Using Ferric Maltol instead of intravenous iron treatments in Diagnosed Iron Deficiency Anaemia (IDA)

Managing Iron Deficiency Anaemia

This paper assumes clinicians have excluded or are simultaneously managing red flag causes for iron deficiency anaemia.

The World Health Organisation (WHO) defines anaemia as haemoglobin less than 13 g/dl in men or less than 12g/dl in non-pregnant women[4]. Reduced mean cell volume is common in IDA but low serum ferritin is the most powerful test for iron deficiency. [4]

The British Society of Gastroenterology (BSG) and BMJ Best Practice treatment algorithm recommends that oral iron preparations such as ferrous sulphate are first line treatments for IDA[5]. Such products should be tried for three months to see if the anaemia is improving.

Patients should be warned of the side effects of oral iron – bowel habit changes such as black and more tarry stool, constipation, nausea, sometimes diarrhoea and indigestion. Patients should also be encouraged to maximise iron in their diet and signposted to appropriate guidance on such.

Ferrous salts show only marginal differences between one another in efficiency of absorption of iron. Haemoglobin regeneration rate is little affected by the type of salt used provided sufficient iron is given.

Absorption of non-haem iron in plants and dairy requires acid for digestion. Absorption is enhanced by ascorbic acid (Vitamin C) and meat and inhibited by calcium, fibre, tea, coffee, and wine.[5] Some patients will benefit from taking ascorbic acid (500mg bd), with their iron supplement, to aid absorption of oral iron and this should be considered when response to oral iron is poor.[5] (Orange juice only contains approximately 50mg Vitamin C per 100ml and a medium orange contains about 70mg so tablet supplementation [OTC rather than prescription] is probably more convenient)[6].

Complete intolerance to oral iron supplements happens in relatively few patients. It can be minimised by:

- Recommending a laxative to people with constipation – See RSS guidance here
- Recommending iron is taken with meals
- Reducing the frequency of the iron supplement. Lower doses may be as effective and better tolerated and should be considered in patients not tolerating traditional doses.
- Trying different iron compounds such as ferrous sulphate or ferrous gluconate. Encourage patients to try each for at least a month.
- Evidence suggests that oral iron supplementation administered as a single dose on alternate days (e.g., Monday, Wednesday, and Friday) may optimise iron absorption and offer more convenient dosing compared with daily oral iron supplementation.[5]

These measures should be tried before giving up on the most cost-effective oral iron products.

Modified-release preparations of iron are licensed for once-daily dosage, but have no therapeutic advantage and should not be used. These preparations are formulated to release iron gradually; the low incidence of side-effects may reflect the small amounts of iron available for absorption as the iron is carried past the first part of the duodenum into an area of the gut where absorption may be poor.[1]

The haemoglobin concentration should rise by about 2 g/100 mL (20 g/litre) over 3–4 weeks. When the haemoglobin is in the normal range. With oral iron the reticulocyte count should peak at 1 to 2 weeks with normalisation of haemoglobin after 2 to 4 months and replacement of iron stores after 6 months.[5]

Oral iron should be continued for 3 months after the iron deficiency has been corrected so that stores are replenished.[4]

Iron salt/amount	Content of ferrous iron	Daily dosing	Cost for 28d	When to use
ferrous fumarate 322 mg	100mg	1 od-bd	£1.00-£2.00	First line
ferrous sulfate, 200 mg	65 mg	1 bd-tds	£2.58-£3.87	Second Line
ferrous gluconate 300 mg	35 mg	2 bd-tds	£2.18-6.54	
ferrous fumarate 210 mg	65 mg	1 bd-tds	£2.66-3.99	
ferric maltol 30mg	30mg	1 bd	£47.60	
Do not use routinely – Use in special situations only				

If patients are unable to tolerate oral iron or those who do not respond, the next line of treatment would traditionally have been parenteral iron via secondary care.

Parenteral iron has its problems however. There is a risk of serious hypersensitivity (life threatening and fatal anaphylactic) reaction to it, even after successful previous administration.[7] Parental iron cost administration itself is expensive and can take 0.5-6 hours depending on the product used. Such treatments are inconvenient for most patients, impossible for housebound patients and are more environmentally damaging. Oral alternatives (e.g. ferric maltol) to parenteral iron may be a preferred option as a part of a management strategy to reduce hospital day case admissions, and keep immunosuppressed people out of hospital, and to enable social distancing within the day case unit plus shielding of high-risk patients during the COVID-19 pandemic.

Using Ferric Maltol instead of intravenous iron treatments in Iron Deficiency
Ferric Maltol remains intact before it is absorbed across the gastro intestinal tract. This increases bioavailability and reduces the amount of free iron in the gastro-intestinal tract, potentially reducing gastro-intestinal toxicity associated with free iron.[3]

Ferric Maltol is an oral product that had a license that was restricted for use in patients who Hb is >9.5 and who have IBD. This was widened in March 2018 to *adults with iron deficiency though no new evidence supports the license extension.*[3] Trial evidence (AEGIS 1 and AEGIS 2 studies, n=128) showed after 12 weeks, Ferric

Maltol led to a statistically significant improvement (p<0.0001) in Hb of 2.25g/dL from baseline to week 12 (**compared [unhelpfully] to placebo**, not other types of oral iron), with the median time to normalisation of Hb levels being 57 days.[2]

Use of Ferric Maltol is indicated in patients who have been intolerant of other oral iron despite best efforts to remedy this and whose iron levels are in the ranges below

