Functional capacity in a late-onset Pompe disease patient: Effect of enzyme replacement therapy and exercise training

Sir,

Pompe disease is a rare inherited autosomal recessive disorder caused by the partial or total deficiency of acid α-glucosidase, resulting in lysosomal accumulation of glycogen.[1,2] Since 2006 enzyme replacement therapy (ERT) with recombinant human α-glucosidase was introduced; this changed decisively the progress of the infantile form of the disease.[3] However, the results were only moderate for the late-onset form: Limited improvements or stabilization of the symptoms. Exercise training has been considered as a supportive treatment to compensate for the muscle dysfunction in Pompe patients receiving ERT, resulting in increases in muscular strength and 6 min walking ability.[4] However, it remains unknown whether exercise training-induced adaptations acquired with simultaneous ERT, are maintained after cessation of the ERT. In the current case report, muscular strength, forced vital capacity (FVC), 6 min walking distance, and body composition were measured in an ambulatory male late-onset Pompe disease (LOPD) patient before and after discontinuing ERT, who continuously performed exercise training. The patient was 45-year-old (IVS1-13 T > G and c. 2066-2070dup, α-glucosidase enzyme activity in fibroblasts 0.26 nmol/mg/min) and followed ERT (20 mg/kg, every 14 days) for 3 years and then decided to withdraw. Supervised exercise training under close supervision, 3 times/week, was initiated 2 years after initiation of ERT. Each training session started with 20–30 min of bicycling at 110–120 heart beats per minute, mild stretching of the major muscle groups and then resistance exercise for the major muscle groups for 3 sets × 10 repetitions with free weights, machines, fit balls, and soft straps, at approximately 50–75% of maximum strength. Muscular strength, FVC, 6 min walking distance, and body composition (dual-energy X-ray absorptiometry) were evaluated every year.

Maximal isometric strength was increased after 12 months of ERT and continued to increase for a year after the initiation of exercise training. Muscle strength decreased 1 year after withdrawing from ERT, whereas it was restored during the last 2 years of exercise *per se* [Figure 1]. FVC decreased during ERT *per se*, recovered with ERT + exercise and slightly decreased with exercise *per se*. Six minutes walking distance was increased during the first 12 months after initiation of ERT and remained unaltered thereafter. Only minimal alterations were observed in whole body, lean body mass, and bone mineral density.

The increase in muscle strength and 6 min walking distance with ERT *per se* or in combination with exercise training may be due to a mild degradation of glycogen from skeletal muscle.[5] A few months after termination of ERT our patient suffered from muscular pain although it was impossible to identify the origin of this pain. As a consequence, exercise training frequency and intensity were reduced for 6 months; only one or two training sessions were performed each week with 20–30% lower resistance, which may explain the reduction in muscular strength 1 year after withdrawal from ERT. Thereafter, muscle pain disappeared, and exercise training frequency and intensity returned to the previous level. The higher FVC was attained with the combination of ERT and exercise training. The current data suggest that the combination of moderate intensity resistance and aerobic exercise may sustain functional capacity and muscle strength in ambulatory LOPD patients after voluntary withdrawal from of ERT. Exercise training should be of moderate intensity to avoid possible detrimental effects of excessive loading, especially in patients with cardiac involvement along with myopathy.

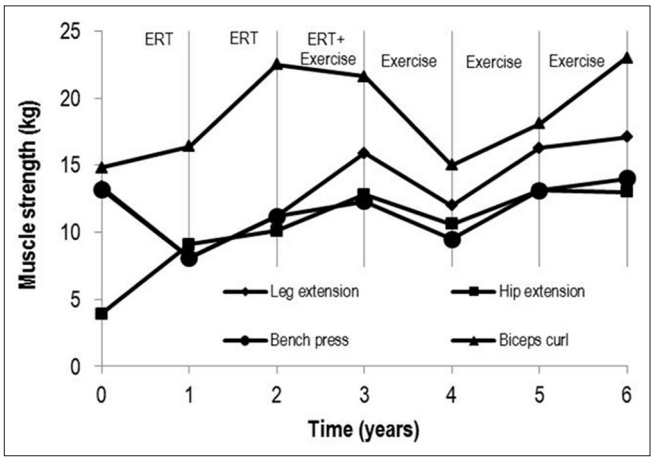

Figure 1: Muscular strength changes over 6 years in one male late-onset Pompe disease patient under enzyme replacement therapy (enzyme replacement therapy, 24 months), enzyme replacement therapy and regular exercise training (enzyme replacement therapy + exercise, 12 months), and under exercise training *per se* (exercise, 36 months)

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Conflicts of interest
There are no conflicts of interest.

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