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QUANTIFICATION OF MUSCLE STRENGTH AND MOTOR ABILITY IN PATIENTS WITH DUCHENNE MUSCULAR DYSTROPHY ON STEROID THERAPY

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ABSTRACT - *Objetive:* An assessment protocol was applied to quantify and describe muscular strength and motor abilities of 32 patients with Duchenne muscular dystrophy (DMD), aged between 5 and 12 years on steroid therapy. *Method:* Assessments were made monthly for the first six months and with intervals of two months thereafter until the 14-month end point. The tests employed included: the Medical Research Council (MRC) scale; the Hammersmith *motor ability score;* maximum weight lift; timed rise from floor and nine-meter walk. *Results:* The results showed that loss of muscular strength and motor abilities were slowed in comparison to that observed in the natural evolution of the disease according to the literature. *Conclusion:* We conclude that a swift and objective assessment may be performed using the MRC scale for lower limbs and trunk, the Hammersmith *motor ability score,* timed nine-meter walk and weight lifts.

KEY WORDS: Duchenne muscular dystrophy, corticosteroids, muscle strength, motor ability, MRC scale, Hammersmith motor ability score.

Quantificação da força muscular e habilidades motoras em pacientes com distrofia muscular de Duchenne em corticoterapia

RESUMO - *Objetivo:* Um protocolo de avaliação foi aplicado com o objetivo de quantificar e descrever evolutivamente a força muscular e as habilidades motoras de 32 pacientes com distrofia muscular de Duchenne (DMD), com idades variando de 5 a 12 anos, em corticoterapia. *Método:* As avaliações foram aplicadas mensalmente durante os primeiros seis meses e bimensais até completar um período de 14 meses. Os testes empregados foram: escala da "Medical Research Council" (MRC); Hammersmith "*motor ability score"*; levantamento da carga máxima de peso; cronometragem do tempo para levantar-se do chão e percorrer nove metros. *Resultados:* Os resultados demonstraram que a perda da força muscular e das habilidades motoras foi mais lenta do que a observada na evolução natural da doença, como descrito na literatura internacional. *Conclusão:* Concluímos que uma rápida e objetiva avaliação pode ser executada utilizando a escala MRC para membros inferiores e tronco, Hammersmith *motor ability score,* cronometragem do tempo para percorrer 9 metros.e o levantamento de peso.

PALAVRAS-CHAVE: distrofia muscular de Duchenne, corticosteróides, uso terapêutico, força muscular, habilidade motora, escala Medical Research Council (MRC), Hammersmith *motor ability score.*

Duchenne muscular dystrophy (DMD) is characterized by muscle weakness in the pelvic girdle commencing between the second and fourth year of life, at which time classic hypertrophy of the calves becomes evident; between six and seven years of age occurs weakness in the scapular girdle and between nine and twelve years, loss of ambulation. Cardiac or respiratory insufficiency are the most common causes of death in the second or third decade of life.

In the absence of an effective treatment, palliative therapy based chiefly on rehabilitation, steroid therapy and continuous multidisciplinary support is fundamental to prevent the orthopedic deformities and clinical complications which accompany the physical restrictions resulting from the disease. Steroid therapy with prednisone, prednisolone or deflazacort is universally utilized in a bid to slow the rate of muscle strength loss (MS), that was well document-

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ed by Scott in 1982[1], and to delay confinement to a wheelchair along with its associated rapid progression of scoliosis[2-22]. There are several studies on physical and functional assessment[2-6,11,16,17,19,20,23,24] which employ an array of different methods aiming uniform steroid therapy results.

We sought to select a sequence of tests which can be applied in a practical and swift fashion in an outpatient setting to assess patients' response to steroid therapy. Tests were drawn from those already standardized to assess MS and motor ability in patients with neuromuscular diseases.

METHOD

A total of 32 patients with DMD aged 5 years or older, who were able to walk unaided and were willing to collaborate in the applying of the tests, were put on steroid therapy regimens using either deflazacort (1 mg/kg/day in single daily dose) or prednisolone (0.75 mg/kg/day in an intermittent course of 10 days on, followed by 10 days off the drug), Patients who were not already enrolled onto rehabilitation programs were referred to one at first assessment. During the study, patients who underwent orthopedic surgery or who interrupted steroid therapy were excluded. All patients underwent a physiotherapy assessment including tests assessing parameters for MS and motor abilities:

1. parameters for MS assessment: medical research council scale (MRC)[24], applied to 30 muscle groups (total MRC) or only to lower limb and trunk muscles (MRC of lower members and trunk); weight lifting, where patients were asked to lift dumbbells by flexing at the elbows.

