Conduction velocity in human muscle
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MUSCLE FIBER CONDUCTION VELOCITY IN CHRONIC MYOSITIS

J.H. van der Hoeven, M.J. Zwarts.

(submitted)

ABSTRACT

Muscle fiber conduction velocity (MFCV) was measured in the brachial biceps muscle of 36 patients with chronic myositis, some of whom used steroid medication. Both an invasive and a surface EMG determination technique were used. In the non-steroid treated patients an increase in scatter of conduction velocities was found in combination with a slight decrease in mean MFCV. The deviations here appeared to be related to muscle fiber atrophy and hypertrophy. In the steroid treated patients a large decrease in MFCV was found together with a further increase in scatter; these two abnormalities seemed to be related to muscle fiber atrophy, a partial membrane depolarization and associated membrane alterations. We hypothesize that MFCV changes due to steroid medication and steroid myopathy are both manifestations of the catabolic effects of steroids on the muscle. It is concluded that invasive determination of the MFCV shows clear abnormalities in all myositis patients. The possible role changes in conduction velocity play on the form of the motor unit action potential is discussed.
INTRODUCTION

The electrodiagnosis of inflammatory myopathies is often difficult. The classic triad of (1) polyphasic, short duration motor unit potentials, (2) fibrillation, positive sharp waves, increased insertional irritability, and (3) bizarre, high-frequency, repetitive discharges is suggestive of polymyositis - dermatomyositis (Bohan and Peter 1975). However, these "classic" findings are strongly dependent on disease activity and are generally found only in the active stages of the disease (Partanen and Lang 1982). In the chronic stages the motor unit action potentials (MUAPs) can be both short or long in duration, and the amplitude tends to increase. The existence of the so-called "satellite potentials" makes a reliable judgement based on visual inspection even more difficult (Lang and Partanen 1976). These, sometimes contradictory, phenomena are due to a combination of changes in the muscle fiber and the terminal innervation pattern (Mechler, 1974; Henriksson and Stalberg, 1978; Nebeker et al. 1990). Additionally, steroid medication, which is commonly used, can also influence MFCV (Gruener and Stern, 1972; Troni et al. 1990) and hence change the MUAP (Nandedkar and Sanders, 1989). We investigated the muscle fiber conduction velocity (MFCV) in chronic polymyositis and dermatomyositis with regard to a possible diagnostic use. MFCV was determined by an invasive and a surface EMG determination method.

METHODS

Patients
The 29 patients (11 men and 18 women) with chronic myositis whom we investigated ranged in age from 27 to 73 with a mean age of 50.1 years. All patients were diagnosed as having polymyositis or dermatomyositis, or myositis in combination with SLE, sclerodermia or MCTD. All received clinical testing, CK measurements and standard EMG investigation. Part of the patients also underwent muscle biopsy. The diagnosis myositis was established according to the criteria of Bohan and Peter (1975) and only patients with definite or probable myositis were included. 24 measurements were performed on patients who had used no steroids for at least one year. 12 measurements were performed on patients receiving various dosages of corticosteroid medication, with a minimum of 30 mg prednisone a day, during at least six weeks before measurement. Eight patients were measured more than once in different stages of the disease, with or without medication. A total of 43 measurements were made.

Controls
Normal values were derived from a group of 49 healthy individuals, 29 men and 20 women. These subjects, who ranged in age from 21 to 74, with a mean age of 38.4 years, had no complaints about their neuromuscular system. None of the subjects used medication and all measurements were performed after obtaining informed consent.
MFCV estimation

