Enzyme replacement therapy for late-onset Pompe disease: a systematic review

Guilherme I. P. S. Gertsenchtia,b, Ida V. D. Schwartza,b

aHospital de Clínicas de Porto Alegre, Porto Alegre, Brazil; bFederal Univeristy of Rio Grande do Sul, Porto Alegre, Brazil.

Introduction

Pompe disease (PD) is an inherited disorder characterized by deficiency of acid alpha-glucosidase, leading to progressive glycogen accumulation in the body’s organs and tissues.

Previous systematic reviews (SR) on enzyme replacement therapy (ERT) for late-onset PD (LOPD) haven't evaluated important endpoints as quality of life (QOL) and safety, creating the need for reassessing clinical outcomes.

Objective

To evaluate evidence available on the efficacy and safety of ERT for LOPD.

Methods

We systematically searched PubMed and Embase for prospective clinical studies published until May, 2017 evaluating ERT for LOPD.

Outcomes of interest were defined a priori. Only studies with n>5 were included. Assessment of quality of evidence (QOE) was performed according to the GRADE criteria.

Results

A total of 1172 articles were identified, 185 studies were eligible for abstract and full text reading and 25 articles were included in our analysis.

From a total of 10 endpoints evaluated, 4 had moderate or high GRADE Score: QOL, 6MWT, Muscle strength and AE.

Two endpoints defined a priori was not assessed by any of the studies: Sleep quality and Swallowing.

Quality of life outcome was evaluated in 6/25 studies and 5/6 used the SF-36 questionnaire, which measures physical and mental components. In spite of heterogeneous results across studies, GRADE score was moderate and the final results favors ERT.

Most AE were considered to be mild or moderate symptoms, such as urticarial rashes, flu-like symptoms, pruritus and hyperhidrosis. None of these AE caused discontinuation of the treatment.

In AE evaluation, one concern is antibody formation. In 4/5 studies, antibody anti-aglucosidase was analyzed and although all patients developed antibodies there was no correlation with severe AE and infusion-associated reactions (IARs) nor with treatment efficacy. Most IARs were mild to moderate in severity. The results suggest that ERT is safe in patients with PD.

Other outcomes had low or very low QOE, such as WGMS, Survival, Ventilation hours/day. In all 5 studies evaluating WGMS there was no improvement shown, however more data has to be assessed considering the very low QOE.

Discussion

Our results corroborate previously published SR on ERT impact on 6MWT and show positive effect of ERT on QOL and MS.

Our findings also suggest that ERT is safe in LOPD, once most AE were mild to moderate and antibody formation did not seem to interfere with any outcome evaluated.