2. parameters for motor abilities: time required to rise from the floor (Gowers manoeuvre); time required to walk 9 meters; Hammersmith *motor ability score*[1].

Ten physiotherapy assessments were scheduled (visits 1 to 10), which accompanied medical assessments of steroid therapy results, on a monthly basis from visits 1 through 6, and then every two months from visits 7 to 10, allowing a ±15 day leeway.

In order to minimize possible subjectivity, a concordance test was carried out through participation of a second physiotherapist for eight patients over the 10 assessments, where concordance found ranged from moderate to very good, with a prevalence of good to very good.

This study was approved by the Ethical Committee for research projects analysis of our Institution under the number 183/03 and all parents from the 32 patients gave their informed consent.

Statistical methods – The continuous quantitative variables were reported as average, standard deviation, median and minimum and maximum values. Non- parametric test were applied due to the nature of the data. The agreement between the two examiners was evaluated by the coefficient kappa and its significance was tested; the level of significance of 0.05 was chosen and values <0.05 were considered significant.

RESULTS

Among 32 initial patients, two abandoned treatment and four were excluded: two due to orthopedic surgery and two owing to irregular medication use. Following data collection, two distinct groups were defined for result interpretation: Group 1, comprising 18 patients who completed the 10-visit protocol while maintaining independent gait; Group 2, comprising 8 patients who lost ambulation during the assessment period, and who remained on the protocol up to the point of loss (Chart 1).

Results were interpreted based on classification of improvement, stability and worsening of parameters assessed in both patient groups, and were presented in three categories: evolutional study of Group 1 over follow up period; evolutional study of Group 2 over follow up period up until loss of gait; analysis of correlation between patient age at end point

Chart 1. Casuistic of 26 patients: age at initial steroid therapy and age at loss of unaided ambulation (Group 2 patients).

Case	Age at initial steroid therapy	Age at ambulation loss
1	5 y 8m	
2	5 y 3 m	
3	5 y 6m	
4	5 y 2m	6 y 6 m
5	6 y 9m	
6	6 y 10m	
7	6 y 5m	
8	6 y 10m	
9	7 y 7m	
10	7 y 8m	
11	7 y 5m	8 y 2m
12	7 y 7m	8 y 3m
13	8 y 7m	
14	8 y 3m	9y
15	8 y 6m	9 y 10m
16	8 y 3m	8 y 9m
17	8 y 6m	
18	10y	
19	7y	
20	6 y 3m	
21	6 y 9m	
22	7 y 6m	
23	6 y 7m	
24	6 y 7m	
25	8 y 4m	8 y 10m
26	8 y 8m	9 y 10m

Table 1. Summary of overall results in Group 1.

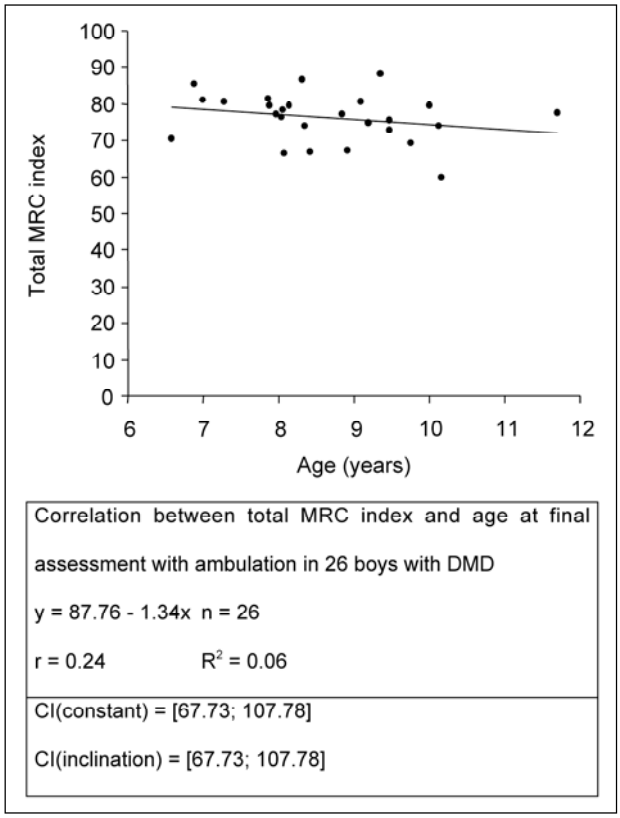
	Total MRC	MRC lower limbs and trunk	Score on HMA	Rising from floor	Distance 9 m	Weight
Improvement	4	6	4	8	13	11
Stability	4	1	6	2	4	6
Worsening	10	11	8	5	1	1
Total	18	18	18	15*	18	18