Invasive MFCV (I-MFCV) estimation
Experiments were performed in the left brachial biceps (short head) with a method adapted from Troni et al. (1983) and performed on a Nicolet Viking I EMG apparatus (van der Hoeven et al. 1993). A stimulation needle electrode (Dantec 13L64, area of uninsulated tip: 2 mm²) was placed in the distal part of the resting muscle with a silver surface electrode as anode 10 to 15 mm distally. The muscle was stimulated with gradually increasing strength (suprathreshold) until a clear twitch was palpable (1 - 2 mA, 0.2 msec, 1 Hz). Guided by the twitch, the examiner placed a concentric needle electrode (Dantec 13L58) 50 - 60 mm proximally and manipulated until a reproducible polyphasic action potential was seen, amplitude 20 - 500 µV. The signals were amplified and bandpass filtered, 500 Hz - 10 kHz; the time base varied between 5 - 10 msec per division. Care was taken to place the electrodes perpendicular to the skin. A 4-trace storage was used to ensure the reproducibility of the action potentials. Only spikes larger than 20 µV were used for calculations. All latencies were measured at the positive turning points. The I-MFCV calculation was based on the distance between the electrodes and the latencies. The parameters used were: mean I-MFCV, fastest and slowest I-MFCV, and ratio fastest/slowest I-MFCV (F/S ratio), which indicates the scatter in conduction velocities.

Surface EMG recording
The experiments were performed on the left biceps brachii muscle. Each subject was seated in a chair with his left arm fixed in a horizontal semiflexed position at an angle of 120 degrees and supported at the elbow and the supine wrist. The isometric force of the elbow flexion was measured at the wrist with a strain gauge and the exerted force was displayed in front of the subject on a voltmeter. Three silver electrodes (diameter 2 mm) were placed in a rigid bipolar array with a common centre electrode, interelectrode distance 10 mm. The localization of the electrodes was parallel to the fiber direction, nearly halfway between the innervation zone and the distal tendon. The two EMG signals were amplified differentially (Disa EMG amplifier type 14C13) and bandpass filtered (20 - 500 Hz). They were then digitized synchronously by a 12-bit A/D converter with two different sample rates: 6024 Hz (velocity estimation) and 1024 Hz (power spectra) over two connected signal periods of 0.34 and 2.05 sec respectively.

Data were analyzed by a microcomputer (PDP 11/23) off line. The surface MFCV (S-MFCV) was calculated after interpolation, which raises the sample frequency to 12048 Hz, by the cross correlation method (Lynn 1979, Naeije and Zorn, 1983). Only correlation coefficients higher than 0.85 were accepted. The rectified integrated EMG (IEMG) was also calculated. All measurements were performed at different force levels in duplicate: 20-30-50-75 and 100% maximum voluntary contraction. On the basis of the summarized results, the mean S-MFCV was then calculated.

Procedure
All subjects were examined with the invasive method in the left biceps brachii muscle. Some of the subjects (23 patients) were also investigated by surface EMG. Knowledge of the fiber direction facilitated the positioning of the surface electrodes. Additionally, the muscle force of the elbow
TABLE 1. Results of invasive (I-MFCV) and surface (S-MFCV) MFCV measurements (SD) in controls and myositis patients. The patient group is divided according to the use of steroid medication.

<table>
<thead>
<tr>
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<tr>
<td><strong>I-MFCV</strong></td>
<td></td>
<td></td>
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<tr>
<td>mean (m.s⁻¹)</td>
<td>3.20 (0.25)</td>
<td>2.75 (0.49)</td>
<td>2.98 (0.44)</td>
<td>2.36 (0.28)</td>
</tr>
<tr>
<td>slow (m.s⁻¹)</td>
<td>2.77 (0.28)</td>
<td>1.58 (0.49)</td>
<td>1.79 (0.45)</td>
<td>1.23 (0.34)</td>
</tr>
<tr>
<td>fast (m.s⁻¹)</td>
<td>3.72 (0.33)</td>
<td>3.91 (0.64)</td>
<td>4.14 (0.66)</td>
<td>3.52 (0.37)</td>
</tr>
<tr>
<td>F/S ratio</td>
<td>1.35 (0.15)</td>
<td>2.70 (0.92)</td>
<td>2.43 (0.61)</td>
<td>3.14 (1.16)</td>
</tr>
<tr>
<td>spikes pro ins</td>
<td>7.4 (2.5)</td>
<td>15.9 (6.4)</td>
<td>14.1 (4.8)</td>
<td>18.9 (7.4)</td>
</tr>
<tr>
<td>n</td>
<td>49</td>
<td>36</td>
<td>24</td>
<td>12</td>
</tr>
</tbody>
</table>

