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Hammersmith Functional Motor Scale and Motor Function Measure-20 in non ambulant SMA patients

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Abstract

The aim of this prospective longitudinal multi centric study was to evaluate the correlation between the Hammersmith Functional Motor Scale and the 20 item version of the Motor Function Measure in non ambulant SMA children and adults at baseline and over a 12 month period. Seventy-four non-ambulant patients performed both measures at baseline and 49 also had an assessment 12 month later. At baseline the scores ranged between 0 and 40 on the Hammersmith Motor function Scale and between 3 and 45 on the Motor Function Measure 20. The correlation between the two scales was 0.733. The 12 month changes ranged between −11 and 4 for the Hammersmith and between −11 and 7 for the Motor Function Measure 20. The correlation between changes was 0.48. Our results suggest that both scales provide useful information although they appeared to work differently at the two extremes of the spectrum of abilities. The Hammersmith Motor Function Scale appeared to be more suitable in strong non ambulant patients, while the Motor Function Measures appeared to be more sensitive to capture activities and possible changes in the very weak patients, including more items capturing axial and upper limb activities. The choice of these measures in clinical trials should therefore depend on inclusion criteria and magnitude of expected changes.

Keywords: Spinal muscular atrophy; Outcome measures

1. Introduction

Spinal muscular atrophy (SMA) is a neuromuscular disease characterized by degeneration of alpha motor neurons in the spinal cord. In the last years a better

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understanding of the mechanisms underlying the disease has allowed the development of a number of possible therapeutic approaches, with some of them already being used in clinical trials [1–3]. The prospective of clinical trials has highlighted the need for identifying methods of assessments that could be used as outcome measures and to collect natural history data [3–5]. An international Clinical Outcomes Group consisting of clinicians, scientists, patient and advocacy groups has suggested that in non ambulant patients functional scales should be used as primary outcome measures, as they provide clinically meaningful information on the course of the disease by assessing different aspects of function that are related to activities of daily living [6].

The Hammersmith Functional Motor Scale (HFMS) [7] and the Motor Function Measure (MFM) [8] are the scales that have been more frequently used and reported. Validation studies and natural history data are available [8–17] and both have also been used in some of the most recent clinical trials in non ambulant SMA [18–20]. While the HFMS was developed including activities that could all be achieved even by young infants [7], the original version of the MFM was validated starting from the age of 7 years. Recently, a subset of 20 items also suitable for young children were identified and these were used to constitute the MFM 20, a shorter scale structured according to the same 3 functional domains used in the larger original 32 item scale [12]. The ability to assess young children is important. In our recent clinical trials, children in the age range between 3 and 5 years appeared to be the ones who responded better to treatment [18,20].

The HFMS and the MFM 20 have some overlap, with some activities such as sitting independently or rolling, present in both, but have different constructs with the HFMS specifically designed for assessing non ambulant SMA patients and the MFM exploring three different domains and a wider range of items assessing trunk, proximal and distal abilities in order to cover different neuromuscular disorders with different patterns of weakness. No systematic study has been performed to investigate how the two scales relate to each other or the correlation between changes in the two scales over time. The aim of our longitudinal multi centric study was to prospectively establish the correlation between the two measures in non ambulant SMA children and adults at baseline and over a 12 month period.

2. Subject and methods

This prospective study was performed as part of a large European multicentric natural history study of SMA including 8 participating sites from 6 countries. Patients were enrolled in the present longitudinal study if they (i) had a genetically confirmed diagnosis of SMA with a homozygous deletion of exon7 in the SMN1 gene (ii) were non ambulant, (iii) did not have unstable medical conditions that would preclude participation. To reduce selection bias, all patients seen in the neuromuscular clinics who fulfilled eligibility criteria were consecutively offered enrollment until the target of recruitment was reached.

2.1. HFMS

The scale consists of 20 items, investigating the child's ability to perform various activities (Table 1). Each activity (item) is scored on a 3 point scoring system, with a score of 2 for unaided, 1 for assistance and 0 for inability. A total score can be achieved by summing the scores for all the individual items. The total score can range from 0, if all the activities are failed, to 40, if all the activities are achieved. All items have to be tested without spinal jacket or orthoses.

As we only included non ambulant patients the HFMS used in this study is the original version of the scale that does not include the items related to standing and walking integrated in the expanded and extended versions that can also be used in ambulant SMA patients [15,21].

2.2. MFM20

The scale consists of 20 items (Table 1) subdivided in three functional dimensions: D1 standing and transfers, D2 axial and proximal motor function and D3 distal motor function. Each item is scored as follows: 0, cannot initiate the task or cannot maintain the starting position; 1, partially performs the task; 2, performs the task with compensatory movements and 3, performs the task fully. The total score is obtained by adding up all item scores from each dimension. According to the manual, the scores can also be expressed as a percentage of the maximum possible score but, in order to make the results more comparable with the HFMS scores, this was not used in our study.

