GUEST EDITORIAL

Thalassaemia (part 2)

Thalassaemia ranks among the most common genetic diseases worldwide, with around 60 000 severely affected live births annually, and a prevalence of around 288 000. Most children with thalassaemia are born in low-income countries. Increasing global migration has resulted in a wider dispersion of people at risk of hereditary anaemias, which have become increasingly prevalent in countries where these diseases are not endemic. Thalassaemia was frequently lethal in childhood or early adulthood due to insufficient access to transfusion and chelation, with death resulting from anaemia and/or iron overload of various organs. Management initially only focused on transfusions to prevent symptomatic anaemia. This was accompanied by a high rate of splenectomy. Chelation with desferrioxamine (DFO), a drug only available as a parenteral formulation, was accessible from the 1960s. DFO has a very short half-life of 20 - 30 minutes, hence is only effective if administered continuously (usually given subcutaneously) for around 10 hours a day through an infusion pump. Compliance was suboptimal for this reason. With the advent of oral iron chelators, viz. deferiprone and deferasirox, which were made available in 1987 and 2005, respectively, compliance improved significantly.

Worldwide, the availability of safe and adequate transfusion remains a challenge, and mortality from iron overload will remain unacceptably high unless an available and potentially inexpensive oral iron chelator is licensed more widely.

The Thalassaemia International Federation was formed in 1987, and has been critical in promoting care, leading to improved survival and quality of life through guidelines for the management of thalassaemia. The past few decades have seen remarkable improvements in the survival of patients with access to treatment. Transfusion therapy evolved to hyper-transfusion to maintain physiological levels of haemoglobin concentration, and reach a post-transfusion haemoglobin concentration of 14 g/dl, which thenceforth necessitated intensification of iron chelation therapy. [1,2]

Assessment of iron overload previously required an invasive liver biopsy. Since 2005 there have been significant advances in non-invasive assessment of iron overload of the heart and liver using magnetic resonance imaging, which guides judicious intensification of chelation to reverse iron overload and mitigate end-organ damage.

Exploration of novel therapeutic approaches continues, with a number of agents and approaches under study. These include: (*i*) agents that minimise haemolysis and thereby reduce transfusion requirements (e.g. luspartecept); (*ii*) targeted agents that negatively regulate hepcidin with a consequential decrease in iron absorption and total iron burden; (*iii*) advances in the bone marrow transplantation sphere; and (*iv*) gene therapy. Currently, haemopoietic stem cell transplantation remains the only realistic chance of a cure. However, this is limited by the availability of human leukocyte antigen-matched donor stem cells, and the high cost of the procedure. Gene therapy is a high-tech procedure with remarkable success in pilot patients and has the potential to cure patients on a large scale in the future. At present, management of thalassaemia is largely confined to supportive care, with blood transfusion and iron chelation being the mainstays of treatment. A multidisciplinary team effort is required for optimal management of patients with thalassaemia.

Prevention of live births with thalassaemia major requires committed screening in high-risk populations. Premarital and antenatal prevention programmes aim to identify and counsel couples who carry the relevant genes, and offer different options to prevent having a child with thalassaemia. Neonatal screening allows for early detection and management planning. Screening programmes in high-risk populations such as in Cyprus and Sardinia have demonstrated notable success in reducing the number of live births with thalassaemia major and stabilisation of patient numbers.[3,4]

The second of this 2-part series on thalassaemia focuses on management issues, including conventional and currently available treatment modalities and recent advancements.

The authors are indeed grateful for being part of the educational CME on the subject of thalassaemia.

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