Diagnosis and management of anaemia in children with IBD

Jochen Kammermeier and Astor Rodrigues on behalf of the IBD working Group UK

Background:

Anaemia is common in children with IBD. Published prevalence rates vary widely with figures reported as high as 70% [1]. Iron deficiency anaemia (IDA) and anaemia of chronic disease (ACD) are the two most common types of anaemia in IBD.

The aetiology of IDA is multifactorial; low dietary intake, impaired absorption as well as blood loss are contributing factors [2].

ACD is due to the dysregulation of iron homeostasis resulting in increased uptake and retention of iron within the cells of the reticuloendothelial system. The diversion of iron from the circulation into storage sites of the reticuloendothelial system, results in reduced availability of iron for erythroid progenitor cells and iron-restricted erythropoiesis [3]. During the inflammatory process, cytokines such as TNFα and IL-1 and 6 decrease erythropoiesis directly and indirectly by inhibiting erythropoietin production. The expression of the acute phase protein hepcidin is induced by proinflammatory cytokines such as IL-6 and diminishes iron absorption from the duodenum as well as iron release from macrophages [3].

Diagnosis:

To diagnose and evaluate anaemia in children with IBD we propose the following tests as first line investigations:

1. Haemoglobin (Hb), haematocrit (Hct) and mean cell volume (MCV)
2. Ferritin
3. Transferrin saturation (TfS)
4. Inflammatory markers: C- reactive protein (CRP) / erythrocyte sedimentation rate (ESR)

Typically, Hb, Hct, MCV, ferritin and TfS are low in children with IDA. In the presence of inflammation (raised CRP and/or ESR), ferritin becomes an unreliable marker and is frequently found within normal range or elevated. For patients on thiopurines, MCV values need to be interpreted with care, as they are frequently elevated as an effect of the drug. A basic diagnostic flow chart is provided below. For further guidance see reference [4 5].

Treatment:

The effects of chronic iron deficiency (ID) on cognitive development and function, immune regulation and growth are well established [6] and ID should be diagnosed early and treated promptly. Treatment with oral iron preparations is recommended in children with mild to moderate anaemia (Hb>10) and quiescent disease. The daily absorption capacity of elemental iron from the duodenum is approximately 10-20mg. It has therefore been suggested that

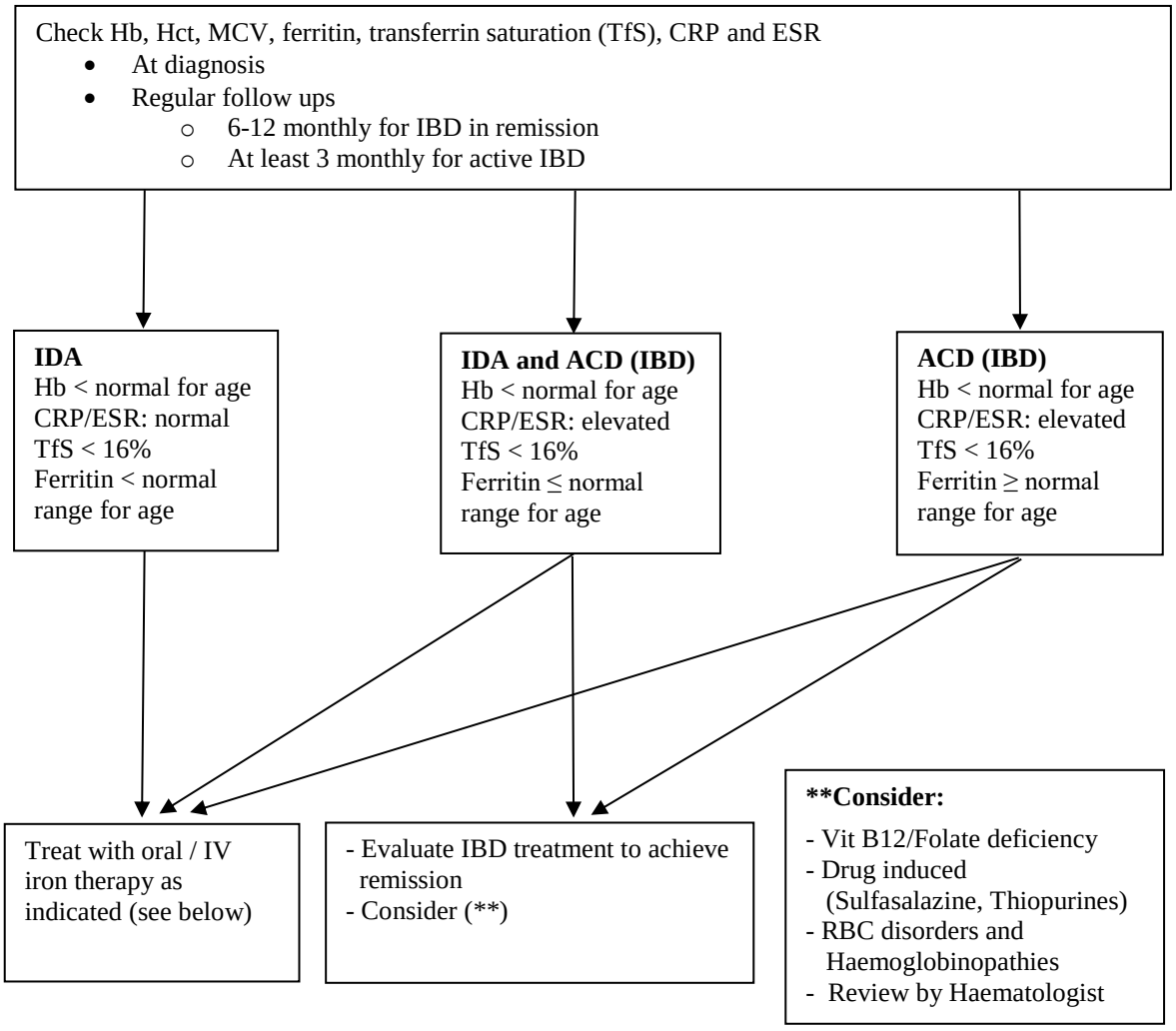
higher oral iron doses in adult patients with IDA might not be beneficial and could result in a higher risk of developing iron-associated adverse reactions [7]. Some evidence from animal and human studies suggests that luminal iron exposure may exacerbate intestinal inflammation [8 9]. In addition, poor absorption of iron from the inflamed intestine (see above) often renders the parenteral route of iron administration necessary. Over recent years, safer and more efficient intra-venous (IV) iron preparations have become available and are now commonly used in adult IBD practice [5].

