

Abstract

Sickle cell disease (SCD) is the most common genetic disease in the world. Approximately 150,000 Nigerian children are born each year with SCD, making it the country with the largest burden of sickle cell disease in the world. SCD is the most common cause of stroke in children and results in considerable morbidity in affected children. The current primary prevention approach of regular monthly blood transfusion therapy of children at high risk of stroke (identified by elevated transcranial Doppler measurements) is not feasible in a low income country such as Nigeria due to scarcity of supply, cost, and high rate of blood borne infections. In the United States, hydroxyurea (HU) is standard therapy for adults with SCD and may be a reasonable primary stroke prevention alternative to regular blood transfusions for high-risk children. Given large absolute numbers of individuals with SCD in Nigeria, HU therapy for all individuals with SCD may not be initially feasible; however, a targeted strategy of HU use for primary prevention of strokes is an alternative to the standard therapy (observation) for high-risk individuals. We therefore propose a feasibility study to determine the acceptability of randomization to HU vs. placebo for primary prevention of strokes in Nigerian children with sickle cell anemia (SCA) in preparation for a NIH sponsored multicenter, phase III Trial. We will establish a safety protocol for using HU in a clinical trial setting and complete the necessary preparations for a definitive phase III trial. To accomplish these aims we have assembled a strong multidisciplinary team representing Vanderbilt University and two premier in-country institutions: Aminu Kano Teaching Hospital, Nigeria, and Friends in Global Health-Nigeria. Completion of a definitive trial will not only benefit children with SCA in sub-Saharan Africa, where the majority of children with SCA live in the world, but could provide reasonable evidence for an alternative to blood transfusion therapy for the primary prevention of strokes in the US. To our knowledge this would be the first stroke prevention trial in Nigeria and could establish a precedent to expand to secondary stroke prevention for children and adults with SCA, as regrettably, no therapy is available to prevent recurrent stroke in these high-risk patients in resource-poor nations.