P4.39
Enzyme replacement therapy during pregnancy and lactation in Pompe disease
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In 2006 Enzyme Replacement Therapy (ERT) with alglucosidase alfa was registered as a treatment for Pompe disease. So far it is unknown whether alglucosidase alfa can be safely administered during pregnancy and lactation. In pregnant women with other lysosomal storage diseases continuation of ERT seemed to be safe for the unborn child. For Pompe disease there are no such cases published in medical literature. We present a patient who continued receiving ERT during pregnancy and lactation. We carefully monitored the pregnancy and lactation period of a primiparous 42-year-old woman with adult-onset Pompe disease. She had moderate limb-girdle weakness and used nocturnal ventilation. She continued receiving alglucosidase alfa in a dose of 20 mg/kg every other week during pregnancy and lactation. After delivery pharmacokinetic studies were performed in breast milk and plasma to determine the milk/plasma concentration ratio of alglucosidase alfa. The mother’s clinical condition remained stable until the 25th gestational week. Thereafter she experienced more mobility problems and increased respiratory effort. Fetal growth was normal as monitored by regular ultrasound investigations. At a gestational age of 38 weeks, a healthy baby-boy was born. There were no maternal complications and the child developed normally. In breast milk, α-glucosidase activity levels peaked 2 h after the end of the infusion, which was 2 h later than in plasma. The peak activity levels in milk were 250 nmol/ml h versus 80 nmol/ml h in plasma. The α-glucosidase activity in breast milk disappeared over a period of 25 h after the infusion. This case report indicates that ERT with alglucosidase alfa can be administered safely during pregnancy and lactation. Alglucosidase alfa transfers in small amounts into breast milk. Based on our findings, we recommend refraining from breastfeeding on the day of the infusion.

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P4.40
Enzyme Replacement Therapy and prognostic factors for response: An ongoing open-label cohort study in adults with Pompe Disease
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Enzyme Replacement Therapy (ERT) for Pompe disease was approved for clinical use in 2006 based on the efficacy of alglucosidase alfa in classic infantile patients. More recently, treatment efficacy was demonstrated in adults. We evaluated the long-term effects of ERT and compared effects with the natural disease course. Furthermore prognostic factors for treatment response were identified. In this ongoing prospective study, we included 71 adults who were treated with 20 mg/kg alglucosidase alfa every other week. Muscle strength (by manual muscle testing and hand held dynamometry) and pulmonary function (Forced Vital Capacity (FVC) in upright and supine position) were assessed every 3 months. In patients who had also participated in a prospective follow-up study before start of ERT, effects of ERT were compared with the natural course. The median treatment duration was 23 months (range 5–47 months). Muscle strength increased significantly after start of ERT: 1.4% points/year for manual muscle testing and 4.0% points/year for hand held dynamometry. The calculated difference between natural course and treatment course was 3.3% points/year for manual muscle testing (P < 0.001) and 7.9% points/year for hand held dynamometry (P < 0.001). During ERT, FVC remained stable in upright position and declined further in supine position. For FVC in upright position, the calculated difference between natural course and treatment course was 1.75% per year (P = 0.08). Favorable prognostic factors for treatment response were female gender for muscle strength and younger age for pulmonary function. Our study shows that ERT significantly alters the natural course in adult patients with Pompe disease. During treatment, muscle strength increased and pulmonary function in upright position stabilized, while both parameters declined before start of ERT. The course of FVC in supine position did not change substantially.

