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Neuromuscular Disorders 15 (2005) 610–617

www.elsevier.com/locate/nmd

Quantification of mobility impairment and self-assessment of stiffness in patients with myotonia congenita by the physiotherapist

Elisabet Hammarén[a,b,*], Gunilla Kjellby-Wendt[b], Christopher Lindberg[a]

[a]*Neuromuscular Centre, Sahlgrenska University Hospital, 431 80 Mölndal, Sweden*
[b]*Department of physiotherapy, Sahlgrenska University Hospital, 431 80 Mölndal, Sweden*

Received 6 June 2005; accepted 6 July 2005

Abstract

We investigated test–retest reliability and responsiveness in two functional measuring instruments, Timed Up&Go (TUG) and Timed-Stands Test (TST), and in three self-assessment scales, Visual Analogue Scale (VAS), Borg's Category-Ratio Scale (BorgCR10) and Myotonia Behaviour Scale (MBS) when quantifying myotonic stiffness and mobility impairment. These methods were used in the assessment of treatment efficacy of mexiletine. Six male patients with myotonia congenita followed a standardised protocol with time scoring and rest on two occasions, with and without mexiletine. Time scoring of TUG and TST and self-assessments of stiffness were performed. A 14-day stiffness diary was used at home. Timed Up&Go and TST showed very good test–retest agreement (ICC = 0.87–0.95) and significant to change ($P = 0.005$ and 0.001, respectively). All self-assessment scales revealed excellent responsiveness and good test–retest reliability. The measurement instruments possess great capacity to detect functional impairment in the myotonia congenita patient group, and sensibility to identify true changes due to treatment. When considering the results, three instruments are favoured; Timed Up&Go and BorgCR10 for short, and MBS for long-term evaluations.

Keywords: Functional measuring instruments; Self-assessment; Reliability; Sensibility to change; Timed Up&Go; Timed-stands test; VAS; BorgCR10; Myotonia behaviour scale

1. Introduction

Myotonia congenita (MC) is a group of inherited neuromuscular disorders characterised electrophysiologically by repetitive electrical discharges (myotonic runs), and clinically by involuntary muscle contractions. Myotonia congenita exists in two variants: MC Thomsen, with dominant inheritance, and MC Becker with recessive [1]. The disorders are caused by mutations in the gene of skeletal muscle voltage-gated chloride channels (CLCN1) [2].

Patients with MC have muscle symptoms with onset in early childhood that continue and progress throughout life. The muscle force is normal or slightly reduced, and the possible weakness per se, does not lead to any disability. In MC, the muscle function of the patient is hampered by myotonia rendering the muscles stiff, in particular after muscle rest, due to inability of the muscle to relax after contraction. In some patients, the myotonic stiffness is severe and significantly reduces the ability of the patient to perform activities of daily living. Patients with recessive MC typically have transient weakness following the initial myotonia, due to a severe muscular block after depolarisation [3]. Myotonia in MC markedly decreases after 'warming-up' and can also be diminished by drugs that reduce the increased membrane excitability in muscle fibres, i.e. local anaesthetics and class 1b antiarrhythmic drugs, of which mexiletine is most often used. Myotonia is objectively observed, but not quantified, by electromyography (EMG), and the method is thus not applicable for monitoring clinical disease severity. Several measurements have been used in investigations of MC: ascending stairs after seated position (10 steps, time in seconds); maximum eye opening after eye closure (time in seconds); hand opening after sustained maximum grip (time in seconds) [4,5]. Becker et al. [1] classified the

* Corresponding author. Fax: +46 31 343 1900.
E-mail address: elisabet.hammaren@vgregion.se (E. Hammarén).

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doi:10.1016/j.nmd.2005.07.002

disability of patients with MC following a four-degree scale from mild to severe form of myotonia. However, there is no well-established validated instrument used clinically to assess myotonia with respect to quantification. The efficacy evaluation of treatment in clinical praxis is therefore today mainly based upon subjective statements of the patients.

Hence, a lack of reliable measurement instruments exists. There is a wide inter- and intra-patient variation in myotonia severity. Such an instrument would therefore allow quantification of all functional impairment from mild to severe. This tool should be of significant use as the patient comes for intervention follow-up by the neurologist or the physiotherapist.

