Current Treatment Modalities and Therapies under development for Lysosomal Storage Diseases

Alsayed M[1], Awada N[1], Moslmany R[2], Al-Otaibi L[3], Alhazzaa S[4] Al-Wadai A[5], Al-Jaber R[2]

X European Conference on Rare Diseases
"Bringing Rare Diseases Closer"

July 6-8, 2012, Cedzyna, Poland

Lysosomal Storage Diseases (LSDs) are individually rare but collectively not uncommon group of over 40 diseases. Most LSDs are autosomal recessive disorders that result from a genetic alteration of genes encoding for lysosomal enzymes. Management and treatment of LSDs is quite challenging, due to their progressive nature, multisystem involvement, central nervous system affection and paucity of medical staff with experience in treatment of these disorders.

In the past, no specific treatment was available for the affected patients: management mainly consisted of supportive care and treatment of complications. Hematopoietic stem cell transplantation (HSCT) as a treatment for LSDs was first reported by Hobbs and co-workers in a MPS I patient in the early 1980's. Over 500 LSD patients have received allogenic bone marrow and more recently, cord blood transplants. In general, somatic disease is improved for most LSDs but skeletal and corneal manifestations remain relatively unaffected after HSCT. The microglias of the central nervous system, which are of bone marrow origin, are believed to be the source of enzyme in the brain after HSCT. The neuropsychological outcomes have varied widely after HSCT. The timing of HSCT is critical for CNS disease. One of the main limitations of HSCT is the high rate of mortality especially during the 1st year post transplantation. HSCT has been performed in our institute for some LSDs with variable outcome.

Although first suggested by de Duve in 1964, enzyme replacement therapy (ERT) for Lysosomal Storage Diseases (LSDs)) did not become a reality until the early 1990s when its safety and effectiveness were demonstrated in type 1 Gaucher disease. The first product (Ceredase for the treatment of Gaucher disease) was approved in 1991. Currently several ERTs are commercially available for Gaucher Disease (Cerezyme, Velagluceraze), Fabry disease (Replagal and Fabrazyme), MPS I (Aldurazyme), MPS II (Elaprase, Hunterase), MPS VI (Naglazyme), Pompe Disease (Myozyme). ERT is under development for other LSDs like MPS IVa, Metachromatic Leucodystrophy and Niemann-Pick disease. Enzyme replacement therapy (ERT) represents a significant progress in treatment of LSDs. However, the success of ERT with Gaucher disease type 1 was not fully reproduced in other LSDs and responses have been variable. Treatment costs are very high as well.

Furthermore, novel approaches including substrate inhibition therapy and enzyme enhancement therapy are under development. Proof of concept for gene therapy using animal models has been already established and further developments are expected in the near future. The currents treatment modalities for LSDs will be highlighted. New developments in this field will also be discussed.

[1]Deparment of Medical Genetics, [2]Pharmacy Services, [3]Department of Radiology, [4]Department of Surgery, [5]Department of Cardiology, King Faisal Specialist Hospital& Research Center, Riyadh, Saudi Arabia