MRC indexes, weight-lifting tests and time taken to walk 9 m (p<0.001*); HMA: Hammersmith motor ability score test; *3/18 did not perform the manoeuvre.

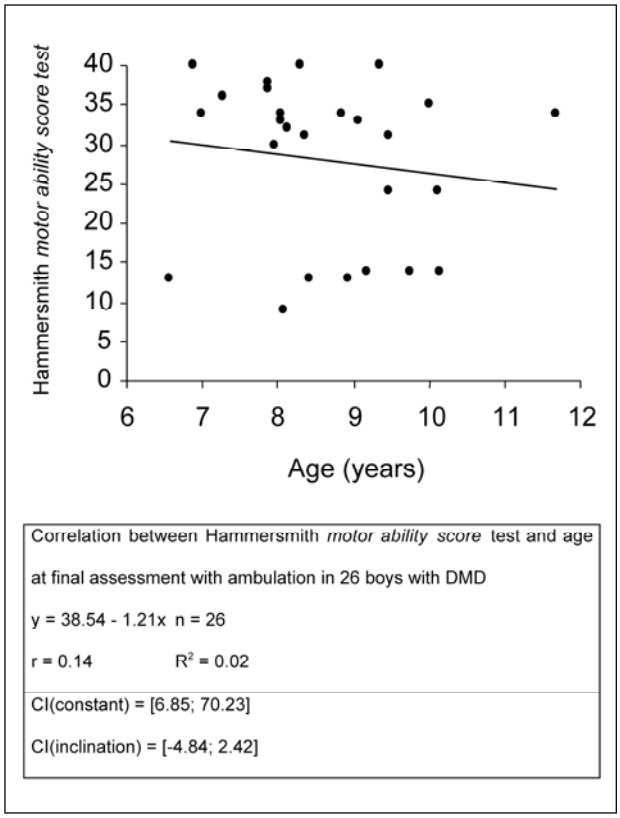
Table 2. Summary of overall results in Group 2.

	Total MRC	MRC lower limbs and trunk	Score on HMA	Rising from floor	Distance 9 m	Weight
Improvement	–	–	–	–	–	1
Stability	–	–	–	–	–	6
Worsening	8	8	8	2	8	–
Total	8	8	8	2*	8	7**

Total MRC index (p=0.020*); HMAScore: Hammersmith motor ability score test; *6/8 did not perform the test; **1/8 did not perform the test.



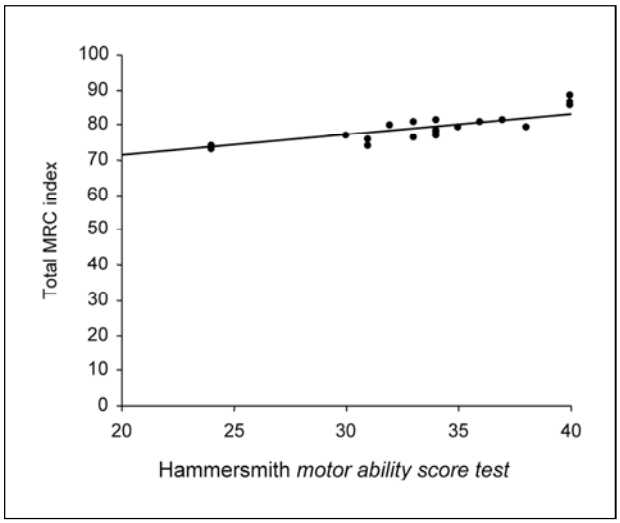
Graph 1. Correlation between total MRC index and age at end point.



