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Enzyme replacement therapy and white matter hyperintensity progression in Fabry disease

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Study objective

To determine whether enzyme replacement therapy (ERT) or clinical characteristics are associated with white matter hyperintensity (WMH) progression in Fabry disease (FD).

Summary results

ERT is not associated with WMH progression in FD, but higher total cholesterol is associated with slower WMH progression.

What is known and what this paper adds

ERT improves various microvascular, cardiac, and renal measures in FD, but its effects on WMH remain undetermined. This study addressed this lacuna in the FD literature.

Participants and setting

This study examined data for 149 patients with FD (44% male; baseline age, 39.7 ± 12.8 years) who participated in a preexisting observational study (NCT00196742) at the Mark Holland Metabolic Unit of Salford Royal Hospital (Salford, UK). The selected participants underwent ≥2 brain MRIs over ≥2 years between December 2006 and August 2016.

Design, size, and duration

A semiautomated procedure was used to calculate the total WMH volume in each MRI scan, and linear regression was used to calculate each participant's rate of change in WMH volume. Multiple linear regression was used to determine whether receiving ERT at any time between the baseline and final MRI was associated with the rate of change in WMH volume. Other metabolic measures were obtained.

Main results and the role of chance

Over a median observation period of 6.1 years (interquartile range [IQR], 3.7 years), the median number of available MRIs was 6 (IQR, 4), and the median interval between consecutive MRIs was 13 months (IQR, 3 months). The number of participants who received ERT at any time between the baseline and final MRI was 104 (70%). Receiving ERT was not associated with the rate of change in WMH volume (p = 0.22). Higher total cholesterol was associated with slower WMH progression (p = 0.03).

Table Multiple linear regression of select participant characteristics against the rate of change in WMH volume

Characteristic	B coefficient (95% CI)	*p* Value
Age at baseline MRI	0.001 (0.001 to 0.002)	<0.0005
Smoker at any time between baseline and final MRI	0.002 (−0.012 to 0.016)	0.74
Total cholesterol at baseline MRI	−0.008 (−0.015 to −0.001)	0.03
History of peripheral pain	0.018 (0.003 to 0.033)	0.02
ERT at any time between baseline and final MRI	0.012 (−0.007 to 0.031)	0.22

Bias, confounding, and other reasons for caution

The MRI scanners and protocols were nonuniform, and follow-up MRIs could not be coregistered to baseline MRIs. The selection of patients for ERT was nonrandom for this observational study. This study lacked a control group. The lack of an observed relationship between ERT and WMH progression does not preclude an association between ERT and stroke incidence.

Generalizability to other populations

This study's single-center nature may limit the generalizability of the results.

Study funding/potential competing interests

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A draft of the short-form article was written by M. Dalefield, a writer with Editage, a division of Cactus Communications. The authors of the full-length article and the journal editors edited and approved the final version.

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