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Review Article

Sickle Cell Anaemia: A Review

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Abstract: This paper reviews Sickle cell anaemia.Sickle cell anaemia is a homozygous form of HbS(HbSS).This result from single point replacement of glutamine by valine at position 6 of β- globin chain.This reduces solubilty of the red cells which in turn leads to polymerisation and vaso-occlussion in the vasculature. The β - globin gene is found on the short arm of chromosome 11. The association of two mutant β -globin subunits forms haemoglobin S (HbS). Under low - oxygen conditions, the absence of a polar amino acid at position of six of the β - globin chain promotes the non - covalent polymerization of haemoglobin, which distorts red blood cells into a sickle shape and decreases their elasticity. In sickle cell disease, low oxygen tension promotes red blood cell sickling and repeated episodes of sickling damage the cell membrane and decreases the cell's elasticity. These cells fail to return to normal shape when normal oxygen tension is restored. As a consequence, these rigid blood cells are unable to deform as they pass through narrow capillaries, leading to vessel occlusion and Ischaemia. The actual anaemia of the illness is caused by haemolysis, the destruction of the red cells inside the spleen.Those suffering from this illness are present with chronic anaemia which those with normal adult haemoglobin genotype will not survive because of the misshape of the cells leading to destruction of the cells at the spleen.
Keywords: Sickle cell disease, Sickle cell anaemia,pathophysiology,Genetics of Sickle cell anaemia,Inheritance,Crisis and Management.

INTRODUCTION

Sickle - cell disease or sickle cell anaemia (or depanocytosis) is a life -long blood disorder characterized by red blood cells that assume an abnormal, rigid, sickle shape. Sickling decreases the cells' flexibility and results in a risk of various complications. The sickling occurs because of a mutation in the haemoglobin gene. Life expectancy of 42 and 48 years for males and females, respectively [1]. Sickle cell disease, usually presenting in childhood, occurs more commonly in people from parts of tropical and sub -tropical regions where malaria, since the infestation of the malaria plasmodium is halted by the sideling of the cells which it infests. The prevalence of the disease in the United States is approximately 1 in 5,000, mostly affecting African Americans according to National institute of Health.

HISTORY OF SICKLE CELL ANAEMIA

This collection of clinical findings was unknown until the explanation of the sickle cells in 1904 by the Chicago cardiologist and a professor of medicine k James B. Herrick (1861 - 1954) whose intern Ernest Edward Irons (1877 -1959) found "peculiar elongated and sickle - shaped" cells in the blood of Walter Clement Noel, a 20 - year - old first-year dental student from Canada after Noel was admitted to the Chicago Presbyterian Hospital in December 1904 suffering from anaemia. Noel was readmitted several times over the next three years for "Muscular rheumatism" and "bilious attack". Noel completed his studies and returned to the capital of Grenada to practice dentistry. He died of pneumonia in 1906 and is buried in the catholic cemetery as Sauteurs in the north of Grenada.

The disease was named "Sickle cell anaemia" by Vernon Mason in 1922. However, some elements of the disease have been recognized earlier: A paper in the southern journal of medical pharmacology in 1846 described the absence of a spleen' in the autopsy of a runaway slave. The African medical literature reported this condition in the 1870s, where it was known locally as ogbanjes ("Children who come and go") because of

the very high infant mortality rate caused by this condition. A history of the condition tracked reports back to 1670 in one Ghanian family [2, 3].

Linus pauling and colleagues were the first, in 1949, to demonstrate that sickle cell disease occurs as a result of an abnormality in the haemoglobin molecule. This was the first time a genetic disease was linked to a mutation of a specific protein, a milestone in the history of molecular biology, and it was published in their paper "sickle cell Anaemia, a molecular Disease".

The origin of the mutation that lead to the sickle cell gene was initially thought to be in the Arabian Peninsula, spreading to Asia and African. It is now known, from evaluation of chromosome structures, that there have been at least four independent mutational events, three in Africa and a fourth in either Saudi Arabia or central India. These independent occurred between 3,000 and 6,000 generations ago, approximately 70 - 150,000 years [3].

