Recent advances in prevention and treatment of sickle cell anaemia - literature review

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ABSTRACT: Sickle cell anaemia is a haemoglobinopathy which is inherited in the autosomal recessive manner. It causes haemolytic anaemia and reoccurring instances of vascular occlusion that gives rise to pain, this condition is common among people with African background. Previously, blood transfusion was carried out for patients having sickle cell anaemia. Recent advances include, hydroxyurea which is considered in patients having recurring episodes of acute chest syndrome with three or more crisis that requires hospitalisation. Another recent advance is by having the patient to undergo a bone marrow transplant but in order for the success of this treatment; an identical match is needed with at least 8 out of 10 human leukocyte antigen. Recent studies have demonstrated by carrying out aggressive transfusion therapies are not the best conservative and conventional approach towards a cure as it requires a long postoperative procedures by ingesting non-steroidal anti-inflammatory drugs. Conservative transfusion treatment is seen to be as effective as an aggressive regimen in preventing perioperative complications in patients with sickle cell anaemia, and the conservative approach resulted in only half as many transfusion-associated complications. Research is currently being carried out into hydroxyurea, gene therapy and bone marrow transplants as well a huge range of new drugs are being tested clinically for the treatment of sickle cell anaemia. With these new therapies and treatment procedures, it may be possible to help improve the anaesthetic course of the patients with sickle cell disease as well as reduces postoperative complications and allow the patient to be discharged out of the hospitals in a faster time.

KEYWORDS: Sickle cell anaemia, treatment, therapies

INTRODUCTION

Sickle cell haemoglobin are pathologically polymerised and deformed red cells due to a single nucleotide change in the beta-globin which causes a poor micro vascular blood flow with consequent tissue ischemia and infarctions. Sickle cell diseases comprises of a group of inherited disorders that alters red blood cells and ultimately leads to haemolytic anaemia and recurrent instances of vascular occlusion that produces acute and chronic pain. Vascular occlusion of small and large vessels can cause chronic damages to the brain, lungs, bone, spleen, liver and kidney.

Haemoglobin are capable of undergoing reverse polymerisation when it is deoxygenated to form a network of fibrous polymers that stiffens the erythrocyte membrane. The haemoglobin are also capable of increasing viscocity and causes dehydration due to potassium leakage and calcium influx. These would cause changes in the red cell causing it to have a sickle shape which would not allow it to pass through blood capillaries. 

The recent advancements in treatment of sickle-cell anaemia being carried out are bone marrow transplants, hydroxyurea, gene therapy and new drugs. Bone marrow transplant can cure sickle cell disease and is mainly used in young patients with severe sickle cell disease. However this procedure is really risky due to the requirement that the transplant has to come from a closely matched donor.

Hydroxyurea on the other hand is given in dosages and is much more conservative method compared to bone marrow transplantation and gene therapy. However, the patients that are consuming this drug have to be monitored closely to ensure that dosages are adjusted according to time to prevent cytopenia which can be fatal.

Gene therapy are currently being studied as a possible treatment for sickle cell disease. This method is planned to be carried out in a way that the new gene which is normal would be able to be placed in the bone marrow of a sickle cell anaemia patient to have the body produce normal red blood cells.

New drugs are being studied to treat as well as prevent sickle cell anaemia by helping with the sickling of the haemoglobin, prevention of cells from sticking to the vessel walls as well as increasing the level of haemoglobin in the foetus itself.

REVIEW

Sickle cell anaemia is a disease that is autosomal, recessive disorder which is characterised by a single amino acid change in the beta globulin chain of the haemoglobin which would cause pathological polymerisation, cell rigidity and poor micro vascular blood flow with consequent ischemia and infarction. The patients suffering from sickle cell anaemia would need to constantly undergo surgery due to the vasoconstriction of blood vessels. A lot of pain would also be experienced due to this as sickle cell anaemia can lead to an early death. Due to the vaso-occlusive, symptoms such as fever, acidosis, hypoxia, stress, exposure to cold as well as sleep apnea and physical exhaustion would occur.

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Preoperative complications in patients with sickle cell anaemia are common and many researches are being made into the recent advances in prevention and treatment of sickle cell anaemia. Early reviews reported preoperative mortality rates as high as 10 percent and the rate of postoperative complications are at 50 percent. The clinical course of sickle cell disease is highly variable and difficult to predict, we attempted to identify patients at risk for poor outcomes before extensive organ damage due to sickle cell disease occurred.

This problems may arise from preoperative hypoxia, hypo perfusion and acidosis which causes erythrocyes to sickle, thus precipitating vast-occlusion and organ dysfunction. This problems are similar to that applied in patients with beta thalassemia major. In a collaborative multicentre trial, risks and benefits of allogeneic bone marrow transplantation in children with symptomatic sickle cell disease. The hematopoietic stem cell transplantation can be used to cure sickle cell anaemia.

