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FABRY DISEASE

Enzyme replacement in Fabry disease

Researchers in Norway report that long-term enzyme replacement therapy (ERT) in young people with Fabry disease can lead to the complete clearance of globotiaocylceramide (GL3) deposits in glomerular endothelial and mesangial cells, and that reduction in GL3 deposits in podocytes is dependent on ERT dose.

"A major problem in treatment decisions in Fabry disease is the timing of treatment initiation," say two of the authors, Camilla Tøndel and Einar Svarstad. "We wanted to explore the 'window of therapeutic opportunity' to determine whether early ERT treatment of young patients with a normal glomerular filtration rate (GFR) and microalbuminuria could prevent progression of the cellular damage that is thought to be a precursor of progressive proteinuria and GFR decline."

The researchers followed up 12 patients (11 male) aged 7–33 years with Fabry disease who received treatment with agalsidase alfa or agalsidase beta for about 5 years. Renal biopsy samples were analysed at baseline and after 5 years.

After a median of 65 months, all patients showed total clearance of GL3 deposits in endothelial and mesangial cells. "Both drugs showed similar effects on reduction of deposits in endothelial and mesangial cells after 5 years," note the authors. "A clear dose-dependent effect was seen on reduction of deposits in the podocytes, with patients receiving the highest doses having the greatest clearance of podocyte deposits and normalization of microalbuminuria. This effect was most conspicuous in the youngest patient (aged 7 years at initation of ERT), whose podocytes almost completely normalized." Tøndel *et al.*'s findings need to be confirmed in larger patient cohorts.

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Original article Tøndel, C. *et al.* Agalsidase benefits renal histology in young patients with Fabry disease. *J. Am. Soc. Nephrol.* **24**, 137–148 (2013)