|                  |               |               |               |              |
| **S-MFCV**       |               |               |               |              |
| S-MFCV (m.s⁻¹)   | 4.23 (0.41)   | 4.07 (0.85)   | 4.44 (0.64)   | 3.49 (0.51)  |
| IEMG (µV)        | 514 (267)     | 172 (151)     | 188 (179)     | 145 (76)     |
| Force (N)        | 224 (32)      | 120 (60)      | 136 (64)      | 97 (42)      |
| CK (0-50 U.l⁻¹)  | 148 (142)     | 164 (144)     | 120 (133)     |              |
| n                | 49            | 23            | 14            | 9            |

Abbreviations: mean: mean I-MFCV, slow: mean of slowest measured fibers, fast: mean of fastest measured fibers, F/S ratio: mean ratio between fastest and slowest measured fibers, spikes pro ins: number of spikes pro insertion, IEMG: rectified integrated EMG at maximal voluntary contraction, force: mean maximal force of elbow flexors, CK: creatine kinase serum level, n = number of investigations. Statistical analysis students t-test, unpaired samples, 2-tailed significant difference with controls, * significant difference between steroid and non-steroid treated patients.

flexors was measured by a hand-held dynamometer according to a standardized procedure (Van der Ploeg et al. 1991).
Differences between the groups were analyzed by means of the Students t-test, unpaired samples, 2-tailed. Statistical significance was accepted at a level of 5%.

RESULTS

For a summary of the results see table 1. All myositis patients showed a lower mean I-MFCV than the controls. Although the discrepancy between the two groups with respect to the mean fastest I-MFCV was small, the differences in mean slowest I-MFCV and the F/S ratio were significant. The same was true for the number of spikes per insertion and the muscle force of the elbow flexors. Nearly all patients showed an increased F/S ratio, sometimes even in combination with a (nearly) normal force (fig. 1). The mean force was lower in the myositis group. There were, however, also
significant differences among the patients depending upon their use of steroid medication. The mean I-MFCV as well as both the slowest and fastest I-MFCV were definitely lower among those myositis patients receiving steroid medication. Plotting the slowest vs the fastest I-MFCV result emphasized this distinction (fig. 2). Furthermore, the tendency of the mean F/S ratio toward higher values was more pronounced in the steroid group (fig. 3). The creatine kinase (CK) levels were found to be slightly, but not significantly, higher in the patients who were not treated with steroids.

When the mean I-MFCV is plotted against the mean S-MFCV, a linear correlation between the two methods can be found ($r=0.51$, $p<0.0001$). The S-MFCV was always higher than the mean I-MFCV (fig. 4). Examples of invasive measurements are given in figure 5.

**DISCUSSION**

We measured the conduction velocity along muscle fibers with both an invasive and a noninvasive method. The invasive method has the advantage of direct, non-volitional muscle activation (Troni et al. 1983). The main finding in this study is that all myositis patients show abnormalities in the I-MFCV estimation (fig. 1 and 2). Since only one muscle was measured, this indicates a highly sensitive measuring technique. Nearly all patients showed an increased F/S ratio in combination...
with a decrease in mean I-MFCV. Additionally, the influence of steroid use on the MFCV was important.

The chronic myositis patients without (recent) steroid therapy shared certain disturbances. The F/S ratios, the mean fastest I-MFCV and the mean S-MFCV values were increased in all patients, together with a slight decrease in mean I-MFCV. Additionally, lower IEMG values were found in combination with a loss of force.

