ACRM
AMERICAN CONGRESS OF REHABILITATION MEDICINE

Archives of Physical Medicine and Rehabilitation

journal homepage: www.archives-pmr.org

Archives of Physical Medicine and Rehabilitation 2013;94:1555-61

ORIGINAL ARTICLE

Responsiveness of the Motor Function Measure in Patients With Spinal Muscular Atrophy

Carole Vuillerot, MD, PhD,[a,b,c,d] Christine Payan, MD,[e] Jean Iwaz, PhD,[b,c,d,f] René Ecochard, MD, PhD,[b,c,d,f] Carole Bérard, MD,[a] and the MFM Spinal Muscular Atrophy Study Group

From the [a]Hospices Civils de Lyon, Hôpital Femme-Mère-Enfant, L'Escale, Service de Médecine Physique et de Réadaptation Pédiatrique, Bron; [b]Université de Lyon, Lyon; [c]Université Lyon I, Villeurbanne; [d]CNRS UMR 5558, Laboratoire de Biométrie et Biologie Evolutive, Equipe Biostatistique Santé, Pierre-Bénite; [e]Assistance Publique-Hôpitaux de Paris, Hôpital Pitié-Salpétrière, Institute of Myology, Paris; and [f]Hospices Civils de Lyon, Service de Biostatistique, Lyon, France.

Abstract

Objective: To assess the ability of the Motor Function Measure (MFM) to detect changes in the progression of spinal muscular atrophy (SMA).

Design: Observational, retrospective, multicenter cohort study.

Setting: Seventeen departments of pediatric physical medicine.

Participants: Volunteer patients with SMA (N = 112) aged 5.7 to 59 years with no treatment other than physical therapy and nutritional or respiratory assistance.

Interventions: Not applicable.

Main Outcome Measures: The distributions of the MFM scores (total score and 3 subscores) were analyzed per SMA subtype. The relationships between scores and age were studied. The slopes of score changes (reflecting MFM responsiveness) were estimated in patients with at least 6 months' follow-up and 2 MFMs. Hypothetical sample sizes for specific effect sizes in clinical trial scenarios are given.

Results: In 12 patients with SMA type 2 and 19 with SMA type 3 (mean ± SD follow-up, 25.8±19mo), there was a moderate inverse relationship between age and the MFM total score. Patients with less than 6 months' follow-up showed little score changes. Patients with longer follow-ups showed a slow deterioration (−0.9 points/y for type 2 and −0.6 points/y for type 3). Substantial responsiveness was obtained with the MFM Dimension 2 subscore (proximal and axial motricity) in patients with SMA type 2 (standardized response mean [SRM] = 1.29), and with the MFM Dimension 1 subscore (standing and transfers) in patients with SMA type 3 aged 10 to 15 years (SRM = .94).

Conclusions: If further confirmed by larger studies, these preliminary results on the relative responsiveness of the MFM in SMA will foster its use in monitoring disease progression in patients who participate in clinical trials.

Archives of Physical Medicine and Rehabilitation 2013;94:1555-61

Spinal muscular atrophy (SMA) is a recessively inherited neuromuscular disease characterized by a degeneration of the spinal cord motor neurons. The clinical spectrum of SMA is highly variable and ranges from early infant death to normal adult life. The severity of muscle weakness depends mainly on the patient's age at disease onset and, most importantly, on the maximal motor milestone acquired (ability to hold head up, sit, or walk).[1] This led some authors to propose defining SMA stages by the ability to sit or walk.[2-5]

The recent understanding of the pathogenesis of SMA raised hopes that specific therapeutic approaches might be possible.[6] Many clinical trials—planned, in progress, or completed—have chosen motor function as the primary or secondary outcome.[6] Indeed, in children with SMA, motor function assessment tools appeared to be more reliable than quantitative muscle testing in monitoring the course of the disease.[7,8] Nonetheless, valid and responsive outcome measures are still needed to assess the effect of a treatment on the motor function of patients with SMA.[9,10]

Supported by the Association Française contre les Myopathies.

No commercial party having a direct financial interest in the results of the research supporting this article has or will confer a benefit on the authors or on any organization with which the authors are associated.

0003-9993/13/$36 - see front matter © 2013 by the American Congress of Rehabilitation Medicine
http://dx.doi.org/10.1016/j.apmr.2013.01.014

Today, few clinical outcome measures, except survival, are available for patients with SMA type 1, the most severe form of the disease.[11] Therefore, a motor function measure that allows an assessment of patients with SMA, regardless of the disease type, is welcome. Validation studies of many scales applied to SMA have already been published—for example, the Gross Motor Function Measure (GMFM),[12] the Hammersmith Functional Motor Scale for SMA (HFMS),[13,14] the Expanded HFMS (ExpHFMS),[15,16] and the Upper Limb Module for Nonambulant SMA Patients.[17] However, the validation processes of most scales lack specific responsiveness assessments (ie, sensitivity to change studies).[18]