Graph 2. Correlation between Hammersmith motor ability score test and age at study end point.

and parameter values, as well as correlation amongst the parameters themselves.

Evolutional study group 1 – In Group 1, statistical analysis of parameter values from visits 1 to 10 showed that worsening of MRC indexes reached significance (p<0.001*), as did (p<0.001*) improvement in results of weight-lifting tests (p<0.001*), weight increase and time taken to walk 9 m (shorter time). Global results for Group 1 are shown in Table 1.



Graph 3. Correlation between MS test with total MRC index and the Hammersmith motor ability score test.

Evolutional study group 2 – Statistical analysis was carried out in Group 2 up to the 5th visit when patients started to loose gait. This analysis showed significant variation for worsening of total MRC index (p=0.020*) and on the assessment prior to ambulation loss, children in this group presented an MRC index of lower limbs and trunk of around 50-60%. All patients from this Group presented worsening in all tests applied, except in the weight-lifting test where one patient improved and the others remained stable. Overall results for Group 2 are shown in Table 2.

Analysis of correlation between different parameters and age in the final assessment, and amongst parameters themselves – The correlation between age at study end point of 14 months and total MRC index, as well as scores in the Hammersmith *motor ability test* showed a tendency for MS (from 80 to 70) and motor ability (functional score from 31 to 25) to decline proportional to the chronological increase in age (Graphs 1 and 2).

Correlation between total MRC index and Hammersmith *motor ability test* showed a tendency for scores to increase (varying from 20 to 40) in line with any MS increase (total MRC variation from 71% to 80%) (Graph 3).

DISCUSSION

Firstly, we wish to highlight that the intervals proposed for assessments, namely every month up to visit 6 and every two months thereafter, were devised to take advantage of patients' visits for medical appointments and analyze whether such frequent physiotherapy assessments would yield differential data enabling improved interpretation of functional-physical assessment parameters. Given that this supposition proved unfounded, we currently use the longer intervals adopted by similar studies, of three months at outset then six months, for all new patients[3,5,6,11,15,22]. Given the progressive decline characteristic of the disease course, the classification adopted of improvement or stability can be considered indicative of a positive response, although a worsening may not necessarily represent a negative effect, if this occurs at a slower rate than that described for natural evolution of the disease.

Results analysis revealed no significant variation between results from total MRC index and MRC index for lower limbs and trunk, emphasizing that delayed, slower loss of strength in upper limbs has little influence on the phase of evolution of the disease where the child still retains the ability to walk unaided. Therefore, to simplify test application for patients in this phase of disease evolution, we opted to apply the manual muscle strength test to lower limbs and trunk only. The eight patients who lost their ability to walk have not been followed over the full study period. However, their data were considered for the analysis of the clinical course and of the evaluation parameters and were registered until the last visit prior to the loss of walking. Therefore, we formed two groups, 1 and 2, that were essentially different concerning the clinical course and the time of follow-up.

Statistical analysis of Group 1 as a whole, despite each individual patient having presented variability in test results, indicating improvement, stability or worsening, was significant (p<0.001) for variation indicating worsening of total MRC and MRC for lower limbs and trunk indexes, and indicating improvement in relation to the load of lifted weight and time taken to cover 9 meters. Since the number of children who presented a worsening on total MRC and MRC indexes of lower limbs and trunk was greater than the number presenting improvement or stability, had this been the only test applied, we would have drawn the conclusion that steroid therapy offered no positive results. However, no significant variation was seen in the Hammersmith *motor ability score test,* denoting stability. Moreover, the number of children who presented improvement and stability in both weighting-lifting and timed 9-meter walk tests was higher than those presenting worsening, which can be considered a positive outcome

of steroid therapy. Taken together, these data demonstrate that MS measurement alone is insufficient for proper assessment, and that tests analysing function end execution time should also be applied. Statistical analysis could not be performed on the timed test for rising from the floor, because children lost the ability to do this at different points in the study.

