Royal College of Nursing

Iron Deficiency and Anaemia in Adults

RCN guidance for nursing practice

CLINICAL PROFESSIONAL RESOURCE

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Publication

This is an RCN practice guidance. Practice guidance are evidence-based consensus documents, used to guide decisions about appropriate care of an individual, family or population in a specific context.

Description

Iron deficiency anaemia (IDA) is a widespread problem affecting an estimated two billion people worldwide and is the most common cause of anaemia seen in primary care. This guidance has been developed by expert nurses from several relevant specialties and is for the use of nurses, health care assistants (HCAs), midwives and health visitors from all specialties and backgrounds.

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The Nine Quality Standards

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Evaluation

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Background

Iron deficiency anaemia (IDA) is a widespread problem affecting an estimated two billion people worldwide (Zimmermann and Hurrell, 2007) and is the most common cause of anaemia seen in primary care. It causes more than 57,000 emergency admissions to hospital each year, at a cost to the NHS of £55.48m across the UK (Goddard and Phillips, 2014).

Fatigue, weakness and impaired physical function are typical symptoms that can adversely affect an individual's quality of life and wellbeing and results in a greater demand for health services. Nursing staff in all clinical settings will encounter people affected by IDA but effective identification and management is often overlooked. Dealing with IDA improves a person's physical condition, prevents complications and blood transfusion use; an estimated cost saving of £8.43m per year (Goddard and Phillips, 2014).

This RCN guidance has been developed by expert nurses from several relevant specialties. It is written for the use of nurses, health care assistants (HCAs), midwives and health visitors from all specialties and backgrounds.

This publication:

- gives clear information on identifying IDA and escalating effective management
- makes it easier to understand when, why and how IDA occurs
- provides information on good dietary advice and the use of oral iron supplements
- encourages the use of intravenous iron and provides practical tips for its delivery
- provides good patient and public information website links
- offers specialist guidance to nursing staff working in the following specific therapeutic areas: chronic kidney disease (CKD), inflammatory bowel disease (IBD), heavy menstrual bleeding, pregnancy and postpartum, patient blood management, perioperative care and heart failure.

Definition

Anaemia is defined as a reduced number of red blood cells (RBCs) or less than the normal amount of haemoglobin (Hb) in the blood. It can also be defined as a lowered ability of the blood to carry oxygen.

World Health Organization (WHO) Haemoglobin thresholds used to define anaemia (Pavord et al., 2011)

Age or gender group	Hb threshold (g/l)
Children (0.5 to 5 years)	110
Children (5 to 12 years)	115
Teens (12 to 15 years)	120
Women, non-pregnant (over 15 years)	120
Women, pregnant	110 in first trimester 105 in second and third trimesters 100 post partum (up to six weeks post-delivery)
Men (over 15 years)	130

The normal range for Hb also varies between different populations in the UK. There are several different types of anaemia and each one has a different cause, although IDA is the most common. IDA is a condition where a lack of iron in the body leads to a reduction in the number of red blood cells. Iron is normally stored in the liver and is essential to red blood cell production. If there is a shortage of stored iron then red cells become depleted.

Iron homeostasis and pathophysiology

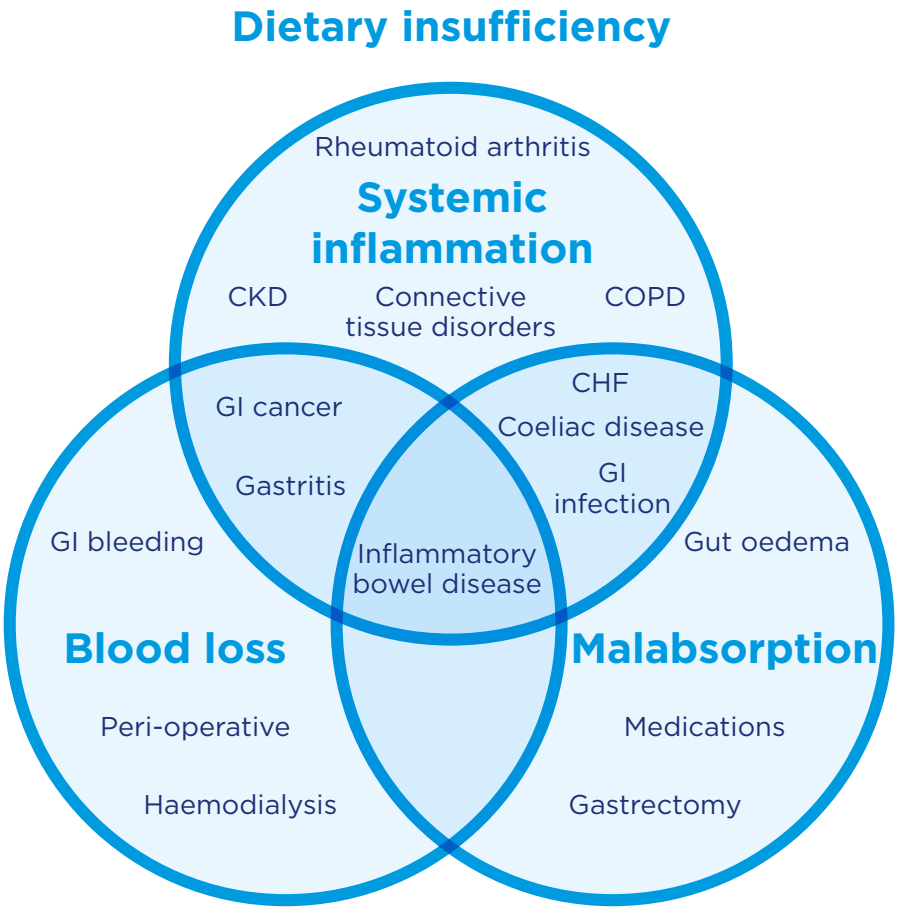
Iron

Iron homeostasis involves a number of important processes, including the regulation of intestinal iron absorption, the transport of iron to the cells, the storage of iron, the incorporation of iron into proteins, and the recycling of iron after red blood cell (RBC) degradation. Under normal physiological conditions, as there is no active iron excretion mechanism, iron homeostasis is strictly controlled at the level of intestinal absorption.

Storage of iron

In healthy individuals, about 25% of the total body iron (800 to 1,000mg) represents storage iron, mainly as ferritin in the liver and skeletal muscle; consequently, serum ferritin is a useful marker for iron stores.

Hepcidin is a naturally occurring protein, secreted by the liver. It acts as a regulatory hormone controlling the amount of iron in the body. In inflammation, hepcidin levels rise causing iron to be trapped within macrophages and liver cells. Therefore serum iron levels fall. This typically leads to anaemia due to an inadequate amount of serum iron being available for developing red cells. This leads to functional iron deficiency (FID), which develops under conditions where the demand exceeds iron availability.



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Measuring iron status

If Hb is reduced, further blood iron studies identify if the anaemia is caused by iron deficiency. Iron tests can also help differentiate iron deficiency from other causes of anaemia (such as pernicious anaemia or anaemia of chronic disease).

	Absolute iron deficiency	Absolute iron deficiency in the presence of inflammation	Functional iron deficiency
Iron tests	Ferritin <30	Ferritin 30–100 + iron saturation <20% or C-reactive protein (CRP) >5	Ferritin >100 + iron saturation <20% or C-reactive protein (CRP) >5

Serum Ferritin Levels

This is a measure of iron storage in the body. Reduced serum ferritin is always the first iron study to fall and show iron deficiency. However, it is not always accurate as it may increase if the patient has:

- inflammation/infection
- liver disease
- malignancy.

Transferrin

Transferrin is a plasma protein that transports iron through the blood to wherever it is needed. Testing the blood transferrin levels provides an indicator of functional iron availability. This test measures transferrin saturation (in %) – that is the degree of circulating transferrin loaded with iron. Levels will fall in iron deficiency.

Hypochromic microcytic red blood cells

This test measures the size of red blood cells. Iron deficiency results in a failure to synthesise haemoglobin. In cases of hypochromia the MCH (mean cell haemoglobin) is reduced as there is less haemoglobin within the red blood cells. This makes the cells appear pale. The lack of haemoglobin also makes the cells smaller than they should be, leading to a reduced MCV (mean cell volume).

Causes of absolute iron deficiency (AID)

Inadequate dietary intake

Poor nutrition.

Chronic alcoholism.

Vegetarianism (decreased consumption of animal protein).

Poor vitamin C (ascorbic acid) intake.

Decreased consumption of animal proteins and ascorbic acid.

Increased iron demands

Pregnancy.

Infancy/adolescence.

Dialysis.

Surgery.

Gastrointestinal bleeding.

Blood donation.

Menstruation.

Nose bleeds.

Haemodialysis.

Puerperium.

Inadequate gastrointestinal absorption

Malabsorption syndromes, for example, coeliac disease.

Interference with certain drugs/foods, for example, proton pump inhibitors.

Bariatric surgery, for example, gastric bypass.

Common symptoms of anaemia

The following are the common signs and symptoms of anaemia. It is important to remember that they can be overlooked or missed due to their vagueness and ability to be attributed to several causes. Individuals rarely present with only one of the symptoms listed and often present them as a part of a list of other symptoms, sometimes obscuring information.

- Weakness.
- Shortness of breath.
- Dizziness.
- Fatigue.
- Fast or irregular heartbeat.
- Pounding or 'whooshing' in the ears.
- Headache.
- Cold hands or feet.
- Pale skin.
- Chest pain.
- Lack of concentration.
- Mouth ulcers or cracks at the corners of the mouth.
- Slow or poor wound healing.
- Tinnitus.

(Arnott et al., 2013)

Important questions to ask

To determine the underlying cause of anaemia, questions about an individual's lifestyle and medical history should be asked. These questions should cover the following areas.

Diet

Certain types of food preferences or intolerances may lead to a diet that does not contain sufficient iron-rich foods.

Medicines

A comprehensive list of all medicines being taken is vital. Many people will mention over the counter, homeopathic and/or herbal remedies alongside any medications that are regularly prescribed by a clinician. There can be contraindications and a comprehensive list will allow identification of any type of medicine that might cause gastrointestinal bleeding (bleeding from the stomach and intestines), such as ibuprofen or aspirin.

