Anaemia and use of Carboxymaltose (Ferinject ®) in Pregnancy and the Postnatal Period – Guideline for Management

University Hospitals of Leicester NHS Trust

C1/2012

1. Introduction and Who Guideline applies to

This guideline is aimed at all Health Care Professionals involved in the management of women with severe anaemia in pregnancy and the initial postnatal period.

Background:

Iron deficiency is the most common form of malnutrition in the world affecting more than 2 million people. Oral iron therapy and advice regarding dietary iron intake, are the simplest measures which can be employed to improve the haemoglobin (Hb) level. However, in the event that this is not possible there are alternatives. Although iron absorption from the diet increases three-fold in pregnancy, iron requirements increase even further and an iron deficit builds up.

Maternal anaemia has implications in pregnancy and postpartum period. Iron deficiency may contribute to maternal morbidity through effects on immune function with increased susceptibility or severity of infections (Eliz *et al,* 2005), poor work capacity and performance (Haas *et al,* 2001) and disturbances of postpartum cognition and emotions (Beard *et al,* 2005).

It has been shown to increase the risk of postpartum haemorrhage (PPH). In a large prospective observational study at 2 maternity services in the UK found that 60% of women with Hb <85g/l sustained PPH, with a quarter progressing to severe PPH. One explanation is impaired uterine contractility due to reduced oxidative capacity. (Briley et al, 2014). Evidence suggests that maternal iron depletion increases the risk of iron deficiency in the first 3 months of life, by a variety of mechanisms (Puolakka *et al*, 1980, Colomer *et al*, 1990). Impaired psychomotor and/ or mental development are well described in infants with iron deficiency anaemia and may also negatively contribute to infant and social emotional behaviour (Perez *et al,* 2005)

Ferinject® can be used as a second line treatment when oral therapy is deemed inappropriate or has failed.

Intravenous iron is the chosen method of treatment for severe iron deficiency anaemia in pregnancy and the postnatal period.

Ferinject® usage in pregnancy is limited. However, Ferinject® is now licensed for use in the second and third trimester of pregnancy

Contents

Definition:

There is variation in definition of normal haemoglobin levels in pregnancy. UK guidelines from the BCSH suggest definitions of anaemia as <110g/l in the first trimester and <105g/l in the second and third trimesters. Postpartum anaemia is defined as a haemoglobin <100g/l.

WHAT'S NEW?

- Once daily dosing of oral iron
- The Maternity Assessment Units on both sites now have a daily slot (Mon-Fri) for administration of Ferinject®
- Other preparations of IV iron use such as Monofer
- Removed Vit B12 pathway from the flowchart in Appendix 4 (UHL lab doesn't measure accurately the Vit B12 component levels that would alter management in pregnancy)
- Appendix 4 folate level change from <2ng/ml to < 2.6
- Updated anaphylaxis treatment in line with Resuscitation Council UK 2021
- Added specialist nurse/midwife referral criteria for parenteral iron infusion
- Skin staining risk statement added

Related documents:

- Booking bloods and urine test UHL Obstetric Guideline
- Sickle Cell and Thalassaemia (haemoglobinopathy) Screening in Pregnancy UHL Obstetric Guideline
- Aseptic Non Touch technique UHL Guideline
- Hand Hygiene UHL Policy
- MHRA Drug Safety Update, Volume 7,Issue 1 August 2013: Intravenous iron and serious hypersensitivity reactions: new strengthened recommendations to manage and minimise risk.

2. Guideline Standards and Procedures

2.1 Screening:

- **All women/pregnant people** in pregnancy should have a screen for haemoglobinopathies at the first booking visit as per the guidelines for Sickle Cell and Thalassaemia. The result should be reviewed and documented in the health record.
- Women/pregnant people with known haemoglobinopathy should have assessment of serum ferritin and folate before supplements are commenced.
- All women/pregnant people should have a FBC taken at booking and at 28 weeks in accordance with NICE guidelines. The results should be clearly documented in the health care records at next antenatal clinic visit.

2.2 Assessment:

- All anaemic women/pregnant people should be contacted by the health care professional to assess wellbeing and if symptomatic clinical review arranged.
- All women/pregnant people with anaemia should be offered a trial of oral iron without delay (see 2.3 below).
- Non-anaemic women/pregnant people considered to be at risk of iron deficiency should have serum ferritin taken.
- **At risk women/pregnant people who are not yet anaemic should be given oral iron if ferritin level is <30ug/l.**

The clinical symptoms of iron deficiency anaemia in pregnancy are non-specific. Fatigue is the most common symptom but women may also present with pallor, weakness, headache, palpitations, dizziness, dyspnoea irritability, and restless legs. A craving for non-food items such as ice (pagophagia) and soil (pica) may develop (Lumish et al, 2014).

