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Artículo:

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New Directions in Sickle Cell Disease

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Children with sickle cell disease are at risk for several unpredictable complications. In the past few years, several developments have brightened the outlook for patients with sickle cell disease. These include:

1. The therapeutic benefit of hydroxyurea in reducing the frequency of painful episodes and acute chest syndrome
2. The use of transcranial Doppler ultrasound to identify children at risk for CVA prior to the event
3. The introduction of a conjugate pneumococcal vaccine that will theoretically reduce the risk of pneumoccocal infection and sepsis in these susceptible children

Hydroxyurea

Vaso-occlusive complications of sickle cell disease are due to deformation of red blood cells, especially in the small blood vessels. The polymerization of deoxygenated HbS results in hemoglobin precipitation and formation of the characteristic, irreversibly sickle d cell. Interventions that cause a reduction in the intraerythrocytic concentration of Hb S have been shown to reduce the rate of sickle cell formation. One way to dilute the intraerythrocytic Hb S concentration is to increase the concentration of HbF. A number of antitumor agents including 5-azacytadine, cytarabine and, hydroxyurea, have been shown to increase the production of fetal hemoglobin in nonhuman primates as well as in humans.

Hydroxyurea increases the number of red cell that contain hemoglobin F (F cells), the percentage of HbF and the amount of Hb F, per F-containing cell. A prospective, double-blind, placebo-controlled clinical trial in adults with sickle cell disease (>18 years old) showed a reduction in the number of episodes of severe pain and acute chest syndrome. This study paved the way for FDA approval of hydroxyurea for adults for treatment of painful episodes and acute chest syndrome. More recent work in children (5–18 years of age) has shown that, at the same doses used in adults, hydroxurea is well-tolerated in children and that similar hematologic toxicities are to be expected. The starting dose of hydroxyurea is 20 mg/kg administered orally, once per day. Hematologic toxicities are to be expected and must be carefully monitored.

Transcranial Doppler (TCD)

Stroke is one of the most difficult complications of sickle cell disease. The prevalence of clinically apparent stroke is estimated between 8–11% in childhood. The risk of silent infarction, detected by MRI scanning, is even higher. Most sickle cell-related strokes of childhood are infarctive due to occlusive vasculopathy. Until recently, strokes were treated only after a child was noted to have a clinically obvious neurological deficit. Long-term management for prevention of recurrence of stroke is best accomplished with red blood cell transfusions, maintaining Hb S% concentration at <30%.

The recent demonstration that transcranial Doppler ultrasound (TCD) can identify a group of children at high risk for stroke has provided a means for implementing stroke prevention. TCD measures flow velocity through cerebral vessels. High (>200 cm per second) flow velocities detected in either distal ICA or proximal MCA are associated with a significant risk of subsequent stroke. Once identified, at-risk children can be started on a chronic transfusion program for primary stroke prevention.

Pneumoccal vaccination

S. pneumoniae infection is a significant cause of morbidity and mortality in young children with sickle cell disease. In those without penicillin prophylaxis or pneumococcal vaccination, the risk of invasive disease is 30 to 100 times greater than in healthy children.

Routine administration of penicillin prophylaxis reduces the risk of pneumoccal infection. Immunization with the 23 serotype vaccine at the age of 2 years with

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a booster 2 years later provides protective antibodies against the 23 serotypes represented in the vaccine. Although the combination of penicillin prophylaxis and pneumococcal immunization has resulted in fewer cases of pneumococcal disease, sepsis can still occur in the immunized patient on prophylaxis; infants remain at the greatest risk. Recently, a conjugate vaccine has been licensed for immunization of all infants in the U.S. This 7-valent pneumococcal (PCV-7) vaccine is bound to a cross-reacting diphtheria variant and is marketed under the name Prevnar. Immunization of infants with sickle cell disease with the conjugate vaccine has been shown to cause a rise in antibody concentrations to levels at least as high as those observed in infants without sickle cell disease. The currently recommended schedule for young infants with sickle cell disease is three doses of Prevnar 6–8 weeks apart followed by a booster at the first birthday.

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