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IRON DEFICIENCY

Iron is an important essential trace element in the body. Iron stores maintain the oxygen carrying capacity of the blood and is crucial for oxygen transport, delivery and utilisation. It is a key component of haemoglobin, myoglobin and many other enzymes critical to body function. Iron deficiency can significantly impair a person's quality of life. Anaemia is one of the many consequences of iron deficiency.

Iron-deficiency anaemia in older people is recognized as a risk factor for negative outcomes, such as reduced physical performance and muscle strength, frailty, falls and fractures, hospitalization, cognitive impairment, depression, and mortality.

Iron in the body

Iron deficiency can be absolute, when total body iron is decreased; or functional, when total body iron is normal or increased but sufficient iron is not available to target tissues, for example in patients with inflammatory conditions. Serum ferritin correlates strongly with body iron stores.

Symptoms

Symptoms or iron deficiency, with or without anaemia, include chronic weakness, paleness, fatigue, lethargy, difficulty concentrating, tinnitus, headache and exercise intolerance. It may promote restless leg syndrome. Occasionally patients may present with abnormal cravings to eat ice or dirt (pica). Iron deficiency may also be asymptomatic.

Risk factors

Risk factors for iron deficiency include female gender, advanced heart failure, and higher levels of B-type natriuretic peptide (BNP) and C-reactive protein CRP). Vegetarians are more likely to be iron deficient and have lower iron stores.

Causes

Absolute iron deficiency can occur with inadequate iron intake and uptake, and blood loss. Iron deficiency and iron-deficiency anaemia can commonly occur with coeliac disease. Iron absorption in women who are overweight and obese is lower than in women in the healthy weight range. People with chronic inflammatory conditions can experience iron deficiency.

Gastrointestinal blood loss is an important cause of iron deficiency in men and postmenopausal women. Many medications can cause or exacerbate gastrointestinal blood loss, including:

- Aspirin
- Antiplatelets
- Anticoagulants
- NSAIDs
- Prednisone/prednisolone
- SSRI antidepressants

Gastric acidity is important for dietary iron absorption. Long-term use of antacids, proton pump inhibitors (PPIs) and histamine-2 receptor antagonists (e.g., ranitidine, famotidine, nizatidine) increases the risk of iron deficiency. Helicobacter pylori infection is associated with iron deficiency, and eradication improves iron stores.

Heart failure

Anaemia and iron deficiency can occur in people with heart failure. Nearly 50% of patients with heart failure, with or without anaemia, have low levels of available iron. Iron deficiency in patients with heart failure is an independent predictor of worse functional capacity, outcomes and survival, as well as impaired quality of life.

Guidelines recommend that all patients with heart failure should be tested for anaemia and iron deficiency with serum ferritin and transferrin saturation tests.

Absolute iron deficiency in heart failure can result from reduced intake because of anorexia, cardiac cachexia, or impaired iron absorption.

Intravenous iron replacement therapy is associated with a significant reduction in the risk of hospitalisation for worsening heart failure. It also improves functional capacity, symptoms, quality of life in patients with symptomatic iron-deficiency and heart failure. Oral iron supplements are not absorbed well in people with heart failure.

Treatment

The underlying cause should be determined in people with iron deficiency. The aim of treatment is to replenish iron stores and normalise haemoglobin if anaemia is present. Treatment primarily consists of oral or parenteral iron replacement.

Dietary iron intake should be encouraged. Dietary iron occurs as haem iron in meat and non-haem iron from plant sources. Haem iron is best absorbed. Non-haem iron dietary sources include nuts, legumes and fortified foods. Iron absorption from these foods can be increased by ascorbic acid (vitamin C).

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Phytates found in seeds and grains, calcium, and tannins (tea and coffee) inhibit non-haem iron absorption.

Many people cannot tolerate oral iron supplements or may have a poor response leading to poor adherence to therapy. Intravenous iron therapies have become increasingly common in recent years and may be preferred in many people with iron deficiency. Oral and parenteral iron should not be used together. Intramuscular injections of iron are now discouraged.

Oral iron therapies

Many oral iron supplements are available in varying doses and formulations. Treatment duration is usually 3 to 6 months.

- Ferrous fumarate
- Ferrous sulfate
- Ferrous gluconate
- Iron polymaltose complex

All oral iron supplements can cause dark coloured stools, and gastrointestinal upset (nausea, constipation, diarrhoea); and liquid products can cause tooth discolouration.

Oral iron supplements are available as immediate or controlled-release formulations. Controlled-release formulations may cause less GI upset. Ferrous salt formulations may be combined with ascorbic acid (vitamin C) to improve absorption. The iron content in multivitamin products is usually too low to treat iron deficiency.

Iron absorption is most efficient with intermediate doses (50-100mg elemental iron) and on alternate days. High doses and dosing two or three times daily is inefficient and is now discouraged.

Most oral iron supplements should be taken on an empty stomach, avoiding cereals, milk, tea and coffee as they may reduce iron absorption. They may interfere with the absorption of antibiotics such as tetracyclines and fluoroquinolones, and should be administered at least 2 hours apart. Oral iron supplements should also be administered at least 2 hours apart from bisphosphonates, levodopa, methyldopa and levothyroxine.

Iron polymaltose complex (Maltofer) tablets or syrup may be administered with food and may be mixed with fruit or vegetable juice. Interactions with other medicines are not significant.

Intravenous iron therapy

Intravenous (IV) iron therapy should be considered first-line treatment of functional iron deficiency. It is preferred in patients with heart failure and in inflammatory bowel disease with moderate to severe anaemia. For patients with chronic kidney disease, IV iron produces higher haemoglobin concentrations and improves morbidity and mortality from cardiovascular events.

IV iron therapy repletes iron stores faster than oral iron supplements and is usually better tolerated. It can be used when oral treatment is ineffective or not tolerated. IV iron generally promotes better haemoglobin improvements. Iron studies can be repeated at least 4 weeks after administration.

Intravenous iron therapies include:

- Ferric derisomaltose (Monofer)
- Ferric carboxymaltose (Ferinject)
- Iron polymaltose complex (Ferrosig)
- Iron sucrose (Venofer)

Common adverse effects of intravenous iron therapies include nausea, hypo- or hypertension, flushing, bronchospasm, tachycardia, hypophosphataemia (abnormally low serum phosphate) and dizziness. Leakage of ferric carboxymaltose at the injection site can leave long-lasting or permanent brown discolouration and irritation of the skin.

Summary

Iron deficiency is a leading contributor to the burden of disease among older persons. Iron deficiency can occur with or without anaemia, and is common in people with heart failure. Intravenous (but not oral) iron therapy has a role in patients with heart failure and iron deficiency. IV iron therapy provides rapid, safe iron replacement. Medication reviews may identify medication-related causes.

References

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