Tests and reference ranges:

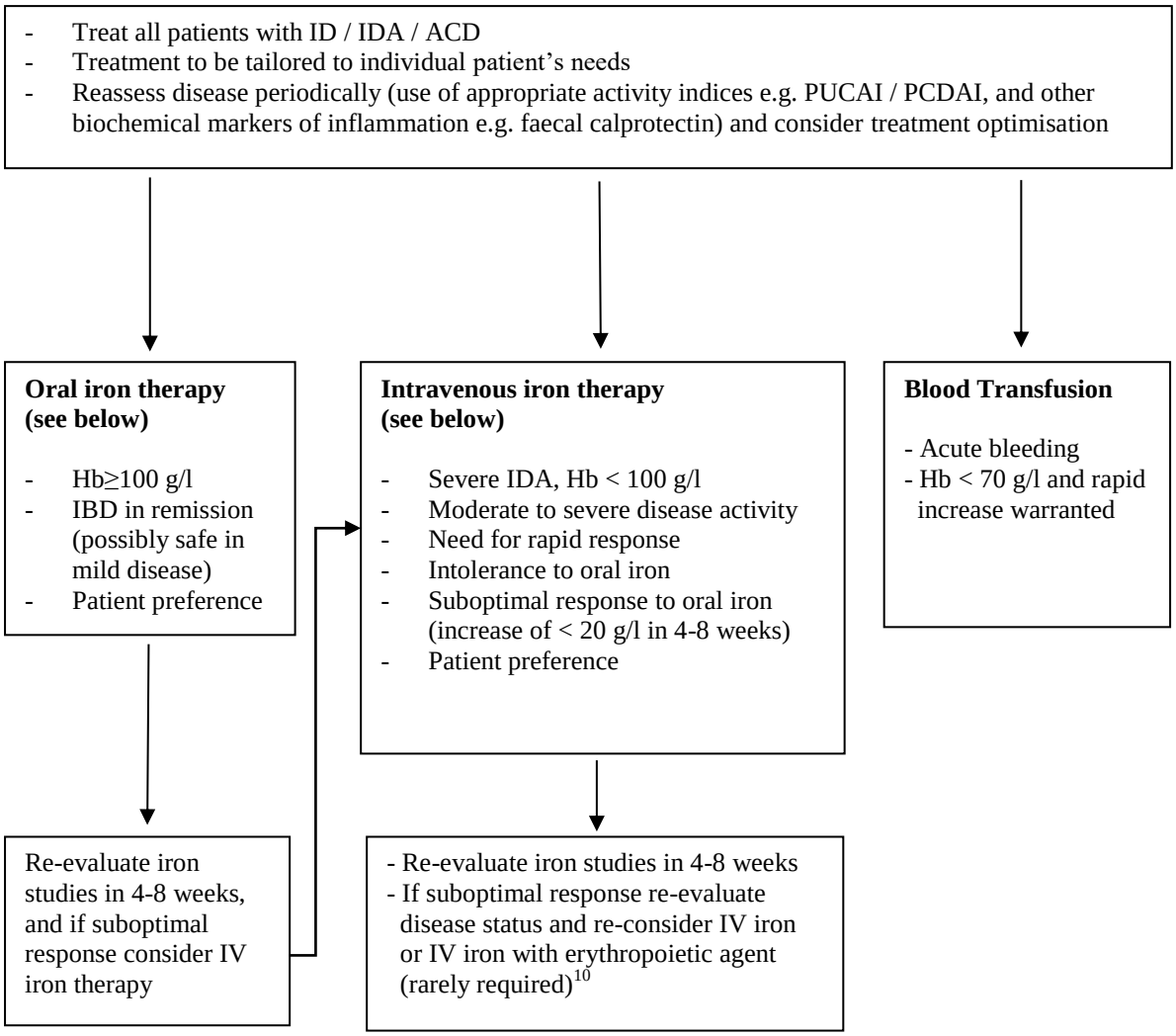
Age Group	HB (lower limit in [g/l])	HCT (lower limit in [%])	MCV (fl)	Ferritin (ug/l)	Transferrin saturation
18 months to 3 years	105*	33*	70 – 86*	4-74*	>16%
3 to 7 years	115*	35*	75 – 87*		
7 to 13 years	115*	35*	77 – 94*	11-93*	
14 to 18 years, female	120*	36*	78 – 102*	4-122*	
14 to 18 years, male	130*	37*	78 – 98*	10-98*	

