Practice Perspective

The Management of Sickle Cell Disease in a Primary Care Setting

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Abstract

With increasing burdens placed on Primary Care Physicians in the prevention and management of Sickle Cell Disease (SCD), it is imperative that there is some basic understanding of the same. Needless to say, its management is a multifocal, multidisciplinary approach which includes a collaborative effort between patients, family members and the healthcare team.Primary Care Physicians must be familiar with the pathophysiological processes, diagnostic evaluation, and current standard of care, new treatment options, clinical research advances and medical management of sickle hemoglobinopathies and their complications.The guidelines should include new born screening and assessment, accessible medical records for those diagnosed with SCD, system support and prevention, management of complication and crisis periods and home management (dietary and lifestyle modifications).

Keywords: Primary care, screening, management, vaso-occlusive, thalassemia, sickle cell trait, fetal hemoglobin, hemoglobin, Iron, Total Iron-Binding Capacity, Unsaturated Iron-Binding capacity, C-Reactive protein, erythrocyte sedimentation rate, comprehensive metabolic panel

Introductory Statement

With increasing burdens placed on primary care physicians in the prevention and management of sickle cell disease (SCD), it is imperative that there is some basic understanding of this condition. Its management is a multifocal, multidisciplinary approach which includes a collaborative effort between patients, family members, and the healthcare team.

Primary care physicians must be familiar with the pathophysiological processes, diagnostic evaluation, and current standard of care, new treatment options, clinical research advances, and medical management of sickle hemoglobinopathies and their complications.

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Let us Review the Basics

Fetal hemoglobin or HB(F) is the main oxygen carrying protein in a fetus during the last 7 months of gestation and up to 6 months after birth. It has a greater binding capacity for oxygen. HB(F) production is basically switched off after birth and the production of Hemoglobin A ensues. Children with SCD however produce a defective form of hemoglobin called Hemoglobin S. Hemoglobin S unfortunately clumps together and causes the red blood cells to become "sickled" shaped. This adversely impedes circulatory flow which produces the painful vaso-occlusive episodes that classically present during a sickle cell crisis. There are a variety of gene mutations a part from SCD. They include: Hemoglobin AS/Sickle Cell Trait (one sickle gene (HbS) and one HbA gene), sickle-hemoglobin C disease (HbSC), sickle beta-plus-thalassemia (HbS/β+), and sickle beta-zero-thalassemia (HbS/β0). The thalassemias are a group of disorders in which the normal hemoglobin protein is produced in lower amounts than usual. In other words, there is an issue with quantity and not quality.[1]

Screening and Diagnosis

The hallmark screening method for SCD and it variants is Hbelectrophoresis; an electric field applied to a gel matrix is used

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to separate the various types of hemoglobin. A qualitative and quantitative analysis is then done to determine if there is normal Hemoglobin A or one of the defective hemoglobinopathies. A recent blood transfusion may obscure the accuracy of the test.

Prevention and Management

So SCD has been identified; what next? The primary drug used in SCD is hydroxyurea/hydroxycarbamide;[2] an antineoplastic drug used to increase HB(F) levels. Recent studies have shown that combined therapy with recombinant erythropoietin greatly enhances its effects and is thus considered superior over monotherapy.[3] Standard medical management should never be abandoned unless appropriately advised by your qualified health care provider. It is important for the health care provider to be aware of the side effects of hydroxyurea. These include gastrointestinal problems, headache, drowsiness, and skin and nail changes. On rare occasions, there have been reports of hallucinations and seizures. Long-term use of hydroxyurea (3 years) may induce leg ulcers in certain patients. There is some concern that it may also pose a slight long-term risk for cancers, such as leukemia, however, more research needs to be done in this area. Hydroxyurea should be avoided during pregnancy.

The Social and Emotional Impact

Having to deal with the negative impacts of SCD can have an emotionally devastating effect on both the sufferer and their family. This affects self-esteem, finances, academics, and social isolation, particularly for children who are unable to function normally because of pain. Appropriate referrals for counseling are prudent. Many support organizations can also offer great help for sufferers.

There are a number of preventative approaches and lifestyle changes that can be used to minimize the complications of SCD. The following list is in no way exhaustive but instructive.

