

Overview of sickle cell anaemia



Sickle cell anaemia is a genetic disorder that affects the haemoglobin within erythrocytes, which delivers oxygen to cells within the body. It is caused by a mutation in the HBB (haemoglobin subunit beta) gene. The HBB gene provides instructions for making beta globin, a subunit of haemoglobin. One of the various mutations of beta haemoglobin is called haemoglobin S. In individuals with sickle cell anaemia, both of the two beta-globin units are replaced with haemoglobin S. Sickle cell anaemia is an inherited disease which is inherited in an autosomal recessive pattern. Both parents are carriers of the disease and carry one copy of the mutated gene each. ²

Sickle cell anaemia can be diagnosed by a blood test/screening. If the haemoglobin found is haemoglobin S, further blood screening is undertaken to confirm the diagnosis of sickle cell. Two haemoglobin S have to be found to have sickle cell. One indicates carrier. Neonatal screening for sickle cell is administered to pregnant women who are at high risk of being a sickle cell carrier. This is done before the mother is 10 weeks pregnant. If the mother turns out to be a carrier, the father can also be screened. ¹⁴

Individuals with sickle cell anaemia may possess a range of different complications as well as symptoms. This is due to the fact that sickle cell anaemia is a multi-organ system disorder, and nearly every organ in the body can be affected. One of the main symptoms of sickle cell anaemia include vascular occlusions. Vascular occlusions occur due to the polymerisation of deoxygenated sickle haemoglobin, this results in the deformation of the erythrocyte creating a crescent 'sickle' shape. ⁴ Due to the deformation, sickle erythrocytes can block the blood vessels, causing

exceeding amounts of pain. The pain develops and can occur typically in the lower back, in different joints/extremities. Blood flow through the chest, abdomen and joints is reduced/blocked. The pain, a constant throbbing sensation, may also migrate, or be localised. ³ The name for these painful episodes can be called crises. Another symptom of sickle cell anaemia are strokes. Cerebral infarctions occur mostly commonly in young children. They are caused by sickle shaped erythrocytes clumping together within the walls of larger arteries in the brain which causes damage to the vessel walls allowing more sickle red blood cells to gather, this as a results narrows the blood vessel. ⁵ Other symptoms include pulmonary infarctions e. g. pneumonia, pulmonary hypertension, ischemic cardiomyopathy, chronic kidney disease, splenic disorders, skeletal abnormalities/joint damage e. g. avascular necrosis, retinopathy, acral erythema, priapism delayed growth and puberty, ulcers. ³

One of the most effective treatment methods is the use of the medicine hydroxyurea (also called hydroxycarbamide). Hydroxyurea was first synthesised in Germany in 1869, however its biological significance was not recognised till 1928. ⁶ In 2011, Winfred Wang leads research to the use of hydroxyurea in children, which is the only approved drug approved by the Food and Drug Administration on February 25th 1998 for the treatment of sickle cell so far. Hydroxyurea is a cytotoxic drug, which means it has the potential to damage normal tissue, most are also teratogenic, meaning it can cause disruption in the embryo or foetus, as a result causing a birth defect. ⁸,

⁹ In individuals with sickle cell, the medicine needs to be taken for months till positive effects of the drug are noticed. ¹⁰

Hydroxyurea works by enhancing the production of fetal haemoglobin (HbF) in the blood. ¹⁰ When levels of fetal haemoglobin are increased, the kinetics and thermodynamics of haemoglobin S polymerisation are altered. Increased levels of fetal haemoglobin inhibits the growth of erythroid colonies in individuals with sickle cell anaemia. ¹¹ Haemoglobin stimulates the production of HbF by gathering many erythroid precursors that can continue γ -chain synthesis till fully developed, then remain dormant within the bone marrow unless constricted when red blood cells expansion occurs.

Another common treatment/maintenance method is frequent blood transfusions. . In 1997, it was shown that regular blood transfusions reduced the risk of children with sickle cell disease who were susceptible to strokes by 90%. ¹² Blood transfusions reduce vaso-occlusive crises by replacing haemoglobin S with the normal haemoglobin, haemoglobin A (HbA) from a donor. This reduces vaso-occlusive crises by increasing perfusion as followed by cellular oxygen delivery. ³ Blood is transfused every 3-4 weeks, which raises the concentration of HbA in the blood and consequently reduces the concentration of HbSS(haemoglobin sickle cell anaemia). This therefore improves the blood flow of non-sickled shaped red blood cells as less sickle shaped red blood cells are circulating in the blood and hence suppressing the production of sickled red blood cells. ³

A new and evolving form of treatment which is still under research is bone marrow transplant. Bone marrow transplant, also called haematopoietic stem cell transplantation, is the only permanent cure for the disease. In 2009, a study discovered that modified blood adult stem cell transplant cures sickle cell anaemia in 9 out of 10 adults.¹² In haematopoietic stem cell transplantation from unrelated donors, the use of cord blood transplantation has been investigated as it has a low immunogenicity, this is the ability for a medical immune response to be induced. As a result of cord blood transplantation having a low immunogenicity, this results in a decreased association with graft versus host disease.¹³

Sickle cell anaemia has a great impact on the individuals as well as family. Frequent crisis often result in low attendance which can affect the economy if individuals are out of work. Parents with children with sickle cell have to stay home to look after them which also affects the economy as they cannot go to work as well as not earn money for living. Economic factors of sickle cell are highlighted in a study by Nuffield trust in 2013 which concludes that hospital admissions for minor conditions has been growing over the last decade, occupying an estimate of £1.4 billion pounds a year. Between the years 2010 and 2011, England had 6077 admissions primary due to crisis. In total, the cost for these admissions was £18798255.¹⁵

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