Iron supplementation in the pharmacy

Iron is involved in multiple critical functions in the body. It is a component of haemoglobin and myoglobin and is required for many enzyme-based biochemical processes. It is essential for the transportation and storage of oxygen, and is required for normal growth, development, and immune function.

The terms “iron deficiency” and “iron-deficiency anaemia” are often used interchangeably. Iron deficiency is a continuum that ranges from depleted iron stores without functional or health impairment, to iron-deficiency anaemia, which affects the functioning of several organ systems.

Iron deficiency is a concern because it can:
- Delay normal infant motor function or mental function;
- Increase the risk of small, or preterm babies during pregnancy;
- Cause fatigue that impairs the ability of adults to do physical work;
- Affect the memory or other mental function in teens.

### Iron requirements

Iron metabolism is unusual in that it is controlled by absorption, rather than by excretion. This is because the body recycles iron, and when red blood cells die, the iron in them is returned to the bone marrow to be used again in new red blood cells. The body only loses large amounts of iron when red blood cells are lost through bleeding.

Iron is poorly absorbed by the gastrointestinal tract (5-10% of dietary intake is absorbed), and usual dietary intake barely meets the daily requirement for most people.

The recommended dietary allowance (RDA) for iron is listed in Table I.

### Causes of iron deficiency

Iron deficiency results when iron demand by the body is not met by iron absorption from the diet (see Table II). Therefore, patients with iron-deficiency anaemia may have an inadequate dietary intake, hampered absorption or physiologic losses, e.g. menstruation in a woman of reproductive age. Iron-deficiency anaemia could also be a sign of blood loss, known or occult.

### Symptoms of iron-deficiency anaemia

Too little iron can impair body functions, but most physical signs and symptoms are not present until iron-deficiency anaemia occurs. Symptoms include:
- Feeling tired and weak
- Headache
- Dizziness
- Shortness of breath
- Pallor
- Irritability
- Difficulty maintaining body temperature
- Decreased immune function
- Glossitis (an inflamed tongue).

Iron deficiency may cause pica (a craving for non-foods) and spoon nails, and is associated with restless legs syndrome.

### Diagnosis

A comprehensive patient history, including diet, should be recorded. Blood tests are used to diagnose anaemia. Iron levels can be measured in the blood, as well as transferrin levels (the protein that carries iron not contained in the red blood cell).
Iron supplements

Numerous iron supplements are available, including tablets, capsules, syrups and sustained-release preparations. The choice of the iron preparation depends upon the severity of the illness, as well as the patient’s ability to tolerate iron preparations.7

Multiple salt forms of iron exist. Close attention must be paid to the salt form when ordering and administering iron. Incorrect selection or substitution of one salt for another without proper dosage adjustment, may result in serious over- or underdosage.

There are two main iron salt forms: ferric and ferrous irons, and numerous formulations, e.g. amino acid chelates, carbonyl iron, polysaccharide iron complex and combination products.9 All dietary iron has to be reduced to the ferrous form to enter the mucosal cells. Therefore, ferrous iron is absorbed three times more readily than the ferric form.8

Iron supplements are usually in the form of soluble ferrous salts: ferrous sulphate, ferrous gluconate or ferrous fumarate6 (see Table IV). There are marginal differences between the different types of ferrous salts regarding efficiency of iron absorption.9 Ferric polymatose is as effective as the ferrous salts in raising haemoglobin, and is well tolerated.4

Compound preparations

Some oral preparations contain ascorbic acid to aid iron absorption. About 200 mg of ascorbic acid is needed to increase the absorption of elemental iron.8 There is no justification for the addition of other ingredients such as the B group of vitamins (except folic acid for pregnant women).9

Modified-release preparations

Iron is not absorbed in the stomach, and is best absorbed from...
the duodenum and proximal jejunum. Therefore, enteric-coated or sustained-release capsules, which release iron further down the intestinal tract, are less efficient sources of iron and should not be recommended.\textsuperscript{4,6,7,9}

Table IV: Elemental content of ferrous salts\textsuperscript{6}

<table>
<thead>
<tr>
<th>Ferrous salt</th>
<th>Amount</th>
<th>Iron (elemental)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferrous sulphate (dried)</td>
<td>200 mg</td>
<td>65 mg</td>
</tr>
<tr>
<td>Ferrous sulphate</td>
<td>300 mg</td>
<td>60 mg</td>
</tr>
<tr>
<td>Ferrous gluconate</td>
<td>300 mg</td>
<td>35 mg</td>
</tr>
<tr>
<td>Ferrous fumarate</td>
<td>200 mg</td>
<td>65 mg</td>
</tr>
</tbody>
</table>

General principles about the use of iron supplements:

- In general, iron preparations should be taken on an empty stomach, as food can decrease absorption by 40-50%.\textsuperscript{8} However, this increases the likelihood of stomach upsets and increased patient adherence should be weighed against the inferior absorption.\textsuperscript{4}
- Preparations must be kept out of reach of children as accidental iron poisoning is a common cause of poisoning deaths in children.\textsuperscript{6,10}
- Liquid preparations may discolour the teeth, and should be consumed through a straw.\textsuperscript{6,10}
- Iron may decrease the absorption of several medicines and dosing may need to be separated if iron supplementation is to be used concurrently:\textsuperscript{10}
  - Quinolone and tetracycline antibiotics
  - Bisphosphonates
  - Levodopa
  - Levothyroxine
  - Methyl dopa
  - Mycophenolate mofetil.
- Iron should be given two hours before, or four hours after, the ingestion of antacids.\textsuperscript{7}

Adverse reactions include gastrointestinal irritation, epigastric pain, nausea, diarrhoea, dark stools and constipation.\textsuperscript{10} The incidence is approximately 10-20%.\textsuperscript{7} Gastrointestinal tract symptoms seem to be directly related to the amount of elemental iron ingested.\textsuperscript{7} This means that the reported low incidence of side-effects for some preparations can be explained by their low iron content.\textsuperscript{9} Discolouration of urine (black or dark) has also been reported.

Managing gastrointestinal adverse reactions\textsuperscript{6,7}

- Slowly increase the dose.
- Take with meals, although this will decrease absorption.
- Laxatives, stool softeners and adequate intake of liquids can alleviate constipation.
- Patients with persistent intolerance to oral iron tablets may tolerate ferrous sulphate elixir. Patients can titrate the dose up or down to the level at which gastrointestinal symptoms become acceptable.

Parenteral iron therapy is generally reserved for use when oral therapy is unsuccessful because the patient cannot tolerate oral iron, or does not take it reliably, or there is continuing blood loss or malabsorption.\textsuperscript{7} Also, many patients with chronic renal failure, who are receiving haemodialysis, require intravenous iron regularly.\textsuperscript{7} Parenteral iron should be used with caution because there is a 2-3% risk of anaphylaxis, some cases of which result in death. Iron polymatose is administered intramuscularly, and iron sucrose is administered either by slow intravenous injection or by intravenous infusion.\textsuperscript{7} Interestingly, the haematological response to parenteral iron treatment is not faster than the response to oral iron.\textsuperscript{7}

Conclusion

Iron supplementation has a key role in both the treatment and prevention of iron deficiency. In the pharmacy, we can provide valuable input regarding selection of an appropriate supplement and the best use of such products.

References

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