Within the specific context of SMA, the HFMS and the Modified HFMS (MoHFMS)[19] are used only in nonambulant patients with SMA types 2 and 3. The 6-minute walk test is now routinely used to assess patients with neuromuscular diseases, especially Duchenne muscular dystrophy and SMA. Although convenient and useful in patients with SMA type 3,[20] this test becomes useless when ambulation is lost during follow-up, especially during a clinical trial. The ExpHFMS has added 13 items from the GMFM to capture various aspects of ambulation. Its reliability and validity have been validated in SMA types 2 and 3,[15] but the methodology used for its construction has been the object of some criticism.[18] The Motor Function Measure (MFM) is a reliable tool designed for most of the neuromuscular diseases and is applicable to a wide range of disease severities in ambulant and nonambulant patients between 6 and 60 years of age.[21] The MFM showed good convergent validity and excellent correlations with the Vignos, Brooke, and FIM scales, as well as with a visual analog scale of overall motor impairment used by some physicians.[21] The preliminary results concerning responsiveness in a population of 152 patients with various neuromuscular diseases (of whom 15 had SMA) showed good responsiveness, especially in Duchenne muscular dystrophy.[22,23]

The aim of the present study was to monitor motor function impairment in patients with SMA types 1, 2, and 3 using the MFM in order to study the responsiveness of the MFM in this disease and provide estimations of the number of patients with SMA needed for clinical trials to prove the effectiveness of a given drug.

Methods

Participants

For the present study, data were collected from patients followed up in 17 departments of pediatric physical medicine located in France, Belgium, and Switzerland. These centers use the MFM in the everyday management of patients with a wide variety of neuromuscular diseases, and their physiotherapists were given specific training in administering the MFM with a high interrater reliability.[21] The protocol of the study was approved by the ethics committee of Hospices Civils de Lyon on June 26, 2009.

The inclusion criteria were as follows: (1) patients older than 5 years at first MFM testing; (2) a clinical diagnosis of SMA type 1, 2, or 3 with laboratory confirmation of a mutation of the survival motor neuron (SMN) gene; (3) at least 1 MFM testing by a trained physiotherapist during routine follow-up; and (4) no treatment other than physical therapy, nutritional assistance, and respiratory assistance.

In the present study, in agreement with the International SMA Consortium,[1,24] SMA is classified into 3 clinical types: (1) SMA type 1 (severe) with onset between birth and 6 months of age (patients unable to sit without support and/or death occurring usually before 2y of age), (2) SMA type 2 (intermediate) with onset before 18 months of age (patients able to sit but unable to stand or walk unaided and/or death occurring usually after 2y of age); and (3) SMA type 3 (mild) with onset after 18 months of age (patients able to stand and walk and/or death occurring in adulthood).

List of abbreviations:

ExpHFMS	Expanded HFMS
GMFM	Gross Motor Function Measure
HFMS	Hammersmith Functional Motor Scale for SMA
MFM	Motor Function Measure
MFM D1	Motor Function Measure, Dimension 1 subscore
MFM D2	Motor Function Measure, Dimension 2 subscore
MFM D3	Motor Function Measure, Dimension 3 subscore
MoHFMS	Modified HFMS
SMA	spinal muscular atrophy
SMN	survival motor neuron
SRM	standardized response mean

Motor Function Measure-32

The MFM-32 consists of 32 task items in 3 dimensions that provide a detailed profile of the physical impairment: D1, standing and transfers; D2, axial and proximal motor function; and D3, distal motor function. The scoring of each task uses a 4-point Likert scale based on the subject's maximal abilities without assistance: 0, cannot initiate the task or maintain the starting position; 1, performs the task partially; 2, performs the task incompletely or imperfectly (with compensatory/uncontrolled movements or slowness); and 3, performs the task fully and "normally." The 32 scores are summed to yield a total score expressed as the percentage of the maximum possible score (the one obtained with no physical impairment); the lower the total score, the more severe the impairment.

In routine follow-up of patients with neuromuscular diseases, the MFM scores of each patient are automatically reported by the physiotherapist on a specific scoring sheet allowing a longitudinal follow-up. Furthermore, the cooperation of the patients is also rated as null, moderate, or optimal.

Data collection

By the end of 2009, the scores of MFM tests administered to 112 patients in the 17 centers between 2005 and June 30, 2008, were collected by a clinical research assistant. For each patient, a specific clinical questionnaire was filled out from the medical records; it included detailed information on motor deterioration milestones (eg, loss of ambulation, defined as the inability to walk 10 steps without assistance).

Statistical analysis

The MFM scores were presented as mean, SD, and range per SMA type and walking ability. The relationship between the MFM total score and age at first visit was analyzed in patients with SMA types 2 and 3 by using regression modeling. The assumption of homogeneity of the regression slopes was tested using an analysis of covariance.

The responsiveness was studied according to the SMA type (in types 2 and 3) by analyzing the slopes of change in patients with at least 6 months' follow-up. Precisely, for each patient, the repeated