The aim of this investigation was to evaluate two functional measuring instruments 'Timed Up&Go' (TUG) and 'Timed-Stands Test' (TST) and three self-assessment scales, Visual Analogue Scale (VAS), Borg's Category-Ratio Scale (BorgCR10) and a Behaviour Scale. The evaluation was done in relation to test–retest agreement, correlation between the functional measurement instruments and the self-assessment scales, and further, the possibility to detect known changes (after rest compared to after warming-up) and changes due to medication with mexiletine.

2. Patients and methods

2.1. Patients

Six patients (all men, aged 31–61, median 40 years) with MC, known at Neuromuscular Centre at Sahlgrenska University Hospital, gave their written consent to participate. Diagnostic criteria for MC were: (1) congenital/early onset of symptoms; (2) clinical myotonia; (3) myotonia confirmed with EMG-examination. Myotonic Dystrophy type 1 was excluded through DNA-testing when appropriate. The Ethics Committee of The Sahlgrenska Academy of Göteborg University approved the study.

2.2. Measuring instruments

2.2.1. Functional measurement instruments

2.2.1.1. Timed Up&Go (TUG). The subject is asked to rise from an armchair of 45-cm height, walk 3 m, turn around, walk back and sit down again in a self-selected speed [6]. Normal values of TUG are not definitely set; they differ between investigators [7]. Reference values according to the original paper are: ≤ 10 s, normal; 11–20 s, independent mobility indoors and outdoors; >30 s, dependent of assistance [6]. Timed Up&Go has shown intra- and inter-reliability and correlates well with log-transformed scores of more extensive measuring instruments, such as the Berg Balance Scale and gait speed [6,7].

2.2.1.2. Timed-stands test (TST). The time that it takes to stand up (to upright position) and sit down 10 times from an armless chair of 45-cm height, as quickly as possible, is measured with a stopwatch. Mean predicted times of TST ranges from 10.8 s at 30 years to 16.6 s at 60 years for men. In healthy subjects, the time correlates strongly with age. It is considered a both valid and reliable measure of lower extremity function [8,9].

2.2.2. Self-assessment scales

2.2.2.1. Visual Analogue Scale (VAS). The Visual Analogue Scale [10] is a well-established tool of self-assessment with a broad field of application [11–13]. The construction of VAS in our study was as an absolute measure, with a straight, horizontal, 10 cm line having the endpoints 'No stiffness at all' and 'Stiffness as worst possible'. The subject responses were scored on the line to the nearest millimetre (a 100-point scale) [14]. In our study, the scale was evaluated using only the ordered structure of the data.

2.2.2.2. Borg's Category-Ratio Scale (BorgCR10). This ordinal scale is constructed as a category scale anchored with verbal expressions and ranges from zero—'no symptom at all' to 10—'very, very severe stiffness'. Beyond 10 lies 'maximal' without a score. It is considered easy to understand by most people. The BorgCR10 is proposed to be used for determining subjective symptoms, and has shown test–retest reliability and sensibility to change [15–17]. The scale was evaluated using the ordered structure of the data.

2.2.2.3. Myotonia behaviour scale (MBS). The Behaviour Rating Scale originally developed by Budzynski, Stoyva, Adler and Mullaney as a pain measurement instrument [18], has been modified in our study for application in the MC patient group. The subject chooses one out of six framed sentences, which most closely describe the impact of the stiffness on everyday life (Fig. 1).

2.3. Procedure

The patients were invited for two sessions with 2–5 weeks in-between. Four out of six were on their usual medication, i.e. mexiletine, during the first session, but on the second occasion had not taken medication for at least 12 h. They were all given standardised information at the first session about the procedure and how to grade their stiffness on the self-assessment scales. They were also instructed how to register their stiffness at home over a 2-week period. After the first part of assessments during the second session, they all were given mexiletine. All tests and assessments were performed identically on each occasion. Standardised 10-min rests took place on the chair used in the coming test. Warming-up consisted of

0. No stiffness
1. Some stiffness exists, which can be ignored
2. Some stiffness exists, which can be ignored at times, but doesn't impair daily activities
3. Stiffness exists, which demands a higher level of mental awareness when performing **some** duties and activities
4. Severe stiffness exists, which impairs **every** duty and activity
5. Incapacitating stiffness exists, which demands constant moving not to be totally locked up, with regard to movement

Fig. 1. The Myotonia Behaviour Scale (MBS).

the TUG twice or the TST once before respective test. All TUG performances were videotaped.

