A double-blind placebo-controlled trial of triheptanoin in adult polyglucosan body disease

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BACKGROUND: Adult polyglucosan body disease (APBD) is a progressive neurogenetic disorder caused by a deficiency of glycogen branching enzyme. Patients develop in the 5th or 6th decade of life neurogenic bladder, progressive spastic paraparesis, sensorimotor peripheral neuropathy and sometimes dementia. There currently is no effective therapy. We hypothesized that decreased glycogen degradation leads to cellular energy deficit and that anaplerotic therapy via triheptanoin may augment energy production thus preventing or reversing cellular damage.
METHODS: This was a two-site randomized crossover study over one year of 23 patients (age 35-73 years; 63% male). Vegetable oil served as placebo. Outcome measures included a 6-minute walk test (primary), balance testing, and SF-36 health survey questionnaire for all subjects; the Spastic Paraplegia Rating Scale, finger tap and dynamometer testing in French site subjects. Safety monitoring included adverse events, blood chemistries, urine organic acids and acyl carnitine profile in blood. The linear mixed model was used to analyze this study.
RESULTS: Nineteen patients were eligible for data analysis. At baseline, patients could walk a mean 389±164 meters (range 95-672). The overall mean difference between subjects on triheptanoin versus placebo was 6 meters; 95% CI: (-11, 22); p=0.49. Motion capture gait analysis, gait quality, stair climbing did not show a consistent direction of change. SF36 questionnaire showed significant improvement in mental and physical quality of life scores on triheptanoin. There was no significant difference in the number of patients experiencing adverse events in the two treatment groups. Patients were followed on the open label study for up to 5 years. Most parameters showed progressive decline over time.
DISCUSSION: Triheptanoin had a good safety profile. However, from this study we cannot conclude that it is effective in the treatment of APBD over a 6-month period. We quantified gait, balance, and quality of life data over time to be used in future clinical trials.