The HFMS was administered before the MFM20. Patients were allowed to rest in between the two assessments if needed. For the overlapping items, present in both scales, these were performed only once and scored on both scoring proforma according to the instruction of each scale.

2.3. Training sessions

One of the physiotherapists organized training sessions with the physiotherapists from the other centers. This consisted in assessing training videos of several patients, having the opportunity to discuss results and possible bottlenecks in scale administration and scoring. Inter and intra observer reliability of the two measures have already been reported [13,22].

Table 1
List of items in the MFM20 (top) and in the HFMS (bottom).

Item/starting position	Motor Function Measure 20	Domain
	Task description	
1. Supine	Holds the head for 5 s in midline position and turns it completely from one side to the other	D2
3. Supine	Flexes the hip and knee more than 90° by raising the foot during the whole movement	D2
4. Supine	From the plantar flexion, dorsiflexes the foot to at least 90° in relation to the lower part of the leg (D3)	D3
5. Supine	Raises the hand and moves it to the opposite shoulder	D2
6. Supine	Lower limbs half-flexed, kneecaps at the zenith and feet resting slightly apart: maintains for 5 s the starting position then raises the pelvis; the lumbar spine, the pelvis and the thighs are aligned and the feet slightly apart	D1
7. Supine	Turns over into prone and frees both upper limbs from under the trunk	D1
9. Seated on the mat	Without upper limb support, maintains the seated position for 5 s and is then capable of maintaining contact 5 s between the two hands	D2
10. Seated on the mat	Tennis ball placed in front of the PERSON: without upper limb support, leans forward, touches the ball and sits back again	D2
11. Seated on the mat	Without upper limb support, stands up	D1
12. Standing	Without upper limb support, sits down on the chair with the feet slightly apart	D1
14. Seated on the chair or in the wheelchair	From head in complete flexion, raises the head then maintains it raised for 5 s, the head stays in midline position throughout the movement and the holding position	D2
18. Seated on the chair or in the wheelchair	Goes round the edge of the CD with the same finger without hand support on the table	D3
21. Seated on the chair or in the wheelchair	Picks up the tennis ball, and turns the hand over completely holding the ball	D3
22. Seated on the chair or in the wheelchair	One finger on diagram places finger on 8 squares	D3
23. Seated on the chair or in the wheelchair	Places the two forearms and/or the hands on the table at the same time without moving the trunk	D2
24. Seated on the chair	Without upper limb support, stands up with the feet slightly apart	D1
25. Standing with upper limb support on equipment	Without upper limb support, maintains a standing position for 5 s with the feet slightly apart, the head, trunk and limbs in midline position	D1
27. Standing	Without support, touches the floor with one hand and stands up again	D1
30. Standing without support	Runs 10 m	D1
32. Standing without support	Without upper limb support, manages to squat and gets up twice in a row	D1

Hammersmith Functional Motor Scale
1 Plinth/chair sitting can be over edge of plinth or on plinth/floor
2 Long sitting legs straight = knees maybe flexed, knee caps pointing upwards, ankles <10 cm apart
3 One hand to head in sitting
4 Two hands to head in sitting
5 Supine to side-lying
6 Rolls prone to supine over R
7 Rolls prone to supine over L 8 rolls supine to prone over R
9 Rolls supine to prone over L 10 sitting to lying
11 Props on forearms
12 Lifts head from prone
13 Prop on extended arms
14 Lying to sitting
15 Four-point kneeling
16 Crawling 17 lifts head from supine
18 Supported standing
19 Stand unsupported
20 Stepping

2.4. Statistical analysis

Correlations were evaluated by the Spearman rank correlation coefficients. The level of significance was set at 0.001.

3. Results

Seventy-four non ambulant patients performed both measures at baseline. (71 type 2 and 3 type 3 who lost ambulation) age range 2.67–28.17 years (mean 8.62, SD 6.24).

3.1. HFMS

The HFMS scores ranged between 0 and 40 (mean 13.7, SD 9.9). Fig. 1a shows the distribution of scores according to age.

3.2. MFM20

The MFM20 scores ranged between 3 and 45 (mean 26.7, SD 9.2). Fig. 1b shows the distribution of scores according to age.