Menstrual pattern

Particularly heavy or prolonged periods can lead to anaemia, but this may go unreported if a woman has always had periods of this kind and has not seen a marked difference in what she is used to. Establishing an idea of volume of loss and length of bleeding in days, as well as what is a normal pattern for the individual, is important.

Pregnancy and lactation

Both pregnancy and lactation place heavier demands on the body for the use of iron and iron stores, particularly as the baby develops and when the body responds to the demands to nurture the baby during feeding. In addition, there are greater physical demands on the body when caring for a new born, with the change in sleep and dietary patterns of the mother.

Unexplained and heavy bruising

It is valuable to ask if there has been any unexplained or unexpectedly heavy bruising from an otherwise light injury. This will allow a timeframe to be established for the symptoms and concerns being investigated and may prompt an individual to recall episodes of weakness or dizziness they may have not otherwise mentioned.

Family history

Identification of immediate family members who have been diagnosed and treated for anaemia, or who have a history of gastrointestinal bleeding or blood disorders, can assist in identifying potential patterns or genetic commonalities that can lead to a more specific diagnostic pathway.

Blood donation

Regular donations of blood require a blood test to check that the donor's haemoglobin level is sufficient for them to be able to donate safely. If the person has recently been unable to meet that threshold after previously having no problems, it may give a timeframe for the onset of the anaemia. If a donation has been made within 48 hours of a blood test, then an individual will have a lower haemoglobin level (as their body replaces the red cells that have been donated).

Other medical conditions

It is important to record any other illnesses or symptoms as listed previously.

Travel

Ask about any recent trips or contact with others who have been abroad. This can be instructive as certain destinations may increase the chances of someone having a blood-borne infection or hookworm.

Examination

Investigations to determine IDA usually begin with blood tests.

Full blood count (FBC)

This checks the number and quality of red cells present in the blood sample taken, including the Hb.

Vitamin B12 and folate levels

This checks to see if the levels present are sufficient to make functioning red blood cells.

Ferritin and transferrin saturation levels

This checks the amount of iron stored (ferritin) and the amount available to use (iron saturation).

Urinalysis for haematuria

Just 1% of people diagnosed with IDA will have renal tract malignancy. This may present as obvious or occult haematuria (Goddard et al., 2011).

Managing iron deficiency

Dietary iron

In general, a broad range of foods should be used to prevent iron deficiency. A normal balanced diet contains a total of 12 to 18mg of iron per day. However, only a small amount of iron eaten is absorbed (3 to 5mg per day). It is advised that eating 70g of red meat per day is safe to meet iron requirements. Iron in the diet comes in two forms: haem iron and non-haem iron. Haem iron is found in animal derived foods and non-haem iron in plant derived foods. Non-haem iron (plant iron) is less easily absorbed through the gut. Therefore a balanced diet with iron enhancers is recommended (Derbyshire, 2012).

Foods that enhance or inhibit iron intake and absorption (Derbyshire, 2012)

Foods that enhance iron intake

Lean red meat.

Oily fish.

Vitamin C (fresh fruit and juices).

Fermented products (such as soy sauce and bread).

Foods that inhibit iron absorption

Calcium, particularly from milk and dairy products.

Phytates (present in cereal brans, grains, nuts and seeds).

Polyphenols and tannin (in tea, coffee, herbal infusions, green leafy vegetables).

General tips

Don't drink tea or coffee before or immediately after meals; wait at least one to two hours. Include vitamin C with meals where possible (such as a glass of fruit juice). Eat dairy products as snacks rather than with meals. Eat five portions of fruit and vegetables each day (Food Standard Agency, 2007).

For more patient information on iron in your diet please go to:

www.bda.uk.com/foodfacts/iron_food_fact_sheet.pdf

Oral iron supplements

Oral iron supplements should be considered for all people diagnosed with iron deficiency. These will help to correct anaemia and replenish iron stores. However, there are some instances when it is inappropriate to take oral iron, particularly if someone:

- has inflammatory bowel disease that is active (see Appendix 2 on page 22)
- has an oral iron intolerance
- is taking erythropoiesis stimulating agents.

There are several iron compounds available as tablets (ferrous sulphate, ferrous fumarate, ferrous gluconate). Oral iron preparations contain varying amounts of ferrous iron and the frequency of gastrointestinal side effects related to each different preparation tends to be directly related to the content of ferrous iron.

Iron salt	Dose	Preparation	Content of ferrous iron
Ferrous sulphate	200mg	tablets	65mg
Ferrous gluconate	300mg	tablets	35mg
Sodium feredetate (Sytron)	380mg/ 10mls	elixir	55mg

Limitations to iron supplements

There are several limitations to taking iron supplements. Only a small amount is actually absorbed (particularly if there is inflammation). Between 10 and 40% of people taking oral iron supplements experience gastrointestinal (GI) side effects, including diarrhoea or constipation, and don't fully adhere to the prescribed course.

Tips for successful supplementation

- Lower doses are better tolerated (start daily and build up dosing).
- Check FBC and iron levels monthly. Once Hb is normal, continue oral iron for three months.
- Combine ascorbic acid (vitamin C) as it may help absorption.
- Warn of potential GI side effects.

When people are able to take and tolerate iron supplements effectively, haemoglobin should rise by 2 g/l every three weeks.

Intravenous iron: practical administration

Using iron intravenously (IV) used to be thought as a last resort. However, modern IV iron preparations are becoming standard practice now in the management of IDA (Arnott et al., 2013). Randomised controlled trials show that:

- intravenous iron is at least as effective as oral iron
- intravenous iron delivers a faster response rate than oral iron.

In some instances, using IV iron is recommended as the first line of treatment. For example:

- if surgery is planned less than six weeks after the diagnosis of iron deficiency
- for pregnant women with severe iron deficiency (HB <80g/l) or who are diagnosed with IDA beyond 34 weeks gestation
- for women with severe post-partum anaemia.

IV iron is given when there is an oral iron intolerance/poor adherence, or if there is a poor response to oral iron. It needs to be given in a specialist environment. However, there are a number of contraindications. These include:

- known hypersensitivity to intravenous iron
- anaemias not caused by iron deficiency
- iron overload
- first trimester of pregnancy.

Precautions to take into account include:

- asthma, eczema or other atopic allergy
- liver dysfunction
- acute or chronic infection
- hypotension.

All health care practitioners should refer to the individual Summary of Product Characteristics before prescribing.

Use in pregnancy

Oral iron is generally the preferred method of supplementation for anaemia in pregnancy, although, where anaemia is sufficiently severe, intravenous preparations may be used.

Intravenous iron is contraindicated during the first trimester of pregnancy; whilst for the second and third trimesters it is suggested that pre-pregnancy weight should be used as the basis for iron requirement and dose calculation.

IV iron preparations

Currently five IV iron preparations are available for use.

1. Ferric carboxymaltose (Ferinject®).
2. Iron isomaltoside 1000, 10% (Monofer®).
3. Low molecular weight iron (111) dextran (CosmoFer®).
4. Iron sucrose (Venofer®).
5. Iron isomaltoside 1000, 5% (Diafer®).

All IV iron preparations should be administered in a setting where resuscitation facilities are available and appropriately trained staff are present. The patient should be observed for adverse effects for at least 30 minutes following each administration.

All preparations have been shown to be well tolerated, with few side effects. NICE (CKD) guidance (2015) does not differentiate between them.

Health care professionals are asked to report all suspected adverse drug reactions to these products through the Yellow Card Scheme.

Dosing and infusions differences between IV iron preparations					
	Ferinject (Ferric carboxymaltose)	**Monofer (Iron isomaltoside 1000, 10%)**	**CosmoFer (Low molecular weight iron dextran)**	**Venofer (Iron sucrose)**	**Diafer (Iron isomaltoside 1000, 5%)**
Indication	Iron deficiency	Iron deficiency	Iron deficiency	Iron deficiency	Iron deficiency in haemodialysis
Total vs. Repeated dosing	Total dosing	Total dosing	Total dosing	Repeated dosing	Repeated dosing
Dose estimation	SPC simplified table	SPC simplified table Or Ganzoni formula	Ganzoni formula	Ganzoni formula	No specific dosing. As per dialysis requirements
Max single dose for infusion	Max. single dose 20mg/kg up to 1g Larger doses require separate infusions one week apart	Max. single dose 20mg/kg. No other dose cap Larger doses require separate infusions one week apart	Max. single dose 20mg/kg. No other dose cap Larger doses require separate infusions	Max. single dose 200mg Larger doses separate infusions max. three times/ week	Max. single dose 200 mg. Bolus injection only Larger doses separate infusions max. 1000 mg/week
Administration for infusion	Up to 1000 mg over 15 mins	Up to 1000 mg over > 15 mins > 1000 mg over ≥ 30 mins	Over 4-6 hours	200mg: • minimum of 30 mins by infusion • minimum of 10 mins by injection	Fast push bolus injection

1. Ferinject

Dose calculation for Ferinject

The cumulative dose of iron using Ferinject is determined based on the patient's body weight and Hb level and must not be exceeded. The following table should be used to determine the cumulative dose.

Hb (g/dL)	Patients with body weight 35kg to <70 kg	Patients with body weight ≥70 kg
<10	1500mg	2000mg
≥10	1000mg	1500mg

A single dose of Ferinject by infusion should not exceed 20mg/kg, up to 1000mg of iron. Do not administer 1000mg of iron more than once per week. Patients with a cumulative dose requirement of >1000mg will need a second infusion after seven days or more of the first.

Administration

No test dose required. A cumulative iron dose of 500mg should not be exceeded for patients with a body weight <35kg. For patients with a Hb value ≥14 g/dL, an initial dose of 500mg iron should be given and iron parameters should be checked prior to repeat dosing. Post repletion, regular assessments should be completed to ensure that iron levels are corrected and maintained.

Maximum tolerated single dose

A single dose of Ferinject should not exceed 1,000mg of iron (20ml) per day. Do not administer 1,000mg of iron (20ml) more than once a week.

