Medical / GP Referrals to Patient Blood Management

Anaemia (Hb <130g/dL in males / Hb <118g/dL in females)

Ferritin <15µg/L

IDA

Ferritin <30µg/L

Probable IDA

Commence oral iron
e.g. Ferrous sulphate 200mg b.d.
Consider investigations for causes
Consider repeat Hb in 4-6 weeks to assess response

Responding – continue to 3 months.
Intolerant:

Consider mitigations steps:
Try intermediate or low dose FeSO4
e.g. 200mg o.d or b.d on alternate days.

This reduces side effects and can increases absorption[1]

Patient remains intolerant

Refer to PBM for parenteral iron
Please record in referral:

- mitigation steps;
- symptoms of intolerance;
- duration of trial of oral iron;.

Ferritin 30-100µg/L
MCHr <29pg or
CRP >5mg/L

Functional iron deficiency: anaemia of chronic inflammation *and probable* co-existing iron deficiency

Ferritin >100µg/L
MCHr <29pg or
CRP >5mg/L

Functional Iron deficiency

anaemia of chronic inflammation

Treat underlying cause of inflammation if possible.
Check and replace B12 and folate as needed
Consider trial of oral iron (see tolerance notes)

If intolerant of oral iron or no response after 4-6 week trial, consider referral for parenteral iron if moderate to severe anaemia (Hb <100g/L)

Refer to PBM for parenteral iron
Please record in referral:

- mitigation steps;
- symptoms of intolerance;
- duration of trial of oral iron;.

Ferritin >100 +
MCHr >29pg or
Other indications of non-iron-deficiency anaemia (e.g. MCV >80, MCH >27, B12 / folate deficiency etc)

Not consistent with iron-deficiency and unlikely to benefit from iron replacement.

- Consider other causes and clinical context;
- Review / request blood film comments,
- Iron studies,
- renal and liver function,
- consider further investigations (malignancy, MDS, haemolysis, undiagnosed haemoglobinopathy or haemoglobin variant)

Notes (see also: Iron deficiency. Pasricha S et al. The Lancet December 4th 2020)

- Iron deficiency anaemia is sometimes straight forward to identify but is often obscured by anaemia of chronic inflammation or other co-morbidities making diagnosis sometimes difficult . Sometimes the results will not fit neatly into one category and clinical discretion is advised.
- Check haematinics first, consider requesting reticulocytes and reticulocyte haemoglobin content (MCHr) which measures iron-restricted erythropoeisis and suggestive of iron-deficiency when <29pg. A blood film, CRP and iron studies **(transferrin saturation (Tsat) of <20% is also suggestive of iron-deficiency)** can help identify co-existing iron deficiency anaemia in cases of chronic inflammation. Consider also coeliac serology and IgA antibodies.
- Although ferritin can be useful (particularly if <15ug/L), there is little evidence to support specific cut-off values and it is often confounded by co-existing inflammation. There is no single gold-standard test to diagnose iron deficiency anaemia other than a bone-marrow biopsy which is invasive and rarely justified in this context. The above algorithm is a guideline to support clinical decision making and referral to patient blood management. **Of note is the advice on management of oral iron intolerance by suggesting alternate day, low to intermediate dosing: this improves absorption and reduces side-effects and should be strongly encouraged before referral for parenteral iron.**

Advice for GPs when Patient Encounters Intolerance to Oral Iron Replacement

Side effects of oral iron are common. It is therefore important to prescribe in a way that minimises these and avoids the need for referral for parenteral iron which is more invasive and costly. Clinicians are advised to consider the following measures to optimise tolerance of oral iron:

- intermediate or low dose ferrous sulphate e.g. 200mg o.d or b.d on alternate days: this is proven to reduce side effects and increases absorption.
- we also recommend iron is taken 30 minutes before a meal.
- advice to the patient on dietary improvement to optimise dietary iron intake.
- An alternative preparation such as ferrous gluconate or ferrous fumarate should be tried before abandoning oral iron.