2.3.1. Test–retest reliability

For the test–retest reliability, the TUG and the TST were performed twice in succession during the first session after warming-up (TUG 1 + 2 and TST 1 + 2). Self-assessments on VAS, BorgCR10 and MBS were done directly after TUG 2 and TST 2. Test–retest of the TUG and the TST after rest were performed in the following way: since four of the patients were treated with mexiletine and two were untreated at the first session, the after-rest time scores of the treated patients at the first occasion were compared with the after-rest times after intake of mexiletine on the second occasion. The time scores of the two untreated patients were compared to their untreated after-rest times at the second occasion. Reliability of the self-assessment scales were calculated on test–retest of 'warmed-up assessments', comparing the self-assessments in the same way as for the after-rest time scores of the TUG and the TST.

2.3.2. Correlation between functional measuring instruments and self-assessment scales

After standardised rests, on the chair being used in the coming test, TUG 3 and TST 3 were performed. Assessment of stiffness on the three different self-assessment scales was done after each test. The correlation between time and self-assessment was analysed.

2.3.3. Responsiveness of known changes

The time measured in the TUG and the TST after warming-up at the second session (unmedicated) was compared to the corresponding measures after rest, when a considerable prolonging of time was expected, due to the myotonia stiffness. In the same way, the corresponding self-assessment scales were analysed.

2.3.4. Evaluation of intervention

At the second session, all patients were untreated. After tests as in the first session, all patients were given a standard dose of 100 mg mexiletine. One hour was allowed for the medication to take effect and then all measurements were repeated. The times and assessments of the untreated patients were compared with the results after intake of drugs.

2.3.5. Descriptive study of myotonia—the stiffness diary

All patients filled in the self-assessment scales of stiffness at home, during 14 days. The assessments were done twice daily. In the morning, the patients were asked to describe the 15 min related to getting out of bed. In the evening, the over-all myotonia during the day was assessed. Possible myotonia-affecting situations or activities were noted down voluntarily for each day. Finally, the patients also were asked to consider which of the assessment scales they preferred.

2.4. Statistics

Intra Class Correlation (ICC) was used to estimate the reliability between paired observations of TUG and TST [19], and rank-invariant method [20–22] was used in order to estimate the reliability (i.e. disagreement) of paired observations of the self-assessment scales.

Also, the sign test was used to estimate the systematic disagreement/change between paired observations of self-reported data in order to compare the results with the rank-invariant method. To evaluate the responsiveness to known changes in the TUG and the TST, i.e. increased stiffness due to rest, and to evaluate possible differences due to medication in the functional measuring instruments, a paired sample *t*-test was applied on log-transformed values of the after-rest and the warmed-up measures. The sensibility to change, i.e. responsiveness, in the self-assessment scales was evaluated with the same rank-invariant method as above and again using the sign test, as were the possible differences by medication. The correlation between functional measuring instruments and the self-assessment scales was analysed with the Spearman rank order correlation coefficient. All tests were two-sided and $P < 0.05$ was considered as statistically significant. A 95% confidence interval (95% CI) was estimated for the estimates of the rank-invariant method by the jack-knife method for calculations of the standard error.

The empirical measure of the random part of the disagreement/changes (not explained by the group) is the relative rank-variance (RV). Possible values of RV range from zero to $+\infty$ (infinity). The greater the random disagreement/change is, the higher the value of RV. Relative rank-variance equal to zero indicates a lack of random disagreement/changes. This indicates good reliability. The systematic disagreement/change by the group is expressed by relative position (RP). Values of RP

Table 1
Timed Up&Go and Timed-Stands Test: Effects of warming-up and medication

	Estimated mean value effect[a]		*t*-Test (p)[b]	
	TUG	TST	TUG	TST
Warming-up effect				
Without medication, rest vs. warmed-up	−61%	−56%	0.005	0.001
Effect of medication				
After-rest, without vs. with medication	−18%	−19%	0.035	0.01
Effect of medication				
After warming-up, without vs. with medication	−2.5%	2%	0.54	0.49

TUG, Timed Up&Go; TST, Timed-Stands Test.
[a] *Mean value effect*. Back-transformed (anti-logarithmated) mean values with respect to change in the Timed Up&Go and the Timed-Stands Test.
[b] *t-test*. Paired samples *t*-test of log-transformed scores ($P<0.05$ were considered as statistically significant).

range from −1 to 1 and a value close to zero indicates absence of systematic disagreement/change by the group. The presence of RP (RP≠0) means that the second of the two test occasions has systematically higher (+) or lower (−) ratings.

