Guidelines on the Diagnosis and Management of Iron Deficiency and Anemia in Inflammatory Bowel Diseases

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1. Anemia Evaluation

Definition of Anemia

Statement 1A: The WHO definitions of anemia (Table 2) apply to patients with IBD. All patients with IBD should be assessed for the presence of anemia (Grade D).

TABLE 2. Minimum Hemoglobin and Hematocrit Levels Used to Define Anemia in People Living at Sea Level

	Hemoglobin		Hematocrit
Age or Sex Group	(g/dL)	(mmol/L)	(%)
Children 6 months to 5 years	11.0	6.83	33
Children 5-11 years	11.5	7.14	34
Children 12-13 years	12.0	7.45	36
Nonpregnant women	12.0	7.45	36
Pregnant women	11.0	6.83	33
Men	13.0	8.07	39

From WHO/UNICEF/UNU, 1998. (17)

Screening Parameters

Statement 1B: Hemoglobin, serum ferritin, and C-reactive protein (CRP) should be used for laboratory screening. For patients in remission or mild disease, measurements should be performed every 6 to 12 months. In outpatients with active disease such measurements should be performed at least every 3 months. Patients at risk for vitamin B_{12} or folic acid deficiency (e.g., small bowel disease or resection) need proper surveillance. Serum levels of vitamin B_{12} and folic acid should be measured at least annually, or if macrocytosis is present (Grade D).

Anemia Workup

Statement 1C: Anemia workup should be initiated if the hemoglobin is below normal. The minimum workup includes serum ferritin, transferrin saturation (TfS), and CRP concentration. More extensive workup should be performed if these investigations do not identify the cause of anemia, or if a therapeutic intervention is unsuccessful. More extensive workup includes serum concentrations of transferrin, vitamin B_{12}, folic acid, haptoglobin, lactate dehydrogenase, and creatinine, a reticulocyte, and a differential white blood cell count. Advice from a hematologist is appropriate if the cause of anemia remains unclear after more extensive workup (Grade D).

Iron Deficiency

Statement 1D: Diagnostic criteria for iron deficiency depend on the level of inflammation (Table 3). In patients without biochemical or clinical evidence of inflammation, appropriate criteria are a serum ferritin <30 g/L or TfS <16%. In the presence of inflammation, the lower limit of serum ferritin consistent with normal iron stores is 100 <g/L (Grade B).

TABLE 3. Degree of Iron Deficiency Evaluated by Serum Ferritin or Transferrin Saturation in Adults

	Serum Ferritin (μg/L)	Transferrin Saturation %
Depleted iron stores in healthy adults or patients with quiescent IBD	<30	<16
Depleted iron stores during active IBD	<100	<16
Adequate iron stores	>100	16–50
Potential iron overload	>800	>50

Anemia of Chronic Disease

Statement 1E: In the presence of biochemical or clinical evidence of inflammation, the diagnostic criteria for ACD are a serum ferritin >100 g/L and TfS <16%. If the serum ferritin level is between 30 and 100 g/L, a combination of true iron deficiency and ACD is likely (Grade B).

2. Triggers for Treatment of Anemia

Initiation of Therapy

Statement 2A: Treatment should be considered for all patients with a hemoglobin below normal. The decision to initiate therapy depends on symptoms, etiology, and severity of anemia, rate of change, comorbidity, and potential adverse effects of therapy (Grade D).

Initiation of Iron Supplementation

Statement 2B: Iron supplementation should be initiated when iron deficiency anemia is present (Grade A). For iron deficiency without anemia, different approaches to iron replacement should be considered and discussed with the patient. If patients are likely to develop iron deficiency anemia the monitoring frequency should be increased (Grade D).

Initiation of Erythropoietic Therapy

Statement 2C: The use of erythropoietic agents is effective for the treatment of ACD and may improve the quality of life. It should be considered if the hemoglobin is <10.0 g/dL or if there is no response to intravenous iron therapy within 4 weeks (Grade B).

Initiation of Vitamin Supplementation

Statement 2D: Replacement of vitamin B_{12} or folic acid should be initiated if serum concentrations are below normal (Grade D).

Blood Transfusion

Statement 2E: Indications for replacement of blood after acute or chronic gastrointestinal bleeding vary depending on the clinical situation (including the rate of bleeding, hemodynamic state, hemoglobin, age, concomitant disease) and are best judged by the physician. Management should be directed at diagnosing and stopping intestinal bleeding. Blood transfusion is no substitute for the treatment of iron deficiency anemia with intravenous iron, possibly in combination with erythropoietic agents. Should transfusion be judged necessary, iron replacement therapy is still required (Grade D).

3. Targets of Anemia Therapy

Treatment Goals

Statement 3A: The goals of anemia treatment are to increase the hemoglobin, serum ferritin, and TfS above the lower threshold of normal (Tables 2, 3), to prevent a further fall in hemoglobin, to avoid the use of blood transfusion, to relieve symptoms related to anemia, and to improve the quality of life (Grade D).

Response to Treatment

Statement 3B: The erythropoietic response to iron or hematinic replacement is considered appropriate if the hemoglobin concentration increases by at least 2 g/dL or reaches normal (Table 2) within 4 weeks of treatment (Grade C)

Treatment Evaluation

Statement 3C: To evaluate the response to therapy, hemoglobin should be measured within 4 weeks in asymptomatic patients and sooner in symptomatic patients in order to adjust treatment accordingly. When monitoring oral iron supplementation, a serum ferritin above 100 g/L indicates appropriate iron stores. Serum ferritin is not useful for monitoring intravenous iron supplementation, but a TfS >50% indicates iron overload (Grade D).

4. Treatment of Anemia

Iron Supplementation

Statement 4A: The preferred route of iron supplementation in IBD is intravenous, even though many patients will respond to oral iron. Intravenous iron is more effective, better tolerated, and improves the quality of life to a greater extent than oral iron supplements (Grade A). Absolute indications for intravenous iron include severe anemia (hemoglobin <10 g/dL), intolerance, or inappropriate response (see Statement 3B) to oral iron, severe intestinal disease activity, concomitant therapy with an erythropoietic agent, or patient preference. Dosing and infusion intervals depend on the compound. Oral iron supplements can be used if absolute indications for intravenous iron therapy are not met. If oral iron is used, the response (Statement 3C) and tolerance should be monitored and treatment changed to intravenous if necessary (Grade C). Since side effects of oral iron are dose-related, and because its absorption and efficacy are no greater when high doses are used, no more than 100 mg elemental iron daily should be prescribed (Grade C).

Erythropoietic Agents

Statement 4B: Erythropoietic agents are effective for the treatment of ACD. To optimize the effect of erythropoietic agents, treatment should be combined with intravenous iron supplementation. Dosing and injection intervals depend on the compound used (Grade A).

Adjustment of IBD Therapy

Statement 4C: Azathioprine or 6-mercaptopurine (thiopurines) are not considered a cause of isolated anemia. Nevertheless, for patients with pancytopenia thiopurines should be considered a cause and the dose adjusted appropriately. Patients with a high MCV should be checked for vitamin B_{12} and folate deficiency before macrocytosis is attributed to thiopurines or other causes.