Intravenous injection

Ferinject may be administered by intravenous injection using undiluted solution up to 1,000mg iron (up to a maximum of 15mg per kg of body weight). For doses up to 200mg iron, there is no prescribed administration time. For doses greater than 200 and up to 500mg iron, Ferinject

should be administered at a rate of 100mg/min. For doses greater than 500mg and up to 1000mg iron, Ferinject should be administered over 15 minutes.

Dilution plan of Ferinject for intravenous infusion							
Ferinject			**Iron**			**Maximum amount of sterile 0.9% m/V sodium chloride solution**	**Minimum administration time**
2	to	4ml	100	to	200mg	50ml	–
>4	to	10ml	>200	to	500mg	100ml	6 minutes
>10	to	20ml	>500	to	1000mg	250ml	15 minutes

Note: For stability reasons, dilutions to concentrations less than 2mg iron/ml are not permissible. Ferinject must not be administered by the subcutaneous or intramuscular route.

Minimum observation is required (pulse and blood pressure should be checked before and after infusion). Facilities for cardiorespiratory resuscitation and equipment for handling acute anaphylactic/anaphylactoid reactions should be available, including an injectable 1:1000 adrenaline solution. Additional treatment with antihistamines and/or corticosteroids should be given as appropriate.

Haemodialysis patients

A single maximum daily injection dose of 200mg iron should not be exceeded in haemodialysis-dependent chronic kidney disease patients.

Intravenous infusion

Ferinject may be administered by intravenous infusion up to a maximum single dose of 1000mg of iron (up to a maximum of 20mg per kg of body weight). Ferinject must be administered only by the intravenous route: by bolus injection, or during a haemodialysis session undiluted directly into the venous limb of the dialyser, or by infusion. In case of infusion, Ferinject must be diluted only in sterile 0.9% m/V sodium chloride solution as shown in the table.

2. Monofer (100mg/ml) (iron isomaltoside 1000)

Dose calculation for Monofer

The dose of Monofer can be estimated based on the patient weight and Hb.

Dosing table: Cumulative iron dose		
Hb (g/dL)	**Patients with body weight 50kg to <70kg**	**Patients with body weight ≥70kg**
≥10	1000mg	1500mg
<10	1500mg	2000mg

Administration

No test dose required. The maximum dose per single administration is 20mg of iron per kg body weight. If the cumulative iron exceeds 20mg of iron per kg of body weight, the dose must be split into two administrations, with an interval of at least one week. If possible, it is recommended to give 20mg of iron per kg of body weight in the first administration. Dependent on clinical judgement, the second administration can await follow up blood tests.

Doses of up to 1000mg must be administered over more than 15 mins. Doses exceeding 1000mg must be administered over 30 minutes or more. Monofer should be added to a maximum of 500ml sterile 0.9% sodium chloride.

Minimum observation is required to monitor for adverse reactions (pulse and blood pressure should be checked before and after infusion).

Administration of intravenous bolus injection

No test dose is required for this. Inject up to 500mg (up to three times a week) at an administration rate of up to 250mg of iron per minute. It may be administered undiluted or diluted in a maximum of 20mls of sterile 0.9% sodium chloride.

Haemodialysis patients

Monofer can be administered either as an intravenous bolus injection, as an intravenous drip infusion or as a direct injection into the venous limb of the dialyser.

3. CosmoFer

Dose calculation for CosmoFer

The normal recommended dosage schedule is 100 to 200mg of iron corresponding to 2–4ml, two or three times a week (depending on the haemoglobin level). However, if clinical circumstances require rapid delivery of iron to the body iron stores, CosmoFer can be administered as a total dose infusion up to a total replacement dose corresponding to 20mg of iron per kg of body weight.

Total dose (mg Fe) – Hb in g/l:
(Body weight (kg) x (target Hb – actual Hb) (g/l) x 0.24) + mg iron for iron stores.

Administration

Before administering a slow intravenous injection, 25mg of iron should be injected slowly over a period of one to two minutes. If no adverse reactions occur within 15 minutes, the remaining portion of the injection may be given.

Low dose infusion

Add the CosmoFer dose to 0.9% sodium chloride solution or in 5% glucose solution. CosmoFer, in a dose of 100 to 200mg iron (2–4ml), may be diluted in 100ml. On each occasion, the first 25mg of iron should be infused over a period of 15 minutes. If no adverse reactions occur during this time, the remaining portion of the infusion should be given at an infusion rate of not more than 100ml in 30 minutes.

Total dose infusion

Add total dose of CosmoFer to 500ml of sodium chloride 0.9% or 5% glucose solution; infuse the volume intravenously over four to six hours. The first 25mg of iron should be infused over a period of 15 minutes. Minimum observation is required (pulse and blood pressure should be checked before and after infusion). The patient must be kept under close medical observation during this period. If no adverse reactions occur, then the remaining portion of the infusion should be given. The rate of infusion may be increased progressively to 45 to 60 drops per minute. Patients should be observed carefully during the infusion and for at least 30 minutes after completion.

Patient monitoring for all intravenous iron

Iron infusions should only be administered if there are trained staff available to evaluate and manage anaphylactic reactions, and should take place in an environment which has resuscitation facilities. The patient should be observed for adverse effects for at least 30 minutes following each treatment. If hypersensitivity reactions or signs of intolerance occur during administration, the treatment must be stopped immediately.

Hypotensive episodes may occur if IV iron is administered too quickly. Signs include: flushing to the face, acute chest or back pain and tightness, with breathlessness. The infusion should be stopped and the patient's observations checked. The symptoms should disappear shortly after and usually do not reoccur if the administration is restarted at a lower infusion rate.

4. Venofer

Dose calculation for Venofer
Total iron deficit (mg) = body weight (kg) x (target Hb – actual Hb) x 0.24 + depot iron (mg).
• Below 35kg body weight: target Hb = 130 g/l and depot iron = 15mg/kg body weight.
• 35kg body weight and above: target Hb = 150 g/l and depot iron = 500mg.
*Factor 0.24 = 0.0034 x 0.07 x 1000.

The total amount of Venofer required in mg is determined by the following calculation: iron content of haemoglobin 0.34%; blood volume 7% of body weight; factor 1000 = conversion from g to mg. The total single dose must not exceed 200mg of iron given and not more than three times a week.

Administration

No test dose is required. Venofer may be administered by slow intravenous injection at a rate of 1ml undiluted solution per minute and not exceeding 10ml of Venofer (200mg of iron) per injection. Patients should be observed carefully during the infusion and for at least 30 minutes after completion.

Haemodialysis patients

Venofer may be administered during a haemodialysis session. Administer directly into the venous limb of the dialyser.

5. Diafer

Diafer is indicated in adults for the treatment of iron deficiency in patients with chronic kidney disease on dialysis.

Dosing calculation

No specific dose calculation is recommended, as Diafer is used for haemodialysis patients only. The iron dose must be individualised based on the clinical response to treatment including evaluation of haemoglobin, ferritin and tranferrin saturation, concommittant treatment with an erythropoiesis stimulating agent (ESA).

Administration

Diafer can be administered either as an intravenous bolus injection or during a haemodialysis session directly into the venous limb of the dialyser. It may be administered undiluted or diluted in up to 20ml sterile 0.9% sodium chloride.

Diafer should not be administered concomitantly with oral iron preparations, since the absorption of oral iron might be decreased.

Blood transfusion

There are many reasons a blood transfusion may be considered as part of a patient's care pathway. Whatever the cause or clinical decision that leads to a transfusion, it is important to provide evidence and information to support discussions with the patient about this treatment option. These discussions should take place as part of the process of obtaining informed consent.

Since the creation and implementation of the Department of Health's *Health Service Circular: Better Blood Transfusion: safe and appropriate use of blood* in 1998, and the subsequent initiatives of 2002 and 2007 to improve the safe, effective and appropriate use of blood, there has been an emphasis to reduce inappropriate and over use of blood transfusions. There has also been a greater consideration of alternative treatments to ensure blood stocks are conserved and available to everyone at all times, as well as an effort to reduce the risks of unnecessary and inappropriate use of a live human product where an alternative treatment could be used as effectively. In July 2014, *Patient Blood Management – an evidence based approach to patient care* was published and provides clear recommendations on how patient blood management (PBM) should be implemented in hospitals.

PBM is a multidisciplinary concept with the patient at the centre of the decision-making process. It has a clear focus on improving patient outcomes through appropriate use and employing alternatives to transfusion. It puts the patient at the heart of the decisions being made about blood transfusion to ensure they receive the best treatment and avoidable, inappropriate use of blood and blood components is reduced. *Guidance for Blood Transfusion* (NICE, [NG24] 2015) recommends that using alternatives to blood transfusion for individuals having surgery should be a priority.

In March 2011, the Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO) (a Department of Health expert committee) initiated a public consultation on patient consent for blood transfusion, and as a result made a number of recommendations including:

- valid consent for blood transfusion should be obtained and documented in the patient's clinical record by a health care professional
- the provision of patient information is vital for valid consent.

There are patient information leaflets available from NHS Blood and Transplant (NHSBT) such as *Will I need a blood transfusion?* These can help with discussions and decision making, ensuring person-centred care and obtaining informed consent to treatment in a non-emergency setting. Although blood transfusion is often used for iron deficiency anaemia, it can be an inappropriate choice. Evidence of inappropriate practice is shown in the box below.

National Comparative Audit of Blood Transfusion (RCP and NHSBT, 2013)

The audit (which included 1,592 individual cases) revealed that 747 patients were identified as having possible reversible anaemia and that transfusion could have been avoided in 187 (25%) of these. Of those patients who received avoidable transfusion, 18% were not investigated to determine the cause of the anaemia and, in 60%, the anaemia was not adequately treated. Of the 552 patients with possible iron deficiency, 372 were documented as having definite iron deficiency. Only 73% of the 372 were prescribed iron therapy (252 oral and 20 parenteral). Of these, 37 (15%) were intolerant of oral iron and only eight (22%) were given parenteral iron.

Why were patients with potentially reversible anaemia being transfused?

The main reasons identified in the audit were:

- inadequate recognition, investigation and treatment of anaemia
- significant symptoms/signs of anaemia, according to the consultant reviewers.

Why were patients being transfused above the thresholds set in the audit?

