In situ measurements of muscle fiber conduction velocity in Duchenne muscular dystrophy

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ABSTRACT

Objective: To measure the muscle fiber conduction velocity in Duchenne muscular dystrophy patients.

Methods: The muscle fiber conduction velocity of the biceps brachii and tibialis anterior was measured with the needle electrode. Eighteen controls and 32 Duchenne muscular dystrophy patients were studied. Clinical neurological examination, serum cretin kinase level estimation, conventional electromyogram were carried out for every individual and 17 of the Duchene muscular dystrophy patients were biopsied for further histological and histochemical examination.

Results: The muscle fiber conduction velocity of the control group showed good reproducibility. The frequent distribution of the Duchenne muscular dystrophy data characterized by multi-peaks curve as compared to the control group. This is demonstrated as significant slowing ($P<0.005$) of the muscle fiber conduction velocity in the two muscle examined of the patients group.

Conclusions: The slowing of the muscle fiber conduction velocity is proposed to be due to the small size of the regenerating and splitting fibers. The multi-peaks frequency distribution curve indicates a great variability in the muscle fiber diameter. The muscle fiber conduction velocity is a useful tool for diagnosing myopathies.

Keywords: Duchenne muscular dystrophy, muscle fiber conduction velocity, needle techniquem biceps brachii, tibialis anterior.

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Duchenne muscular dystrophy (DMD) or the pseudohypertrophic variety is inherited as a sex-linked trait. The diagnosis of the disease is based routinely on the family history, clinical criteria and supported by raised creatin kinase (CK) actively and conventional electromyography (EMG). However, muscle biopsy and histochemical studies are also important in the diagnosis of the disease especially when a positive family history can not be obtained.

Several hypothesis were postulated to explain the underlying pathogenesis of muscular dystrophies such as failure of muscle cell regeneration after an injury, a primary collagen abnormality with external fibrosis and a vascular hypothesis. In the mid-seventies and later, the concept of generalized and systematic plasma membrane defect of the muscle fiber in the muscular dystrophies was raised (the membrane leaking theory).[1,2] Muscle fiber conduction velocity (MFCV) is a valuable non-vasive approach to test the functional state of the muscle fiber and its sarcolemma.[3] Thus, the MFCV may reflect at least in part the structural integrity of the muscle fiber and its diameter. Accordingly, the MFCV was included as a part of the investigation for muscular dystrophies and its pathogenesis.[4] The conduction velocity in skeletal muscle of muscular dystrophy patients has been carried out using different techniques.[5-9] Different studies showed variable and contradictory results.[10-12] The aim of this study was to investigate MFCV in the biceps brachii

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and tibialis anterior of DMD patients and try to explain the results in accordance with the histological, histochemical, as well as CK and conventional EMG studies.

Methods. ***Subjects.*** A total of 50 individuals were examined. Eighteen healthy boys aged 6-12 years (mean age = 8.55±1.85) used as control group. The patients were comprised of 32 DMD subjects aged 6-12 years (mean age = 9.03±1.43). The duration of the disease was ranging from 1 to 7 years taking in consideration the onset of the start of the symptoms. Diagnosis of DMD was confirmed by consultant neurologist and primarily made by clinical criteria, serum enzyme studies, and conventional EMG. Seventeen out of the DMD patients were biopsied for further histological and histochemical examination using Gomori trichrome stain. The MFCV was conducted in the Neurophysiology Unit-University Hospital. The room temperature is maintained at 20-24°C. Dantec counterpoint 4-channel electromyograph was used throughout. The measurement was performed on the muscle biceps brachii and the muscle tibialis anterior of the right side. The method was essentially the same as that one which was previously reported by Troni et al[3] with modification. The subjects were relaxed in supine position. A pickup concentric needle electrode (Dantec 13L58) was placed between the proximal and middle third of the muscle. A supra-maximal square pulses at a rate of 1 Hertz and duration of 2 milliseconds was applied by means of bipolar surface recording electrode (Dantec 13L36) on two sites at the distal portion from the recording electrode as far a way possible from the endplate region. Care was taken to pickup the electromyograph activity of the same set of muscle fibers during the test and this is achieved by the similarity of the shape of the compound muscle action potential. The latency was measured at the initial positive deflection. The MFCV was calculated by dividing the distance between the two sites of stimulation by the difference in the latency of the two evoked compound action potential. The signals were amplified with a band-pass filter of 1 Hertz to 10 kilohertz. The time base was 5 milliseconds per division. The measurements were repeated three times for reproducibility and the least reading was taken for further calculation.