- females: Hb g/dl >9.5 and <12
- males: Hb g/dl >9.5 and <13

Follow-up
Once normal, the Hb concentration and red cell indices should be monitored at intervals.[4,5]

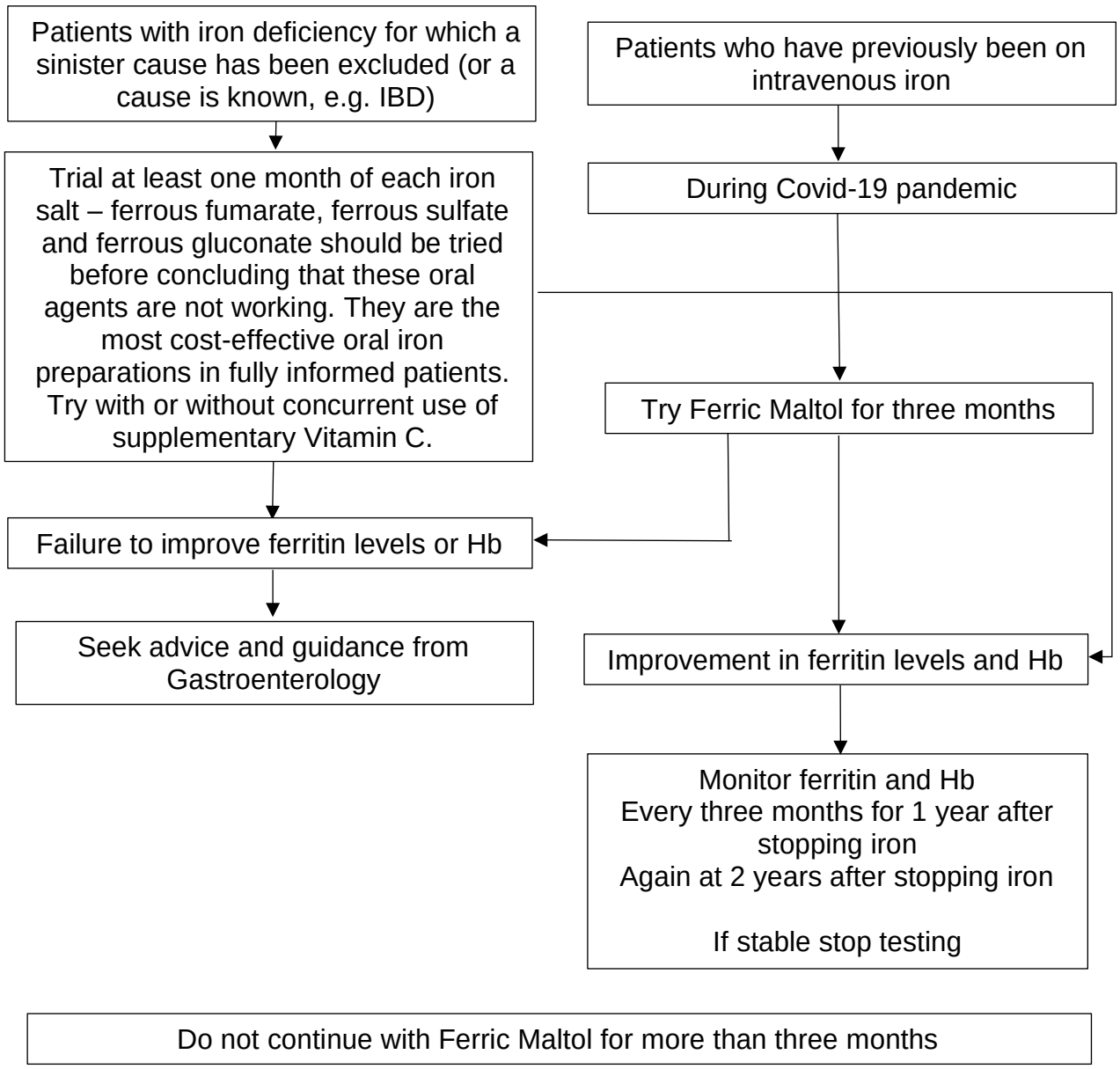
We suggest 3 monthly for 1 year, then after a further year, and again if symptoms of anaemia develop after that. Further oral iron should be given if the Hb or red cell indices fall below normal (ferritin concentrations can be reserved for cases where there is doubt).

Further investigation is only necessary if the Hb and red cell indices cannot be maintained in this way. It is reassuring that iron deficiency does not recur in most patients in whom a cause is not found after upper GI endoscopy, testing for coeliac disease, and large-bowel investigation.

Reference

1. BNF – Medicines Complete, accessed 8th April 2020
2. London Medicines Evaluation Network Review May 2016
3. Northern Treatment Advisory Group Ferric Malton for the Treatment of iron deficiency Sept 2018
4. Goddard AF et al. Guidelines for the management of iron deficiency anaemia. Gut 2011;60:1309-16.
5. BMJ Best Practice: Iron Deficiency Anaemia" Last updated: Mar 05, 2020 Accessed 8/4/20
6. US Department of Health and Human Sciences, National Institutes of Health, Office of Dietary Supplements Fact Sheet for Health Professionals Updated 27th February 2020 https://ods.od.nih.gov/factsheets/VitaminC-HealthProfessional/ Accessed 8th April 2020
7. Intravenous iron and serious hypersensitivity reactions MHRA August 2013

Summary



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