The main reason identified in the audit was:

- significant symptoms/signs of anaemia, according to the consultant reviewers.

Why were patients being over transfused?

The main reason identified in the audit was:

- in many cases, the use of a standard prescription of two units which led to a higher increment than required (particularly in patients of lower body weight).

Although other reasons for transfusion were not specifically audited, the logistics of emergency patient care and the pressure on inpatient beds may mean that transfusion is selected as a matter of expediency. Unnecessary and over transfusion may result in patient harm and a waste of precious resources.

Careful consideration should be given to the risks and benefits of using blood transfusion as a treatment option for the correction of iron deficiency anaemia only and the ease of use against the alternative treatments available. Nurses often hold a vital role as the central part of the multidisciplinary team and patient advocate when decisions are made.

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Further reading

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Useful websites and resources

The following list of websites provide information and/or resources to help with good practice in the treatment of anaemia and iron deficiency and will also help nursing staff signpost patients to useful online resources.

Iron deficiency anaemia

https://patient.info/health/anaemia-leaflet/iron-deficiency-anaemia

www.nhs.uk/Conditions/Anaemia-iron-deficiency-/Pages/Diagnosis.aspx

Patient blood management

https://hospital.blood.co.uk/patient-services/patient-blood-management

Blood transfusion practice

www.nhs.uk/Conditions/Blood-transfusion/Pages/Introduction.aspx

www.transfusionguidelines.org.uk/index.aspx

Preoperative assessment

www.aagbi.org/sites/default/files/preop2010.pdf

www.pre-op.org

Perioperative care

www.afpp.org.uk

Appendices

People diagnosed with IDA should be aware that the increase in Hb is a slower process with oral iron and iron infusions than with a blood transfusion and that this may be a contributing factor to the clinical recommendations made. Following treatment, they should be encouraged to see their GP or usual health care practitioner to find the underlying cause of the iron deficiency anaemia (if not identified) and to check that the treatment has been effective. They should have Hb monitoring blood tests to ensure that treatment is given in a timely manner and its effectiveness monitored.

Appendix 1: Gastroenterology

Introduction

Gastrointestinal conditions account for the most common causes of IDA (Goddard et al., 2011) and these may present both with and without GI symptoms. Nursing staff working within GI practice will encounter patients with IDA in all areas of care, whether in outpatient clinics, during investigative procedures, in inpatient care or in specialist roles with patients pre-operatively or with inflammatory bowel disease (IBD) or coeliac disease.

The main body of this guidance has covered the principles of the nursing management of patients with IDA and this appendix aims to inform the care of GI patients in more detail.

GI causes of IDA

The most common cause of IDA in adult men and postmenopausal women is blood loss from the GI tract. There are other causes which include:

- colonic and gastric cancers (these can present with asymptomatic iron deficiency)
- malabsorption (most commonly from coeliac disease)
- gastrectomy or bariatric surgery
- inflammatory bowel disease
- helicobacter pylori (this decreases iron uptake)
- Giardia lamblia.

GI history

When taking a GI history of a patient with IDA consider:

1. use of aspirin and NSAIDS
2. family history, to include:
    - haematological disorders
    - colorectal cancer
    - coeliac disease
    - iron deficiency.
3. history of blood donation
4. epistaxis (nosebleeds)
5. diet and lifestyle (for example, heavy alcohol intake, vegetarianism/veganism).

Investigation

This should include:

- screening for coeliac disease (blood tests for coeliac antibodies)
- upper and lower GI evaluation (oesophago-gastroduodenoscopy, colonoscopy, CT colonoscopy)
- small bowel investigation if poor response to oral/parenteral iron therapy (small bowel video capsule endoscopy, MRI enteroclysis, CT enterography)
- stool culture if the patient reports diarrhoea.

Coeliac disease

Coeliac disease (CD) is a chronic, autoimmune enteropathy that affects the small intestine. It is caused by exposure to gluten (a protein in wheat, rye and barley) in the diet. Eating gluten causes small bowel inflammation and blunting of the intestinal villi. This, in turn, leads to a range of nutritional deficiencies, particularly IDA.

CD affects up to 1:100 of the population, although only about 10 to 15% of people living with it are diagnosed (NICE, 2009). In children and adults, CD can present with a broad range of signs and symptoms. The most frequent include: abdominal pain, cramping or distension, chronic or intermittent diarrhoea, failure to thrive or faltering growth in children, fatigue, iron deficiency anaemia, nausea or vomiting, weight loss.

Studies have shown that 3% of patients undergoing endoscopy for investigation of iron deficiency anaemia will be diagnosed with coeliac disease. Anyone with IDA should be offered serological blood testing for CD. These serological tests should include:

- IgA tissue transglutaminase (tTG)
- IgA endomysial antibodies (EMA) if the tTG is equivocal
- check for IgA deficiency if tTG is negative.

Serological testing should be carried out in primary care settings, but for those with positive serology tests, they should be referred for an intestinal biopsy which will confirm CD. Once diagnosed, treatment is to remove gluten from the diet, and this requires specialist dietetic support. Iron levels should be monitored, and iron supplemented, whilst the child or adult adjusts to a gluten-free diet. Once gluten free, iron absorption should return to normal.

Case study

Miss Rogers is a 25-year-old fashion student who went to her GP feeling tired and run down and with a long history of unpredictable bowel habit which she had always assumed was an irritable bowel. The GP found her to be anaemic and iron deficient (Hb 92 g/l, ferritin 10 µg/l).

She was given some oral iron supplements and sent for coeliac serological blood testing. tTGA (coeliac antibodies) was found to be positive (73 units). She was immediately referred to the nurse-run coeliac clinic in secondary care for gastroscopy and duodenal biopsy.

The biopsy confirmed coeliac disease, and with support from the nurse specialist and the GI dietitian, she started a gluten-free diet. During this time, she struggled to take oral iron (it caused constipation), therefore she had one dose of intravenous iron, which corrected her iron deficiency.

Appendix 2: Inflammatory bowel disease (IBD)

In the UK, IBD is estimated to affect approximately 400 people per 100,000 (Rubin et al., (2000).

IDA occurs in 60 to 80% of people with IBD (Arnott et al., 2013). Reasons for this include:

- an increase in hepcidin, a protein produced in response to inflammation
- intestinal bleeding
- poor iron absorption
- dietary restrictions.

Diagnosing IDA in IBD

The implications of not diagnosing IDA in IBD are significant. Symptoms can substantially reduce quality of life and complications can lead to an increase in admission and post-operative problems. There are two common types of anaemia in IBD: iron deficiency anaemia (IDA) and anaemia of chronic disease (ACD). Distinguishing between the two is most important.

As more nurses are carrying out specialist roles in IBD they have increasing responsibility for interpreting and acting on blood tests. The minimum monitoring blood tests should include haemoglobin, serum ferritin, transferrin saturation and c-reactive protein (CRP). Iron deficiency can be identified using the ferritin and saturation levels but interpreting these depends on the level of inflammation (CRP).

Serum ferritin levels increase in acute inflammation, so where CRP is raised, patients may appear to have a normal ferritin level. Therefore, when CRP is raised, the cut of ferritin level indicating iron deficiency increases to <100 µg/l. In quiescent disease (where CRP is normal) the standard value (<30 µg/l) applies.

Options for oral iron

Ferric maltol (Feraccru) is an option for the oral treatment of IDA in patients with IBD. There is some evidence (Schmidt et al., 2016) to suggest that patients unable to tolerate ferrous iron, can tolerate oral ferric maltol (this should be given twice a day), with only mild to moderate adverse events, and it can improve Hb levels.

The IBD nursing role

Identifying and appropriately managing IDA is an essential part of the IBD nursing role. The role should cover the following areas.

- Ensure monitoring blood tests cover iron studies and CRP. Remember that a normal ferritin level does not always exclude iron deficiency disease.

Case study

Mr Patel is a 46-year-old taxi driver with long standing Crohn's disease. His bowel symptoms fluctuate but have been reasonably controlled with azathioprine and Pentasa. He has been feeling tired for many months and finds it significantly affects his home and work life. He calls the IBD nurse advice line with a recent increase in diarrhoea and some rectal pain. The nurse looks back over his blood tests whilst she is talking to him on the phone and sees that he has been anaemic for some time. However, his iron levels have not been measured.

She organises to see him in the outpatient clinic where she carries out a full range of screening blood tests (including iron studies). His tests show Hb 94 g/l, CRP 27, Ferritin 46 ug/l and reduced iron sats. This enables her to identify active inflammation and iron deficiency and escalate his care to include suitable iron supplementation.

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Appendix 3: Heavy menstrual bleeding and irregular bleeding

Definition of heavy menstrual bleeding (HMB)

NICE guidelines (2007, updated in 2018) changed the definition of HMB to a more subjective one (away from the traditional blood loss of 80mls or more) to:

"HMB should be defined as excessive menstrual blood loss which interferes with the woman's physical, emotional, social and material quality of life, and which can occur alone or in combination with other symptoms. Any interventions should aim to improve quality of life (QoL) measures."

HMB or heavy periods can be as a result of conditions such as fibroids, which impact on the endometrium and increase the surface area or polycystic ovary syndrome, where there is an ovulation leading to a disturbance of the feedback system (causing the endometrium to be thicker under the influence of oestrogen and not to shed regularly due to no ovulation and lack of progesterone). However, in up to 50% of women a cause may not be found.

HMB is the most common cause of IDA in the developed world and has an impact on quality of life (in excess of the periods) by causing weakness, fatigue and impaired cognitive function.

NICE quality guidelines (2013) highlight the need for women with HMB to have a FBC and look at the possibility of IDA. However, an audit by the Royal College of Obstetricians and Gynaecologists (2014) found that a third of women who presented with HMB in primary care, were not investigated for IDA.

Prevalence

HMB is one of the most common and economically significant gynaecologic complaints and reasons for referral to secondary care. It is estimated that it affects approximately 10% of women of childbearing age. This may be an underestimate as women may not seek help or recognise that they have heavy periods, and it may change throughout a women's lifespan.