PATHOPHSIOLOGY OF SICKLE CELL ANAEMIA

Sickle cell anaemia is caused by a point mutation in the β - globin chain of haemoglobin, causing the amino acid glutamic acid to be replaced with the hydrophobic amino acid valine at the sixth position. The β - globin gene is found on the short arm of chromosome 11. The association of two mutant β - globin subunits forms haemoglobin S (HbS). Under low - oxygen conditions, the absence of a polar amino acid at position of six of the β - globin chain promotes the non - covalent polymerization of haemoglobin, which distorts red blood cells into a sickle shape and decreases their elasticity. The loss of red blood cell elasticity is central of the patho physiology of sickle cell disease. Normal red blood cells are quite elastic, which allows the cells to deform to pass through capillaries. In sickle cell disease, low oxygen tension promotes red blood cell sickling and repeated episodes of sickling damage the cell membrane and decreases the cell's elasticity. These cells fail to return to normal shape when normal oxygen tension is restored. As a consequence, these rigid blood cells are unable to deform as they pass through narrow capillaries, leading to vessel occlusion and Ischaemia..

The actual anaemia of the illness is caused by haemolysis, the destruction of the red cells inside the spleen, because of their misshape. Although, the bone marrow attempts to compensate by creating new red cells, it does not match the rate of destruction [4]. Healthy red blood cells typically live 90 - 120 days, but sickle cells only survive 10-20 days according to Emedicine.

GENETICS OF SICKLE CELL ANAEMIA

A single amino acid change causes haemoglobin protein to form fibres. Sickle cell gene mutation probably arose spontaneously in different geographic areas, as suggested by restriction endo nuclease analysis. These variants are known as Cameroon, Senegal, Benin and Saudi- Asian. Their clinical significance springs from the feet that some of them are associated with higher HbF levels, example Senegal and Saudi- Asian variants, and tend to have milder [5].

In people heterozygous for HbS, the polymerization problems are minor, because the normal allele is able to produce over 50% of the haemoglobin. In people homozygous for HbS, the presence of long-chain polymers of HbS distort the shape of the red blood cell, from smooth dount-like shape to ragged and full of spikes, making it fragile and susceptible to breaking within capillaries. Carriers have symptoms only if they are deprived of oxygen or while severely dehydrated. Under normal circumstances, these painful crises occur 0.8 times per year per patient. The sickle-cell disease occurs when the seventh amino acid (if we count the initial methionine), glutamic acid, is replaced by valine to change its structure and function [6]. The gene defect is a known mutation of a single nucleotide (A to T) of the p-globin gene, which results in glutamate to be substituted by valine at position 6.Haemoglobin S with this mutation are referred to as HbS, as opposed to the normal adult HbA. The genetic disorder is due to the mutation to a single nucleotide, from a GAG to GTG codon mutation. This is normally a benign mutation, causing no apparent effects on the secondary, tertiary, or quaternary structure of haemoglobin. What it does allow for, under conditions of low oxygen concentration, is the polymerization of the HbS itself. The deoxy form of haemoglobin exposes a hydrophobic patch on the protein between the E and F helices. The hydrophobic residues of the valine at position 6 of the beta chain in haemoglobin are able to associate with the hydrophobic patch, causing haemoglobin S molecules to aggregate and form fibrous precipitates [7].

The allele responsible for sickle cell anaemia is autosomal recessive and can be found on the short arm of chromosome II. A person that receives the defective gene from both father and mother develops the disease; a person that receives one defective and one healthy allele remains healthy, but can pass on the disease and is known as a carrier. If two parents who are carriers have a child, there is a 1 - in - 4 chance of their child's developing the disease and a 1 - in - 2 chance of their child's being just a carrier since the gene is incompletely receive, carriers can produce a few sickled red blood cells, not enough to cause symptoms, but enough to give resistance to malaria. Because of this, heterozygotes have a higher fitness than either of the homozygotes. This is known as heterozygotes advantages.

Due to the adaptive advantage of the heterozygotes, the disease is still prevalent, especially among people with recent ancestry in malarial –stricken areas, such as Africa, the Mediterranean, India and the Middle East [8]. Malaria was historically endemic to southern Europe, but it was declared eradicated in the mid 20"[1] century with the exception of rare sporadic cases.

The malaria parasite has a complex life cycle and spends part of it in red blood cells. In a carrier, the presence of malaria parasite causes the red blood cells with defective haemoglobin to rupture prematurely making the plasmodium unable to reproduce. Further, the polymerization of Hb affects the ability of the parasite to digest Hb in the first place. Therefore, in areas where malaria is a problem, people's chances of survival actually increase if they carry sickle cell trait.