Invasive measurements of MFCV in myogenic disturbances have rarely been performed. Buchthal et al. (1960) found an MFCV within the normal limits in 5 cases of advanced myopathy. Also data exist on cases of periodic hypokalemic paralysis (van der Hoeven et al. 1994) and Duchenne muscular dystrophy (Cruz Martinez et al. 1990), where a general reduction in MFCV was found. In acute and chronic polymyositis an increased scatter of conduction velocities in combination with a reduction in the mean I-MFCV was found in several investigations using different needle techniques (Chino et al. 1984, Troni et al. 1988, Zwarts 1989). A differentiation based on the use of steroid medication had, however, not yet been made. The increase in MFCV variability was described as an adaptive effect of the muscle resulting in faster conducting, probably hypertrofied fibers compensating for the loss of force, in combination with fiber atrophy. To catch this behaviour, Zwarts (1989) introduced the ratio between the fastest and slowest measured fiber (F/S ratio). In our much larger patient group a clear increase in F/S ratio was found as well.

In histological investigations in chronic myositis an increased range of fiber diameters due to a combination of hypertrophy and atrophy has been found. Increased diameter variation will result in an increased scatter of I-MFCVs because of the relation between fiber diameter and

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**Figure 2.** Plot of slowest conducting fibers (slowest I-MFCV) vs fastest conducting fibers (fastest I-MFCV) in both myositis groups and in the healthy controls. Note the clear separation between the three groups.
conduction velocity (Håkansson 1956). Other frequently found histological abnormalities in chronic myositis include segmental necrosis, fiber splitting, a decrease of motor unit area and changes in the terminal innervation pattern (Bertorini 1988). The "late" potentials which we often find after direct muscle stimulation have been interpreted as a manifestation of slow conducting fibers. However, linked potentials due to fiber splitting or ephaptic transmission between different muscle fibers at "low-threshold" sites cannot be excluded completely (Trontelj and Stalberg 1983, van der Hoeven et al. 1993).

The patients treated with steroid therapy differed remarkably from the non-treated patients. The mean I-MFCV and S-MFCV were substantially lower (fig. 4), as were the fastest and slowest measured I-MFCV result (fig. 2). Also the mean F/S ratio was higher in the steroid treated patients (fig. 3). These differences could have been the result of (1) a generally higher disease activity in the steroid treated patients or (2) an (additional) effect of steroids on the muscle fiber. The second hypothesis seems more likely since nearly all non-treated patients complained of (a slowly) progressive loss of force (suggesting higher disease activity) and because CK levels in the non-treated group were generally higher (table 1).

Few studies on the effects of steroid medication on the MFCV have been performed. Gruener and Stern (1972) found a decrease in muscle membrane potential in steroid treated rabbits. Troni et al. (1990) showed a decrease in MFCV in a heterogenous group of patients during steroid therapy. Several factors could be responsible for the MFCV decrease: changes in muscle fiber diameter (Håkansson 1956), membrane potential, or other membrane parameters such as ion

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Figure 3. Relation between the mean muscle fiber conduction velocity, invasive method, (mean MFCV) and the ratio between fastest and slowest conducting fibers (F/S ratio) of the myositis groups and healthy controls. Note the higher F/S ratio in both patient groups; the mean MFCV is clearly lower in all steroid treated patients.
channel density (Gruener et al. 1979). In (experimental) steroid myopathy a general muscle fiber atrophy occurs, mainly in the type 2 fibers (Smith 1964, Kelly et al. 1986), which normally show the higher diameter values, especially in males (Jennekens et al. 1971). Denervation atrophy results in a rapid decrease in MFCV (van der Hoeven et al. 1993). Hence it is likely that progressive atrophy forms the major cause for the general decrease in the MFCV. Two other factors which could cause the decline in MFCV are changes in depolarization rate and capacitance (Gruener et al. 1979, van der Hoeven, in press).