Investigations

All women with heavy periods or bleeding should have a full history taken. As well as establishing the impact HMB is having on their life, it is necessary to fully assess their periods. To do this comprehensively, questions should include:

- is the cycle regular? – minimum and maximum length of time from the first day of one cycle to the first day of the next
- total days bleeding, if over seven consider heavy or excessive
- total number of days of bleeding that are heavy, this can be established by asking about the use of protection (tampons or pads and the absorbency of these) and what types. Also ask about length of time between changes. For example, using double protection and changing one-hourly would be considered heavy
- any flooding?
- any clots?
- the use of any medication, and if this helped
- any pain with, or around, periods?
- any bleeding with sex or in between periods?

A full pelvic and speculum examination should also be undertaken and referral for an ultrasound if there is pathology suspected.

Treatment options

NICE guidelines (2018) discuss a number of treatment options for HMB, including pharmacological and surgical interventions, depending on the cause of the HMB. Any treatment of the IDA, in any form, will not treat the underlying problem so will need to be in combination with a strategy to reduce the periods. This can be in the form of medication, contraceptive pills, Mirena intrauterine system (IUS), an operation (such as removal of fibroids or removal of the womb lining) and, ultimately, hysterectomy if all other interventions fail.

These all need to be balanced with the need for contraception and fertility wishes in the future. Many of the treatments used to treat heavy periods will also provide contraception (such as the IUS), subsequently, if a woman wishes to conceive and there is no cause then there are limited options. One of the issues for women who need surgery is achieving Hb and iron stores to an optimum level pre-operatively, especially if they continue to bleed in that period.

The nursing role

The nursing role in supporting women with heavy periods can be varied and it is important that nursing staff in primary care ensure that women who present with HMB have their Hb monitored. Nursing staff in secondary care who are working in a specialist role need to ensure that Hb has been checked and acted upon, and that the cause (if known) or the treatment for the periods is working. The role involves trying to stop the cause of the blood loss. Nursing staff in pre-assessment clinics may need to refer women to have iron infusions if operations are needed and the above steps have not rectified the IDA.

All nursing staff working with women need to be aware that HMB is a very common cause for IDA and should ensure that women are aware of this and are taking good dietary iron to help to try and prevent IDA in the future.

Case study

Mrs Brown was referred to a gynaecology clinic with heavy periods and some irregular bleeding by her GP. She was 45 years old, had two children and was using condoms for contraception. Her GP had examined her and found that her uterus was enlarged. Simple medication, such as tranexamic acid, had not helped and she was having her periods every 21 days and she was bleeding for up to 10 days during each cycle. Five of these days she was using tampons and pads and having to change these every 45 to 60 minutes. She was also flooding and had clots, the flooding was worse at night and she was finding it difficult to go out during her periods.

Her scan showed that she had fibroids, one was submucosal and impacting on the endometrial cavity. Her Hb on referral was 64 g/l. She was placed on oral iron by her GP but was not taking it regularly as she did not like the GI side effects. After being seen in a clinic, she was booked for a resection of fibroids. In order to optimise her preoperatively, she was assessed and given iron infusions by the anaemia clinic team. The gynaecology team prescribed pre-operative medication which put her into a temporary medical-induced menopause.

Post-operatively, her bleeding in between periods stopped, her periods were now of five days duration and she no longer required double protection and only needed to change every few hours. Her Hb was checked at four months, post-operation, after she had been on the oral iron and was 124 g/l.

References

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Appendix 4: Patient blood management

Patient blood management (PBM) is a multidisciplinary, evidence-based approach to optimising the care of patients who might need a blood or blood component transfusion as part of their planned or emergency stay in hospital.

Patient Blood Management – an evidence-based approach to patient care (NBTC, 2014) provides recommendations on how PBM should be implemented in hospitals. PBM has been rolled out across England and North Wales, to date. Local, national and international experts are supporting doctors, nurses, scientists and other health professionals to work together with patients on a case-by-case basis to deliver PBM.

PBM should be considered in every case where a transfusion may be an appropriate treatment consideration, regardless of the specialty and in elective, long-term and emergency scenarios. It puts the patient at the heart of the decision making and ensures they receive the best treatment and avoids an inappropriate use of blood components. PBM focuses on measures for blood avoidance and the correct use of blood when it is needed, with improved patient outcomes as the key driver.

Recent studies suggest that if the three basic principles of PBM are followed (and transfusion is reduced or avoided) patients have:

- fewer complications
- faster recoveries
- shorter stays in hospital.

The three basic principles

1. Optimising blood volume and red cells before treatment

This means making sure patients are as healthy as possible before surgery or treatment to help them recover afterwards. It includes identifying and treating anaemia well in advance of any planned surgery or medical treatment.

2. Minimising blood loss throughout the treatment process

This is done by using modern techniques and medicines to prevent patients from losing blood in the first place. This includes using modern surgical tools and medicines, and intraoperative cell salvage to reduce blood loss in the operating theatre.

3. Maximising the body's own abilities to cope during recovery

The body has a natural ability to adapt to lower haemoglobin or blood counts without resorting to a blood transfusion. However, to increase an individual's own capabilities, improving their iron intake through diet might help in their recovery.

The use of iron tablets or an intravenous iron infusion might also need to be considered as a method to help increase their haemoglobin. The NHSBT has prepared a suite of patient information leaflets that cover all key aspects of blood and blood component transfusion and these are designed to help patients make an informed decision about the treatments they are being offered. Leaflets are available for all age groups and for specific types of transfusion and include:

- Will I need a blood transfusion?
- Will I need a platelet transfusion?
- Information for patients needing irradiated blood
- Iron in your diet
- Will my baby need a blood transfusion?
- Will my child need a plasma transfusion?
- Will my child need a blood transfusion?
- Information for patients who have received an unexpected blood transfusion
- Patient blood management
- Anaemia
- Fresh frozen plasma (FFP) and cryoprecipitate.

These can all be ordered through the hospital transfusion practitioner or downloaded at: https://hospital.blood.co.uk/patient-services/patient-blood-management/patient-information-leaflets/

Case study

Miss Smith, a 19-year-old female presented in the emergency department following a road traffic accident. Routine blood tests on admission revealed her Hb was 88g/l. She was distressed and feeling very unwell, showing signs and symptoms of anaemia as she was feeling short of breath and dizzy with palpitations and a headache. Her attending doctor discussed how she felt and, during the conversation, learned that she had started to suffer from very heavy and prolonged periods recently but had not had treatment for this. Taking this and her low Hb into account, as well as her symptoms, she decided that a blood transfusion would be beneficial and explained this to her. She left her with patient information leaflets on having a blood transfusion and took further samples to send to the laboratory for cross matching so that the unit for transfusion could be authorised and prepared.

As part of the preparation for the transfusion a nurse went to see Miss Smith to take a set of baseline observations and found her to be very distressed and upset. He sat with her as she explained she was very squeamish and afraid of the sight of blood and the thought of a transfusion was making her feel sick. Further conversation revealed that she was a first-year student away from home for the first time and that her diet and lifestyle had undergone significant changes. She had decided to become vegetarian as well. Although she had understood the information given to her, she was becoming increasingly distressed by the idea of having a blood transfusion and asked the nurse if there was anything else she could have instead.

In his role as patient advocate, the nurse went to the authorising physician and discussed this and the balance between the risks and benefits of a transfusion against the use of alternatives were considered. It was agreed that, as Miss Smith was otherwise fit and healthy and, although the need for a transfusion could be said to be clinically indicated, it could be managed appropriately by use of an alternative to an allogeneic blood transfusion. This would prevent a possibly inappropriate transfusion and exposure to a live human product. This option would decrease Miss Smith's anxiety and allow her to remain a blood donor if, and when, her Hb was high enough. This was explained to her and she was relieved and happy; she felt that she had been able to be involved in her treatment plan and understood the options given to her.

The dietician prescribed oral iron (with clear instructions on how and when to take it) and provided advice on diet and lifestyle, including the NHSBT patient information leaflet *Iron in your diet to support sensible choices in a vegetarian diet*.

At discharge, a letter was sent to her current GP and a copy was given to Miss Smith. She agreed that she would take this copy and register with the GP on campus and make appointments for regular Hb checks to ensure she was getting the corrective treatment needed and if it was effective.

Reference

National Blood Transfusion Committee (2014) *Patient blood management. An evidence-based approach to patient care*. London: NBTC.

Useful websites and resources

Online transfusion training
www.learnbloodtransfusion.org.uk

Serious Hazards of Transfusion (SHOT) – the United Kingdom's independent professionally lead haemovigilance scheme
www.shotuk.org

The British Society for Haematology
https://b-s-h.org.uk

Patient information leaflets

Patient (and donor) information
https://hospital.blood.co.uk/patient-services/patient-blood-management/patient-information-leaflets

www.blood.co.uk

Transfusion in surgery
www.transfusionguidelines.org.uk

Appendix 5: Chronic kidney disease

Chronic kidney disease

Chronic kidney disease (CKD) is defined as abnormalities of kidney function or structure which are present for more than three months, with implications for health. This includes all people with markers of kidney damage and those with a glomerular filtration rate (GFR) of less than 60 ml/min/1.73m² on at least two occasions, separated by a period of at least 90 days.

CKD has been classified into different categories using a combination of GFR and albumin creatinine ratio (ACR). An increased ACR is associated with increased risk of patient adverse outcomes and this multiplies the risk of poor patient outcomes when coupled with a decreased GFR (NICE, 2015).

Classification of chronic kidney disease using GFR and ACR categories

GFR and ACR categories and risk of adverse outcomes			ACR categories (mg/mmol), description and range		
			<3 Normal to mildly increased	3–30 Moderately increased	>30 Severely increased
			A1	A2	A3
GFR categories (ml/min/1.73m2), description and range	≥ 90 Normal and high	G1	No CKD in the absence of markers of kidney damage		
	60–89 Mild reduction related to normal range for a young adult	G2			
	45–59 Mild-moderate reduction	G3a[1]			
	30–44 Moderate-severe reduction	GSb			
	15–29 Severe reduction	G4			
	<15 Kidney failure	G5			

Increasing list

Increasing risk

[1] Consider using eGFRcystatinC for people with CKD G3aA1 (see recommendations 1.1.14 and 1.1.15)

Abbreviations: ACR, albumin:creatinine ratio; CKD, chronic kidney disease; GFR, glomerular filtration rate

Adapted with permission from Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group (2013) KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney International (Suppl. 3): 1–150

Renal anaemia

Moderate to severe CKD may affect the ability of the kidneys to help stimulate production of red blood cells, which carry oxygen around the body. Anaemia occurs when the quality or quantity of red blood cells are below normal. If untreated, anaemia can increase the risk of cardiovascular complications (for example, left ventricular hypertrophy) and exacerbate symptoms (for example, tiredness, lethargy, sleep disturbance and shortness of breath).