*Reference ranges, Great Ormond Street Hospital, London. Please also consult local laboratory for guidance

Diagnosis of anaemia:



Treatment of ID/IDA/ACD in IBD:



Oral Iron Preparations (as per BNFc)

The recommended oral dose for the treatment of ID is 3-6mg/kg/day (max 200mg/day) to be given in 2-3 divided doses. Limited duodenal iron absorption (10-20mg/day - see above) suggests that high iron doses might have no beneficial effect and might increase the risk of adverse drug reactions. Consider treating in the low dose range instead.

Iron salt	Brand name	Ferrous Iron/Amount
Ferrous Sulfate	Ironorm drops Ferrous Sulfate coated tabs	25mg/125mg/ml 65mg/200mg/tab
Ferrous Fumerate	Ferrous Fumarate tabs Ferrous Fumarate syrup Fersaday Galfer Capsules Galfer syrup	68mg/210mg/tab 45mg/140mg/5ml 100mg/322mg/tab 100mg/305mg/tab 45mg/140mg/5ml
Sodium Feredetate	Sytron	27.5mg/190mg/5ml
Ferrous Gluconate	Ferrous Gluconate coated tabs	35mg/300mg/tab

BNFc listed parenteral iron preparations (preference may vary in between centres please refer to local pharmacy protocols; please acknowledge MHRA/CHM advise below)

Iron salt	Brand name	Licenced age	Ferrous Iron	Dosing (see also product literature)
Ferric Carboxymaltose	Ferinject	≥ 14 years	50mg/ml	Do not exceed 20mg/kg/dose (max 1000mg/dose)
Iron Dextran	CosmoFer	≥ 14 years	50mg/ml	Do not exceed 20mg/kg/dose (max 200mg/dose)
Iron Sucrose	Venofer	≥ 18 years	20mg/ml	Do not exceed 3mg/kg/dose (max 200mg/dose)

Total iron deficit can be calculated as per Ganzoni Formula:

Total Iron Deficit = Weight [kg] x (Target Hb [g/l] – Actual Hb [g/l]) x 2.4 + Iron Stores [mg]

(Iron Stores: Body weight <35kg = 15mg/kg; Body weight >35kg = 500mg)

MHRA/CHM advice

Serious hypersensitivity reactions with intravenous iron (August 2013)

Serious hypersensitivity reactions, including life-threatening and fatal anaphylactic reactions, have been reported in patients receiving intravenous iron. These reactions can occur even when a previous administration has been tolerated (including a negative test dose). Test doses are no longer recommended and caution is needed with *every* dose of intravenous iron.

Intravenous iron products should only be administered when appropriately trained staff and resuscitation facilities are immediately available; patients should be closely monitored for signs of hypersensitivity during and for at least 30 minutes after every administration. In the event of a hypersensitivity reaction, treatment should be stopped immediately and appropriate management initiated.

The risk of hypersensitivity is increased in patients with known allergies, immune or inflammatory conditions, or those with a history of severe asthma, eczema, or other atopic allergy; in these patients, intravenous iron should only be used if the benefits outweigh the risks.

Intravenous iron should be avoided in the first trimester of pregnancy and used in the second or third trimesters only if the benefit outweighs the potential risks for both mother and fetus.

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