GeNeDit

Gene Therapy & More: Options for Treatment of Hemophilia

Editorial

The long-awaited option of gene therapies for monogenic disorders has become a reality. This is exciting for medical geneticists who have been closely following the ups and downs in this area of research. Some clinicians in India have had an opportunity to treat patients of spinal muscular atrophy (SMA) with gene therapy. Hemophilia was thought to be an ideal target for gene therapy as production of as little as 5% of coagulant factor level can make a tremendous change in the quality of life. The success of gene therapy for hemophilia B by ex vivo strategy was reported almost a decade back, but studies failed to show long-term continued expression. Recent studies with adeno-associated virus-based therapy for hemophilia A have been successful. Experience of two to four years has shown the long-term efficacy of the gene therapy. In 2022,Valoctocogene roxaparvovec has been approved for patient care. This is a great news for the hemophilia community. The factor levels achieved with gene therapy were significant, though showed about 40% loss of response after the second year. In one trial the factor level achieved was 150% causing the trial to stop. The landmark paper of the phase 3 trial to evaluate the efficacy and safety of valoctocogene roxaparvovec in male patients with severe hemophilia A is included in the GenExpress of this issue. Other strategies based on CRISPR-Cas9 gene editing using lipid nanoparticles have shown efficacy in mice.

Along with developments in gene therapy the long half-life factor preparations and non-factor replacement therapies like emicizumab have changed the hemophilia treatment scenario markedly. With these easy prophylactic therapies available, gene therapy will have a tough competition. The treatment strategy will change from one-size-fits-all as the available options increase. In the decision-making about gene therapy vs other factor and non-factor therapies, education and involvement of patients and families with hemophilia will be needed. What patients need to know needs to be understood. Easy-to-read educational resources are being made and these will be helpful to the hemophilia physicians for conducting discussions with the patients and their families to empower them with knowledge about this novel treatment strategy. What is known and what is not known about the long-term effects, have to be communicated with the families. The decisions will also depend on the age, previous experience and the outcome of treatments taken by the patient. Research in these aspects is also needed. Hemophilia patient groups, the treating physicians and paramedical hemophilia experts are working together for many decades and have a strong base worldwide. The centres providing holistic treatment for hemophilia and bleeding disorders have established protocols and experience of long-term follow ups. They will be closely working with the gene therapy groups and the strong bonds within the existing hemophilia community will be helpful in smooth transitions to the novel therapies of the new era for hemophilia.

At this juncture, India also has long experience of government-funded hemophilia management program of more than a decade. Though the treatment is still far from optimum, long-acting factors, emicizumab and bypassing agents are available to the patients. Many hemophilia treatment centres,their networking, and activities of the Indian Association for Haemophilia and Allied Disorders will go a long way to change outcomes of hemophilia patients. Hemophilia is among the commonest of the rare disorders. The activities for hemophilia are evolving as a prototype for the management of rare genetic disorders in India.Same will be true about long term outcomes of gene therapy which the future only will be able to tell.

The Genexpress in this issue covers recent developments in the various issues related to hemophilia management.

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