THE APPROACH OF MOLECULAR MEDICINE TO THE TREATMENT OF GAUCHER DISEASE

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Introduction. Gaucher disease presents a metabolic rare disease with the autosomal recessive transmission. The cause of this monogenic disease is the mutation of the gene GBA. As a consequence of this mutation, a deficiency of synthesis of the enzyme β- gucocerebrosidase occurs. As a result, glucocerebrosides accumulate throughout the body, especially in the bone marrow, spleen and liver. Three different forms of Gaucher disease have been determined, distinguished by the absence or presence and extent of neurological complications. Currently, five therapies for the treatment of Gaucher disease are described. This review study provides the most recent information on the therapies approved for the treatment of the disease. Material and methods. Narrative synthesis of specialized literature in databases: *PubMed, Gene Cards, National Library of medicine, Google Scholar* and *Hinari* of the years 2014 to 2024 were analyzed. Results. Enzyme replacement therapy is an effective tool in the treatment of Type 1 Gaucher disease. Treatment is done via infusion of imiglucerase. This is a synthetic substance called glucocerebrosidase. It ensures the breakdown of accumulated lipids. Substrate reduction therapy uses a small molecule drug miglustat and eliglustat tartrate that inhibits the first committed step in glycosphingolipid biosynthesis. Chaperone therapy treatment with non-inhibitory chemical chaperones can increase glucocerebrosidase levels and activity in lysosomes. Gene therapy as a potential therapeutic approach for the treatment of GD type 1, ex vivo autologous bone-marrow-derived GD 1 hematopoietic stem cells were genetically corrected by infection with self-inactivating lentiviral vectors expressing WT GBA1 induced by different cellular promoters. Hematopoietic stem cell transplantation, involving the replacement of affected stem cells with healthy stem cells is a treatment that can provide a permanent source of enzyme to people with Gaucher disease and is a

considerably less expensive procedure. People with Type 3 Gaucher disease showed no further neurological deterioration. The important limitations of HSCT are the mortality and morbidity associated with the procedure and the non-availability of HLA-matched donors. Conclusions. The different methods of Gaucher disease treatment have been permanently researched. Advances in this field are promising regarding the increase in life quality of patients. The treatment choice should be personalized by the severity of the disease as well as other associated medical conditions. The most commonly applied therapy is still enzyme replacement. Even though this therapy form is the one that is well-tolerated by the patient, healthcare providers should be aware of any unexpected complications.

References:

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