2.3 Treatment:

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- First line treatment for anaemia should be an oral iron only supplement such as Ferrous Fumarate 322mg. Women/pregnant people should be advised on the correct method of administration and also receive dietary advice (see appendix 4).
- Women/pregnant people who are confirmed on venous sampling to be anaemic and who do not have a known haemoglobinopathy should be commenced on oral iron therapy.
- Women/pregnant people who have either Thalassaemia trait or sickle cell trait should only be commenced on oral therapy if they have evidence of iron deficiency i.e. low serum ferritin.
- All women/pregnant people should be instructed regarding the correct way to take oral iron and dietary advice should be given. (see Anaemia leaflet)
- Oral iron should be taken on an empty stomach 1hour before or after food and should be taken with a vitamin C rich drink.
- If a woman/pregnant person is iron deficient prior to delivery and on iron therapy, she should continue oral iron for at least 3 months post-partum.

To ensure good compliance and minimize side effects, a once daily dose is advised. Higher doses potentially increase side effects such as gastric irritation, nausea and disturbed bowel function affecting compliance (Smith G. 2014 Cochrane database). Recent data has also shown that absorption of iron is maximized if given once daily rather than more frequently. (Moretti 2015)

2.4 Monitoring:

- Once treatment has been commenced a repeat FBC should be taken after 2 weeks.
- These results should be clearly documented in the woman's/pregnant persons health care records.
- If the Hb is improving treatment should continue. Further assessments of FBC may be required if there is concern about compliance, tolerance or significant anaemia (see appendix 4).

2.5 Poor response/intolerance:

- If there is no response after two weeks, if the Hb is not improving ferritin and folate levels should be checked and a referral should be made to secondary care.
- If after 2 weeks the FBC is not improving because there has been intolerable side effects limiting compliance, the woman/pregnant person should be given a different preparation of oral iron therapy e.g. Ferrous Sulphate or Sytron. (see appendix 4)
- If the woman/pregnant person has symptomatic anaemia, is over 34 week's gestation or is not tolerating any oral therapy then her Obstetric Lead Clinician should be consulted. If the Obstetric Clinical Lead is unavailable, then the Haematological Team should be consulted for further advice.

2.6 Absolute intolerance or non-compliance

- If there is absolute intolerance or non-compliance with oral iron, IV iron should be considered providing iron deficiency has been confirmed with a low serum ferritin.
- The decision to prescribe Ferinject® should be made by the Clinician following this guidance.
- Ferinject® **MUST NOT** be given in the first trimester of pregnancy

Indications for Ferinject ®:

- Women/pregnant people with confirmed iron deficiency anaemia with a serum ferritin of <30ug/L who:

1. Are intolerant to oral iron preparations or
2. Fail to respond to oral iron therapy or
3. Have malabsorption of oral iron

All care providers should discuss the option to use Ferinject® with either the Lead Obstetric Clinician or the Haematological Obstetric Team.
Referrals to HaemObs team can be made via e-mail to - haemobsmailbox@uhl-tr.nhs.uk

2.7 Ferinject® dosing and prescribing

- The dose of Ferinject® should be calculated according to the woman's/pregnant persons **booking** weight.
- Ferinject® should only be prescribed on the drug chart.

The regime that should be used is:

PATIENT WEIGHT	MAXIMUM DOSE OF FERINJECT®
< 50kgs	20mgs / kg
≥50kgs	1000mgs

2.8 Ferinject® administration:

- Provide patient information leaflet and ensure that details of who to contact with any adverse reactions or queries is highlighted
- Ferinject® should be administered as an infusion. (See Appendix 2) Ferinject® should be diluted in 250mls of 0.9% saline and be given over 15 minutes. A pump should be used to control the rate of infusion.
- If the Ferinject® leaks out of the vein, it can cause skin staining. It is important to flush the cannula after insertion prior to commencing Ferinject® to ensure the cannula is correctly placed in the vein.
- Administration can only be undertaken in a clinical area where emergency equipment is available as there is a risk of anaphylaxis. The Maternity Assessment Unit (at both sites) have one daily slot (weekdays only) to facilitate administration of Ferinject®.
- The risk of anaphylaxis is very rare but it is recommended Adrenaline should be available as first line treatment in case of severe reaction.
- Patients should be closely monitored for signs of hypersensitivity during and for at least 30 minutes after every administration of an IV iron product.
- Caution is needed with every dose of intravenous iron that is given, even if previous administrations have been well tolerated.
- If the woman has experienced signs of hypersensitivity to Ferinject® consideration should be given to other preparations of intravenous iron (e.g. Monofer®)
- If signs of hypersensitivity have been experienced during the current or previous intravenous iron infusion administration, ensure the preparation that has triggered the reaction, is identified and documented in the hospital/electronic records.