3. Results

3.1. Functional measurement instruments

3.1.1. Timed Up&Go and Timed-Stands Test without medication

After warming-up, all subjects showed decreased time scores compared to their after-rest state, both for the TUG, mean from 29.5 to 11.7 s (range 16.9–59.2 and 9.1–14.9 s, $P=0.005$) and for the TST from 66.1 to 28.8 s (range 47.1–116.1 and 16.3–45.9 s, $P=0.001$) (Table 1, Figs. 2a and 3a).

3.1.2. Timed Up&Go and Timed-Stands Test after medication

After rest, all patients showed decreased time scores compared to their state without drugs, both for the TUG, geometric mean from 29.5 to 24.6 s (range 16.9–59.2 and 11.0–45.0 s, $P=0.01$) and for the TST from 66.1 to 53.7 s (range 47.1–116.1 and 34.6–98.4 s, $P=0.035$). In the warmed-up state, mexiletine gave no additional improvement. The geometric mean for the TUG was 11.5 s compared to 11.7 without medication (range 8.8–13.9 and 9.1–14.9 s, $P=0.54$), and for the TST 29.5 compared to 28.8 s (range 16.5–45.9 and 16.3–45.9 s, $P=0.49$) (Table 1, Figs. 2a and 3a).

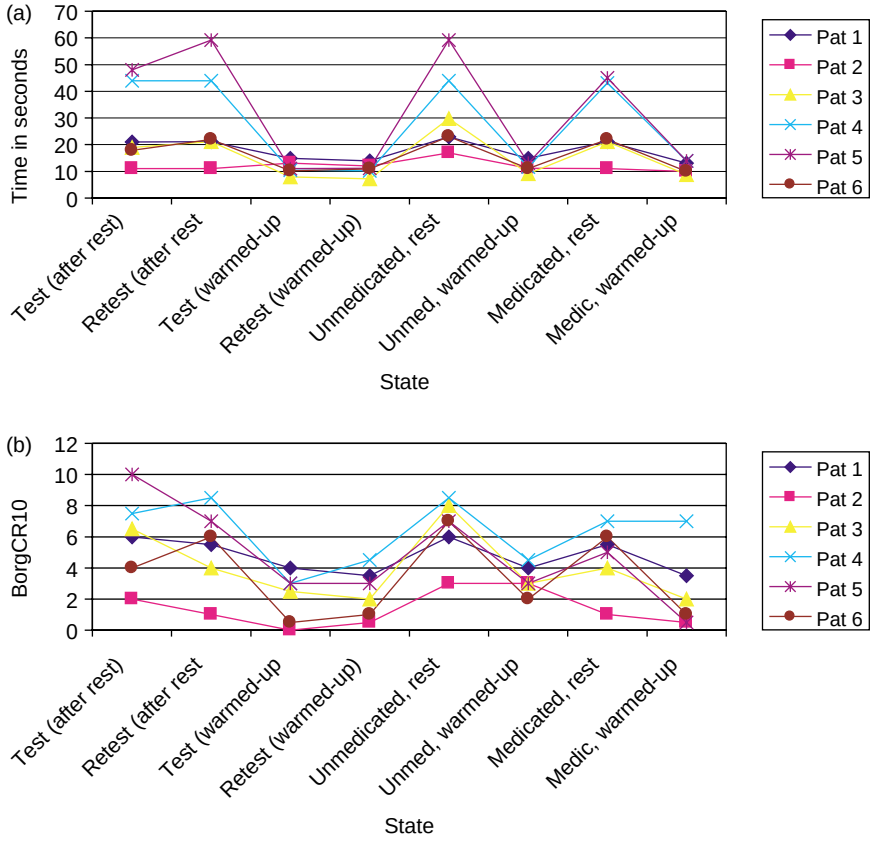

Fig. 2. Times in seconds to perform TUG (a) and momentary assessment of stiffness (b) after performing TUG in different states.