In the USA, where there is no endemic malaria, the prevalence of sickle - cell anaemia among blacks is lower (about 0.25%) than in West Africa (about 4.0%) and is felling. Without endemic malaria from Africa, the condition is purely disadvantageous, and will tend to be bred out the affected population. Another factor limiting the spread of sickle - cell genes in North America is the absence of cultural proclivities to polygamy.

INHERITANCE OF SICKLE CELL ANAEMIA

Sickle cell anaemia are inherited from parent the same way as blood type, hair colour and texture, eye colour and other physical traits. The type of haemoglobin a person makes in the red blood cells depend upon what haemoglobin genes are inherited from his parents.

1. If one parent has sickle cell anaemia (SS) and the other has sickle cell trait (AS), there is a 50% chance of a child's having sickle cell disease (SS) and a 50% chance of a child's having sickle cell trait (AS).
2. When both parents have sickle cell trait (AS), they have a 25% chance of a child's having sickle cell disease (SS).

CLASSIFICATION OF SICKLE CELL DISEASE

Sickle cell anaemia is the name of a specific form of sickle cell disease in which there is homozygosity for the mutation that causes HbS. Sickle cell anaemia, is also referred to as "HbSS", "SS disease", "haemoglobin S" or permutations thereof. In heterozygous people, only 1 sickle gene and one normal adult haemoglobin gene, it is referred to as "HbAS" or sickle cell trait. Other rarer forms disease include sickle haemoglobin C disease (HbSC), sickle beta - plus thalassemia (Hbs/B) and sickle beta - zero – thalassemia (HbS/P). These other forms of sickle cell disease are compound heterozygeous states in which the person has only one copy of another abnormal haemoglobin allele. The term "disease" is applied since the inherited abnormality causes a pathological condition that can lead to death and severe complications. Not all inherited variants of haemoglobin are detrimental, a concept known as genetic polymorphism.

SIGNS AND SYMPTOMS

Sickle cell disease may lead to various acute and chronic complications, several of which are potentially lethal. VASO - OCCLUSIVE crisis

The vaso -occlusive crisis is caused by sickle - shaped red blood cells that obstruct capillaries and restrict blood flow to an organ, resulting in ischaemia, pain and often organ damage. The frequency, severity, and duration of these crises vary considerably.

HAEMOLYTIC CRISIS

Premature destructure of sickle erythrocytes occur both extra vascularfy and intravascularly. Extra vascular haemolysis results from abnormalities of the sickle cell that permit its recognition and phagocytosis by macrophages (Hebbel, and Miller, 1984) and from impaired deformability of sickle red cells, enabling their physical entrapment [9].

Elevations of free plasma haemoglobin in patients suggest that one-third the total haemolysis in sickle cell anaemia is intravascular [10]. One mechanism of intravascular haemolysis is sickling - associated exo vesciculation [11,12] of vesicles rich in phosphatidy linositol anchored membrane proteins [13] depleting the cell of the complement regulatory proteins DAF and MIRL and leaving the cells susceptible to complement - mediated intravascular lysis [14]. Another component of intravascular haemolysis is increased mechanical fragmentation of sickle cells [15]; which accounts for the accelerated haemolysis of sickle cell patients during exercise [15].

Haemo globinuria and oliguria may be present. Pallor develops rapidly and icterus is common. Frequently the pallor, listlessness and mild icterus develop more insidiously. The urine may be dark in colour due to the presence of excess urobilinogen. The anaemia is usually ortho chromic but it may be either normocytic or macrocytic. Reticulocytosis is often marked and there may be many erythroblasts in the peripheral blood [16].

SEQUESTRATION CRISIS

In sequestration crisis, there is massive pooling of red blood cells in visceral organs especially splenomegaly may be marked but sometimes disappears in later childhood, splenectomy is indicated when there is hypersplenism [17].

IMMUNE DEFICIT

The propensity of children with sickle cells disease to streptococcus pneumoniae infection is related to impaired splenic function and diminished serum-

opsonizing activity [18]. The decreased litre of antibody against S. pneumoniae antigens following splenectomy in individuals without sickle cell disease [19] suggest that splenic hypo function may mediate the opsonic deficiency of sickle cell disease. This conclusion is consistent with the earlier loss of splenic function in genotypes characterized by more rapid haemolysis [20], the correlation between free plasma haemoglobin levels and the rate of consumption of alternate complement pathway components [21], and the suppression of B - lymphocyte activity of phosphatidyl serine rich viscles [22,23].