Anaemia is a common consequence of CKD and becomes worse over time as the kidney function declines. It is twice as prevalent among people with CKD compared with the general population (15.4% vs 7.6%) (*Renal & Urology News*, 2017).

The use of IV iron in CKD

Patients with CKD should receive iron supplementation to maintain:

- serum ferritin levels between 200 and 500 µg/L. Ferritin is the iron stored in the liver. Serum ferritin levels can become elevated in iron overload, but also in the presence of infection or inflammation
- transferrin saturation level above 20% (unless ferritin is greater than 800 µg/l). Transferrin saturation is the amount of circulating free iron in the blood
- percentage of hypochromic red cells (% HRC) less than 6% (unless ferritin is greater than 800 µg/L, HRC are 'pale' red blood cells and indicate iron deficiency) (NICE, 2006).

IV iron therapy (at doses of more than 100mg) should be stopped for at least one week before performing these measurements to avoid the IV iron abnormally influencing the test results.

Anaemia is a common symptom of CKD and is primarily caused by a reduction in endogenous erythropoietin (EPO) production. EPO is predominantly produced by peritubular cells in the kidney and is the hormone responsible for the production of red blood cells. CKD leads to a loss of peritubular cells, resulting in a low level of circulating EPO (NICE, 2006).

The introduction of erythropoietin stimulating agents (ESA) was an important therapeutic innovation in the treatment of anaemia in CKD and has largely replaced the need for blood transfusions in this group of patients. ESAs are usually administered by a subcutaneous injection which may be done by the patient, a family member or a community nurse. Iron levels and other haematinics are usually monitored by the specialist team but can be measured in the community if more convenient. Treatment with an ESA should continue for as long as the patient can benefit from it. ESAs are not interchangeable and the patient should continue on the preparation prescribed by the specialist team.

Target haemoglobin range in CKD

NICE (2011) advises health care professionals treating anaemia of CKD with erythropoiesis stimulating agents to maintain the haemoglobin range between 100 and 120 g/l for adults. NICE is also urging clinicians to not wait until a patient's haemoglobin levels are outside of these ranges before adjusting their treatment (for example, they should act when the patient's haemoglobin levels are within 5 g/l of the range's limit).

The 2015 NICE guidelines recommend that anaemia should be investigated and managed if Hb drops below 110 g/l or a patient develops symptoms of anaemia.

Patient monitoring

- Take blood samples to check iron status no earlier than one week after receiving IV iron and at intervals of four weeks to three months routinely.
- Hb every two to four weeks (induction phase) or one to three months (maintenance phase) during ESA therapy.
- Hb more actively after adjusting ESA dose.
- Monitor in a clinical setting agreed with the patient.
- Maintain iron levels (see NICE's online resource: **Anaemia of chronic disease overview**).
- Serum ferritin 200–500 µ g/l in both haemodialysis and non-haemodialysis patients and either TSAT greater than 20% (unless ferritin greater than 800 µg/l), or % HRC less than 6% (unless ferritin greater than 800 µg/l).

Blood pressure (BP) should be monitored closely in all patients with CKD, particularly during the initiation of ESA therapy. A rapid increase in Hb may be associated with a rise in BP. Antihypertensive therapy may need to be initiated or current antihypertensive medication increased.

The ESA dose may need to be reduced, especially if there is a rapid increase in Hb (more than 10–20 g/l (1–2 g/dL) per month) (NICE, 2006).

Examples of erythropoietin stimulating agents

Drug	Cautions	Side effects	Route/dose
Epoetin beta (for example, NeoRecormon)	Inadequately treated or poorly controlled blood pressure, sicklecell disease; exclude other causes of anaemia; ischaemic vascular disease, thrombocytosis, epilepsy, malignant disease	Dose-dependent increase in blood pressure or aggravation of hypertension in isolated patients with normal or low blood pressure; dose-dependent increase in platelets, influenza-like symptoms, thromboembolic events, sudden loss of response as a result of pure red cell aplasia	By subcutaneous injection **Correction phase** Until Hb 105–115 g/dL use 20 units/kg three times per week **Maintenance phase** Reduce dose by half then adjust accordingly to Hb level at intervals of two weeks. Reduce frequency to once weekly injection
Darbepoetin alfa (for example, Aranesp)	Inadequately treated or poorly controlled blood pressure, sickle-cell disease; exclude other causes of anaemia; ischaemic vascular disease, thrombocytosis, epilepsy, malignant disease, hepatic disease	Peripheral oedema; dose-dependent increase in blood pressure or aggravation of hypertension in isolated patients with normal or low blood pressure; dose-dependent increase in platelets, influenza-like symptoms, thromboembolic events, sudden loss of response as a result of pure red-cell aplasia Contraindicated if breastfeeding	By subcutaneous injection **Correction phase** 450 nanograms/kg for one week 750 nanograms/kg once every two weeks, adjusted according to response by 25 per cent of initial dose at intervals of four weeks **Maintenance phase** Dose required in correction phase to achieve target Hb can now be changed to once monthly

Treatment with ESAs is highly effective, correcting the anaemia of CKD in approximately 90 to 95% of treated patients. Side effects are very rare owing to the similar genetic make-up as endogenous (derived internally) EPO.

Between 1988 and 1998, antibody-associated pure red-cell aplasia (PRCA) was reported in renal patients treated with ESAs (Bennett et al., 2004). The condition has a number of causes, including pharmacological treatment. PRCA can be determined by the presence of anti–EPO antibodies, which neutralise the action of the ESA, a low reticulocyte count (immature red blood cells), and anaemia (NICE, 2006). The Hb concentration declines at a rate of 1 g/dL per day and it may be necessary to transfuse one unit of red blood cells per week to avoid severe anaemia (Macdougall, 2004).

Regular monitoring of anaemia in patients with CKD is vital for early intervention with IV iron and ESA.

Case study

Mrs Brown is an 84-year-old lady with stable stage 4 CKD due to diabetic nephropathy. She comes to the clinic complaining of feeling increasingly tired, a little short of breath and feels cold most of the time. She is taking Aranesp 40mcg once a fortnight.

What is your differential diagnosis for her symptoms?

What tests/investigations would you order?

Her renal function could have declined. She could have an under-active thyroid. She could be anaemic despite being on an ESA. A full history and physical assessment are needed to rule out other causes for her symptoms. For example, does she report any dysuria which could indicate a urinary tract infection? Does she report any chesty coughs, temperature or flu like symptoms?

Infection and inflammation affect both iron absorption and the efficacy of ESA. She did not complain of any recent infections. Bloods were checked for U and Es, FBC, CRP and iron studies. Hb was 90 g/L. Iron levels were low, serum ferritin was 74 µg/l. TSATS (transferrin saturation) 20%. CRP was within normal range.

What is your diagnosis? What is your clinical management plan?

Mrs Brown was diagnosed with absolute iron deficiency. The ESA was less effective due to iron deficiency; her Hb had dropped to below the target range. Mrs Brown was booked into the nurse-led anaemia clinic for one dose of intravenous iron which she had infused without any adverse reactions.

What would your follow-up plan and advice be to Mrs Brown?

Mrs Brown was booked back into the clinic in two weeks to recheck her symptoms and check bloods for FBC to measure the response to iron. She was advised to call should she experience any side effects from the iron infusion. A follow-up appointment letter for two weeks later was given to Mrs Brown with the contact details of the nursing team.

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Renal & Urology News (2017) 'Iron deficiency anaemia in non-dialysis CKD'. Available at: www.renalandurologynews.com/chronic-kidney-disease-ckd/iron-deficiency-anemia-in-non-dialysis-ckd/article/676170/

Useful websites

Johnston S and Noble H (2010) Pharmacological management of chronic kidney disease. Nurse Prescribing Online subscription CPD module.

NICE: Anaemia of chronic disease overview, available at: pathways.nice.org.uk/pathways/anaemia-management-in-people-with-chronic-kidney-disease

Appendix 6: IDA in pregnancy, primary postpartum haemorrhage and post-delivery

Anaemia is the most common medical disorder in pregnancy. Pregnancy causes a two to three-fold increase in requirement of iron and 10 to 20 fold increase in folate requirement. In pregnant women who are anaemic in the UK, 90% of them are iron deficient. Iron deficiency causes maternal morbidity due to increased susceptibility to infections, physical weakness, pre-term labour, increased risk of primary postpartum haemorrhage (PPH), low birth weight babies and postnatal depression. The chronic tiredness that it can cause is also often blamed for new mothers abandoning breastfeeding, which has major health benefits for both mother and baby. Maternal iron depletion also increases the risk of iron deficiency in the neonate. Managing anaemia in pregnancy will therefore help to prevent adverse fetal and maternal outcomes as well as reduce the need for allogeneic red blood cell transfusion.

Definition

The definition of anaemia in pregnancy is Hb levels of:

<110g/l in the first trimester

<105g/l in the second and third trimesters

<100g/l in the postpartum period (defined by WHO as up to six weeks post-delivery).

(British Committee for Standards in Haematology, 2011)

Clinical signs and symptoms

Pregnancy anaemia can be asymptomatic and may be diagnosed following routine screening. The signs and symptoms are often non-specific, with tiredness being the most common. Women may also complain of weakness, headaches, palpitations, dizziness, dyspnoea and hair loss.

Signs of anaemia can occur in the absence of a low Hb. In this instance it would be diagnosed by a full blood count with a reduced MCV (mean cell volume) and MCHC (mean corpuscular haemoglobin concentration). In these women, their ferritin needs to be checked and if it is <30 µg/l iron therapy should be commenced.

