EVIDENCE REPORT

Evidence-Based Management of Sickle Cell Disease

Expert Panel Report, 2014

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

One RCT, six observational studies, and nine case reports addressing both acute and chronic complications were evaluated. There were no RCTs that addressed acute complications and the single RCT addressed chronic complications; acute renal complications were only discussed in five retrospective observational case series.[40,168-171] No controlled trials or prospective studies addressed the recognition or management of acute renal failure in people with SCD, and few studies addressed evaluation or treatment of renal complications of SCD. The systematic review did not identify any literature to guide diagnostic or management recommendations for renal papillary necrosis. Therefore, management recommendations are based on the application of therapies for ARF from other patient populations to people with SCD as noted in the observational reports.

Recommendations

1. In the setting of an acute rise in serum creatinine of ≥0.3 mg/dL,
   - Monitor renal function daily, including serum creatinine and fluid intake/output. ***(Consensus–Panel Expertise)***
   - Avoid potential nephrotoxic drugs and imaging agents. ***(Consensus–Panel Expertise)***
   - Evaluate the patient thoroughly for all potential etiologies in consultation with a nephrologist as needed. ***(Consensus–Panel Expertise)***
2. Do not give blood transfusions to treat ARF unless there are other indications for transfusion. (***Consensus–Panel Expertise***)
3. Use renal replacement therapy (e.g., hemodialysis) when needed for acute renal failure. (***Consensus–Panel Expertise***)

Priapism

Background

Priapism is a sustained, unwanted painful erection lasting 4 or more hours. Stuttering priapism is the occurrence of multiple self-limited episodes of shorter duration (<4 hours) and can be a harbinger of sustained events.[172] Priapism is a common complication of SCD, affecting 35 percent of boys and men.[173] It is usually of the low-flow ischemic type and characterized by pain and a soft glans. Blood aspirated from the corpora cavernosa of the penis is dark, with a low pO_2, pH, and glucose concentration.[173] Prompt recognition of priapism and initiation of conservative medical management may lead to detumescence and limit the need for more aggressive and invasive intervention. Delayed diagnosis and therapy can result in impotence.

Key Question

KQ12. In males with SCD presenting with acute priapism, what is the relative efficacy of conservative management, pharmacological management, transfusion, and surgery on the outcomes of detumescence and the incidence of future impotence?

Summary of the Evidence

Seven observational studies and 39 case reports described priapism in the setting of SCD. Overall, the quality of the evidence in this area was low due to the observational and uncontrolled design of the available studies.

The observational studies included more than 220 people and studied approaches such as shunts, aspiration, exchange transfusion, hydroxyurea, hormonal therapy (e.g., stilbestrol, finasteride, and leuprolide), bicalutamide, hydralazine, sildenafil, oxygen, and hyperhydration to treat priapism in men and boys with SCD. Results were limited, reporting variable success.[174-179] Several of the studies highlighted the importance of prompt recognition and initial conservative medical management with analgesics, intravenous fluids, oxygen, and sedation if needed.[180-183]

Red blood cell transfusion therapy was inconsistently associated with improvement in acute priapism.[184-193] In addition, case reports of acute neurological events following exchange transfusion for priapism further limit enthusiasm for routine adoption of this therapy in the absence of proven benefit.[194] Both observational studies and case reports found that a variety of subsequent interventions used to treat symptoms that persist after initial conservative medical management appear to result in detumescence and retained potency. These include penile aspiration,[195,196] corporal irrigation using α-adrenergic agents (e.g., pseudoephedrine, epinephrine, etilefrine),[197-203] and the use of oral agents (e.g., PDE-5 inhibitors, pseudo-ephedrine).[204] Surgical intervention, including shunting, has been utilized most often after more conservative measures fail, with inconsistent benefit.[190,205-209]

In developing recommendations for the care of males with SCD presenting with acute priapism, the expert panel placed great value on preventing pain and future long-term sequelae.

Recommendations

1. For an episode of priapism lasting 4 hours or longer, initiate interventions to include
   - vigorous oral or intravenous hydration and oral or intravenous analgesia (***Strong Recommendation, Low-Quality Evidence***); and
   - consultation with a urologist who can perform further evaluation and intervention for symptoms which do not remit with initial conservative medical management. (***Consensus–Panel Expertise***)
2. Do not use transfusion therapy for immediate treatment of priapism associated with SCD. (***Moderate Recommendation, Low-Quality Evidence***)
3. Consult with a hematologist for possible preoperative transfusion if surgical intervention is required. (***Consensus–Panel Expertise***)

Hepatobiliary Complications

Background

Biliary tract abnormalities are common in people with SCD in general and in those with HbSS in particular. These abnormalities include cholelithiasis, acute cholecystitis, biliary sludge, and acute choledocholithiasis.[210,211] Hemolysis of any etiology results in increased secreted unconjugated bilirubin that tends to precipitate and leads to gallstones and sludge.

Cholelithiasis and Acute Cholecystitis

Ultrasound-identified rates of gallstones in people with SCD increase with age from 12 percent in those aged 2 to 4 years to 43 percent by 15 to 18 years of age.[212,213] In adults with SCD, the prevalence of gallstones can be as high as 70–75 percent.[214-217] Although gallstones are usually asymptomatic, they can be associated with acute infection and inflammation involving the gallbladder, and they may also lead to obstruction of the cystic or bile ducts and acute pancreatitis.