LIFE EXPECTANCY

In 1973 Diggs reported that the mean survival of patients with sickle cell disease was 14,3 years; in 1994 Platt et al reported a life expectancy of 42 years for men and of 48 years for women with sickle cell anaemia. Prolonged survival is the result of improved general medical care than of successful anti sickling therapy. The ability of prophylactic penicillin therapy to prevent mortality from pneumococcal sepsis may now be having an impact on survival [24].

CHRONIC ANAEMIA

Chronic hemolytic anaemia is a hallmark of sickle cell disease. Sickle erythrocytes are destroyed randomly with a mean life span of 17 days [25]. In addition erythropoietin levels are inappropriately low [26], suggesting the presence of subclinical renal disease.

EXACERBATIONS OF ANAEMIA

Haemolytic anaemia may be exacerbated by any of several events: aplastic crisis, and acute splenic sequestration or, less commonly, sequestration in other organs, chronic renal disease, bone marrow necrosis, deficiency of folic acid or iron and hyperhaemolysis.

ACUTE PAINFUL EPISODE

An episode of acute pain was originally called a "Sickle cell crisis" by Diggs, who used the expression "crisis" to refer to any new rapidly developing syndrome in the life a patient with sickle cell disease. In modern parlance, the term acute painful episode is favored over crisis.

Acute pain is the first symptom of the disease in more than one - fourth of patients, the most frequent symptom after age 2 years [27], and the complication for which patients with sickle cell disease most commonly seek medical attention [28]. The frequency of pain peaks between the age of 19 and 39 years. After the age of 19, more frequent is associated with higher mortality rate [29].

Pain may be precipitated by events such as cold, dehydration, infection, stress, menses, and alcohol consumption, but most painful episodes have no identifiable cause [30]. It can affect any area of the body, may vary from trivial to excruciating, and is usually endured at home without a visit to the emergency department. Painful episodes are bio psycho social events [31] caused by vaso - occlusion in an area of the body having nociceptors and nerves.

PSYCHOSOCIAL ISSUES

Modern insights into the psychosocial adjustment of patients with sickle cells disease are beginning to provide a level of understanding that permits interventional therapy [32, 33]. While most patients with sickle cell disease are generally well adjusted, the disorder is associated with risks of depression, low self - esteem, social isolation, poor family relationships, and withdrawal from normal daily living [34, 35, 36]. Well - adjusted patients have active coping strategies, family support, and support from the extended family unit common in African- American society [37]. Interventional approaches should emphasize recognisizing and reinforcing individual strengths, confronting pathologic behaviour, and establishing coping skill through reinterpreting pain, diverting attention from pain, and using support systems.

GROWTH AND DEVELOPMENT

By 2 years of age, children with sickle cell disease have detectable growth retardation, which affects weight more than height and has no clear gender difference in Platt *et al.;* [38]. Normal height is achieved by adulthood, but weight remains lower than that of controls. Skeletal maturation is also delayed. Girls with sickle disease have retarded sexual maturation and are associated with elevated ganadotrophin levels for the stage of sexual development and with delayed menarche. Boys also have delayed sexual maturation due to primary hypogonadism, hypopituitarism, or hypothalamic insufficiency. It has been possible to restore normal growth by nutritional supplementation [39].

NEUROLOGICAL COMPLICATIONS

The neurological complications occurring in 25% of patients with sickle cell disease include transient ischaemic attacks, cerebral infarction, cerebral haemorrhage, seizures, unexplained coma, spinal cord infarction or compression, central nervous system infection, vestibular dysfunction, and sensory hearing loss [40].

ACUTE CHEST SYNDROME

Symptoms and signs of the acute chest syndrome include dyspnea, chest pain, less commonly abdominal pain, fever, tachypnea, leucocytosis, and a pulmonary infiltrate on the chest radiograph. This event that has an approximate 10% risk of mortality. The process is usually due to infection or vaso -occlusion, but it may also be the result of non cardiogenic pulmonary edema or of pulmonary remobilization from a distant thrombus or bone marrow infarction.

Whatever the etiology, the major danger of the acute chest syndrome is hypoxemia and its attendant wide spread sideling and vaso -occlusion, which create a risk of multi organ failure.