The polymers for the formation of intra cellular haemoglobin has a direct impact on the red blood cell plasma membrane which usually leads to the extra cellular exposure of proteins epitopes and glycolipids that are normally found inside the cell. The pathophysiology pathway starts from the deoxygenated on of red blood cells to the polymerisation of haemoglobin to the sickling of red blood cells to the endothelial damage. Next, red blood cells and leukocytes sticks to the endothelium of the blood vessels causing vasoconstriction which causes vaso-occlusion, organ ischemia and end - organ damage. Due to this acute episodes of severe such as red cell aplasia, acute splenic sequestration and acute haemolysis will take place.

For bone- marrow transplantation in the course of sickle cell anaemia remains uncertain in part because of the unpredictable nature of the disease. The idea of replacing the bone marrow, which is the source of the defective sickle cells, with bone marrow that produces normal red blood cells is an intuitive therapeutic approach in sickle cell diseases. Bone marrow transplant have significant risks in transplants are not appropriate for every patient. Bone marrow transplant that are used primarily in young patients who have severe sickle cell disease. The decision of treatment is made on a case- to- case basis. Clinical trials that have been conducted on children with sickle cell diseases by bone marrow transplant have a 90% long-term survival rate when compared back to those days when the mortality rate of the procedure itself was 20%. Patients whose bodies did not accept the transplant of bone marrow would go under grartification.

Hydroxyurea treated patients have shown a positive result as there is a 50% decrease in the number of painful vaso-occlusive episodes. Patients treated with hydroxyurea requires fewer blood transfusions and hospitalisation compared to other methods of treatments. Hydroxyurea therapy in sickle cell disease have shown that the F strain haemoglobin is an effective inhibitor of gelation. The benefits of red blood cell effects in sickle cell diseases causes an increase in F-cell numbers and Hb F concentration per F cell. There would be an inhibition of cation depletion and dense cell formation. There is also an inhibition of sickle red cell endothelium adhesion. Besides that, there would be an inhibition of sickle erythrocyes adhesion to extra cellular matrix components.

The efficiency of hydroxyurea can only be made once the patient has completed about 9 months of therapy. Hydroxyurea patients should be monitored on a strict basis to prevent cytopenia. Cytopenia can develop when the dosage of the drug is not adjusted according to the blood levels and this could cause fatality. The limitations or barriers towards hydroxyurea are pregnancy, neutropenia, fears of the public as it is a new way of treatment, they are unsure about the long term affects as well as concerned if it is an experimental drug. Unlike bone marrow transplants and gene therapy, the public aren't sure about hydroxyurea as a therapeutic option. The patient is not willing to corporate and come in for frequent monitoring and does not follow the strict treatment regimen. There is also a perception that is unclear by the public that hydroxyurea is currently the only therapy that directly modifies the process of the disease. The long term administration of hydroxyurea to stimulate the production of feral haemoglobin and the transfusion of red cells to lower sickle haemoglobin levels are other therapies now available for the treatment of patients with symptomatic sickle cell disease.

In gene therapy, uses hematopoietic stem cell from a patient's own blood, is being researched to create a revolutionary alternative to current sickle cell disease treatment as it creates a self-renewing normal red blood cells by inserting a gene that has anti-sickling properties into hematopoietic stem cells. This therapy approaches for sickle cell disease are to find ways to reduce haemoglobin S polymerisation. This could increase haemoglobin F and to prevent sickle cell dehydration. A large number of epidemiological, clinical and laboratory observation have converged to support the notion that haemoglobin F administration can ameliorate the clinical severity of sickle cell diseases. Gene therapy offers and enormous promise as a potential curative therapy but concerns over the safety of random genomic insertions should be resolved first. Researchers are studying gene therapy as a possible treatment for sickle cell disease. Researches wants to investigate a normal gene can be placed in the bone marrow of a person with sickle cell, which would help it make normal red blood cells. They are trying to find out if there is a way they can switch the gene on and off to make the red blood cells to behave more normally. There might be a new breakthrough, about a century after sickle cell disease was first described, gene therapy might have genetic information to target specific aspects of the diseases and reduce the mortality rate.

New drugs are being studied to interfere with the sickling of haemoglobin, preventing the cells from sticking to blood vessel walls and drugs that are able to treat pre natal symptoms. The molecular methods of identifying the sickle mutation in utero and post natal are well established but the same beta globin is responsible for the spectrum of the pathophysiology of the disorder, the clinical manifestation of the disease are extremely heterogeneous. The evolving role of researchers of studying into new drugs and medications needs to control clinical trials to investigate the risks and benefits of the indications for medical intervention in sickle cell anaemia.
CONCLUSION
Recent advances in prevention and treatment of sickle cell anaemia is based on the resultant vaso occlusion and pain control can potentially change the anaesthetic course of patients with sickle cell diseases. By this, it can conclude that gene therapy, new drugs and hydroxyurea are capable of reducing haemolysis and sickling of the red blood cells on the blood vessels as well as in the process of creating a breakthrough to find the best treatment to overcome this disease.