Diagnosis

A trial of oral iron therapy can be both diagnostic and therapeutic. If haemoglobinopathy status is unknown, then it is reasonable to start oral iron therapy whilst screening is carried out. A trial of oral iron should demonstrate a rise in Hb within two to three weeks. If there is a rise, then this confirms the diagnosis of iron deficiency. If there is no rise, further tests must be carried out. In women with a known haemoglobinopathy, serum ferritin should be checked first. Ferritin levels below 30 µg/l should prompt treatment and levels below 15 µ/l are diagnostic of established iron deficiency.

Management

NICE guidelines (2008) recommend that women are screened for anaemia at booking and again at 28 weeks gestation. All women should be given advice regarding diet in pregnancy, with details of foods rich in iron, along with factors that may promote or inhibit the absorption of iron. This should be complemented with written information. Dietary changes alone are not sufficient to correct an existing iron deficiency in pregnancy and iron supplements are necessary.

Antenatal

If at booking levels are Hb <110g/l, start on a trial of oral iron. The necessary dose is 100–200mg of elemental iron daily.

Dose and elemental iron content per tablet

Preparation	Dose per tablet	Elemental iron	Number of tablets per day
Pregaday		100mg	1
Ferrous sulphate	200mg	65mg	3
Ferrous gluconate	300mg	35mg	6
Ferrous fumarate	210mg	68mg	3

Pregnant women should receive advice and guidance on how to take oral iron supplementation. It should be taken:

- on an empty stomach
- one hour before meals
- with a source of vitamin C to maximise absorption.

Other medications, antacids, tea or coffee should not be taken at the same time. Women with a normal Hb but a low MCV should have their ferritin checked and if ferritin is <30 µg/l, oral iron should be commenced.

Repeat Hb level check three weeks after commencement of iron therapy and a rise in Hb should be demonstrated (this should fit in with the 15–16 week antenatal appointment). If there is no rise in Hb, despite compliance with therapy, serum ferritin should be checked and concomitant causes of the anaemia need to be excluded. Referral to a consultant obstetrician will be required.

If at booking Hb <90 g/l: oral iron – 200mg elemental iron in divided doses each day should be commenced and follow up as above. Refer to a consultant obstetrician if symptomatic.

If at booking Hb <70 g/l: send an urgent referral to joint obstetric/haematology clinic to investigate further and make management plan. Do not offer blood transfusion unless symptomatic or currently actively bleeding. Consider total dose IV iron infusion. 200mg of elemental iron each day. If 200mg ferrous sulphate is used, three to four tablets will be needed each day. If taken correctly this will give a rise in Hb of 20 g/l every three weeks.

Once Hb is within the normal range, treatment should be continued for a further three months.

At 28 weeks: all women should have their Hb rechecked (NICE, 2008).

If at 28 weeks Hb <105 g/l: trial of oral iron as above. Recheck Hb in three weeks. If no response, check serum ferritin and refer to consultant obstetrician to consider total dose iron infusion.

If at 28 weeks Hb <90 g/l: start oral iron – 200mg elemental iron in divided doses each day, as above. Refer to a consultant obstetrician if symptomatic.

If at 28 weeks Hb <70 g/l: urgent referral to joint obstetric/haematology clinic to investigate and make management plan. Do not offer blood transfusion unless symptomatic or currently actively bleeding. Consider total dose IV iron infusion. Gastrointestinal toxicity affects 35 to 59% of women and can result in non-adherence to treatment with oral preparations (Auerbach and Ballard, 2010). These effects can be reduced by taking oral iron with food or taking a reduced dose.

Parenteral iron should be considered from the second trimester onwards and during the third trimester for women with confirmed iron deficiency that fail to respond to, or are intolerant of, oral iron. Intravenous iron is the appropriate treatment for those women where oral preparations are not tolerated or contraindicated.

Management of labour and delivery

With effective management of anaemia antenatally, anaemia at delivery is usually avoided. If this occurs, all measures must be taken to avoid blood loss at delivery.

- Deliver in consultant unit.
- Ensure IV access and group, and screen on admission.
- Active management of third stage of labour.
- In the event of a PPH, prompt active management is required to stop bleeding.
- Consider the use of prophylactic syntocinon infusion.
- Postnatal FBC and serum ferritin on day one and iron replacement (see below).

Postnatal

Hb <100 g/l in postnatal period: Haemoglobin measurement is not required following an uncomplicated, normal birth. Check FBC and serum ferritin on day one post-delivery in the following cases:

- PPH of >500mls
- uncorrected antenatal anaemia

- known iron deficiency anaemia
- any patient with signs or symptoms of anaemia.

Clinical assessment alongside Hb concentration is necessary postpartum to make a decision on the best method of iron replacement. In fit, healthy asymptomatic women there is little evidence to support blood transfusion.

Hb 80–100 g/l: If asymptomatic and haemodynamically stable, offer 200mg elemental iron per day for three months. FBC and ferritin should be checked after a month to ensure that Hb and iron stores are replete.

Hb<80 g/l: Consider total dose intravenous iron. Repeat FBC and ferritin at 10 days to ensure response and at three months (in community) to ensure Hb and iron stores are replete.

Hb<70 g/l: Consider and discuss alternatives with the patient. Consider transfusion and/or total dose IV iron.

IV iron has been shown to increase Hb and replenish iron stores faster when compared with oral iron therapy (Bhandal, 2007; Van Wyk and Martins, 2007; Breymann et al., 2008). Consider minimum transfusion volumes and review after one unit.

Women who are symptomatic of anaemia, haemodynamically unstable or continuing to bleed heavily will need a full senior obstetric review to investigate the origin of the blood loss and decide further treatment.

Contraindications and precautions for IV iron therapy

- First trimester of pregnancy.
- Previous hypersensitivity to IV iron.
- Anaemia not attributable to iron deficiency.
- Iron overload.
- Acute infection/inflammation.
- Clinical or biomedical evidence of liver damage.
- Asthma.

Case study

Mrs Hill had an uncomplicated pregnancy other than nausea and had Hb of 107 g/l at 28 weeks gestation. She went into spontaneous labour at 39 weeks + four days. She then went on to have a long labour with a normal delivery. She subsequently had a postpartum haemorrhage with an estimated blood loss of 750mls.

Her Hb was checked following delivery and found to be 75 g/l. She was given total dose intravenous iron as she was very keen to avoid oral iron due to her nausea. Five days postnatally her Hb was checked and found to be 99 g/l and at 14 days it was 111 g/l. She felt well, bonded well with her baby and successfully breastfed as she had wanted to do.

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Useful website

hospital.blood.co.uk/patient-services/patient-blood-management/patient-information-leaflets

Appendix 7: Perioperative anaemia

Perioperative anaemia covers anaemia occurring at, or around, the time of an operation and puts patients at increased risk of longer hospital stays, complications and mortality. The British Committee for Standards in Haematology sets out three key reasons for the identification and management of perioperative anaemia (Kotzé et al., 2015).

- To identify a potential undiagnosed disease, such as malignancy.
- To reduce the likelihood of blood transfusions, thereby limiting the demand on donors and conserving finite blood supplies.
- To avoid unnecessarily exposing patients to the potential adverse effects of anaemia, transfusion, or both.

Pre-operative care

All patients should be suitably prepared for surgery. The inclusion of anaemia screening as a key part of the surgical referral pathway is recommended by NICE (2015), the NHS National Blood Transfusion Committee (2014) and the British Committee for Standards in Haematology (Kotzé et al., 2015). In cases of routine surgery, screening should be carried out as soon as possible after referral to give time for diagnosis and treatment without causing unnecessary delays for the patient. When surgery is urgent, any available time beforehand should be used for anaemia screening and, if necessary, treatment (Kotzé et al., 2015).

Intra-operative care

Intra-operative care aims to reduce the risk of anaemia by minimising blood loss throughout the procedure. This is usually achieved through the use of minimally invasive surgical techniques and medicines that prevent the breakdown of blood clots. During surgery, maintenance of optimal temperature, calcium levels and pH means the body is more able to form blood clots and prevent blood loss naturally. In situations where there is anticipated blood loss, intraoperative cell salvage can be used to return salvaged red blood cells back to the patient (Thakrar et al., 2017).

Post-operative care

Following major surgery, up to 90% of patients may become anaemic and recent changes to transfusion thresholds have resulted in more patients being discharged with anaemia. Simple interventions, such as reducing the number and volume of blood samples and avoiding the use of postoperative drains, can have a significant impact on preventing anaemia. Maintaining adequate oxygen levels in patients who become anaemic can help the body to recover and tolerate the anaemia.

Diagnosis and treatment of anaemia

The measurement of both haemoglobin and ferritin levels prior to surgery can be used to diagnose anaemia and iron deficiency, respectively. The WHO define anaemia as haemoglobin <130 g/l in men and <120 g/l in women, although some guidelines recommend that the <130 g/l cut off should be applied to both men and women. Iron correction should be considered if serum ferritin is <100 µg/l and TSA <20% (Muñoz et al., 2017).

Over 70% of cases of perioperative anaemia are due to iron deficiency anaemia (IDA). When preoperative IDA is diagnosed, oral iron is recommended as a first-line treatment for up to three months before surgery. However, in patients who are intolerant, unresponsive to oral iron, or where the interval between diagnosis and surgery is predicted to be too short, intravenous iron is the preferred treatment.

Perioperative anaemia is a preventable surgical risk factor that all health care professionals should be aware of. The early diagnosis and treatment of anaemia in the perioperative period should be a key component of surgical care pathways. Health care staff should take into account the local surgical cohort, with the aim to always optimise patient outcomes and reduce the need for blood transfusions.

Iron deficiency is both easy to diagnosis and treat and should be avoided in all patients in perioperative care.

Case study

Mrs Adams is a 70-year-old woman, with a fungating vulval tumour, who attended pre-assessment for proposed surgery – wide local excision of vulva. She was seen within two weeks of referral and had a short turnaround to surgery. She also had COPD and her medication included clopidogrel.

