Assessment of disease progression in dysferlinopathy

A 1-year cohort study

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Study objective

To determine which functional measures can detect disease progression in dysferlinopathy over 6-month and 1-year periods.

Summary results

A variety of functional outcome measures including motor performance and strength testing can detect changes in dysferlinopathy over 6-month and 1-year periods.

What is known and what this paper adds

The selection of outcome measures in clinical studies of dysferlinopathy is challenging due to heterogeneity in the condition's manifestation and progression. This study identifies certain functional outcome measures that are sensitive to changes over ≤12 months.

Participants and setting

This study examined 193 participants from the Jain Clinical Outcome Study in Dysferlinopathy, an ongoing study that follows patients with dysferlinopathy through 15 centers in the US, Australia, France, Germany, Italy, Japan, Spain, and the UK. The data analyzed in this study were collected between October 2012 and March 2016.

Design, size, and duration

The participants underwent baseline, 6-month and 1-year follow-up evaluations. During these visits, the participants were assessed with the Motor Function Measure–20 (MFM-20), the Brooke Scale, the Jebsen Test, manual muscle testing (MMT), and hand-held dynamometry. Ambulant patients (77% of cohort) were also assessed with the adapted North Star Ambulatory Assessment (a-NSAA), timed function tests and the 6-minute walk test (6MWT). Participants completed the ACTIVLIM questionnaire. For each test, this study calculated standardized response means (SRMs) for from-baseline changes over the study period. These calculations were performed for the whole cohort, nonambulant participants (i.e., those unable to walk 10 meters unassisted), and subgroups of ambulant participants, classified as mildly, moderately, or severely affected based on baseline a-NSAA scores.

Main results and the role of chance

The a-NSAA was the most responsive as an outcome measure overall (SRM, 0.61) and in mildly (SRM, 0.44) or moderately (SRM, 0.89) affected ambulant participants. The most responsive outcome measure in nonambulant participants was the MMT for wrist flexion (SRM, 0.69).

Bias, confounding, and other reasons for caution

This study considered changes over a relatively short period. The functional scale scores were measuring ordinal rather than continuous data. The changes observed in the outcome measures need to be related to patient reports of functional changes in their ability.

Generalizability to other populations

The inclusion of participants from 8 countries favors the international generalizability of the results.

Study funding/potential competing interests

Table 4 Sample size estimates for a placebo-controlled clinical trial

Target study population	Target treatment effect				
	50% reduction in progression	75% reduction in progression	Halting of progression	20% improvement	50% improvement
All ambulant patients	328	148	90	62	42
Moderate patients only (baseline a-NSAA 11–40)	176	80	46	34	22

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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