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

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

bilateral loss of vision. CRAO has been observed in people with SCD in association with increased IOP secondary to hyphema,[276] moyamoya syndrome,[278] or ACS.[279] CRAO can also occur spontaneously.[280-282]

Orbital infarction is another rare but serious complication of SCD, typically occurring during a VOC. This infarction of the orbital bones is often complicated by hematomas, thought to be a result of ischemic vessel wall necrosis. Because space in the orbital cavity is limited, the inflammatory response generated by infarcted bone may result in further compromise of important eye structures. People typically present with protrusion of the eye, eye pain, and lid and/or orbital edema. On examination, people will have decreased visual acuity and extraocular motility. Differential diagnosis includes periorbital infection due to orbital cellulitis, orbital abscesses, or osteomyelitis, and OCS. Radiographic imaging aids in diagnosis.[283-285] In the case of periorbital infection or orbital bone infarction, rapidly progressive symptoms despite maximal medical management may require surgical intervention.

OCS, also known as orbital apex syndrome, is defined by the presence of compressive optic neuropathy and markedly decreased extraocular motility secondary to involvement of the branches of cranial nerves III and V. Recently, OCS has been described as a result of orbital inflammation after sphenoid bone infarction with subperiosteal hematomas,[285] suggesting significant overlap between orbital infarction and OCS. Prompt initiation of corticosteroids once infection is ruled out can result in reversal of OCS.[285] Diagnostic imaging includes MRI. Surgical intervention may be needed if medical management fails to resolve the compressive optic neuropathy.

Key Question

KQ17. In people with SCD and acute eye symptoms, what is the optimal management strategy to preserve vision and prevent long-term ocular complications?

Summary of the Evidence

Six studies (three RCTs and three observational studies) and 29 case reports described sickle cell-related acute or chronic ocular complications. Of these, the RCTs and the observational studies assessed the management of chronic sickle cell retinopathy, which is discussed in the "Managing Chronic Complications of Sickle Cell Disease" chapter. Twenty-two of the 29 case reports addressed acute complications alone (see evidence tables). Very little data exist to evaluate the most effective therapy to preserve vision during and after acute eye emergencies. The evidence that does exist comes from the case reports, which describe various and often multiple interventions (e.g., calcium channel blockers, intravenous hydration, surgical interventions) for the treatment of hyphema, CRAO, orbital infarction, and OCS. There was not enough evidence to make a recommendation about using transfusion to manage these acute complications.

Due to the paucity of available data, in developing recommendations for acute ocular conditions, the panel placed a high value on the outcome of vision preservation and less value on the burdens and harms of interventions supported with lower quality evidence.

Recommendations

1. Immediately examine for hyphema anyone with SCD who presents with eye trauma. If hyphema is present, immediately refer to an ophthalmologist for further management.
   (Consensus–Panel Expertise)
2. Promptly refer anyone with SCD exhibiting signs and symptoms such as protrusion of the eye, changes in visual acuity (flashers or floaters), and unilateral or bilateral loss of vision to an eye specialist capable of performing a dilated eye exam to assess visual acuity, intraocular pressure, and the peripheral retina.
   (Consensus–Panel Expertise)
3. Manage acute ocular complications in consultation with an ophthalmologist, hematologist, and other specialists with expertise in SCD.
   (***Consensus–Panel Expertise***)