SHORT REPORT

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DECLINE OF MUSCLE FIBER CONDUCTION VELOCITY DURING SHORT-TERM HIGH-DOSE METHYLPREDNISOLONE THERAPY

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The suppressive effect of steroids on membrane excitability and muscle fiber conduction velocity (MFCV) has been noted sporadically in the literature.[5,16] Additional complications of steroid therapy are muscle weakness and, in extreme cases, even steroid myopathy.[2,4] These side effects suggest that steroid therapy is directly related to decreases both in MFCV and in muscle force and sometimes even to steroid myopathy. We tested this relationship by measuring the influence of short-term high-dose methylprednisolone on MFCV and muscle force in a group of multiple sclerosis patients during a relapse. MFCV values were determined using an invasive method.

PATIENTS AND METHODS

Fourteen patients, 6 men and 8 women (mean age 37.0 years, range 21–55 years) with definite multiple sclerosis,[11] were investigated. Because of a relapse all patients were receiving high-dose methylprednisolone therapy consisting of 500 mg methylprednisolone i.v. daily for 5 consecutive days. The patients had mainly pyramidal dysfunction, with disability grades before start of therapy varying between 4.0 and 8.0.[10] None of the patients showed any clinical signs of peripheral nerve or muscle involvement. All gave their informed consent prior to the measuring.

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MFCV measurements were performed in the biceps brachii muscle at rest, by means of needle electrodes as described previously.[15,17] The parameters used were: mean MFCV, fastest and slowest MFCV, and the ratio of the fastest and slowest MFCV result (F/S ratio), which indicates the scatter in conduction velocities.

Force measurements were performed by handheld dynamometry.[18] The force of the elbow flexors on the tested side and the sum score of all tested muscle groups (proximal and distal muscle groups on both sides) were used for calculations.

Protocol. The MFCV and force measurements were performed in one session, within 24 h before starting the therapy, and were repeated within 24 h after stopping the therapy. Muscle strength was first determined and then the MFCV was measured on the side with the highest force at elbow flexion to minimize the effects of changes in the central nervous system (CNS) function. If the force was symmetrical, the MFCV was tested on the left side. In addition serum sodium and potassium values and surface temperature near the uptake electrode were obtained. The patients were allowed to maintain their normal daily routine during the entire therapy period.

RESULTS

The results, summarized in Table 1, show a significant reduction in MFCV in all patients after 5 days of therapy. Not only did the mean MFCV decline, but the fastest and slowest MFCV results were less as well. The F/S ratio (fastest/slowest fibers measured) increased slightly but significantly. The force of the elbow flexors on the tested side showed no significant changes. The muscle sum-score increased significantly. Serum sodium and potassium values and surface temperature did not change significantly.

Table 1. Mean and standard error (SE) in the MFCV and force measurements before and after methylprednisolone therapy in all patients.

	Before		After		Difference	
	Mean	SE	Mean	SE	Mean	SE
Mean MFCV (m/s)	3.29	0.09	2.96	0.10	−0.34*	0.05
Fastest MFCV (m/s)	3.80	0.12	3.55	0.12	−0.26*	0.08
Slowest (m/s)	2.85	0.09	2.41	0.10	−0.44*	0.07
F/S ratio	1.34	0.04	1.49	0.05	0.14*	0.06
Force elbow flexors (*N*)	203	10	211	14	8	7
Sum-score (*N*)	2862	255	3155	271	293*	75
Surface temperature	31.4	0.19	31.2	0.27	−0.19	0.23

F/S ratio: mean ratio between fastest and slowest fibers measured; sum-score: mean force value of all tested muscles. Statistical analysis: Wilcoxon's nonparametric test, paired samples, two-tailed.
**Significant difference.*

DISCUSSION

The main finding of this study is a significant reduction in MFCV during short-term high-dose intravenous methylprednisolone therapy. The decrease was found after 5 days of therapy with a cumulative dose of 2500 mg methylprednisolone. The constant surface temperature argues against a general change in muscle circulation. Since the subjects had no signs of peripheral nerve or muscle involvement, it is likely that the observed decrease in MFCV is due to the effect of methylprednisolone on the muscle fiber.

Studies of MFCV changes during steroid therapy have seldom been performed. Troni et al.[16] did, however, report a slowing of MFCV during long-term steroid therapy in a heterogeneous group of patients.

Long-term steroid therapy can cause a gradual loss of force.[2,4] Steroid therapy tested in animals resulted in severe muscle atrophy which was ascribed to an inhibition of protein synthesis.[8,9,13,14] Muscle fiber atrophy could, therefore, have been the cause of the decrease in MFCV in the test group.[7,17] However, the muscle force of the elbow flexors, which generally is positively correlated with MFCV,[1] showed no significant change during the treatment period. This argues against major muscle atrophy, even though the increase of muscle sum-score due to the effect of the medication on the CNS dysfunction might mask a negative effect of the steroids on the muscle force. Other arguments against atrophy as a major cause for the decrease in MFCV are: (1) the fact that all subjects continued their normal daily activities, which retard glucocorticoid-induced muscle atrophy[3]; and (2) the relatively short treatment period (5 days).

An alternative explanation is a lowering of the membrane potential associated with a slowing down of the conduction velocity.[6] Gruener and Stern[5] found in vitro a lowering of the membrane potential after some days of corticosteroid therapy, especially in type II muscle fibers. They related this decline to changes in intracellular ion concentration or muscle membrane permeability. Ruff et al.,[12] however, were unable to confirm these results in an in vivo experiment on rats using megadoses of steroids. Nevertheless, the corresponding time courses of the depolarization in vitro and the MFCV decrease in vivo make a causal relationship likely. It suggests that the MFCV decline is due to a change in membrane potential secondary to an alteration of the muscle membrane properties, or in intracellular ion concentration. The lack of changes in the serum electrolytes argues against a change in extracellular ion concentration.

The decrease in MFCV was most pronounced in the slowest fibers, resulting in an increase in the F/S ratio. A selective atrophy of (type II) muscle fibers is well known in steroid myopathy.[9] This suggests a relation between early membrane changes and secondary steroid-induced muscle fiber atrophy; both are probably components of the mechanism leading to clinically manifest steroid myopathy.

In conclusion, we found a clear decrease in MFCV during short-term high-dose methylprednisolone therapy. The change in MFCV was not associated with a decrease in force, which argues against muscle atrophy as a major cause. We suggest that a partial depolarization of the muscle membrane is responsible for the MFCV decrease, possibly in combination with slight fiber atrophy.

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