- Need for ongoing iron supplements should be reviewed, depending on clinical circumstances. Further supplements should not be administered within a week of IV Ferinject®**.**

2.9 Post-natal anaemia:

- If the woman/birthing person is symptomatic in the postnatal period, but there is no ongoing bleeding and there is no cardiovascular compromise Ferinject® can be considered in an attempt to reduce transfusion of red cells.
- If there is ongoing blood loss or any haemodynamic compromise iron supplementation may well not be sufficient and the need for a blood transfusion should be discussed with the Obstetric Lead Clinician or the Haematological Team.

3. Education and Training

None

4. Monitoring Compliance

None

5. Supporting References

1. Briley et al., reporting errors, incidence &risk factors for PPH (prospective observational study) BJOG 214;121:876-888
2. Pena-Rosas, Juan Pablo, Luz Maria De-Regil, H. Malave Gomez, Monica C. Flores-Urrutia, and Therese Dowswell. "Intermittent oral iron supplementation during pregnancy." (2015): CD009997-CD009997.
3. Shinar S J, A Skornick-Rapaport, S Maslovitz. Iron supplementation in singleton pregnancy: Is there a benefit to doubling the dose of elemental iron in iron-deficient pregnant women? a randomized controlled trial. Journal of Perinatol 2017; 37: 782-786
4. https://www.resus.org.uk/sites/default/files/2021-05/Emergency%20Treatment%20of%20Anaphylaxis%20May%202021_0.pdf

6. Key Words

Anaemia, Ferinject®, Anaemia in pregnancy, Ferritin, Folate

The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs.
As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.

Contact and review details	
Guideline Lead (Name and Title) N Archer - Consultant	**Executive Lead** Chief Medical Officer
Original Authors: P Coser, L Matthews, M Copple, C Oppenheimer, H Mayberry, S Pavord, K Longmuir and L Sanders **June 2022:** H Maybury – Consultant & S Hayes Obs Haem Nurse Specialist	
Details of Changes made during review: **January 2022:** Added consideration of Other preparations of IV iron use such as Monofer Added MAU now have daily slots Mon-Fri for administering IV infusion Removed Vit b12 pathway from the flowchart in Appendix 4 (UHL lab doesn't measure accurately the Vit B12 component levels that would alter management in pregnancy) Appendix 4 folate level change from <2ng/ml to < 2.6 Updated anaphylaxis treatment in line with Resuscitation Council UK 2021 **June 2022 v3.1** Added specialist nurse/midwife referral for parenteral iron infusion criteria to appendix 5 Added HaemObs email **January 2023 v3.2** If the Ferinject® leaks out of the vein, it can cause skin staining. It is important to flush the cannula after insertion prior to commencing Ferinject® to ensure the cannula is correctly placed in the vein Added common or very common side effects **October 2023** Added statement - to document any adverse reactions to medical records & to provide PIL	

Appendix I: Dose and elemental iron content per tablet of combined oral iron and folate preparations

Combined iron and folate preparation	Iron salt and dose per tablet	Elemental iron content per tablet	Folic acid content per tablet
Pregaday	Fumarate 305mg	100 mg	350 mcg
Fefol	Sulphate 325 mg	47 mg	500 mcg
Galfer FA	Fumarate 305 mg	100 mg	350 mcg
Systron	Feredetate 190mg/5 mls elixir	27.5mg/ 5mls elixir	None
Ferrous Sulphate	200 mg	65 mg	None

