Perioperative anaemia and iron deficiency

Anaemia affects a third of surgical patients and is associated with increased morbidity and mortality. Iron deficiency is the most common cause of anaemia and can be absolute or functional. Patients may require treatment with oral or intravenous iron.

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Background

Anaemia affects around 30% of surgical patients (Richards et al, 2020) and is defined as a haemoglobin concentration <13 g/dl in both men and women (Muñoz et al, 2017). It is associated with higher rates of postsurgical complications, including death, morbidity such as increased length of stay, and higher rates of blood transfusion (Baron et al, 2014). Transfusion itself is also associated with increased morbidity and mortality (Baron et al, 2014). The most common causes of anaemia in surgical patients are absolute iron deficiency and chronic inflammation (Richards et al, 2020). Patient blood management is a multidisciplinary approach to caring for the patient who may need transfusion and includes preoperative optimisation of iron deficiency (Samuel, 2019).

Iron deficiency

If uncorrected, iron deficiency leads to a microcytic, hypochromic anaemia. This can be an absolute deficiency, resulting from poor diet or impaired absorption (eg coeliac disease or following duodenal resection), or a functional deficiency, where inflammation hampers the absorption and use of iron (Baron et al, 2014). Absolute iron deficiency is commonly treated with and responds to oral iron (Clevenger and Richards, 2015). Functional iron deficiency (previously called anaemia of chronic disease) is a disorder of iron absorption and use. It can occur secondary to the action of hepcidin, and it is not reliably correctible with oral iron (D'Angelo, 2013).

The peptide hormone hepcidin (hepatic bactericidal protein) is produced primarily in the liver and causes the downregulation of ferroportin transporters on the surface of duodenal enterocytes and macrophages (D'Angelo, 2013). This reduces iron absorption by enterocytes, and increases the sequestration of iron within macrophages, meaning less iron is transported to the bone marrow where it is a crucial substrate for erythropoiesis. Hepcidin production is stimulated by acute (eg infection or major surgery) and chronic inflammation. This is postulated to be an evolutionary response to reduce the availability of iron during infection (iron is an important substrate for bacterial replication) (D'Angelo, 2013), but this means that following the inflammatory insult of major surgery, enteral iron absorption is reduced. Furthermore, a single dose of supplemental oral iron can reduce further absorption for several hours afterwards, because of increased hepcidin levels (Clevenger and Richards, 2015). Hepcidin levels are only routinely measured in research settings and are not currently used clinically to diagnose functional iron deficiency (Clevenger and Richards, 2015). Research is ongoing to examine a possible role for hepcidin antagonists in the management of anaemia (D'Angelo, 2013).

The diagnosis of anaemia and iron deficiency is outlined in Figure 1 (Muñoz et al, 2017). Once anaemia is identified, the cause should be found and treated, with iron deficiency corrected to the point of both normalising haemoglobin and replenishing iron stores (which will require a higher total dose of iron and may take longer). Iron deficiency anaemia can be treated with oral or intravenous iron. Oral elemental iron given once every 1–2 days at a dose of 65 mg is better tolerated and more effective than conventional (higher) dosing of 65 mg two to three times per day. Absorption can be optimised by taking iron first thing in the morning on an empty stomach, with orange juice (ascorbic acid aids absorption), and avoiding tea or coffee for an hour before and after (tannin and calcium reduce iron absorption). 65 mg elemental iron is equivalent to 200 mg ferrous sulphate.

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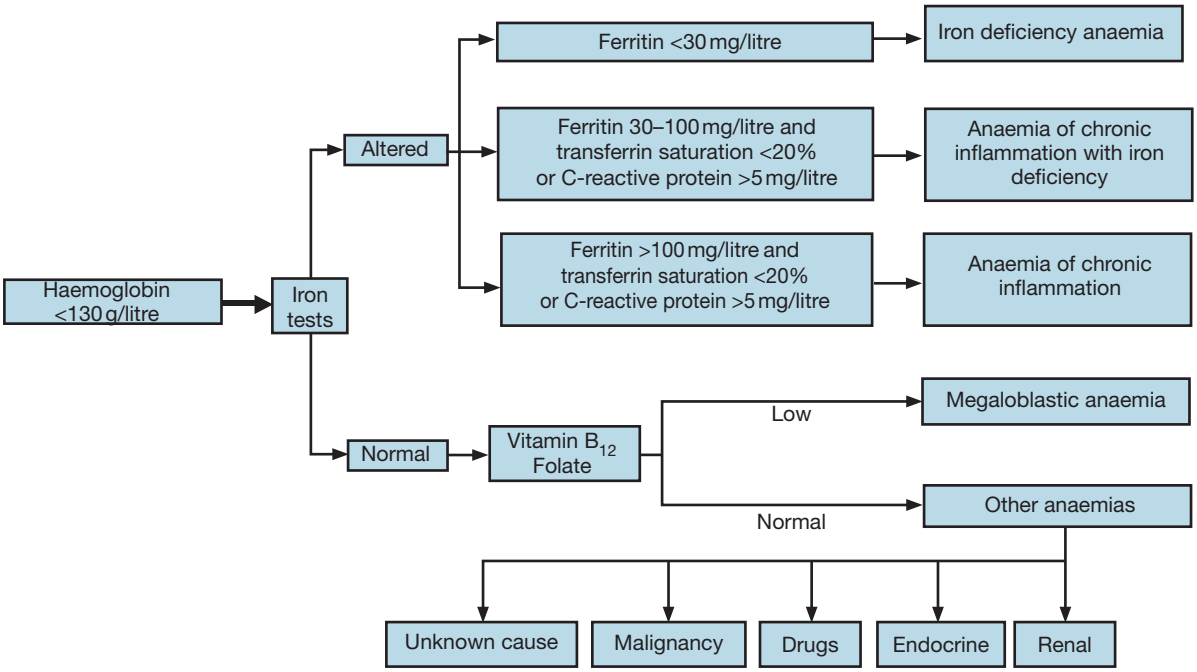

Figure 1. Algorithm for classification of perioperative anaemia. From Munoz et al (2017).

Intravenous iron therapy is safe and effective (Clevenger and Richards, 2015), and can be used if:

- Oral therapy has already failed to increment haemoglobin or not been tolerated
- Surgery is indicated in less than 6 weeks (eg cancer surgery).

If anaemia is the result of chronic inflammation, intravenous iron is likely to be necessary. Where possible, elective surgery should only be performed after anaemia has been investigated and corrected.

The PREVENTT trial randomised anaemic patients undergoing major surgery to receive intravenous iron or placebo (Richards et al, 2020). It did not demonstrate a significant difference in rates of death or blood transfusion. However, further questions remain as subgroup analysis showed reduced rates of readmission in patients randomised to intravenous iron, and any treatment effect may have been diluted by inclusion of patients with milder iron deficiency.

Conclusions

The current postpandemic surgical backlog provides a unique opportunity to optimise patients before their (long delayed) elective surgery, and to improve outcomes. Good understanding of the underlying pathophysiology of anaemia, as well as robust logistical pathways, will be crucial to using this as an opportunity, rather than a setback, within the NHS in the UK and across the world.

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