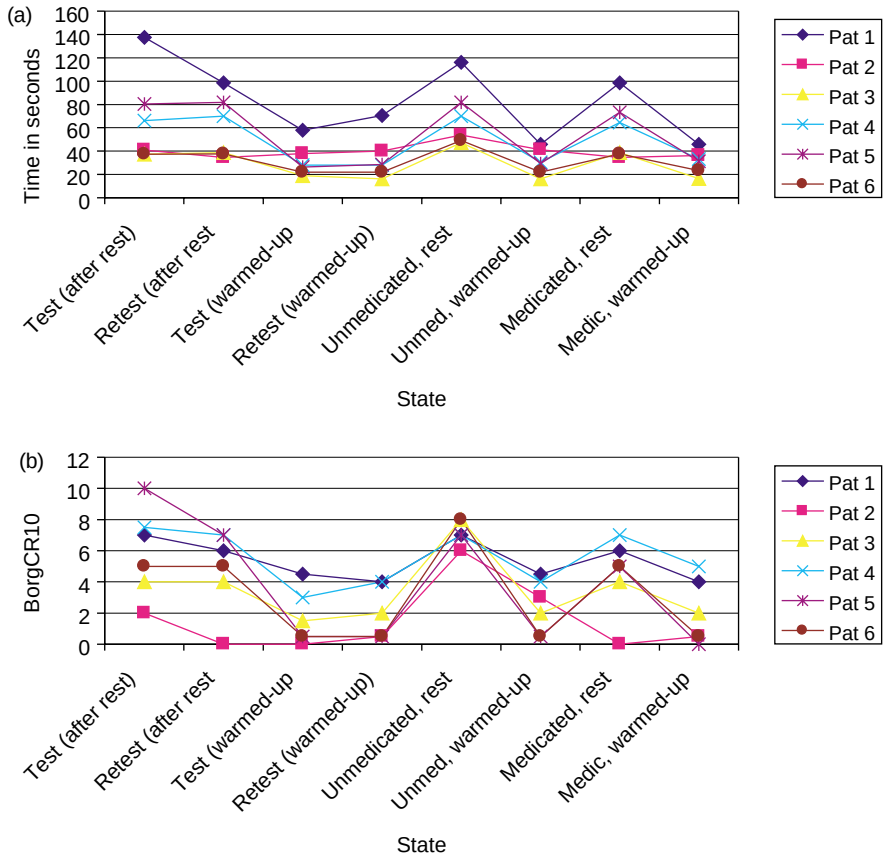

Fig. 3. Times in seconds to perform TST (a) and momentary assessment of stiffness (b) after performing TST in different states.

3.1.3. Test–retest reliability and responsiveness in the TUG and the TST

Intra Class Correlation revealed a very good agreement in test-–retest for both the TUG ($r=0.95$ both after rest and warmed-up) and the TST ($r=0.87$ and 0.94, respectively). The Timed Up&Go and the TST were both significantly sensitive to change according to paired samples *t*-test of log-transformed scores and the estimated effect of known changes was substantial (Table 1).

3.2. Self-assessment scales

3.2.1. Test–retest reliability

The reliability was good because of the lack of statistical evidence for disagreement in RP and RV. No random individual variations (RV) could be detected in MBS for the TUG (test–retest and responsiveness) or in BorgCR10 for the TST (test–retest) (Table 2, Figs. 2b and 3b).

3.2.2. Responsiveness

The rank-invariant method revealed a good responsiveness in all assessment scales. Significant values of relative change in position (RP) were shown in VAS, BorgCR10 and MBS (the confidence interval excluded 0) (Table 2).

3.2.3. Correlation between functional measuring instruments and self-assessment scales

After rest in the first session, the self-assessment scales VAS and BorgCR10 (for momentary stiffness) correlated equally well with the TUG according to Spearman's rank correlation ($r_s=0.94$, $P=0.005$, respectively), MBS showed weaker correlation ($r_s=0.68$, $p=0.14$). No significant correlation with the TST was shown in any of the assessment scales with analysis according to Spearman ($r_s=0.71$ (VAS), 0.66 (BorgCR10) and 0.79 (MBS, $P=0.06$)).

3.2.4. The intervention

A significant effect of medication was shown in after-rest scores in both the TUG and the TST (Table 1, Figs. 2a and 3a). After treatment, the rank-invariant method displayed significant changes in the after-rest assessments in the VAS and the BorgCR10 in connection with the TUG, and in the BorgCR10 and the MBS in connection with TST. No random individual changes were shown in MBS, only systematic. In sign test, the self-assessment scales showed significant changes after rest when the patients were medicated, on VAS and BorgCR10 when performing TUG, and on VAS when performing TST. No significant changes were pointed out when using MBS (Table 2, Figs. 2b and 3b).