Summary of intravenous iron preparations available in the UK

	Cosmofer iron (III) hydroxide dextran complex	**Venofer iron (III) hydroxide sucrose complex**	**FerinJect Iron(III) carboxymaltose**	**Monofer Iron (III) isomaltoside**
Dose of elemental iron	50mg/ml	20mg/ml	50mg/ml	100mg/ml
Test dose required as per manufacturer	Yes, before every intravenous dose, once before intramuscular treatment	First dose new patients only	No	No
Routes of administration	Slow intravenous injection Intravenous infusion of total dose Intramuscular injection total dose	Slow intravenous injection Intravenous infusion	Slow intravenous injection Intravenous infusion	Slow intravenous injection Intravenous infusion
Able to administer total dose	Yes (up to 20mg/kg body weight over 4-6 hours)	No	Yes (up to 15mg/kg body weight maximum of 1000mg/week over 15mins)	Yes (up to 20mg/Kg body weight over 1 hour)
Half life	5 hours	20 hours	7-12 hours	5 hours
Dosage	100-200mg per IV injection up to 3 times a week. Total dose infusion up to 20mg/kg body weight over 4-6 hours)	Total IV single dose no more than 200mg, can be repeated up to 3 times in 1 week	200mg per IV injection up to 3 times a week. Total dose infusion up to 15mg/kg body weight. Maximum weekly dose of 1000mg that can be administered over 15mins.	100-200mg per IV injection up to 3 times a week. Total dose infusion up to 20mg/Kg body weight per week. Doses up to 10mg/Kg body weight can be administered over 30mins, doses greater than

	(100mg IM into alternate buttocks daily in active patients in bed ridden up to 3 times a week)			10mg/kg body weight should be administered over 60 mins.
Use in pregnancy	No adequate data for use in pregnant women, contra-indicated in first trimester thereafter risk benefit based on clinical need	Not in first trimester	Not for use in first trimester	No adequate data for use in pregnant women, contra-indicated in first trimester thereafter risk benefit based on clinical need
Lactation	Risk not known	Unlikely to pass to maternal milk no clinical trials	<1% iron passed into milk unlikely to be significant	Risk not known
Adverse drug related events	5% patients may experience minimal adverse events (dose related) Risk of severe anaphylaxis <1/10 000 Risk of anaphylactoid symptoms >1/1000<1/100 **Common or very common** Dizziness; flushing; headache; hypertension; hypophosphataemia; hypotension; nausea; skin reactions; taste altered	0.5-1.5% of patients may experience adverse events. Risk of anaphylactoid reaction >1/10 000 <1/1000 **Common or very common** Dizziness; flushing; headache; hypertension; hypophosphataemia; hypotension; nausea; skin reactions; taste altered	3% of patients may experience adverse events. Risk of anaphylactoid reaction >1/1000 <1/100 **Common or very common** Dizziness; flushing; headache; hypertension; hypophosphataemia; hypotension; nausea; skin reactions; taste altered	More than 1% of patients may experience adverse events Risk of anaphylaxis <1/10 000 >1/1000 to <1/100 Anaphylactoid reactions **Common or very common** Dizziness; flushing; headache; hypertension; hypophosphataemia; hypotension; nausea; skin reactions; taste altered

Appendix 2:

Equipment required for administration of Ferinject®:

Ferinject®doses 1000mg in 250 mls normal saline 0.9% given in 15 mins.

1 alcowipe
1 green Venflon.
Tape or cannula dressing
Vacutainer blood bottles- FBC.
2 White needles.
1 x 5 ml syringe
1 x 20 ml syringe
5mls of 0.9% sodium chloride (to flush the cannula)
1 bag of 0.9% sodium chloride 250 mls.
Giving set (appropriate giving set to use with correct pump)
Gauze.

Procedure for administration of Ferinject® infusion.

Baseline observations:
Prepare infusion of ferinject®.
Prepare the skin in accordance with the aseptic non touch technique policy.
Insert venflon according to UHL guidelines.
Secure cannula in position with tape or cannula dressing.
Take blood as required via the cannula.
Flush with 2mls of 0.9% sodium chloride.
Connect infusion of ferinject® and infuse via pump calculated to the correct rate for the infusion.
Observe patient for any adverse events.
Remove cannula following completion of infusion.
Post infusion observations.

IM/IV Adrenaline should be available for immediate use in the event of a severe adverse drug reaction.

Appendix 3:

