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Therapeutic apheresis in Fabry disease

Jessica Ugalde-Altamirano[1], Jordi Rovira Juarez[2], Josep Maria Campistol Plana[3], Miquel Lozano[4], Joan Cid[4], Gaston Piñeiro[4], Maria Jose Ramirez[2], Vicente Corral-Velez[5], Ignacio Revuelta[4], Ramon Roca[6], Jordi Calls[6] and José Vicente Torregrosa Prats[4]

[1]Hospital Universitario de Mollet, Hospital Clinic de Barcelona, Mollet del Valles, Spain
[2]Instituto de Investigaciones Biomédicas August Pi i Sunyer (IDIBAPS), Barcelona, Spain
[3]Hospital Clinic de Barcelona, Instituto de Investigaciones Biomédicas August Pi i Sunyer (IDIBAPS), Barcelona, Spain
[4]Hospital Clinic de Barcelona, Barcelona, Spain
[5]Hospital de Bellvitge, Hospitalet de Llobregat, Spain
[6]Hospital Universitario de Mollet, Mollet del Vallés, Spain

Background and Aims: Fabry's disease (FD) is a rare lysosomal disorder linked to the X chromosome due to a mutation in the gene encoding alpha-galactosidase A (alpha-Gal A). This mutation leads to a defect in the metabolism of glycosphingolipids, causing the progressive accumulation of globotriaacylceramide (GB3) or LysoGB3 in cells, tissues, and organs. In the treatment of FD, we have enzyme replacement therapy (ERT) with Agalsidase-alfa (Replagal®), Agalsidase-beta (Fabrazyme®), and chaperones (Migalastat®). However, there are limitations such as disease progression and morbimortality. Regarding ERT, the development of circulating immunoglobulin G (IgG) antibodies against agalsidase (aGAL) in the long term appears to be associated with a loss of effectiveness.

The use of Therapeutic Apheresis (TA), such as plasma exchange therapy (PE) and low-density lipoprotein apheresis (LDL-apheresis), is employed in the treatment of various pathologies due to its ability to eliminate plasma, antibodies, low-density lipoproteins, apolipoproteins, and the adaptability of therapy to the molecule to be removed.

The aim was to demonstrate that LDL-apheresis and PE favor Lyso-Gb3 elimination, and PE also eliminates IgG-aGAL as an adjunctive treatment in FD and conducted a proof-of-concept study.

Method: Two branches of intervention were established, where patients were classified into two groups based on the presence or absence of anti-agalsidase IgG antibodies.

If they have the presence of antibodies, they would be eligible for plasma exchanges with two objectives: removing pre-formed antibodies and eliminating Lyso-Gb3. Conversely, in the absence of pre-formed antibodies, LDL-apheresis is performed with the aim of eliminating Lyso-Gb3.

The proof-of-concept study was done with two FD patients undergoing ERT were identified, one with IgG-aGAL and the other with very low levels. PE was performed on the first patient, and LDL-apheresis on the second.

Lyso-Gb3 levels were titrated in blood before and after LDL-apheresis, and in the washout bag of the column.

For antibodies, titration was done in pre and post PE blood and in the extracted plasma from PE.

Results: After applying TA techniques, we observed that PE reduces IgG-aGAL by 85%, and in the case of LDL-apheresis, there was a 28% reduction in IgG-aGAL. While the ability to eliminate LysoGb3 showed a reduction of 25.5% in PE and 39.7% for LDL-apheresis.

To eliminate a potential confounding factor, LysoGb3 determination in albumin was within normal limits.

Conclusion: With these results, we confirm that PE is more efficient in removing IgG-aGAL but also eliminates LysoGb3, whereas LDL-apheresis is a very effective technique for removing Lyso-Gb3 but also contributes to antibody removal. Based on these findings, we consider TA to be an effective adjunctive tool for FD treatment, even as a standalone treatment. However, these are very preliminary results and should be reproduced with a larger number of patients.