EVIDENCE REPORT

Evidence-Based Management of Sickle Cell Disease

Expert Panel Report, 2014

U.S. Department of Health and Human Services
National Institutes of Health
National Heart, Lung, and Blood Institute

http://www.nhlbi.nih.gov/guidelines

Acute Anemia

Background

Nearly all people with SCD have chronic anemia, but individual baseline hemoglobin values vary widely depending upon hemoglobin genotype (HbSS, HbSC, HbSβ^+-thalassemia, HbSβ^0-thalassemia), current and recent therapies (blood transfusions and hydroxyurea in particular), and other unknown factors. It is important for the patient and his or her primary care provider to know the baseline or "steady state" hemoglobin value to inform ongoing monitoring and management during acute complications. Baseline values are typically 6–8 g/dL for people with SCA, 10–15 g/dL for people with HbSC, and 9–12 g/dL for people with HbSβ^+-thalassemia.

Acute anemia, defined as a decline by 2.0 g/dL or more in hemoglobin concentration below the patient's baseline value, can have diverse causes. Potential etiologies such as splenic sequestration in a child or an aplastic episode at any age may require urgent evaluation and therapy.

During acute events, the reticulocyte count is an important addition to the CBC to assess whether diminished red blood cell production (low reticulocyte count, as can occur in parvovirus infection resulting in aplastic crisis), accelerated hemolysis, or sequestration in the lungs, spleen, or liver is responsible for the acute anemia.

Aplastic Episode

An aplastic episode or "crisis" is a common feature of SCD, especially in children with HbSS.[237,238] The usual clinical picture is gradual onset of fatigue, shortness of breath, and sometimes syncope. Fever is quite common as well. Physical examination may reveal lethargy, rapid heart rate, and occasionally frank heart failure. The hemoglobin value (typically 3–6 g/dL) is usually far below the person's baseline level, and the reticulocyte count is reduced or even zero.

It has been noted that people with SCD rarely have recurrences of aplastic crisis, and several people with SCD in the same household frequently develop aplastic crises simultaneously or sequentially. This pattern suggests an infectious etiology. In the early 1980s, it was shown that parvovirus B19, the cause of fifth disease in young children, is in fact the etiology of these events.[238] This virus destroys erythroid precursors in the bone marrow, so people with an extremely short red blood cell lifespan such as those with SCA are susceptible to rapid decline in their hemoglobin concentration. Resolution of the aplastic crisis is heralded by marked reticulocytosis and rising hemoglobin concentration, concomitant with the appearance of immunoglobulin G (IgG) antibodies which neutralize the offending virus. The resulting humoral immunity is lifelong, preventing recurrent events. However, siblings or others with SCD who are exposed to a person with an aplastic crisis in the acute phase are at risk. Aplastic crises are most commonly seen in children with SCA. People with other genotypes, whose hemolysis is less severe, more often have clinically silent events. Occasionally, parvovirus B19 may also be responsible for or contribute to the development of ACS and/or stroke.

Other Causes of Acute Anemia

Acute splenic sequestration is a major cause of acute anemia, especially in children with SCA. This complication and the recommendations for its management will be described separately (see page 44).

A decline in hemoglobin concentration below the baseline is a common feature of ACS and can be its initial manifestation in a patient experiencing a VOC. Acute anemia may also occur as a result of sequestration of blood in the liver or accelerated hemolysis due to a delayed hemolytic transfusion reaction, septicemia, or another serious infection. Acute blood loss due to papillary necrosis or unrelated to SCD, such as

gastrointestinal hemorrhage, can also occasionally be responsible for a rapid decline in hemoglobin concentration. Slow but progressive reduction in hemoglobin values should raise concern about renal failure in the older child or adult with SCD.

Summary of the Evidence

An adequate systematic review of the literature with fair sensitivity and specificity for all studies indexed by SCD terms and the symptom of acute anemia was not feasible. A large and nonspecific return of studies with significant heterogeneity, high miss rate, and low-quality evidence (lack of comparative studies) was anticipated. No systematic evidence review was conducted, and the panel used a consensus process to develop a proposed strategy for triaging and promptly managing acute anemia.

Recommendations

1. During all acute illnesses in people with SCD, obtain a CBC and reticulocyte count, repeat daily in all hospitalized patients, and compare the results with the patient's prior measurements.
   (***Consensus–Panel Expertise***)
2. Assess people with SCD whose hemoglobin concentration is 2 g/dL or more below their baseline (or less than 6 g/dL when the baseline is unknown) for acute splenic sequestration, an aplastic episode, a delayed hemolytic transfusion reaction, ACS, and infection.
   (***Consensus–Panel Expertise***)
3. Use simple transfusion in people with SCD and acute anemia whose symptoms are due to anemia.
   (***Consensus–Panel Expertise***)
4. Perform a CBC and reticulocyte count promptly and again 7 to 10 days later in siblings and others with SCD who are exposed to a person with an aplastic episode.
   (***Consensus–Panel Expertise***)
5. Manage aplastic events with immediate red blood cell transfusion aimed at restoring the hemoglobin to a safe (not necessarily baseline) value. Isolation of hospitalized patients (droplet precautions) is required to prevent spread of the parvovirus B19 to pregnant women and others with SCD or compromised immunity.
   (***Consensus–Panel Expertise***)

Splenic Sequestration

Background

Splenic sequestration is defined as sudden enlargement of the spleen and reduction in hemoglobin concentration by at least 2 g/dL below the baseline value. It is a major cause of acute anemia. During splenic sequestration, the reticulocyte count and circulating nucleated red blood cells are usually elevated, and the platelet count is generally decreased because both red cells and platelets are trapped in the spleen. Sequestration usually develops without warning or known cause. It may occur as early as several months of age,[239] although it is more typical in children between the ages of 1 and 4 years old. Parents may note an enlarging mass in the left upper quadrant. Involution and autoinfarction of the spleen usually occurs by age 5, so sequestration events are less common in older children and adults with HbSS. In people with HbSS, the lifetime prevalence of acute splenic sequestration has been reported to be between 7 percent and 30 percent. In people with HbSC and HbSβ^+-thalassemia, splenic sequestration often occurs later in childhood or even during the adult years. Splenic sequestration in older patients is often accompanied by severe pain from splenic infarction, which can be documented by imaging studies.[240]