Drugs and Therapeutic Backgrounder:

Optimizing the use of oral iron supplementation in the treatment of iron deficiency anemia

In most cases, oral iron therapy is first line therapy for iron deficiency anemia. Regimens should be patient-specific and based on tolerability. Oral iron tolerability strategies include using a low starting dose and using an intermittent (every other day) dosing schedule.

Background

Iron deficiency is the most common cause of anemia worldwide[1]. Iron deficiency anemia (IDA) is defined as reduced iron levels that occur concurrently with reduced hemoglobin (Hb) levels. Iron deficiency or IDA could be asymptomatic, however if syptomatic, patients could present with pallor of the skin, fatigue, dyspnea on exertion, headache, weakness, poor work productivity, vertigo, or syncope[1].

Goals of treatment include:

1. Symptom improvement
2. Identifying and treating the cause of IDA
3. Restoring Hb concentration and iron stores

The **Towards Optimized Practice (TOP) Guidelines for IDA** recommend oral iron as the initial and mainstay therapy[2]. **UK guidelines** now recommend an adult target treatment dose of **40 - 100 mg elemental iron/day**[14]. 30-70% of patients on oral iron report GI side effects (e.g., nausea, vomiting, dyspepsia, constipation, diarrhea, dark stools), thereby affecting tolerance and adherence[3, 4]. Rates of adverse effects are similar between ferrous salts when equivalent doses of elemental iron are given[2]. Every other day dosing is a good option for those 30-70% who report GI side effects.

Hepcidin is the main hormone that regulates iron absorption. Increased hepcidin levels decrease the amount of iron absorbed from the GI tract, and when hepcidin levels are low, the body is able to increase the amount of iron it can absorb[5, 6]. Hepcidin levels are affected by inflammation, the body's iron stores, and genetic factors (e.g. hemochromatosis). There is a negative correlation between oral iron dosing and hepcidin levels, suggesting that as doses of oral iron increase, hepcidin decreases the amount of iron the body can absorb from the GI tract[7]. Unabsorbed iron primarily causes the GI side effects. Alternate day or intermittent dosing of oral iron may improve oral iron absorption and decrease GI side effects[8-10].

Guidance[2]

- Oral iron therapy should be used for asymptomatic patients with a Hb >60 g/L
- It takes 3-6 months to replenish iron stores with oral iron therapy
- Oral iron may not be the first choice for patients who are post-bariatric surgery
- GI adverse reactions are typically temporary and wane with continuous therapy with the exception of dark stools[4]

To improve oral iron absorption:

- Approximately 10-20% of an oral iron dose is absorbed at the beginning of therapy, and may drop to 5% after 1 month of therapy[11, 15].
- Oral iron is absorbed to a greater extent on an empty stomach, but administration with food may improve tolerability and adherence[1,4]
- Ascorbic acid may enhance iron absorption; there is no evidence that it is effective in improving IDA [2, 12, 13]
- Low dose oral iron and intermittent dosing (every other day) may be as effective as standard dose regimens for treating IDA in elderly patients. Limited studies have found significant increases in fractional and total iron absorption and similar increases of Hb and ferritin levels with this approach[8-10]
- To maximize absorption, take oral iron in the morning when hepcidin levels are low and avoid consumption of calcium products or high-oxalate foods (e.g. coffee, tea, spinach)[2]
- Proton pump inhibitor and other acid reduction therapies may decrease oral iron absorption. Consider **deprescribing proton pump inhibitors**

To improve oral iron tolerance:

- Use the lowest effective dose and titrate slowly (at least 4-5 days)[2, 4]
- Alternate day or intermittent dosing schedules reduce incidence and severity of GI adverse effects[10]
- Other tolerability strategies[2]:
  - Liquid iron formulation for smaller dose titrations
  - Taking with food
  - Taking at bedtime
  - Try another oral iron formulation, or the iron polysaccharide complex

In the general population, parenteral iron therapy may be considered when[2]:

- Clinical symptoms of IDA persist and adherence to oral iron therapy was optimized
- Hb continues to decline while on oral iron therapy (<90 g/L)
- Inadequate response (increase in hemoglobin of <10 g/L in 4-6 weeks) to oral iron after 3 months of oral treatment dosing
- Patients continue to suffer intolerability although they have tried a variety of oral iron formulations, including the heme or polysaccharide products

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