Table 2
Visual Analogue Scale, BorgCR10 and Myotonia Behaviour Scale: analysis of self-assessments of stiffness in conjunction with functional measurement instruments

	Applied with the functional measurement instrument	Visual Analogue Scale			BorgCR10			Myotonia Behaviour Scale		
		Sign test (P)[a]	RIM: RP[b] (95% CI)	RIM: RV[c] (95% CI)	Sign test (P)	RIM: RP (95% CI)	RIM: RV (95% CI)	Sign test (P)	RIM: RP (95% CI)	RIM: RV (95% CI)
Test–retest reliability: in warmed-up state, first vs. second occasion	TUG	0.69	−0.28 (−0.73:0.17)	0.17 (0.0:0.68)	1.0	0.14 (−0.12:0.40)	0.06 (0.0:0.25)	0.5	0.17 (−0.03:0.36)	0.0 (0.0:0.0)
	TST	1.0	−0.17 (−0.69:0.35)	0.39 (0.0:1.31)	0.62	0.11 (−0.09:0.31)	0 (0.0:0.0)	0.62	0.17 (−0.18:0.51)	0.06 (0.0:0.25)
Responsiveness: without medication, warmed-up vs. rest	TUG	0.22	0.72 (0.16:1.0)	0.17 (0.17:0.17)	0.06	0.81 (0.41:1.0)	0.44 (0.0:1.38)	0.03	0.89 (0.67:1.0)	0.0 (0.0:0.0)
	TST	0.03	0.94 (0.78:1.0)	0.89 (0.0:2.21)	0.03	1.0 (1.0:1.0)	1.0 (0.0:2.07)	0.03	1.0 (1.0:1.0)	0.56 (0.0:1.79)
Effect of medication: after-rest, without vs. with medication	TUG	0.03	−0.64 (−1.0:−0.16)	0.67 (0.0:1.83)	0.03	−0.58 (−1.0:−0.13)	0.39 (0.0:1.31)	1.00	−0.06 (−0.53:0.42)	0.0 (0.0:0.0)
	TST	0.03	−0.75 (−1.0:−0.34)	0.44 (0.0:1.44)	0.06	−0.83 (−1.0: −0.52)	0.61 (0.0:1.69)	0.25	−0.44 (−0.77:−0.12)	0.0 (0.0:0.0)

RIM, Rank-invariant method; CI, confidence interval; TUG, Timed Up&Go; TST, Timed-Stands Test.

[a] *Sign test*. $P<0.05$ were considered as statistically significant.

[b] RP, relative disagreement (test–retest) and relative change (responsiveness and effect) in position. Values of RP range from −1 to 1. As for test–retest, a value near zero shows high repeatability. As for responsiveness and effect, a value near 1 or −1 shows positive or negative changes, respectively. A 95% confidence interval, CI, which excludes zero, shows significance.

[c] RV, Relative rank-variance for the individual random part not explained by RP. Possible values of RV, ≥ 0. A value near zero shows low random variance.

3.2.5. The stiffness diary

All subjects completed the 14-day diary of myotonia self-assessment. The results of the diary showed large inter- and intra-individual variances in myotonic stiffness. Other factors, e.g. alcohol consumption, stress or infections did affect the stiffness according to the comments. We could not find any systematic pattern of myotonia besides increase after rest. The subjects expressed a preference for different self-assessment scales; however, there was no general agreement. Two out of six patients scored their degree of stiffness as four (4) on the MBS (see Fig. 1), on every assessment occasion, which could be seen as an indication of the large impairment that might be connected to MC.

4. Discussion

Patients with MC show a substantial variation in impairment. This is caused by myotonia and in particular in the more severe Becker cases of a transient muscle weakness on initiation of a muscle contraction after rest [2,3]. A disadvantage in all self-assessment scales we have used is the fact that the patients were asked to assess 'stiffness'. The impact of the possible transient weakness was not separated. The functional measurement instruments, however, includes this weakness and thus a comparison between these and the self-assessment scales is only in part adequate.

