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Iron deficiency anaem

Case presentation

A 22 year old female University student attends your GP clinic accompanied by her mother. She complains of progressive lethargy and weakness, making it difficult for her to concentrate on her studies.

On further questioning, she informs you that she has been having heavier regular menses for the past six months. Her last menstrual period was one week ago. During menstruation, she feels very weak and has to stop halfway up a staircase because of shortness of breath. She has been very busy lately finalising her thesis and her mother complains that she is hardly eating anything at home. The patient states that she feels hungry but doesn't have time to eat a proper meal. She also claims that she is only having four to five hours of sleep every day. She has no abdominal upsets and does not complain of any irregularity in her stools.

The patient has no significant past medical history and is not on any regular medications. She does not drink alcohol or smoke. She has not been abroad for the past year.

On examination, her skin, nail beds and conjunctivae are somewhat pale. She has strong peripheral pulses. Blood Pressure is 115/75 mmHg and pulse is regular at 90 bpm. Her chest is clear and examination of her neck is normal. Her BMI is 19.5. Rectal examination is normal.

Investigations carried out

- Full Blood Count
  - Haemoglobin - 8 g/dL
  - Red Cell Count - 4 million/mm^3
  - Haematocrit - 30%
  - Mean Cell Volume (MCV) - 65 fL
  - Mean Corpuscular Haemoglobin Concentration (MCHC) - 25 g/dL
  - Serum ferritin - 5 ng/mL

- Thyroid Function Tests - Normal
- Ultrasound Pelvis - Normal

Iron supplements are prescribed and a review appointment is given in four weeks' time.

Discussion

Generalised weakness, lethargy, dyspnoea and history of heavy blood loss during menstruation accompanied by a haemoglobin level of 8g/dL are all suggestive of anaemia. A mean cell volume (MCV) of 60 fL and a mean corpuscular haemoglobin concentration (MCHC) of 25 g/dL classifies the anaemia as a microcytic, hypochromic anaemia, which is suggestive of iron deficiency. However, this may also be due to a thalassaemic trait. The patient does not have a family history of thalassaemia or its trait; nonetheless a serum ferritin test is required. A level <10ng/mL is indicative of iron deficiency anaemia. Hypothyroidism as a possible cause of lethargy and weakness and cardiac compensation has also been excluded. The history of the patient's complaint helps to shed light on the cause of the iron deficiency. There is evident excessive blood loss in the patient's menses. She is not pregnant as she has had her last menstrual period one week before. Dietary intake of iron seems to be somewhat limited as she "doesn't have time to eat a proper meal".

Chronic disease is unlikely because she has previously been healthy and she is not experiencing a loss of appetite. There doesn't seem to be any signs of gastrointestinal blood loss as her stools are normal and she is not taking any medications such as aspirin or non-steroidals (NSAIDs). Besides, she has no abdominal upsets and so coeliac disease would not be greatly considered at this point. Anxiety or depression should also be considered, given her psycho-social context. Thus, the next step in management in general practice is to control her menorrhagia and at the same time start iron supplementation, as well as follow the patient up to monitor response or otherwise. If the patient does not respond, she would be a candidate for further investigation.

Iron Deficiency Anaemia

Anaemia is a condition in which the number of red blood cells, and thus their oxygen-carrying capacity, is insufficient to meet the physiological needs of the body. Anaemia can also occur if the red blood cells don't contain enough haemoglobin. Specific physiological needs vary with a person's age, gender, altitude, smoking behaviour and different stages of pregnancy. Iron deficiency anaemia is thought to be the most common cause of anaemia globally, but other nutritional deficiencies, including folate, vitamin B_{12} and vitamin A, acute and chronic inflammation, parasitic infections, and inherited or acquired disorders that affect haemoglobin synthesis, red blood cell production or red blood cell survival, can all cause anaemia.[1]

nia in general practice

Haemoglobin concentration alone cannot be used to diagnose iron deficiency anaemia. A serum ferritin level is required, since this is the most sensitive marker of early iron deficiency and is the preferred initial diagnostic test. Serum ferritin level correlates with total iron body stores and a low level can be identified before serum iron is affected. The state of the iron stores can be assessed by considering together the serum ferritin, iron and transferrin; the latter is indirectly measured by the total iron binding capacity. Thus, a full blood count and iron studies are required to establish a diagnosis of iron deficiency anaemia.

Aetiology and epidemiology of Iron Deficiency Anaemia

Iron deficiency anaemia occurs in 2–5% of adult men and post-menopausal women in the developed world.[2] While menstrual blood loss is the commonest cause of iron deficiency anaemia in pre-menopausal women, blood loss from the gastrointestinal tract is the commonest cause in adult men and post-menopausal women.[3] Asymptomatic colonic and gastric carcinoma may present with iron deficiency anaemia and exclusion of these conditions is of prime importance. Malabsorption, most frequently from coeliac disease, poor dietary intake, previous gastrectomy, and NSAID use may also give rise to iron deficiency anaemia.

