Management of thalassaemia and promising results in gene therapy

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Thalassaemia is an inherited disorder of the blood that is passed on from parents to their children.

There are two principal forms of Thalassaemia - Thalassaemia minor and thalassaemia major.

Thalassaemia minor is the heterozygous form of the disease. In this condition the patients are free of any disease symptoms. Their life span is normal.

Thalassaemia major is the homozygous and serious form of the disease. This condition is associated with severe anaemia and considerable disability. Thalassaemia intermedia is also homozygous state of the disease but the symptoms are modified and becomes milder by the presence of DNA polymorphism (G-gamma x mnl1).

Haemoglobin E/Beta-thalassaemia is the commonest thalassaemia in Bangladesh. The clinical approach to haemoglobin E/Beta-thalassaemia resembles that for homozygous Beta-thalassaemia. The most important clinical difference between homozygous Beta-thalassaemia and Hb E- beta-thalassaemia relates to the oxygen affinity of the predominant haemoglobin. In thalassaemia major this is Hb F which has high oxygen affinity and release oxygen poorly to the tissues. By contrast in Hb E/Beta-thalassaemia the predominant haemoglobin is Hb E which has low oxygen affinity. Patients can therefore tolerate a low thalassaemia level better than homozygous beta thalassaemia and Hb around 7g/dl often permits acceptable growth and quality of life.

Treatment for thalassaemia mainly focuses on two aspects: Blood transfusion every 3-4 weeks interval as long as the child survives and regular chelation therapy to remove excess iron as long as the child lives. The best chelation is done by Desferal. The recommended method is slow subcutaneous infusion over 8 to 12 hours at least five days in a week. This is a very expensive treatment. Deferiprone is an iron chelator that can be taken by mouth. It is less safe than Desferal and its long term safety and efficacy are unknown2.

In recent years preparations like Butyrate3 and Erythropoietin4 have been tested for their ability to raise hemoglobin level in thalassaemia but with disappointing results.

Splenectomy becomes necessary for the majority of low- transfused patient within first 10 years of life because hypersplenism is common and progressive, and often leads to death5.

The only curative treatment for thalassaemia is bone-marrow transplantation. This procedure is very expensive and not without risk and failure. Even more is the difficulty in getting a fully compatible donor.

Researchers at the Columbia University College of Physicians and Surgeons in

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New York have succeeded for the first time in demonstrating the long-term transfer and high-level long-term expression of normal human beta globin gene in an animal model.

Dr. Arthur Bank and his colleagues at Columbia put a human beta gene into a safe retrovirus, added the virus to mice bone- marrow cells in vivo and transplanted the modified cells into mice. The presence to the human beta globin gene could be detected up to eight months later with high levels of expression. That level of expression could be enough to ameliorate, if not cure, the anaemia of patients with beta thalassaemia.

Researchers are continuing to investigate better gene transfer systems in mouse models of beta thalassaemia and developing better ways to transfer retroviruses into human haemopoietic stem cells.

Their results may lead to clinically successful gene therapy for beta thalassaemia.

References