NB. There is no benefit to enteric coated or modified release iron capsules. Some clinicians recommend giving oral iron with a source of ascorbic acid (vitamin C), either by taking it with orange juice or with a 500mg ascorbic acid tablet. This is based on the hypothesis that ascorbic acid may increase iron absorption. However some recently published studies show no major impact of lowering the pH on iron absorption and we are not aware of any high quality data to support this practice. Therefore we cannot make a strong recommendation on the addition of vitamin C to improve oral iron absorption.

If oral iron is ineffective in improving Hb, then referral to PBM remains appropriate.

References

1. Stoffel NU et al. Iron absorption from oral iron supplements given on consecutive versus alternate days and as single morning doses versus twice daily split dosing in iron depleted women: two open label randomised controlled trials. Lancet Haematol. 2017; 4:e524-33
2. Iron deficiency. Pasricha S. *et al.* The Lancet December 4th 2020 https://doi.org/10.1016/s0140-6736(20)32594-0
3. Ponikowski P et al. Beneficial effects of long term intravenous therapy with ferric carboxymaltose in patietns with symptomatic heart failure and iron deficiency. *Eur Heart J.* 2015; 36:657-68

Notes to Primary Care on Iron Deficiency in the Absence of Anaemia

The primary purpose of the Patient Blood Management Service is the management of patients suffering from anaemia with iron deficiency (IDA) in order to reduce patient exposure to blood transfusions and preserve blood stocks.

Whilst it is recognise that symptomatic iron deficiency in the absence of anaemia can benefit from replacement, it is strongly encouraged that every attempt is made to replace iron stores orally and address the cause in these circumstances[2,3].

The management of oral iron intolerance can be addressed by using oral iron on alternate days at a low (200mg $FeSO_4$) or intermediate dose – this improves absorption and reduces side-effects and should be tried before referral for parenteral iron (see references below).

Where capacity exists, cases of non-anaemic iron deficiency may be considered on a case-by-case basis by PBM, particularly where evidence for replacement is strongest; there is an established regular requirement for replacement (typically patients with inflammatory bowel disease or persistent menorrhagia pending intervention) and capacity within PBM exists.

Where PBM capacity does not allow for this, referrers are encouraged to use alternative facilities for infusional iron, such as within their own specialty departments, where iron infusions can be safely administered.

Elective Surgical Referral Pathway

All patients undergoing preoperative assessment for major surgery of surgery with a potential for >500mls blood loss

Hb <130g/L → Request: haematinics, reticulocyte count, CRP

Ferritin ≥30µg/L and CRP <5 (Other causes of anaemia more likely)

- Check folate and B12 and replace as required;
- Consider further investigation in Primary Care
- consider further tests in clinical context (e.g. co-existing medications; blood film comments; myeloma screening; haemolysis screening, haemoglobinopathy / variant haemoglobin (HPLC) screen,);
- Ensure clear communication with GP/Surgeon

Ferritin < 30 µg/L (with or without anaemia)
or [Ferritin 30-150 µg/L + CRP >5 + MCHr <29]
Probable Iron-deficiency anaemia

Surgery >10 weeks away

Start oral iron: FeSO4 200mg b.d.

Check response at 4 weeks:
if responding proceed to surgery
No response: consider IV iron

Surgery 2-10 weeks away

Book for IV iron via PBM Ferrinject 1000mg (or weight-equivalent)

Surgery <2 weeks away

Options depending on surgical context and severity of anaemia:

1. IV iron post-op given in recovery;
2. delaying surgery and investigate with IV iron at PBM;
3. Blood transfusion / iron in PBM if Hb >100

Check Response
normally 4 weeks post intervention or day of surgery

NB

- Ferritin is a good measure of storage iron but there are no good data to support specific cut -off values to rule out / in iron deficiency anaemia. Other values such as a low MCH, a mean reticulocyte haemoglobin concentration (MCHr) of <29 or, where iron studies are performed, a transferrin saturation of <20% can be helpful to indicate coexisting IDA in context of other causes of anaemia.
- In the context of inflammation (CRP >5) or cancer, ferritin levels can be elevated above 150 with functional iron deficiency (inaccessible iron stores). This can sometimes respond to IV iron and should be considered, particularly if MCHr <29 and other causes (such as B12 / folate deficiency) have been corrected / excluded.

Patient information leaflet available here

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Review date: 15/03/2021
Next Review due 15/03/2022