She was flagged to the blood management clinic for consideration of haemoglobin optimisation, from pre-assessment – Hb 113 g/l (previous Hb was 134 g/l, seven months prior), MCH 27.3, ferritin 36, CRP 24 and MCV 86.6. Her GP was made aware of new anaemia and proposed pre-operative intervention.

Bloods pre-intervention showed a Hb 104 g/l, MCH 25.7, MCV 85.5, reticulocyte count 62.8. A high dose of intravenous iron was given over 30 minutes. No problems were noted during intervention.

Check bloods were organised for 15 days post iron, the same day as surgery. Hb 116 g/l (an increase of 12 g/l), MCH 26.1, ferritin 897 (following surgery this dropped to within normal limits), MCV 87.3, reticulocyte count 99.5.

No transfusion was required; Mrs Adams made a full recovery and was discharged home. At two weeks following her operation Hb 124 g/l. A letter was sent to her GP summarising intervention and her discharge back to primary care.

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Further reading

Perioperative Quality Improvement Programme *Addressing preoperative anaemia: Ten top tips, practical advice and the evidence base* [Online resource]. Available at: **pqip.org.uk/pages/0#**

Appendix 8: Iron deficiency (ID) and anaemia in heart failure

Introduction

Across the UK, there are almost one million people living with heart failure (NICE, 2018). Heart failure is a term used to describe a complex clinical syndrome when the heart's ability to effectively pump blood around the body is impaired, due to either structural or functional problems. Symptoms of heart failure include: breathlessness, fatigue, leg swelling and reduced functional status. It can significantly impact on a person's quality of life and carries a significant burden to patients. Heart failure can occur at any age but is more common in older people, with an average age of 77 years at diagnosis (Conrad et al., 2018).

There are two types of chronic heart failure.

1. Heart failure with reduced ejection fraction (HFrEF) – patients have a left ventricular ejection fraction of less than 40% identified by echocardiography.
2. Heart failure with preserved ejection fraction (HFpEF) – patients have myocardial stiffness and reduced ventricular filling with left ventricular ejection fraction of greater than 50%.

The New York Heart Association (NYHA) Functional Classification of heart failure is the most widely used tool for classifying a patient's heart failure according to the severity of their symptoms.

I – no limitation of physical activity

II – slight limitation of physical activity

III – marked limitation of physical activity

IV – patients who experience symptoms even at rest.

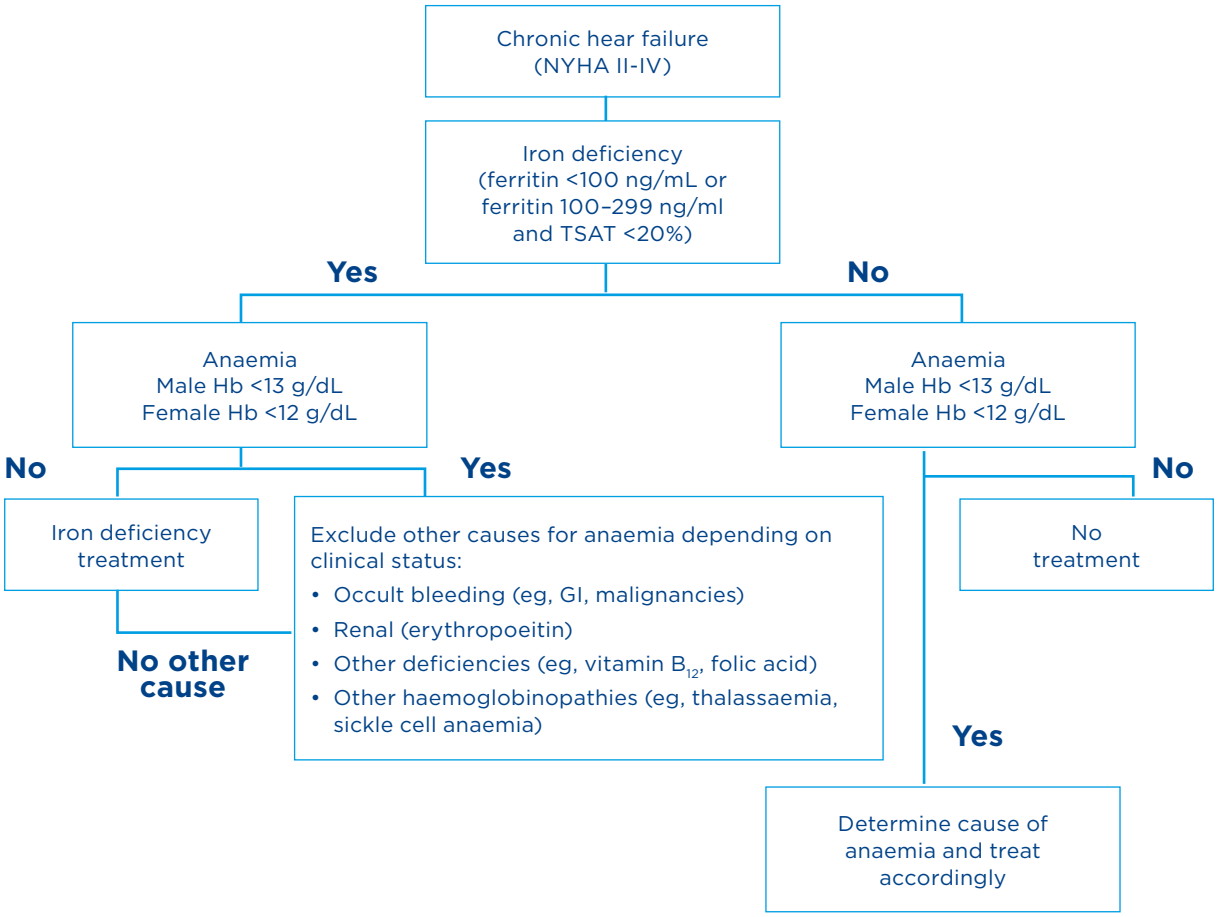
Iron deficiency anaemia in heart failure

Iron deficiency is a known co-morbidity associated with heart failure, affecting up to 50% of patients. It has been associated with a worse prognosis. Iron deficiency can impact on quality of life, reducing exercise capability and physical wellbeing. The symptoms of iron deficiency can be exacerbated or even confused with concomitant heart failure as they are very similar: breathlessness, dizziness, fatigue, weakness, fast or irregular heartbeat, and/or chest pain. Therefore, when patients with heart failure complain of continued debilitating symptoms (despite optimal medical therapies) it is important to check for iron deficiency.

Investigations

Identifying and treating iron deficiency should be a part of the heart failure nurse role. Ferritin, haemoglobin and TSAT tests should be included in routine blood screening. Refer to local protocol for frequency of conducting/repeating iron studies.

Identifying and treating iron deficiency in heart failure patients



McDonagh T and Macdougall IC (2015) Iron therapy for the treatment of iron deficiency in chronic heart failure: intravenous or oral? *European Journal of Heart Failure*, 17(3): 248–62.

Treatment

Even in the absence of low haemoglobin, correcting iron deficiency can not only improve symptoms, but also the quality of life and functional status. Oral iron is often prescribed because it is easy to obtain and relatively inexpensive. However, it is known to have common unpleasant gastrointestinal side effects that can lead to non-adherence. Additionally, oral iron is known to have little effect on correcting iron deficiency in people with heart failure, as demonstrated by the IRONOUT study (Lewis et al., 2017). This study showed no benefit to exercise tolerance with oral iron.

Various studies have demonstrated the benefit of intravenous iron for people with HFrEF; improving self-reported patient global assessment, quality of life, NYHA class, reducing hospitalisations, and increasing exercise capacity. The European Society of Cardiology (2016), Scottish Intercollegiate Guidelines Network (2016) and the American Heart Association (Yancy et al., 2017) all recommend intravenous iron for people with HFrEF and iron deficiency in the absence of anaemia.

NICE guidance (2018) for chronic heart failure in adults makes no recommendation for the routine administration of intravenous/oral iron in the HFrEF population, but recognises there are ongoing trials and the benefits of improved quality of life for people.

Case study

Mr Smith is a 75-year-old gentleman with known chronic heart failure, aetiology ischaemic heart disease having had two previous myocardial infarctions. He has been well for some time (NYHA I) but has found he has been able to do less, with his wife taking on more in the home. His deteriorating symptoms include increasing shortness of breath and fatigue and he is now NYHA II/III. He is unable to play nine holes of golf as he once did and is feeling isolated at home, unable to get out like previously and meet with his friends. His mood is low and his wife is also feeling the impact of his reduced independence.

Mr Smith calls his heart failure specialist nurse who discharged him six months ago due to him being optimised on therapies and feeling well. On clinical examination he has no signs of fluid overload and his vital signs are within normal limits. Bloods are requested TFTs, FBC, LFTs, TSAT, ferritin, U and Es. The results show all are within normal range with the exception of ferritin 89, TSAT 18%, Hb 140.

After discussion at the multidisciplinary team meeting (MDT), the cardiologist agrees to bring Mr Smith in to the day unit for intravenous iron the following week. Two weeks following infusion, Mr Smith is gradually returning to his normal activities and his mood is improved. He agrees this has had a significant impact on his quality of life.

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Acronyms and abbreviations

ACD	anaemia of chronic disease
AID	absolute iron deficiency
ACR	albumin creatinine ratio
BP	blood pressure
CD	coeliac disease
CKD	chronic kidney disease
COPD	chronic obstructive pulmonary disease
CRP	C-reactive protein
EPO	endogenous erythropoietin
ESA	erythropoietin stimulating agents
FBC	full blood count
FID	functional iron deficiency
GFR	glomerular filtration rate
GI	gastrointestinal
Hb	haemoglobin
HFrEF	heart failure with reduced ejection fraction
HFpEF	heart failure with preserved ejection fraction
HMB	heavy menstrual bleeding
HRC	hypochromic red cells
IBD	inflammatory bowel disease
IDA	iron deficiency
MCH	mean cell haemoglobin
MCHC	mean corpuscular haemoglobin concentration
MCV	mean cell volume
PBM	patient blood management
PPH	primary postpartum haemorrhage
PRCA	pure red-cell aplasia
QoL	quality of life
RBC	red blood cells
TSAT	transferrin saturation

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