Drugs and Therapeutic Backgrounder:

Iron therapy in inflammatory bowel diseases

Oral iron can be considered first line therapy in patients with inflammatory bowel disease (IBD) and anemia, or clinically inactive IBD and no history of oral iron intolerance.

Background

Iron deficiency and anemia is a common extraintestinal manifestation of IBD with a prevalence of 6-74% depending on the population[1]. Patients with IBD are susceptible to iron deficiency anemia (IDA) caused by chronic blood loss and decreased iron absorption, as well as anemia of inflammation. Oral iron has limited GI absorption and unabsorbed iron can be harmful to the GI mucosa. Medications to treat IBD have been shown to contribute to anemia[1].

In normal conditions serum ferritin is an accurate indicator of iron stores, however in chronic inflammation, ferritin levels can be elevated[2,3]. Thus, in the presence of inflammation, serum ferritin less than 100 µg/L may indicate iron deficiency[4].

Efficacy

The European Crohn's and Colitis Organization (ECCO) recommends oral iron (maximum 100 mg of elemental iron daily) in most IBD patients with IDA[4]. Patients with mild anemia (Hb >110 g/L) or who are not experiencing an acute IBD exacerbation have shown benefit from oral iron therapy[4,5]. There are a variety of recommendations on the use of oral iron in moderate to severe IBD, but recommendations indicate starting with parenteral iron in these cases[4,6,7]. In patients with gastrointestinal blood loss exceeding oral iron intake (20-30 mL/day), parenteral iron is recommended[2,8].

Guidance The following does not replace clinician judgment[4].

Scenario	Recommended Intervention
Mild IDA (Hb 110-119 g/L in non-pregnant women; 110-129 g/L in men) Clinically inactive IBD No history of oral iron intolerance	• Oral iron therapy for 3-6 months (consider intermittent dosing schedule) • Educate patient on high iron diet. Dietician referral.
Clinically active IBD **with** intolerance to oral iron Hemoglobin <100 g/L Patient requiring erythropoietin stimulating agent (ESA)	• Parenteral iron therapy
Failure to respond to parenteral iron therapy	• ESA with target hemoglobin <120 g/L
Failure with all other therapies Anemia with hemodynamic instability	• RBC transfusion

- After iron stores are replenished with parenteral iron, iron therapy may be continued with intermittent dosing or low dose oral iron on an ongoing basis[2]
- Patients with active IBD should be monitored every 3 months for anemia[4]
- A recurrent drop in ferritin below 100 µg/L or Hb below 120-130 g/L requires re-treatment with parenteral iron[4]

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Sustainability

Appropriate use of healthcare resources is needed to ensure long-term sustainability as there are significant cost differences between oral and parenteral iron therapy.

Safety

Oral iron is commonly associated with GI adverse effects including nausea, heartburn, constipation, diarrhea, and darkened stools. These may be reduced by using an alternate day or intermittent dosing schedule (e.g. every other day)[9,10]. It may difficult to differentiate these side effects from an IBD exacerbation[2]. For patients with moderate to severe active IBD, oral iron may worsen inflammation by altering the luminal microbiota and producing toxic reactive oxygen species. Parenteral iron is preferred in moderate to severe IBD when indicated (*see table on Page 1*)[2-5,11].

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