HEPATOBELIARY COMPLICATIONS

The common hepatomegaly and liver dysfunction in sickle cell disease is related to intra hepatic trapping of sickle cells, transfusion acquired infection, and transfusional haemosiderosis. Histological examination of the liver shows centrilobular parenchyrnal atrophy, bile pigment, periportal fibrosis, haemosiderosis, and cirrhosis. In addition to infection with hepatitis viruses, acute hepatic episodes are unique to sickle cell disease.

OBSTERIC AND GYNECOLOGY ISSUES

Although gynecologic complications delayed menarche, dymenoorhea, ovarian cysts, pelvic infection, and fibrocystic disease of the breast are more frequent in women with sickle cell disease, the major reproductive concern in these patients is pregnancy [41]. The fetal complications of pregnancy most of which are related to compromised placenta blood flow, are the increase incidence of spontaneous abortion, intrauterine growth retardation, pre- eclamsia, low birth weight, and mortality; maternal complications includes increased rates of painful episodes, severe anaemia, infections, and mortality. Better fetal and maternal outcomes in recent years are largely due to generally improved antenatal and obstetric care.

RENAL COMPLICATIONS

The kidney is particularly vulnerable to complications in sickle cell disease because of its hypoxic acidocis and hypertonic microenvironment Clinical manifestations result from medullary and distal tubular, proximal tubular, and glomerular abnormalities. Occlusion of the vase, rectae compromises flow to the medulla resulting in an inability to concentrate the urine, 'as well as papillary infarction with haematuria, incomplete renal tubular acidosis, and abnormal potassium metabolism.

PRIAPISM

Priapism has been defined as an unwanted painful erection. It affects nearly two - thirds of males with sickle cell disease, peak frequencies are at 5-13 years and at 21 - 29 years, and it is most likely to develop in patients with lower HbF levels and reticulocyte counts, increased platelet counts, and the HbSS genotype. Onset can be acute, chronic, recurrent, acute or chronic or "stuttering". The engorgement in priapism affects the corpora cavernosum but spares the glans penis and corpus spongiosum. As a result of recurrent priapism, sickle cell patients have abnormal nocturnal penile tumescence and scared fibrotic corpora which may eventuate in impotence.

OCULAR COMPLICATIONS

Ophthalmologic complications can include anterior chamber ischaemia, tortuosity of conjunctival vessels, retina artery occlusion, angioid streaks, proliferative retinopathy, and retinal detachment and haemorrhage [42]. The retina is particularly vulnerable to vaso - occlusion. Routine retinal examination is part of routine health care maintenance for patients with sickle cell disease.

BONE COMPLICATIONS

Chronic tower skull, bossing of the forehead, and fishmouth deformity of vertebrae are the result of extended hematopoietic marrow causing widening of the medullary space, thinning of the trabeculae and cortices, and osteoporosis [43]. The excruciating pain of bone infarction in the "hand - foot syndrome" that occurs around the age of 12 years is often the first symptom of sickle cell disease [44]. This dactylitis resolves spontaneously and is treated with hydration and analgesic. Necrosis occurs with equal frequency in the femoral and humeral heads, but the femoral heads more commonly undergo progressive joint destruction, as a result of chronic weight bearing (Steinberg and Steinber [45]. Arthritic pain, swelling, and effusion may be related to periarticular infarction or to gouty arthritis. Bone marrow infarction causes reticulo cytopenia, exacerbation of anaemia, a leuko erythro blastic picture, and sometimes pancytopenia.

DERMATOLOGIC COMPLICATIONS

Leg ulcers occur in patients with sickle cell disease beginning in the adolescent years. They usually occur near the lateral or medial malleoli and may become chronic and debilitating. Their pathogenesis presumably is related to tissue 'necrosis. It occurs mostly commonly in males, those with more severe anaemia, and those with lower HbF levels. Treatment of leg ulcers begins with cleansing, debridement, and topical antibiotics. Leg edema retards healing of ulcers and can be treated using elastic wraps or leg elevation. Trauma to the area is to be minimized, and shoes must be selected accordingly. Transfusions may be required. Skin grafting has been successful in the most recalcification cases.

CARDIAC COMPLICATIONS

The chronic anaemia of sickle cell disease is compensated by high cardiac output, which results in chronic chamber enlargement and cardiomegaly, even in young children. While exercise capacity of sickle cell patient is diminished, congestive heart failure is uncommon, and restriction of activity is seldom necessary. An age dependent loss of cardiac reserve [46] creates a greater risk of heart failure in adult patients during fluid over load, transfusion, reduced oxygen - carrying capacity, or hypertension [47]. Cardiac function can be improved by transfusion.