Indications for assessment of serum ferritin

Anaemic women where estimation of iron stores is necessary

Known Haemoglobinopathy
Prior to parenteral iron replacement

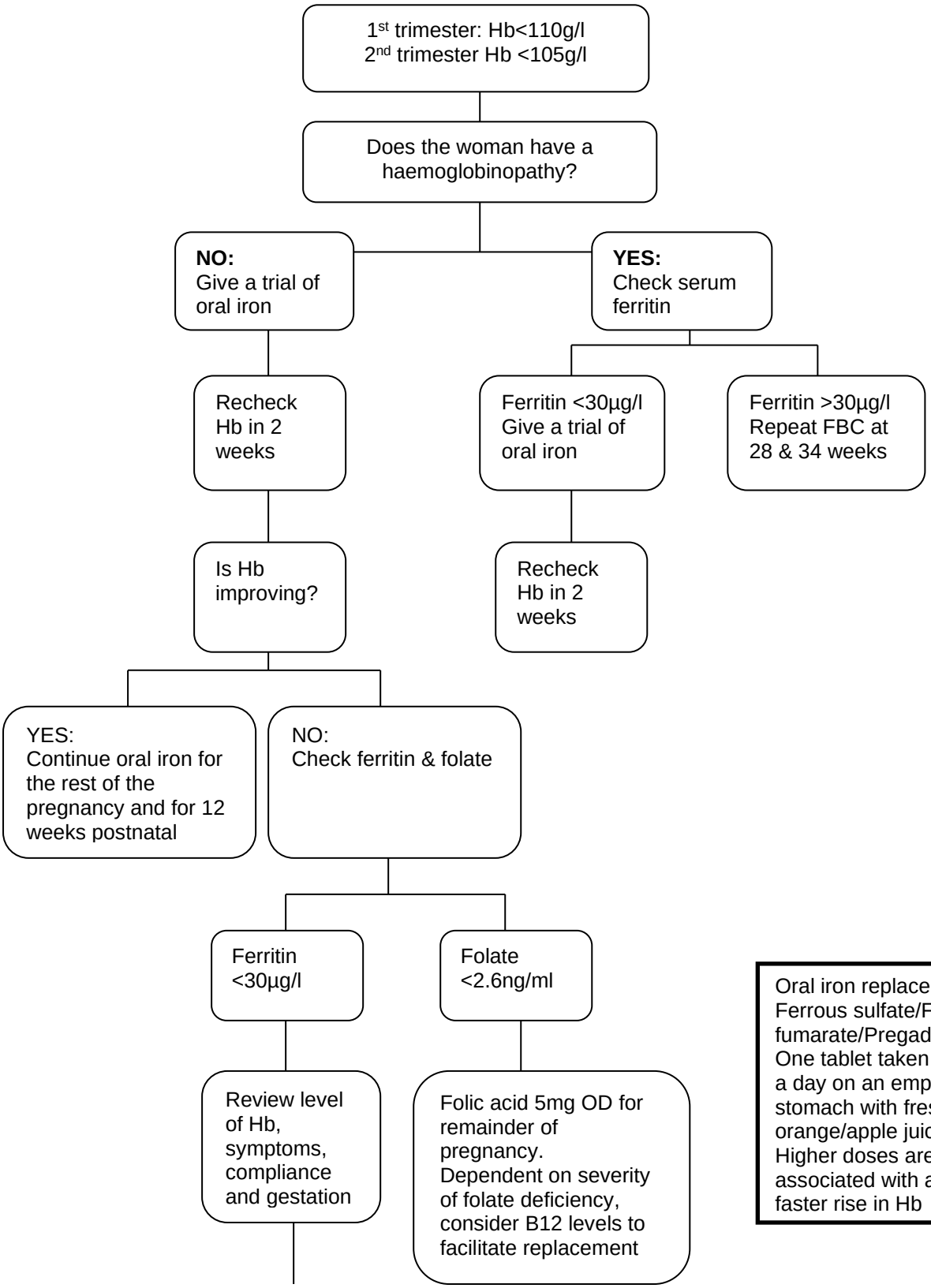
Non-anaemic women with high risk of iron depletion

Previous anaemia
Multiparity >=P3
Consecutive pregnancy <1year following delivery
Vegetarians
Teenage pregnancies
Recent history of bleeding

Non-anaemic women where estimation of iron stores is necessary

High risk of bleeding
Women declining blood products

Appendix 4: Flowchart for the Management of Anaemia in Pregnancy



Consider IV Ferinject or continue oral iron with repeat FBC in 2 weeks.

Appendix 5: Obstetric Haematology Nurse/Midwife led referral for parenteral iron infusion

Registered midwives can arrange IV iron with MAU once approved by lead obstetric clinician or HaemObs team.

An obstetric haematology nurse or obstetric haematology specialist midwife can directly arrange an IV iron infusion without medical review if following criteria is met:

- Gestation 34/40 or higher
- Patient have no haemoglobinopathies - if present medical review needed
- Hb < 90g/l
- Iron deficiency confirmed
- Ferritin level <30 within last 4 weeks
- Folate level checked
- If Folate <2.6ng/ml ensure that Folic Acid 5mg once a day dose prescribed
- No contraindications or allergy to IV iron
- Stop oral iron for 1 week
- Medical review and prescription at MAU before IV iron infusion