It is important to emphasize that even though the variation in MRC index values indicated decline and Group 1 patients presented a total MRC index of over 70% at end point. Values in the present study are higher across all age groups compared to values for the normal course of the disease such as those by Scott et al.[1], demonstrating more satisfactory evolution for patients on steroid therapy. Hence, in Group 1 the worsening of total MRC and MRC indexes of lower limbs and trunk over the course of evolution did not prevent the use of compensatory biomechanical mechanisms which allowed indicators for other parameters assessed to be maintained or even improved. The possibility of utilizing such compensatory mechanisms corroborate the considerations made by Johnson[25], Sutherland et al.[26] and Perry[27].

Statistical analysis was carried out in Group 2 up to the 5th visit when patients started to be excluded due to ambulatory loss. The analysis showed no significant variation in tests investigated, with the exception of total MRC index (p=0.020*). This group revealed prevalence in the number of patients presenting worsening of all parameters applied, except for the weight-lifting test which showed lesser compromise of brachial bicep muscles. On the assessment prior to ambulation loss, children in this group presented an MRC index of lower limbs and trunk of around 50-60%, a value which, according to Fenichel et al.[28] represents the MS percentage at which patients are still able to use compensation mechanisms. Fenichel et al.[28] stressed that beyond this percentage, the slightest increase in deformity leads to loss of independent ambulation.

A variability in motor behavior was observed in Group 1 over the first three months, where evolution became more defined from visit 6 onwards, evidencing a discrete worsening, stability or improvement in parameter values assessed, reflecting a deceleration in the process akin to that described by Griggs et al.[16,17], Angelini et al.[2] and Bonifati et al.[6]. Variability was also seen in Group 2, where some patients had improved parameter values in the first four months and then subsequent decline, whilst other patients presented a steady decline from the outset.

Scott et al.[1] reported the results of 3-years follow up in a group of 61 boys aged between 5 and 12 years, able or unable to walk unaided, with the aim of mapping the profile of the natural evolution of the disease. The cited study today serves as a reference for analyses of strength and functionality assessment in children with DMD. The author analyses the correlation of both the MRC index of 34 muscle groups and the Hammersmith test scores with age. In the present study, correlation between the total MRC index and age in the final assessment showed a tendency for decline in the index from 80 to 70%, directly proportional to age increase. Scott et al.[1] also verified this tendency, albeit with lower indexes (from 72 to 51%). The same correlation occurred between Hammersmith *motor ability test scores* and age at final assessment, where a tendency for a decline in functional score (from 31 to 25) directly proportional to age increase was observed. The same tendency was also reported in the study by Scott et al.[1], although indexes were lower (from 31 to 17). Correlation of the MRC index of lower limbs with age at the last assessment performed in our study cannot be compared with Scott's et al.[1] data which made no such correlation. Further, mirroring Scott's et al.[1] study, we also analyzed correlation between total MRC index, measured at final assessment, and scores from Hammersmith test also taken at final assessment. Scott et al.[1] observed that the variation in MRC index (from 43 to 76%) was proportional to the variation in scores in the Hammersmith *motor ability score test* (from 20 to 40). The present study revealed the same correlation, that is, a total MRC index variation (from 71 to 80%) proportional to variation of Hammersmith test scores (from 20 to 40), *indicating in general,* that the higher the MS, the better the performance in motor abilities. Notwithstanding the subjectivity of the MRC index, the difference between the results of the current study and results by Scott et al.[1] are marked, proving the influence of steroid therapy on evolution of the disease and pointing to the conclusion that progression of the disease in the children on steroid therapy we followed was slower than for the natural course of the disease prior to commencement on steroid therapy. The studies we have reviewed regarding the influence of steroid therapy on motor evolution of DMD patients[2,3,5,7,11-13,16-20,22,28] describe improved MS and functional abilities, or prolonged ambulation period. Moreover, they also highlight that in addition to there being effective improvements between the third and sixth months of therapy, this is also followed by a period of stability and

deceleration in the loss process, as finding being replicated in majority of patients seen at our institution.

Finally, we believe that the influence of steroid therapy in improving the quality of life of DMD patients must remain the subject of future studies employing specific assessment tools. The use of such parameters may facilitate studies on correlation between genotype and steroid therapy response, as well as help in the follow up of patients who are to undergo new therapeutic techniques with stem cells or gene therapy.

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