1. Regular physical examinations perhaps every 3-6 months is recommended. This should include referrals to the ophthalmologist. Other team players may include a hematologist, internist, urologist, and pediatrician; especially where refractory complications arise. Routine examinations may include a complete blood count (CBC), urine test, other tests to monitor the function of the organs of the body, Comprehensive Metabolic Panel (CMP), electrolytes, Erythrocyte Sedimentary Rate (ESR), C-Reactive Protein (CRP), and iron studies. These iron studies may include iron, ferritin, Unsaturated Iron-Binding Capacity (UIBC), Total Iron-Binding Capacity (TIBC), and percent saturation of transferrin which may identify different aspects of the body's iron storage and usage. Iron studies are important to SCD patients who get frequent blood transfusions as the risk increases for iron overload. From age 2 years, a child should get regular transcranial ultrasound, which measures blood flow in the arteries of the head and neck. If test results show a high chance for stroke, the patient may get blood transfusions to lower the risk.
2. Adjunctive treatment with Vitamin B6, B12 and Folic acid play an important role in the reduction of homocysteine. When moderate to severe anemia occurs, a blood transfusion may be necessary. Painful episodes can me managed with a variety of the non-steroid anti-inflammatories available in the market. Acetaminophen is also a popular choice. Aspirin should not be given to children. It is recommended that the child's immunization status be kept up to date.
3. Because of the increased risk of infection, crowded environments should be avoided.
4. Dehydration increases the viscosity of the blood. Adequate fluid intake is crucial.
5. Rest and warmth is important. Adequate rest reduces the demand on the body for oxygen. Low impact exercise provides the benefit of fitness without the risk of vaso-occlusion due to increasing demands on the body. High altitudes should be avoided when it can be.
6. There have been studies indicating some benefits of resveratrol (a compound found in the skin of red grapes) have shown similar benefits to hydroxyurea; however, research is ongoing and adjunctive treatment is preferred over replacement.[4]
7. Diet plays a very important role in the prevention of SCD crisis episodes. Diets rich in leafy green, red, and yellow vegetables may be useful for SCD crisis prevention. Some studies reveal that the use of vitamin C and E supplements reduces the formation of sickled cells. In addition, there seems to be some benefits in using omega 3 fatty acids, which help to maintain the integrity of cell membranes.[5] Weight management and stress reduction is very important.
8. Avoid smoking or environment where smoking is practiced. SCD patients tend to suffer from acute chest syndrome, a common cause of death in SCD patients. Other complications may include priapism (painful, unprovoked and prolonged erection from trapped blood within the penis), gall bladder disease, Legg-Calve Perthes disease/avascular necrosis/osteonecrosis, fatigue, anemia, dactylitis (swelling/inflammation of the hands and/or feet, arthritis, leg ulcers, organ damage (particularly the lung and heart), aseptic necrosis and bone infarcts, hepatomegaly, other options have been exhausted preventative or therapeutic cholecystectomies, rehydration, fluid drainage from the penis, antibiotic treatments, hip replacements, and splenectomies may be employed.
9. Daily antibiotic treatment is recommended for children age 2 months to 5 years as infection prophylaxis; particularly pneumococcal and hemophilus bacterial infections. Vaccination against pneumococcal infection is generally recommended. There is also an increased risk of developing pneumonia, meningitis, and osteomyelitis.

Other Studies

There are some research studies that are inconclusive; however, empirical data support the following supplements:

1. Zinc sulfate appears to help reduce red blood cell dehydration.
2. Magnesium protects against potassium and water loss in sickle cells.
3. Nitric oxide is a substance that helps to relax the blood vessels. The amino acid arginine is converted into nitric oxide. There is a reduction of nitric oxide in sufferers of SCD which further contributes to vaso-occlusive events.
4. L-glutamine is an ordinary amino acid that has shown some success in improving the state of red blood cells in SCD patients.

Bone Marrow or Stem Cell Transplantation

Up to 80-85% of patients who receive bone marrow or stem cell transplantation remain disease free. The diseased bone marrow and stem cells are destroyed and replaced with healthy genetically matched bone marrow. This allows for healthy hemoglobin to be produced. However, only about 7% meet the criteria for this therapeutic "cure." These include patients with sickle pulmonary disease, severe symptoms but no long-term organ or neurological damage, available genetically matched donor, history of stroke and reoccurring acute chest syndrome or vaso-occlusive crises. The risks and limitations of this procedure should be explained to the patient. These risks and complications include increased risk for cancer and infertility, iatrogenic consequences, bleeding, severe infection, pneumonia, and graft-versus-host disease.

Conclusion

Sickle cell disease can have a devastating effect on the quality of life and greatly reduce life expectancy in sufferers. As a primary care physician, there is a great responsibility at hand toward helping with the management of this disorder. Of course, there are many limitations for some doctors who lack the resources necessary to carry out important investigations and/or monitoring of affect patients. In some situations, this responsibility increased where specialist are not readily available. Having a good understanding of the mechanisms and management of SCD can go a long way in improving the quality of life and reducing premature mortality of SCD sufferers.

A quick recap

1. Adequate fluid intake is important.
2. Painful crises should be managed with NSAIDs (but not aspirin as it aggravates abdominal pain).
3. Diets rich in leafy green, red, and yellow vegetables may be useful for SCD crisis prevention.
4. Diet void of refined foods to include sugars, fried food, and alcohol.
5. Smoking cessation.
6. Crowded and unclean environments and high altitudes are to be avoided.
7. Prophylactic antibiotic treatment is generally recommended.
8. Referral to an appropriate specialist is indicated when condition is refractory to standard treatments as outlined within this article.

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