EVIDENCE REPORT

Evidence-Based Management of Sickle Cell Disease

Expert Panel Report, 2014

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content between treatment arms, indicating futility for the composite study end point. Accordingly, the study was closed, and the authors concluded that transfusions and chelation remain a better way to manage children with SCA, stroke, and iron overload.[268]

In addition to the use of transfusion for secondary stroke prevention, the systematic review identified three small observational studies that evaluated the role of hydroxyurea.[94,269,270] The studies enrolled a total of 56 children with a history of stroke who were treated with hydroxyurea. The largest of these studies[270] included 35 children with prior stroke who were discontinued from chronic transfusion therapy. Children were followed on average 42 months with an average hydroxyurea dose of 26.7 mg/kg/d. The stroke recurrence rate for the whole cohort was 5.7 events/100 patient-years, but for children who overlapped transfusion therapy with hydroxyurea treatment, the event rate was 3.6/100 patient-years. The two smaller studies[94,269] showed similar results that were consistent with reduction of stroke recurrence associated with using hydroxyurea. The quality of this evidence was low due to imprecision (small sample size) and the uncontrolled nature of the studies.

Recommendations

1. In people with SCD who present with severe headache, altered level of consciousness, seizures, speech problems, and/or paralysis, evaluate for acute stroke by seeking neurologic consultation and performing an urgent head computerized tomography (CT) scan followed by magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) if available.
   (Consensus–Panel Expertise)
2. In consultation with a sickle cell expert, perform exchange transfusion in people with SCD who develop acute stroke confirmed by neuroimaging.
   (Consensus–Panel Expertise)
3. Initiate prompt evaluation, including neurologic consultation and neuroimaging studies, in people with SCD who have mild, subtle, or recent history of signs or symptoms consistent with transient ischemic attack.
   (Consensus–Panel Expertise)
4. In children and adults who have had a stroke, initiate a program of monthly simple or exchange transfusions.
   (***Moderate Strength, Low-Quality Evidence***)
5. In children and adults who have had a stroke, if it is not possible to implement a transfusion program, initiate hydroxyurea therapy.
   (***Moderate Strength, Low-Quality Evidence***)

Multisystem Organ Failure

Background

Multisystem organ failure (MSOF) is a severe and life-threatening complication usually associated with a VOC and characterized by failure of the lungs, liver, and/or kidneys.[163] MSOF may occur after several days of hospitalization and treatment for a severe VOC, often when pain is beginning to improve. In most cases, patients do not have a history of chronic organ failure. Deterioration is rapid and unexpected. It is usually associated with fever, a rapid decline in hemoglobin concentration and platelet count, and nonfocal encephalopathy. Acute respiratory failure is usually associated with development of ACS. Hepatic failure is associated with marked elevations in total and direct bilirubin, liver enzymes, and blood coagulation screening tests. Acute renal failure is associated with a rapid elevation of serum creatinine, with or without the presence of oliguria and hyperkalemia. Rapid diagnosis and treatment of MSOF is necessary to prevent death.

Summary of the Evidence

An adequate systematic review of the literature with fair sensitivity and specificity for all studies indexed by SCD terms and "multisystem organ failure" was not feasible. No systematic review was conducted, and the panel used a consensus process to develop a proposed strategy for triaging and promptly managing MSOF.

Recommendations
1. In people with SCD who exhibit severe deterioration during a VOC, immediately evaluate for potential MSOF. (***Consensus–Panel Expertise***)
2. In people with SCD and respiratory failure, support respiratory status with supplemental oxygenation and mechanical ventilation when needed. (***Consensus–Panel Expertise***)
3. Use renal replacement therapy (e.g., hemodialysis) when needed for acute renal failure. (***Consensus–Panel Expertise***)
4. In people with SCD and MSOF, immediately initiate either simple or exchange transfusion in consultation with a sickle cell expert or hematologist. (***Consensus–Panel Expertise***)

Acute Ocular Conditions

Background

In persons with SCD, acute ocular complications may occur secondary to trauma, infection, vaso-occlusive episodes leading to occlusion of the eye vasculature, or progression of proliferative sickle retinopathy (PSR). All may have devastating consequences including permanent loss of vision. Hyphema, central retinal artery occlusion (CRAO), orbital and periorbital infections, orbital infarction, and orbital compression syndrome (OCS) all require urgent or emergent assessment and therapy. Although late-stage changes associated with PSR such as nonclearing vitreous hemorrhage and retinal detachment may present with acute visual symptoms, these complications are more fully discussed in the "Managing Chronic Complications of Sickle Cell Disease" chapter of these guidelines.

Hyphema—the presence of blood in the ocular anterior chamber—is often due to blunt injury trauma and typically presents with hemorrhage covering the lower part of the iris and visual abnormalities such as floaters and flashers, light sensitivity, and blurry vision. In persons with SCD, and even in healthy individuals with sickle cell trait, hyphema is especially dangerous due to the hypoxic and acidotic nature of the anterior chamber, which promotes sickling of red blood cells in the aqueous humor. This in turn prevents outflow of sickled erythrocytes and aqueous humor through the trabecular meshwork of the eye and increases pressure in the entire eye. Blood flow in the central retinal artery in the presence of high intraocular pressure (IOP) may result in CRAO and infarction of the optic nerve. Elevated IOP[271,272] is poorly tolerated in people with SCD. The size of the hyphema is poorly correlated with the risk of visual loss.[271-273] In addition, people with SCD tend to have more significant and prolonged hyphema, as well as an increased risk for secondary hemorrhage.[274] Aggressive treatment such as anterior chamber paracentesis or surgical evacuation of a clot may be vision sparing in people with SCD with sustained elevated IOPs that are not responsive to medical management.[271,273-275]

CRAO is a rare cause of acute blindness reported almost exclusively in children and young adults with SCA.[276] It results from thrombus formation in the artery. CRAO causes infarction of the inner retina[277] and results in macular ischemia and potential macular infarction. People typically present with sudden, painless unilateral or