Folate or Cyanocobalamin (vitamin B₁₂) deficiency causes macrocytic anaemias associated with an abnormality in the maturation of haematopoietic cells in the bone .marrow, thus pancytopenia may exist

**Aetiology**

Folate levels could decrease due to dietary deficiency (e.g. poor diet in elderly people), in conjunction with increased folate utilization as in pregnancy and chronic haemolytic anaemias (e.g. Thalassemia), or malabsorption states (e.g. partial GIT removal, crohn's disease, and Coeliac disease). A number of drugs like Phenytoin (an anticonvulsant), Methotrexate (antifolate cytotoxic agent), and Trimethoprim (antibiotic in Co-trimoxazole) have been implicated in causing folate deficiency

B₁₂ deficiency arises from inadequate intake over a prolonged period, e.g. strict vegetarians, or malabsorption states like in removal of distal ileum. Pernicious anaemia is a specific autoimmune form that causes malabsorption of the vitamin due to a lack of intrinsic factor. Total or partial gastrectomy causes B₁₂ deficiency. The onset of anaemia .is usually delayed because the body typically has sufficient stores for 2-3 years

**Clinical manifestations**

In addition to the general features of anaemia, glossitis (sore tongue) may exist. Bilateral peripheral progressive neuropathy presenting as feet tingling characterizes B₁₂ deficiency. Mild jaundice may be present due to the increased breakdown of Hb found .in the abnormal red cells

**Investigations**

Red cell folate concentration accurately reflects folate stores while plasma vitamin B₁₂ diagnoses B₁₂ deficiency. The detection of autoantibodies (intrinsic factor or parietal cell antibodies) is helpful in distinguishing pernicious anaemia from other forms of B₁₂ deficiency

**Replacement therapy**
If it is not possible to delay treatment until a definitive diagnosis is made, both folic acid and B$_{12}$ may be given. Treating B$_{12}$ deficiency with folic acid may lead to resolution of the haematological abnormalities but does not correct the neuropathy.

Folate treatment doses are large enough (5-15 mg daily) that parenteral folic acid is not normally required even in malabsorption states. Treatment continues for 4 months to ensure that the folate deficient red cells are replaced. It is important that products with low folate doses are not used to treat megaloblastic anaemia. N.B. both low and high dose products are available in the Egyptian market under the same trade name.

Prophylaxis with folate (500 µg daily) is now frequently given in pregnancy—often in combination with iron—starting before conception (to prevent neural tube defects) and during the first 12 weeks of gestation.

As for B$_{12}$ deficiency, the standard treatment is Hydroxycobalamin 1 mg I.M. 3 times a week for 2 weeks then 1 mg every 3 months. In case of neuropathy, 1 mg is given on alternate days until no further improvement then 1 mg every 2 months. B$_{12}$ is available also in sublingual and conventional tablets to treat deficiencies that are not intrinsic.

**Monitoring**

Reticulocyte count starts to rise at day 3 or 4 of treatment. The patient should be counseled that Hb takes much longer to return to normal to avoid non compliance. It should rise by approximately 2-3 g/dL each fortnight. Neurological damage may be irreversible.

**Thalassemias (β-Thalassemia Major)**

It is one of the genetic haemolytic anaemias in which abnormal globin chains in Hb lead to red cell destruction. It is a hypochromic microcytic anaemia that is commonly found in North African Mediterranean populations.

History of patient indicates haemolytic anaemias and blood transfusions from infancy thus iron overload precipitates leading to heart failure and various endocrine disorders e.g. Hypothyroidism and Diabetes. Haemoglobin electrophoresis identifies the type of thalassemia.

**Treatment**

Regular blood transfusions every 4-6 weeks to avoid decrease in Hb - Immunization against Hepatitis B should be carried out in all non-immune patients. Treatment for transfusion-transmitted hepatitis C with α-Interferon and Ribavirin is needed if viral genomes are detected in plasma.

Pneumococcal, Haemophilus, and meningococcal infections—resulting from the encapsulated bacteria *Streptococcus pneumonia*, *Haemophilus influenza B*, and *Neisseria meningitides* respectively—are likely if splenectomy has been carried out. In this case, prophylactic oral phenoxymethylpenicillin (Penicillin V) is recommended for life. Erythromycin may be prescribed instead in case of Penicillin allergy. Additionally, vaccination against the previously mentioned infections is recommended.
Daily folic acid therapy indefinitely because of the chronic haemolysis (5 mg daily - which is more than the prophylactic 0.5 mg dose used during pregnancy):

Iron chelation therapy using -

Deferoxamine: Because it is inactive orally, it is given by a separate infusion bag during blood transfusion or by S.C infusion over 8-12 h, 5-7 days weekly. Sometimes the intensive continuous therapy can reverse the heart damage caused by iron overload. Patients should have auditory and fundoscopic examinations regularly because the drug may cause deafness and retinal damage.

Deferiprone: Compliance is better achieved because it is given orally tid.

Endocrine therapy is given as replacement because of end-organ failure e.g. Insulin in case of Diabetes or to stimulate the pituitary gland if puberty is delayed.


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