Perspective

Gene editing as treatment for inherited haemolytic anemia: Is the future here?

Rudrajit Paul[1]

Thalassemia and sickle cell disease are congenital haemolytic anemia syndromes with various systemic manifestations. While thalassemia major makes people transfusion dependent, sickle cell disease is associated with recurrent occlusive crises and other life threatening manifestations. For most patients, lifelong supportive therapy is the only means of management. Bone marrow transplant is able to cure these genetic diseases, but for most thalassemia patients in India, this is not an option due to[1] cost and lack of suitable donors. However, new technology[2] is now offering hope for cure of these genetic ailments.

On January 21, 2021, Frangoul *et al* from USA published a brief report in the NEJM where they have discussed a new therapeutic option for these patients. A brief overview of this method is described here:

CD34+ hematopoietic stem cells were isolated. Then, by electroporation, CRISPR-Cas9 gene editing kit was introduced inside these cells. This gene editing system targeted BCL11A. This is a transcription factor that silences ã-globulin gene expression. Enhancing the ã-globulin gene would lead to more HbF in the RBC and thus, decrease in transfusion requirement. The CRISPR gene editing system would silence the suppressor, which is BCL11A. Hence, fetal hemoglobin would increase. The stem cells, after CRISPR editing, were transfused into the body of patients after myeloablation. Thus, this was a bone marrow transplant procedure, albeit with modified stem cells. At one year, it was seen that the patients had high levels of HbF with marked decrease in transfusion requirement and for sickle cell disease, abolition of further vaso-occlusive crises.

The CRISPR technology is an area of intense research due to its ability to do gene editing with marked precision. In the study mentioned above also, there was no off-target editing. This is a remarkable achievement and the chance of inducing cancerous or dysmorphic mutations is almost nil. This makes CRISPR an ideal tool for clinical use. However, widespread clinical use is still far into the future.

Another method of gene editing is being tried in thalassemia. In September 2020, Gabr et al from Egypt published another study where they took stem cells of thalassemia patients and with CRISPR tool, tried to repair the mutation in the beta-globin gene itself. The edited cells were then cultured and it was found that the mutation had been successfully corrected. These repaired stem cells could then be transfused back into the patient like autologous bone marrow transplantation.

Clinicians of the future must be conversant with this new technology. In the future, when managing a patient of thalassemia, it may be worthwhile to discuss gene editing as a valid therapeutic option.

[1]MD, DNB, MRCP (UK), Consultant Physician, Kolkata

Reference

1 Frangoul H — CRISPR-Cas9 Gene Editing for Sickle Cell Disease and β-Thalassemia. *N Engl J Med* 2021; **384:** 252-60.