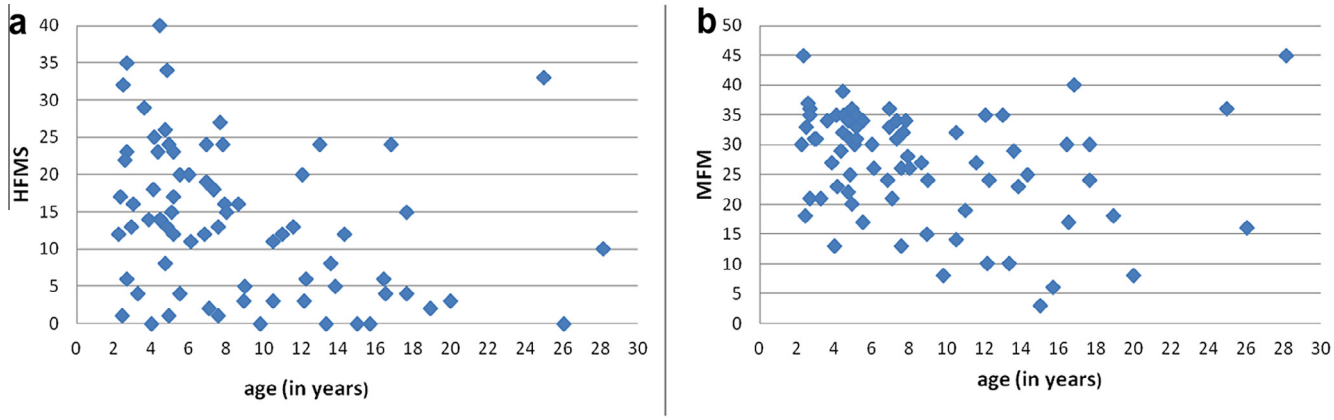

Fig. 1. Distribution of scores of the HFMS (a) and of the MFM 20 (b) related to age showing that low and high scores could be observed at all ages.

The correlation between the two scales at baseline was 0.733 (Fig. 2) ($p < 0.001$).

HMFS total scores of 0–2 on the HFMS (just able to sit) were associated with MFM20 total scores ranging between 2 and 21. In the patients with total HMFS score of 0–2 the MFM 20 items with a score >0 were, in order of frequency, item 23, 14, 22, 18, 1,4, 5, 3. These were related to axial and upper limb proximal function (D2) (items 23, 14 1, 3, 5) or distal motor function (D3) (items 18, 22, 4) (see Table 1 for details of the items).

HMFS scores of 25 or above were associated with a plateau of MFM20 scores that with one exception were between 32 and 36. Seven patients had a ceiling effect, with MFM20 items 6, 11, 12 24, 27, 30 and 32 (all from D1, standing and transfers) having a score of 0 irrespective of the HFMS scores (see Fig. 3 and Table 1 for details of the items).

3.3. 12 month changes

49 subjects completed the 12 month assessment. Among the patients who could not complete the 12 months assessment, 5 underwent scoliosis surgery, 16 entered an intervention study and four were unable to attend the follow up appointment within the allocated schedule. The

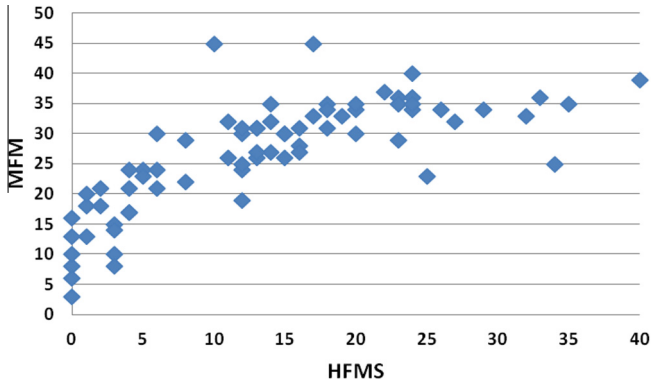

Fig. 2. Correlation of the HFMS and MFM20 baseline scores.

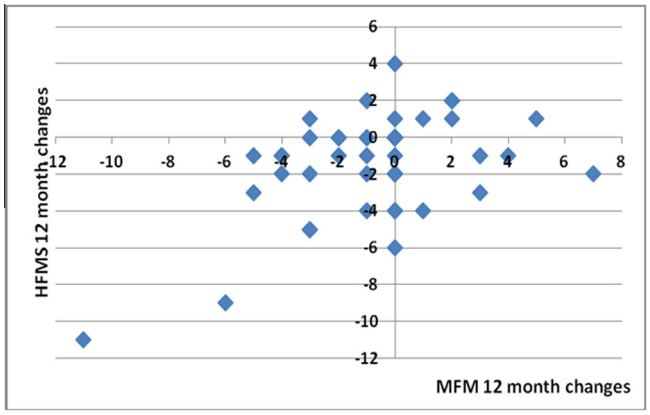

Fig. 3. Correlation of the HFMS and MFM20 12 month changes.

