

A New Era in the Management of Sickle Cell Disease

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Enormous progress in the care of people with sickle cell disease (SCD) has taken place over the past four decades. The median survival has improved dramatically from death typically occurring during early childhood in the 1970s to survival now in the mid-50s for individuals with hemoglobin SS and mid-60s for individuals with hemoglobin SC disease^[1].

From its origins in sub-Saharan Africa SCD became a global health problem spreading to the Arabian Peninsula and the Indian subcontinent. The population migration on the incense trade routes has increased SCD prevalence in areas not previously associated with the disorder, such as the USA, western and northern Europe. In the USA, it affects close to 100,000 people with 3000 affected newborns each year, while in the United Kingdom, it is estimated that 12,500 individuals have SCD with an annual birth rate of 300 affected newborns^[2].

It is estimated that more than 300,000 children are born each year with SCD, about two-thirds of them in Africa; Nigeria, India and the Democratic Republic of Congo bear half the global burden of SCD. Numbers are expected to climb projecting that by 2050, there will be about 400,000 babies born with SCD annually^[3].

The HbS gene frequency in Saudi Arabia in particular ranges between 1-17%. This figure is among the highest in the world; similar figures are reported in several Arab countries that are geographically affected with the migration and the trade routes^[4].

The consequence of the emergence of this disease outside Africa imposing a national and regional health problem was in the form of active scientific research.

Among more than 26,000 published papers more than one thousand were original work from Saudi Arabia, these account for 4% of the globally published work.

Pain management is the most important contributor in improving the quality of life; it needs better evaluation and enhanced research. Similarly, management of acute clinical events, including priapism, intra-hepatic cholestasis, iron overload, multi-organ failure and delayed hemolytic transfusion reactions, need high quality evidence to direct more effective management. The mile stones in the treatment of this disease include: Screening for children at risk of developing stroke by trans cranial Doppler; prevention of stroke by blood transfusion in those at risk; disease modifying treatment options like hydroxyurea and blood transfusion; chelation of iron in the multi-transfused patients; hematopoietic stem cell transplant in patients with severe cases considering the challenges and risks expected^[2].

The new era in managing sickle cell anemia started with the insight into this disease with the clinical trials directed towards active inhibition of adhesion, coagulopathy and the detrimental effect of the inflammatory mediators^[5-7].

The delighting news though, is that we are now observing many competing clinical studies and emerging therapies, using genetic, genome-editing, cell-based and pharmacological approaches as potential disease-modifying treatment options. Different pathways have been explored to utilize matched sibling related donor transplant, including using half matched hematopoietic stem cell transplantation (HSCT) (known as haploidentical) from a family member or the umbilical cord and cells from placenta to overcome the barrier of donor limitations.

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Gene therapy strategies were successful in replacing the defective sickle gene, or manipulating fetal hemoglobin switching^[2,3].

Novel drugs that are currently being evaluated include hemoglobin F inducers, anti-sickling agents, anti-oxidants, anti-adhesive agents, anti-inflammatory agents, anticoagulants and anti-platelet agents^[8].

Several pharmacological agents targeting different parts of the pathophysiological pathway are in the pipeline. The most promising new drug is GBT440, which targets HbS polymerization; Selg1 targeting adhesion, NKT120 (humanized monoclonal antibody) targeting inflammation, SANGUINATE™ targeting vasoconstriction and histone deacetylases (HDAC) inhibitors targeting gamma globin switching. Considering the complexity of the sickle pathophysiology, the optimal therapeutic approach could well include combinations of drugs targeting multiple pathways^[2,3].

The advances in SCD diagnosis and follow up are manifest with the introduction of the biochip, which is a functional adhesion assay, reflecting quantitative evaluation of RBC adhesion, this could be used at baseline, during crises, relative to various long-term complications, and assessing outcome of therapy^[9].

The roadmap for sickle cell anemia treatment is changing with the new insight we have about the pathophysiology of the disease, pharmacogenomics and targeted therapy. The gap in the management is evident and it is speculated that treatment of this disease will soon be revolutionized.

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