These alterations can probably also explain the differences between the S-MFCV in the two myositis patient groups. The mean S-MFCV in steroid treated patients is strikingly low, whereas the non-steroid treated patients show high normal values (table 1). We suggest that the S-MFCV values were biased by the fastest conducting, mainly type 2, fibers (Zwarts, 1989). These fibers show a preferential atrophy in the steroid treated patients. In the non-treated patients, however, a part of the fiber population is hypertrophic which would result in the opposite finding, an increase in S-MFCV.

The MFCV disturbances in the steroid treated patients can, theoretically, be a manifestation of a (subclinical) steroid myopathy. However, the cause of steroid myopathy is not yet completely understood; even the heading "myopathy" is a matter of debate. Dalakas (1988) speaks of "steroid induced muscle weakness, erroneously called steroid myopathy". It is clear that the gradual loss of force associated with Cushing syndrome or during high dose steroid therapy is based on a
preferential atrophy of type 2 muscle fibers (Khaleeli et al. 1983; Lacomis et al. 1993). The loss of force, apparently due to the catabolic effects of corticosteroids, often results in dominant disability, and even in respiratory insufficiency (Bowyer et al. 1985, Dropcho and Soong 1991, Lacomis et al. 1993). We hypothesize that the decrease in MFCV during steroid therapy is a manifestation of this atrophy, and that the degree of atrophy determines the degree of force loss. In our opinion it seems reasonable to speak of "steroid myopathy" when a clinical loss of force occurs due to the use of steroids.

Remarkable are the unspecific findings at concentric needle EMG in steroid myopathy. Myopathic changes are reported in only some of the cases. We suggest the following explanation. The preferential atrophy of type 2 fibers results in a slower MFCV, more or less in the same degree, within the motor unit. A myopathic MUAP pattern based on MFCV differences will then only be found at a larger distance from the end-plate zone. The same reasoning can be applied to the EMG findings in chronic myositis. The increased diameter variation results in an increased scatter of MFCVs, a combination of slower and faster conducting fibers. With concentric needle EMG a slight increase in polyphasic MUAPs will be found along with normal or even increased amplitudes.
These MUAP disturbances are often difficult to judge visually (Lang and Partanen, 1976). This could depend largely on the distance between the end-plate zone and the uptake electrode (Nandedkar and Sanders, 1989). In such cases determination of the MFCV can probably be helpful in showing the presence of abnormalities.

In a previous paper we discussed the role of neurogenic lesions on the MFCV (van der Hoeven et al. 1993). Slower and faster conducting fibers are found in both amyotrophic lateral sclerosis (ALS) and in chronic myositis without steroid therapy. However, in ALS these changes are generally much more pronounced, resulting in a higher F/S ratio. Otherwise, a differentiation between these diseases based solely on MFCV changes seems unlikely.

The MFCV scatter which we found in myositis stresses the role of conduction abnormalities in the phenomenon of the so-called "satellite potentials" during volitional muscle activation at concentric needle EMG (Borenstein and Desmedt 1975, Lang and Partanen 1976). For example, a typical MFCV range of 1.5 to 4.0 m.s\(^{-1}\) in chronic myositis results at a distance of 10 mm from the depolarization point in a latency difference of 4.2 ms, solely based on conduction differences. This difference increases to 20.8 ms at a distance of 50 mm between depolarization point and the uptake electrode. Knowledge of the distance between end-plate zone and uptake area is thus an important parameter, in clinical EMG as well as in automatic MUAP analysis programs.

In conclusion, we found clear disturbances in MFCV in all myositis patients. The non-steroid treated patients showed a slight decrease in mean I-MFCV in combination with an increase in scatter of conduction velocities. We suggest that this is related mainly to a combination of muscle fiber atrophy and hypertrophy. In the steroid treated patients a substantial decrease in mean MFCV was found, together with an increased scatter in conduction velocities. These changes may be related to muscle fiber atrophy and associated membrane alterations due to steroids. Determination of the invasive MFCV seems helpful in showing muscle involvement in possible myositis, and could assist in the interpretation of indistinct concentric needle EMG findings.

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MFCV in Chronic Myositis

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