Statistical analysis. The results of the numerical values were expressed in mean ± standard deviation (SD). Differences between two groups were evaluated with Student "t" test. The results were considered statistically significant when the P value equal or less than 5%. The linear regression analysis and the correlation coefficient "r" is used to study the relationship between some variables such as CK level and the duration of the disease.

Results. The proximal muscles were affected in all the DMD patients whether the upper or lower limbs were examined, while the distal muscle of the upper limbs were affected in 10 patients as compared to 17 patients showed clinical affection of the distal muscles of the lower limbs. Four patients in whom the upper limbs were first to be affected; 28 patients in whom the lower limbs were first to be affected while 18 of the total number presented with affection of both upper and lower limbs. Nine patients presented with hypertrophy of the upper limb muscles versus 23 patients showed hypertrophy in the lower limb muscles. Wasting of the upper limb muscles was present in 6 patients while 2 patients had wasting of the lower limb muscles. The results of the calculated MFCV±SD of the control subjects and DMD patients in the two muscles sampled are summarized in Table 1. The difference in the MFCV between the normal subjects and DMD patients was significant (P<0.005). It is clear that the normal subjects showed normal distribution curve in two muscles examined. On the reverse, DMD patients have an abnormal distribution curve showing multi-peaks. Conventional EMG showed typical myopathic interference pattern characterized by an increase in the percentage of polyphasic potentials of short duration and low amplitude, low mean amplitude of the recruited pattern and condensed interference pattern. The MUP duration in the biceps brachii and tibialis anterior of DMD patients was significantly shorter (P<0.05) and it equals to 5.36±0.71 msec and 5.97±1.52 msec as compared to 8.73±1.05 msec and 11.1±1.02 msec of the control group. Likewise, the MUP amplitude of the DMD patients is significantly reduced (P<0.05) and it equals to 777.21±179.4 μV and 796.97 μV as compared to 969.63±122.08 μV and 1129.5±97.39 μV, of the control group. CK showed increased activity in the DMD patients (mean ± SD = 1081.5±362.9 IU/L) which was significantly higher than 64.4±9.2 IU/L (mean ± SD) in the control group. CK showed lower values as the disease progress with a significant inverse correlation (r = -0.947) with the duration of the illness. A biopsy

Table 1 - The calculated MFCV±SD of the control group and Duchenne Muscular Dystrophy patients in the biceps brachii and tibilis anterior.

Muscle tested	Control group MFCV (m/s)	DMD Group MFCV (m/s)
Biceps brachii	3.59±0.32	2.42±0.48*
Tibialis anterior	3.66±0.35	2.42±0.61*

*=P<0.005 MFCV-Muscle Fiber Conduction Velocity, DMD-Duchenne Muscular Dystrophy

specimen from the muscle quadriceps femoris of DMD patients showed striking muscle fiber diameter variation, hyaline fibers, daughter cells, splitting fibers and an extensive endomysial fibrous tissue proliferation in comparison to the normal mosaic appearance of muscle fibers of the normal subjects.

Discussion. Muscular dystrophies are primary muscle tissue disease involving the muscle itself and attack individual muscle fibers at random giving rise to scattered changes throughout the muscle.[13] Typical myopathic EMG, the hystopathological picture, and raised serum CK activity all confirmed the diagnosis of myopathy. The conduction velocity of the control group showed good reproducibility and is in consistent with the findings of other studies using needle technique.[3,11,14-16] The showing of MFCV in the DMD patients is in accordance with the findings of some authors[4,5,9-12] while it contradict the results of Chino et al[7] Eberstein and Goodgold[8]a nd Yaar and Neils[17] due to the small surface recording area.

The decrease in the MFCV of our patients could be attributed to the higher number of small size muscle fibers found in the biopsy specimen of our patients. Since the cycle of degeneration and regeneration in DMD is continuos so the newly regenerating fibers are short and thin and they have slower conduction velocities than the fully mature fibers. Furthermore, the presence of splitting fibers may add to the increase number of small size muscle fibers. The multi-peaks frequency distribution of the MFCV in the DMD group indicates that different groups of muscle fibers have conduction velocities scattered around a new means depending on their new diameter which is supported histologically by the disorganization of the motor unit and its muscle fibers.[18] This is also found in our study.

The significant inverse correlation between CK activity and the increase in the duration of the illness is suggested to be due to loss of many muscle fibers as a result of extensive fibrous tissue proliferation instead of the normal muscle tissue which have been proved in this study. No grading for our hitochemical findings had done to check for any correlation between CK activity and histochemical criteria.

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