INFECTIONS

Infectious complications of sickle cell disease are a major cause of morbidity and mortality. S. pneumoniae is the most common cause of bacteremia in children with sickle cell disease, accounting for 5-10 episodes, per 100 patients in infants [48]. This event is accompanied by leukocytosis, "a left shift", aplastic crisis, sometimes DIG, a 20-50% mortality rate. The second most common organism responsible for bacteremia in these children, Haemophilus influenzae type b, has accounted for 10-25% of episodes. Prophylactic penicillin, long term - acting broad - spectrum antibiotic ceftriaxone and conjugate H. influenzae type b vaccine have ameliorated the impact of childhood bacteremia. Bacteremia in older patients is more likely due to E. coli and other gram - negative organisms, as are urinary tract infections. Meningitis in sickle cell anaemia is primarily a problem of infants and young children, is caused most frequently by S. pneumoniae. Osteomylitis occurs more commonly in sickle cell disease than in normal individuals, probably as a result of infection of infracted bone. In this patient population, Osteomylitis is commonly caused by salmonella species.

DIAGNOSIS OF SICKLE CELL ANAEMIA

In HbSS, the fall blood count (FBC) reveals haemoglobin levels in the range of 6-8g/dl with a high reticulocyte count. In other forms of sickle cell disease, Hb levels tend to be higher. A blood film may show features of hyposplenism (target cells and Howell-Jolly bodies).

Sickling of the red blood cells, on a blood film, can be induced by the addition of sodium metabisulfite. The presence of sickle haemoglobin can also be demonstrated with the "sickle solubility test". A mixture of haemoglobins (HbS) in a reducing solution (such as sodium dithionite) gives a turbid appearance, whereas normal Hb gives a clear solution. Abnormal haemoglobin form can be detected on haemoglobin electrophoresis, a form of gel electrophoresis on which the various types of haemoglobin move at varying speed. HbSS and HbSC can be identified here.

The diagnosis can be confirmed with high - performance liquid chromatography (HPLC). Genetic testing is rarely performed, as other investigations are highly specific for HbS and HbC. An acute sickle cell crisis is often precipitated by infection. Therefore, a urinalysis to detect an occult UTI to look for occult pneumoniae should be routinely performed.

MANAGEMENT OF SICKLE CELL ANAEMIA

Many of the manifestations of sickle cell disease can be better managed if the diagnosis is made early and regular prospective follow up instituted. The management of sickle cell anaemia is in two phases quiescent stage and crisis stage.

NUTRITION

Sickle cell patients have increased metabolic rate and protein turnover which is balanced by high calories intake. Folic acid requirements are increased by haemolyis above normal levels of 50g/day and as much as 500ng daily has been necessary to reverse established megaloblastic change [49]. Because of low availability of folic acid and the cooking practices, folate deficiency is common and is supplemented with drugs. Red blood cells are rich in zinc. Sickle cell patients tend to acquire an increased total body iron burden especially if they receive blood transfusion. Iron salts are not prescribed routinely.

PROPHYLAXIS AGAINST INFECTIONS

Regular immunization against the common viral and bacterial infections of childhood is especially important and diligence is necessary to ensure that vaccine schedules are completed. Tetanus toxoid "booster" should be given at regular intervals because of the prevalence of leg ulceration. Prophylactic penculin is essential in early childhood to prevent pneumococcal septicemia.

THERAPY OF INFECTIONS

Once infections occur, diagnosis and therapy should be prompt as possible. The hazards of overwhelming septicemia are well recognized and must be remembered in any child with a high fever, or who looks lethargic and ill, and treated accordingly.

AVOIDANCE OF ADVERSE CLIMATIC CONDITIONS

The commonest precipitating factor for the painful crisis is cold and education and proper clothing may minimize its effect so that patients understand the importance of cold and keep warm at the cold wet periods of the year, and at night.

HYDRATION

Dehydration and haemo concentration are known to precipitate painful crisis in some patients. The maintenance of adequate hydration is very important where febrile conditions increase fluid loss, especially in countries with high ambient temperatures.

OXYGEN

During the therapy of acute complications, the use of oxygen is frequently recommended. Patient with SS disease have lowered arterial oxygen saturation in the steady state and this may fall further during acute illness, especially the acute chest syndrome, under these conditions, high levels of inspired oxygen can only be beneficial.