4.1. Functional measurement instruments

For more than three decades, a set of functional measurement instruments, such as the Birnberger stair case test, has been used [2–4]. This test has, however, not been validated or standardised (i.e. step height and depth, chair height). We chose two tests, by well-known physiotherapists, with international evidence of good repeatability to evaluate physical impairment in MC. Both the TUG and the TST showed a very good test–retest agreement and a very good responsiveness for the MC patient group. When warmed-up, the patients showed a TUG score that was normal according to the reference values or just slightly increased, which correlates well with their own assessment of lower level of stiffness when warmed-up. In contrast, the TST the times were all prolonged compared to normal mean values of each age. In the intervention part, mexiletine brought significant changes to the scores only after rest. There was no statistical evidence for change in the TST or the TUG when the patients were warmed-up, comparing pre- and post-medication. One reason to prefer the TUG to the TST as a functional measuring instrument in MC is that the TUG consists of a sequence of different movements. It is thus likely that the TUG could better reflect the myotonia-induced impairment in MC, as different muscle groups are enrolled during the test. Further, the transient weakness of patients with recessive MC does not seem to influence the results as much as in the TST. In fact we have seen that patients with severe transient weakness cannot rise from an armless chair, and thus are unable to perform TST adequately. There is, on the other hand, a warm-up effect in the instrument itself, during the successive repetitions. It also has the disadvantage of being tiring for elderly patients, and influenced by the muscle endurance and strength in the patients.

To sum up, the Timed Up&Go is easily performed in most settings and well known by physiotherapists all over the world as an evidence-based tool of functional assessment, and now also proved suitable for the MC patient group. There is no need for videotaping, since a stopwatch for measuring time is sufficient.

4.2. Self-assessment scales

The choice of self-assessment scales was done with respect to diversity. All assessment scales could detect changes due to the known phenomenon of stiffness after rest in the MC group. The changes due to medication are less. All scales showed excellent responsiveness and good test–retest reliability. In our study, the MBS showed no random individual changes when used together with the TUG, which indicates superiority to the BorgCR10 and the VAS. The achievement of an obvious and clear effect only evident on the group level is very good. A possible disadvantage of the MBS as a behaviour scale is the risk of contamination by other aspects of mobility (weakness, impaired physical fitness) or personality [23]. If the goal of treatment is an improvement of physical functioning in the long term, this could be overlooked. The correlation between the self-assessment scales and the functional instruments seemed high, according to Spearman's correlation coefficient, but due to the few observations, there was no statistical significance. Clinically the BorgCR10 is to be preferred to the VAS as a measurement of short-term effects as it did not show as much random individual change. Further, the patient is given the opportunity to relate to substantial verbal expressions, which makes it easier to use and understand. As a measurement of long-term effects on all-over impairment in MC, the MBS has advantages in the framed sentences and the excellent results of this study, and thus is preferred to the 'diary'.

4.3. Statistics

The TUG and the TST data were analysed with parametric statistics with due respect to the small number of patients, and the self-assessments were evaluated with non-parametric statistics since the data were only evaluated according to their ranks and no numerical interpretation was made.

The rank-invariant method provides estimates to identify and separately measure the level of systematic disagreement

(by group), and random disagreement, a disagreement not explained by the systematic effect, between two test occasions [20–22]. The same method is used for estimating the changes over time, the systematic change and the random individual changes, not explained as a group change. The lack of evidence for significant changes in the sign test indicates that this instrument is inadequate for this kind of assessment; true changes are not detected. The rank-invariant method detects those changes because of the greater statistical power in this method when analysing assessment scales compared to the sign test [20].

5. Conclusion

This study has displayed a large inter- and intra-individual variability in the severity of functional impairment in patients with myotonia congenita. The measurement instruments possess great capacity to catch both mild and severe forms of functional impairment in the MC patient group, and sensibility to accurately identify true changes due to treatment. Together with clinical factors and experiences given by the results, this study speaks in favour of a combination of three instruments, Timed Up&Go and BorgCR10 for short-term and MBS for long-term evaluations of treatment effects. The MBS should be developed further and both the BorgCR10 and the MBS should be expanded with an additional category, weakness.

Acknowledgements

We are indebted to biostatistician Jan Kowalski for excellent professional statistical calculations and advises. The investigation was supported by grants from the Council of Research and Development in Göteborg and southern Bohuslän, Sweden and the Muscle Foundation, Sweden.

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