HFMS changes ranged between −11 and 4 (*mean −1.33, SD 2.74*); the MFM20 scores ranged between −11 and 7 (*mean −0.73, SD 2.94*).

The correlation between changes was 0.48 ($p < 0.001$).

Thirty-three of the 49 had changes of 0 ± 2 points on the MFM20. Of these 33, 25 had also changes of 0 ± 2 points on the HMFS, 7 had a decrease of HFMS scores >2 points (range 3–6) and 2 had an increase >2 points. In the subjects with relatively stable MFM20 scores and decreased HFMS scores, the HFMS changes were mainly observed in rolling and propping on forearms and extended arms.

Another 11 patients (22.4%) had a decrease in MFM20 scores >2 points. Nine of the 11 had also decreased HMFS scores, exceeding 2 points [3–11] in 4/9.

The remaining 5 patients (10%,2%) had an increase in MFM20 scores >2 points, associated in 4 of the 5 with HFMS changes within 2 points.

4. Discussion

The aim of this longitudinal study was to assess a cohort of non-ambulant SMA patients using both the HFMS and the MFM20. Our results confirmed that both scales can be easily used even in younger children from the age of

3.5 years. The reduced number of items in the MFM20 compared to the full version considerably shortens the length and the time of examination, allowing to use the scale in combination with other assessments.

The two scales showed a good correlation at baseline (0.733) even though there were some obvious differences between them especially in patients at the extreme ends of the clinical spectrum. There was a consistent number of patients who had very low HFMS scores (0–2) and were just able to sit independently for a few seconds who were able to achieve a number of activities on the MFM20. These activities were mainly related to axial tone and upper limb performances. In contrast, in the present study, the MFM20 scores appeared to plateau around 32–36. Patients at this functional level had a much wider range of HFMS scores. These non ambulant patients were able to achieve all the activities of the MFM20 that can be performed in sitting or in supine but could not achieve a higher score since the remaining items were related to activities involving standing or walking. The activities in the HFMS that were observed in patients with a plateau of MFM20 scores were propping and rolling, and other activities often assessed from prone, such as four point kneeling.

These differences appear to reflect the fact that the MFM was designed as a general scale for neuromuscular disorders and its 20 items have to cover a wide spectrum of activities to capture different patterns of weakness (e.g. proximal/distal) and different functional levels (ambulant/non ambulant) [22]. In contrast, all the 20 items in the HFMS were specifically selected for non ambulant SMA [7], and this allowed to assess several activities from different starting positions.

In this paper we were also interested in assessing the 12 month changes observed in the two scales. Although it is difficult to compare the magnitude of changes of the two scales because of the different scoring systems, it is of note that in approximately 50% of the patients we found no or little changes on either scales and in an additional 20% there was concordance with both scales improving or deteriorating at the same time. In the remaining 30% there was some discordance.

The changes observed were however very small and larger cohorts may help to establish whether this is due to lack of sensitivity at the extreme or to random variability.

Our data suggest that the HFMS is more suitable in strong non ambulant patients, as it includes a number of items such as the ability to prop or crawl that are not captured on the MFM20. In general the MFM20 appeared to have a gap between a number of activities assessed from sitting or from the supine position that were often achieved by the SMA patients, and the following items that were mainly related to activities involving standing or walking. In contrast, the HFMS appeared to be less sensitive to capture activities and possible changes in the very weak patients, in whom the MFM20 captures axial and more distal upper limb activities, such as going round the edge of a CD with a finger or turning a tennis ball.

The paucity of items assessing upper limb performance in HFMS has recently been addressed as part of an international effort, by producing a module specifically exploring upper limb activities [23]. The module was designed as an easy add on module, that can be performed in 10 min, and has been validated in non ambulant SMA patients, including very weak and young SMA patients. This module was not available at the time the present study was designed but in a recent study, its application, in combination with the HFMS shows that a number of activities assessing upper limb and axial tone can be easily assessed in weak patients who have very low scores on the HFMS therefore reducing the floor effect [23].

These results are in keeping with the results of a recent study in which Rasch analysis on several functional scales used in SMA including the MFM20 and the HFMS was performed. This study showed that the scales had good overall reliability but also had a number of common issues including cohesiveness of items, disordered thresholds and targeting issues with some gaps in the spectrum of activities [11]. Further studies using systematically the HFMS and the upper limb module are in progress to establish the extent to which the combination of the two assessments can solve some of these problems, reducing floor effect and improving the distribution of items, and more generally the reliability of the scales in a well defined cohort of non ambulant patients. This, together with the assessment tools under exploration for the ambulant SMA [24,25] should eventually provide effective and reliable tools to explore patients at the various extremes of the SMA 2 and 3 spectrum.

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