The balance of iron in humans is tightly controlled and designed to conserve iron for optimal utilisation. The only mechanisms by which the body loses iron are menses, gastrointestinal bleeds or other forms of bleeding but also through the loss of epithelial cells from the skin, gut and genitourinary tract. Normally, the only route through which iron enters the body is by absorption from food or oral supplementation; however iron may also enter the body during blood transfusions or injection of iron complexes. A dietary intake of iron is needed to replace the iron that is lost daily in the stools, urine and through the skin. These basal losses represent approximately 0.9mg of iron per day for an adult male and 0.8 mg per day for an adult female.[4] Iron requirements will be increased with heavy menstrual flow, during pregnancy as well as in infants and adolescents.

There are two distinct types of iron found in food – haem and non-haem iron. Haem iron is a constituent of haemoglobin and myoglobin and so is present in meat, fish, poultry and blood products. Non-haem iron is mainly found in vegetables, cereals, tubers and pulses

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Thus, iron deficiency may result from ***excessive loss*** or decreased absorption of iron. Excessive loss might take place as ***occult gastrointestinal blood loss*** caused by:

- Aspirin
- NSAID use
- Benign gastric ulceration
- Angiodysplasia
- Uncommon causes such as oesophagitis
- Colonic carcinoma
- Gastric carcinoma
- Other gastrointestinal tract malignancies

Blood loss might not be gastrointestinal in origin. It might be due to:

- Menstruation
- Pregnancy
- Blood donation
- Rarely, haematuria & epistaxis

Decreased absorption of iron may be due to ***inadequate dietary intake*** of iron in certain subpopulations, example, vegetarians and elderly. It may also arise because of unbalanced diets or because of ***malabsorption syndromes***, example:

- Coeliac disease
- Post-gastrectomy
- Gastric Helicobacter pylori colonisation
- Impaired gastric acid secretion
- The use of proton pump inhibitors
- Parasitic infections
- Uncommon causes such as gut resection and bacterial overgrowth
- Chronic inflammation

Management of Iron Deficiency Anaemia

The aim of the treatment of iron deficiency anaemia should be to restore haemoglobin levels and mean cell volume (MCV) to normal values and to replenish body stores, that is, serum ferritin levels are restored to normal limits. If this cannot be achieved, further investigation may be warranted.

Treatment of the underlying cause should prevent further iron loss; nonetheless all patients should have iron supplementation in order to correct anaemia and replenish body stores. This is achieved most simply and cheaply with ferrous sulphate 300 mg twice daily although ferrous gluconate and ferrous fumarate are as effective.[6] These provide 100-120mg of oral elemental iron per day. A liquid preparation is an alternative when tablets are not tolerated. Patients must also be advised to include more iron in their diet. Iron-rich foods include dark-green leafy vegetables, wholegrains, beans, nuts, apricots, prunes, raisins, iron-fortified cereals and meat.

To ensure a healthy, well-balanced diet, foods from all major food groups should be included in the diet. Ascorbic acid enhances iron absorption[7] and should be advised as a dietary intake, in the form of oranges or other citrus fruits, with the iron supplementation. Patients need to be advised to avoid taking iron supplements with tea or coffee, as tannins can form insoluble complexes with iron, reducing its absorption. Oral iron preparations should be taken on an empty stomach, as food may inhibit iron absorption. However, if oral iron causes gastric upset, it can be taken with or shortly after food.[8] Other drugs such as antacids, calcium, oral bisphosphonates and thyroid hormones should be avoided when taking the oral iron as it forms poorly soluble complexes with them, decreasing iron absorption.[8]

Parenteral iron should only be used when there is intolerance to at least two oral preparations or non-compliance. Parenteral iron treatment is expensive and may cause anaphylactic reactions.[8] Besides, the rise in haemoglobin is no quicker than with oral preparations. If parenteral iron is needed, intravenous iron is preferred; iron administered intramuscularly is painful and is also poorly absorbed from muscle.[9]

The haemoglobin concentration should rise by 2 g/dl after 3–4 weeks. Failure to do so is usually due to poor compliance, misdiagnosis, continued blood loss, or malabsorption. Guidelines vary in their recommendations for the duration of iron therapy after the anaemia has been corrected. Some guidelines suggest an additional 3 to 4 months of treatment.[8,10] Others suggest 4 to 6 months[11] whereas others suggest 6 to 12 months.[12] However iron supplementation should be continued for at least three months after correction of anaemia to replenish adequately the iron stores.[6]

Once normalized, the haemoglobin concentration and red cell indices should be monitored at intervals. It is suggested that monitoring should be done three monthly for one year and then after a further year. Additional oral iron should be given if the haemoglobin or MCV fall below normal levels (a ferritin estimation should also be done in doubtful cases). Further investigation is only necessary if the haemoglobin and MCV cannot be maintained in this way.[3]

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