Sickle Cell Disease Treatment:

Important Information for Patients and Health Care Providers



Sickle cell disease (SCD) is a group of genetic blood disorders that can cause complications ranging from mild, to serious, and even deadly. But many people with SCD are living longer, healthier lives than in the past because more is known about how to prevent and treat dangerous complications. This booklet is designed to help SCD patients and families, together with their health care providers, make informed decisions about their care. Please talk to your primary care doctor or hematologist about any questions or concerns you have.

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Introduction

SCD is group of genetic disorders in which abnormal hemoglobin causes problems with the red blood cells that carry oxygen throughout the body. Normal red blood cells are round, flexible, and slippery and flow easily through small blood vessels. The red blood cells of persons with SCD become quarter-moon or crescent shaped, sticky and rigid when they give up oxygen in the small blood vessels. Sickle red blood cells do not live as long (15-30 days) as normal red blood cells (120 days). This shorter life span of the red cells causes anemia or low hemoglobin level, which may cause tiredness, shortness of breath or decreased energy. The sickled cells can also block the flow of blood in various parts of the body causing pain, infection, acute chest syndrome (severe pneumonia), stroke and major damage to organs. Other health problems include difficulty breathing, jaundice, and delayed growth and development in children.

SCD is found throughout the world. It is most common in people whose ancestors come from Africa, Mediterranean countries (such as Turkey, Greece, and Italy), the Middle East, India, Central and South America and the Caribbean. In the United States approximately 100,000 people have SCD and it is most common in African Americans and Hispanics. There are four common types of sickle cell disease with somewhat different clinical problems and family histories. Sickle cell anemia (Hb SS) and sickle beta zero thalassemia (Hb S β^o Thal) tend to have more problems and hemoglobin SC disease (Hb SC) and sickle beta plus thalassemia (Hb S β^+ Thal) are somewhat milder in childhood.

People with SCD in the United States are living longer, healthier lives because of advances in treatment and prevention of complications. These include:

1. Life-threatening infections in infants and children can be prevented through newborn screening for the disease, family education, immunizations, and use of penicillin.
2. Serious complications of infection can be avoided through early treatment and good general health care.
3. People at high risk for stroke due to SCD can be identified through trans-cranial Doppler ultrasound screening tests and given treatments to reduce their risk of having a stroke.
4. Use of hydroxyurea drug treatment can reduce the severity of anemia, reduce episodes of pain and acute chest syndrome, and increase longevity for people with SCD.

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Prevention of Life-Threatening Infections with Immunization & Penicillin

Immunizations



Infections are the major cause of death in infants and young children with SCD, with children under five years of age at highest risk. One key way to prevent infections is through immunizations, which help the body to build natural defenses against bacteria and viruses. Children with SCD should receive all the routine immunizations recommended for all children. Recommended schedules for these routine immunizations change from year to year but are updated annually by the CDC and the American Academy of Pediatrics, and are well known to most primary care providers. Because infections with pneumococcal and meningococcal bacteria are especially dangerous, additional immunizations for these two infections are also recommended for children with SCD beginning at age two years. The pneumococcal polysaccharide vaccine (PPV) is given at 2 years and repeated five years later. The meningococcal conjugate vaccine is also given at 2 years and repeated 2 months later. Parents should keep their child's immunization record, and insist they receive their immunizations on schedule.

Prophylactic Penicillin

Additionally, the daily administration of oral penicillin has been shown to reduce the incidence of severe pneumococcal infection in children with SCD under five years of age. A leading study published in 1986 found that children treated with penicillin had an 84% reduction in the incidence of life-threatening infection, compared with those not taking penicillin. This study concluded that children should be screened through a newborn screening program for hemoglobin disorders, and those with SCD should receive prophylactic therapy with oral penicillin by 2 months of age in order to decrease morbidity and mortality from pneumococcal septicemia. Thus, Immunizations, and daily penicillin reduce the chance that fatal infections will occur. However because they do not provide protection against all life-threatening infections, it also is important that parents watch their children carefully for signs of infection, and seek urgent medical care for fever.

Prevention of Stroke with Trans-Cranial Doppler (TCD) Ultrasound Screening & Transfusions

Trans-Cranial Doppler

Children with Hb SS and Hb S β^0Thal are 300 times more likely than other children to have a stroke. These strokes are caused by damage to large arteries in the brain which eventually leads to blockage of blood flow or bleeding in the brain. Strokes can permanently affect one's ability to move his or her arms and legs, speak, remember, and learn. Once a child with SCD has had a stroke, their chance of having a second stroke is about 80%, unless they undergo regular blood transfusions. Strokes can also cause death.

Trans-Cranial Doppler (TCD) is a test that uses ultrasound (sound waves) to measure the speed of blood flow in the main blood vessels of the brain to determine whether a child with Hb SS or Hb S β^0Thal is at high risk for having a stroke. Regularly scheduled blood transfusions can then be used to prevent a first stroke. Children with Hb SS and Hb S β^0Thal should begin having annual TCD screening tests at age two years until age sixteen or more often dependent upon the findings. TCD screening is unnecessary and not recommended for children with Hb SC and Hb S β^+ Thal.