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P4.41
Alglucosidase alfa reduces non-invasive ventilation needs in late-onset Pompe disease: Post-hoc analysis from the late onset treatment study
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The Late-Onset Treatment Study (LOTS), a randomized, placebo-controlled trial, showed that treatment of patients with late-onset Pompe disease with alglucosidase alfa led to clinically important improvements in the 6-min walk test (6MWT) and forced vital capacity (FVC) as compared to the placebo group over an 18-month period. To assess another clinically meaningful outcome measure, we performed a post hoc analysis of LOTS data on the effects of treatment upon the need for non-invasive ventilation (NIV) based on the number of hours on NIV per day as recorded in a patient diary. Twenty patients (33.3 %) in treatment group and 11 (36.7 %) in placebo group had a history of using NIV support. In patients who reported the use of NIV at baseline, the mean number of hours per day was 8.7 ± 1 h in treatment group and 7.0 ± 3 h in placebo group. Statistical significance of the between-group difference was assessed using lin-
P4.42
Muscle protein synthesis in patients with Dystrophy Myotonica type 1
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Dystrophy Myotonica type 1 (DM1) is the most common muscular dystrophy. Aerobic exercise improves fitness in DM1 patients. Whether the improvement is caused by improved cardio-respiratory fitness or increased muscle net-protein synthesis is not known. In healthy individuals, especially in combination with protein-intake improved muscle protein anabolic state. Therefore, we investigated how exercise combined with protein-supplement affected skeletal muscle metabolism in DM1 patients. Seven DM1 patients and 6 healthy controls were studied during two trials with and without oral protein-supplementation for 3 h in the recovery phase from exercise. They performed 40 min 1-leg knee extensor exercise kicking at 70% of Wmax. Net protein anabolism was determined across the leg that was exercised with a combination of arterial-femoral venous differences, tracer dilution of continuous infused [1,2-13C]-Leucine, and blood flow. There was no significant difference between DM1 patients and healthy controls in exercise specific physiological and biochemical data; heart rate, blood flow, catecholamines, insulin, lactate, glucose and free fatty acids. In the 3 h post-exercise muscle net protein balance switched from breakdown, measured without protein supplementation, to synthesis after protein supplementation, in both healthy controls (from 0 to 15 μmol/min, p < 0.05) and in DM1 patients (from -3 to 10 μmol/min, p < 0.01). Post-exercise oral protein supplementation induced muscle protein anabolism in patients with DM1. Suggestion that these patients can train their skeletal muscle and improve their muscle quality an possibly mass. This indicates that protein supplementation may be an important add-on to aerobic conditioning in patients with DM1, which should be studied in longer term training trials.

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MYOTONIC DYSTROPHIES: POSTER PRESENTATIONS

P4.43
Therapeutic effect of metformin against insulin resistance in myotonic dystrophy type 1
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A clinical intervention study of metformin was performed to investigate beneficial effects for treatment against insulin resistance in myotonic dystrophy (DM1). Subjects were patients with DM1 who showed hyperinsulinemia on 75 g oral glucose tolerance test (OGTT), and had never been treated by medicine for diabetes. One hundred mg of metformin per day was administered for 12 weeks. Clinical findings, OGTT, routine blood tests including lactic acid were examined before and after the trial. All medicine, diet, exercise, and rehabilitation were fixed during the trial. A summation of serum insulin (IRI) during OGTT (S-IRI) and summated blood sugar (BS) in the same manner (S-BS), are under the curve of IRIs (A-IRI) and BSs (A-BS) during OGTT, and the homeostasis model assessment insulin resistance (HOMA-IR) were calculated. Statistical analyses were carried out by Wilcoxon signed-rank test. Seventeen patients with DM1 were participated (8 females and 9 males). The median value of the age was 55.0, and the number of CTG repeat was 1167. One patient showed diabetes pattern with hyperinsulinemia on OGTT, seven were borderline pattern of OGTT with hyperinsulinemia and nine had only hyperinsulinemia with normal BS pattern. S-IRI, A-IRI and the insulin level at 120 min during OGTT after the trial were significantly decreased compared to those before the trial. BS at 120 min during OGTT and HbA1c after the trial were similarly significantly decreased. HOMA-IR, the fasting BS and IRI, S-BS and A-BS during OGTT had a tendency of decrease by the trial, without significant difference. There was no significant difference between the trial for routine blood tests including lactic acid and body weight. No adverse event was observed through out the trial. Metformin treatment is useful to improve insulin resistance in DM1 without any adverse events for short period observation of 12 weeks.

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P4.44
Methylphenidate reduces excessive daytime sleepiness in patients with myotonic dystrophy
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To evaluate the efficacy and tolerability of methylphenidate for the treatment of excessive daytime somnolence (EDS) in patients with myotonic dystrophy type 1(DM1). Twenty-four patients with DM1 with the Epworth Sleepiness score at ≥10 were invited to participate in a randomized double-blind crossover trial of 20 mg/day methylphenidate versus placebo, with 3 weeks in each arm of the study separated by a 2-weeks washout period. Before and after each trial, subjects completed the Daytime Sleepiness scale (DSS), Epworth Sleepiness Scale (ESS), the quality-of-life measures (RAND 36-item) and the profile of Mood States (POMS). The mean latency sleep (MLS) was measured using the OLSER test. The mean DSS scores decreased from 8.87 ± 0.53 to 6.11 ± 0.51 as compared with placebo (P = 0.0007) and that of ESS decreased from 10.38 ± 0.79 to 7.6 ± 0.69 (P = 0.0032). There was no significant change in MLS (P = 0.237) but methylphenidate significantly (P = 0.04) decreased the number of microsleeps compared with untreated or placebo. The POMS and RNAD 36-item quality of life scale showed no significant change. Three patients withdrew from the study because of side