EDUCATION

Two aspects of education are critical to the child with sickle cell disease, education about the disease and the continuance of formal schooling. Patients learn to cope better with the disease if informed

about its J complications. With reassurance and understanding, patient can be taught to manage mild episodes of painful crisis at home. Education about the use of shoes and socks may reduce the prevalence of trauma - induced led ulceration [50].

BLOOD TRANSFUSION

It is invaluable in the management of acute exacerbation of the disease. In addition to normal hazardous cases of blood transfusion, there are additional dangers of haemosiderosis and precipitation of crisis. Generally, the indication of blood transfusion is haemoglobin level less than 4g/dl to 5g/dl in selected cases, for electric or emergency surgical operations, presence of formidable complicating infections. Normally packed cells are transfused simply to raise the haemoglobin concentration level without increasing the blood volume.

ANTI - MALARIAS

Malaria has been reported as the commonest precipitating cause of crisis in Africa, It is also known that malaria parasitaemia is associated with a fall of 2g/dL in haemoglobin concentration level [51]. Malaria is therefore lethal to sickle cell patients and a special effort is required to prevent it and to render prompt treatment when prophylaxis fails. The drugs used are poludrine and proguanil.

ANALGESICS

Relief of pain is an important aspect in the management of painful crisis. Mild to moderate pain often respond to paracetamol. For more severe pains, pethidine or codeine have reduced the frequency of emergency room visit [51]. Pentazocine or morphine can also be used for severe pains necessitating hospital admission. Intravenous infusion of these drugs gives better and more sustained pain relief but the occurrence of drug dependence in some sickle cell populations has led to reservation in the use of narcotic analgesics.

STREOIDS

Adreno corticotrophic hormone and corticosteroids have been helpful in some cases for controlling pain, swelling and muscle spasm ([52].

INTREVENOUS FLUIDS

Scott et al 1995 reported the disappearance of pain and other symptoms I after intravenous administration of 6% dextrose in 5% fructose [53]. Other fluids prevent increased viscosity of the blood by sickled red blood cells and thereby prevent plugging of end arteries of organs causing their death.

SURGERY

Splenectomy can be done at all stages of life of a sickle cell patient. Sequestration crisis can lead to hypersplenism, which is an indication for removal of the spIeen.The procedure however, is not curative and exposes the individual to the hazards of infection.

CYANATE

Dietary cyanate, from foods containing cyanide derivatives, has been used as a treatment for sickle cell anaemia. In the laboratory, cyanate and thiocyanate irreversibly inhibit sideling of red blood cells drawn from sickle cell anaemia patients. However, the cyanate wound have to be administered to the patient for a life time as each new red blood cell created must be prevented from sickling at the time of creation.

FOLIC ACID AND PENICILLIN

Children with sickle cell disease will undergo close observation by the pediatrician and will require management by haematologist to assure they remain healthy. These patients will take a 1mg dose of folic acid daily for life. From the age of birth to 5 years of age, they will also have to take penicillin daily, due to the immature immune system that makes them more prone to early childhood illnesses.

HYDROXYUREA

The first approved drug for the causative treatment of sickle cell anaemia, hdyroxy urea was shown to decrease the number and severity of attacks in a study in 2003 [54]. This is achieved, in part by reactivating fetal haemoglobin production in place of the HbS that causes sickle cell anaemia.

BONE MARROW TRANSPLANTS

Bone marrow transplants have proven to be effective in children [55].

CONCLUSION

Sickle cell anaemia is a homozygous form of HbS(HbSS). This result from single point replacement of glutamine by valine at position 6 of β- globin chain.This reduces solubilty of the red cells which in turn leads to polymerisation and vaso-occlussion in the vasculature. The association of two mutant β -globin subunits forms haemoglobin S (HbS). Under low - oxygen conditions, the absence of a polar amino acid at position of six of the β - globin chain promotes the non - covalent polymerization of haemoglobin, which distorts red blood cells into a sickle shape and decreases their elasticity. As a consequence, these rigid blood cells are unable to deform as they pass through narrow capillaries, leading to vessel occlusion and Ischaemia. It will be pertinent to have who listic care for those affected. Proper and adequate counseling should be given to intending couple before marriage and haemoglobin genetic counseling and education should be included in the curriculum of pupils and students from primary school to tertiary education levels to avert the pains and the crisis associated with the burden of sickle cell anaemia and the resources to take adequate care of them.

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