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Chronic Transfusions

Treatment with regularly scheduled (usually monthly) blood transfusions can prevent stroke by replacing abnormal sickle blood cells with normal red blood cells. Therefore, chronic transfusions are usually recommended for children who have had a stroke or are identified as being at high risk for stroke through abnormal TCDs, It should be noted, however, that while transfusion therapy can be very effective in preventing strokes, transfusions can cause a number of complications. The following are risks associated with transfusion therapy:

- Hemolytic and allergic reactions to transfusions.
- Development of antibodies against transfused red cells that can cause potentially severe transfusion reactions and may make it harder to find the best units for transfusions in blood banks.
- Iron overload that can damage the liver, heart and other organs. To prevent this organ damage, patients who receive many transfusions need to take a drug to remove the excess iron.
- Transfusion associated infections.

Hydroxyurea

Hydroxyurea, a chemotherapeutic (cancer treatment) drug, has been shown to reduce episodes of pain and acute chest syndrome, reduce anemia and need for transfusion, and improve the quality of life in children and adults with Hb SS and Hb S β^0Thal. There is presently no data to show it benefits individuals with Hb SC and Hb S β^+ Thal. There is now evidence from around the World that individuals with Hb SS and Hb S β^0Thal who are taking hydroxyurea are living longer than those who are not on the drug.

Fetal hemoglobin is the hemoglobin that we all have before we are born, and in persons with SCD, it blocks the sickling of the red blood cells. After birth, the production of fetal hemoglobin decreases, and this benefit is reduced. Hydroxyurea was first tested on SCD in 1984 and has been shown to increase fetal hemoglobin levels in persons with SCD, making the red blood cells less likely to sickle. Hydroxyurea also reduces the white blood cells, platelets, and stickiness of red blood cells that may also be of benefit. Therefore SCD patients on hydroxyurea may experience less of the painful episodes, acute chest syndrome, anemia, stroke, and other health problems associated with SCD.

Benefits

There is still much to be learned about hydroxyurea therapy for SCD patients, but its noted benefits include:

- Decreased frequency of pain episodes
- Less pain and feeling healthier
- Reduced anemia
- Prevention of acute chest syndrome (ACS)
- Decreased need for hospitalization
- Prolonged life.

Potential Side Effects



Hydroxyurea is taken orally and most individuals taking the drug have no side effects and feel better than before they started the drug. The most common reported side effect of hydroxyurea is mild nausea or upset stomach; though most patients have this only for the first few weeks, and taking the medicine at bedtime can reduce these effects. Hydroxyurea also slows production of red blood cells, white blood cells and platelets. The anemia improves because the red blood cells last longer in the blood. Too much reduction in red cell production by hydroxyurea could lead to more severe anemia. Mild suppression of the white blood cells and platelets may also be of benefit but severe reduction can lead to infection and bleeding. Because of this, hydroxyurea dosing needs to be carefully adjusted and blood cell counts monitored every two to four weeks to make sure that the suppression does not become severe. If the blood counts become too low, the hydroxyurea is usually given in a lower dose or stopped for a few weeks and restarted at a lower dose.

Less common side effects of hydroxyurea include allergic reactions, thinning hair, darkening skin or nails, and, rarely, changes in liver or kidney function. These are usually reversible when the drug is stopped. Because this is chemotherapy, there was concern that long-term use could increase the risk of cancer or leukemia. There is no evidence that this is true in individuals with sickle cell disease. It is important that males or females not conceive a child while they are on hydroxyurea in order to avoid the possibility of having a child with birth defects. It is recommended that all individuals on hydroxyurea abstain from sex or use highly effective methods of birth control. So far, the babies born to mothers on hydroxyurea for SCD have not had birth defects. However, it is recommended that hydroxyurea be stopped for at least six weeks before conceiving a baby to avoid this possibility. Another possible effect among men taking hydroxyurea is decreased sperm counts or sperm movement, which may be temporary and reversible.

Some people have worried that hydroxyurea treatment will slow the growth or development of children with SCD. So far, studies of hundreds of children over a few years have not revealed growth and development problems, and newer evidence suggests that hydroxyurea may help reduce or delay the neurocognitive defects associated with SCD.

Bottom Line

Hydroxyurea therapy for a child or adult with sickle cell disease has many possible benefits, several known risks, and potential long-term side effects. All of the benefits and risks will not be known until more research on hydroxyurea treatment is done in sickle cell and large numbers of patients are followed for years on the drug. Most physicians knowledgeable about sickle cell disease presently recommend that most individuals with Hb SS and Hb S β^0Thal consider using hydroxyurea. We strongly recommend individual discussions of the risks and benefits of hydroxyurea with a physician knowledgeable about use of hydroxyurea in SCD to help decide whether you or your child should take the drug.

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Find Out More

Resources and Support:

- Sickle Cell Foundation of Georgia, Inc.: 404-755-1641; toll-free 800-326-5287; sicklecellga.org
- Sickle Cell Information Center: scinfo.org
- CDC Information: www.cdc.gov/ncbddd/sicklecell

Comprehensive sickle cell centers:

- Children's Healthcare of Atlanta: 404-785-1200
- Georgia Regents University: 706-721-2171
- Grady Health System: 404-616-3572

Newborn Screening Program:

- Georgia Department of Public Health: 404-657-4143; health.state.ga.us/programs/nsmscd

For more information and resources, visit: http://ghpc.gsu.edu/project/hemoglobin-disorders-data-coordinating-center/

A 2014 NIH Expert Panel Report includes evidence-based guidelines that recommended increased adoption of hydroxyurea in the care of individuals with SCD.

Update: See the 11/19/2014 media advisory from NIH on new, positive findings regarding hydroxyurea use with TCD to reduce stroke risk.

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