Changes in the Distribution of Nerve Conduction Velocities in Diabetics

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FUJIMURA, Y., YOKOYAMA, K., ARAKI, S. and MURATA, K. *Changes in the Distribution of Nerve Conduction Velocities in Diabetics*. Tohoku J. Exp. Med., 1996, 178 (2), 177-185 — To examine which of the faster or slower large myelinated nerve fibers (alpha fiber group) are affected earlier by diabetes mellitus (DM), the distribution of nerve conduction velocities (DCV) and conventional sensory nerve conduction velocities (SCV) in the median nerve were measured in 10 male DM patients aged 35-58 (mean 50) years. The patients had suffered from DM for 0-30 (mean 11) years; their fasting blood sugar (FBS) levels were 105-363 (mean 219) mg/100 ml. The DCV was expressed by the conduction velocities below which 10, 20,, 80 and 90% of active fibers lie (V10, V20,, V80 and V90 velocities, respectively). In DM patients, the V30 to V90 velocities of the DCV as well as the SCV were significantly smaller than those of age-matched male controls. The results of multiple regression analysis indicated that FBS was inversely related to V50 to V90 velocities; duration of the disease was also significantly related to V80 and V90 velocities. These data suggest that faster nerve fibers are more susceptible to DM than slower fibers are; changes in conduction velocities of the faster fibers are closely associated with FBS and duration of DM. ——— distribution of nerve conduction velocities; peripheral nerve conduction velocity; diabetes mellitus; peripheral neuropathy; blood sugar

Peripheral neuropathy is one of the most common complications of diabetes mellitus (DM) (Thomas and Eliason 1984). To assess early changes of peripheral neuropathy in DM patients, nerve conduction velocity (NCV) studies have been widely used; mild to moderate slowing of motor and sensory NCV (MCV and SCV, respectively) has been reported (Mulder et al. 1961; Downie and Newell 1961; Gilliatt and Willson 1962; Lamontagne and Buchthal 1970; Noel 1973). Some reports have shown linear relationship between fasting blood sugar (FBS) and MCV but not SCV (Graf et al. 1979, 1981; Porte et al. 1981).

Peripheral nerve trunks contain several thousand myelinated nerve fibers with slower and faster conduction in proportion to the fiber diameters. The conventional method of nerve conduction velocity yields only a discrete value

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that reflect maximal velocity of fibers in the nerve trunk; the function of most other fibers cannot be directly assessed.

Three research groups independently developed different transcutaneous techniques to derive the distribution of conduction velocities (DCV) of large myelinated fibers (alpha fiber group) by means of computer analysis (Barker et al. 1979; Cummins et al. 1979; Kovacs et al. 1979). Using the method by Barker et al. (1979), we have found that faster large myelinated nerve fibers of the peripheral nerves are more sensitive than the slower fibers in subjects exposed to lead, thallium, styrene, mixed organic solvents, chronic alcohol ingestion and local vibration (Araki et al. 1986a, 1988, 1993; Yokoyama et al. 1990; Murata et al. 1991a, b, c; Fujimura et al. 1993; Sata et al. 1993).

On the other hand, application of these methods to DM patients have revealed that: (1) both faster and slower fibers were affected (Cummins and Dorfman 1981; Barker 1981; Sax et al. 1981; Suzuki et al. 1992) and (2) faster fibers were earlier affected than slower fibers (Dorfman et al. 1983). However, the relationship between the severity of DM and changes in the DCV has not been demonstrated.

In the present study, to examine which of the faster or slower large myelinated nerve fibers are affected earlier by DM, our technique was applied to 10 DM patients in relation to changes in FBS and duration of DM.

SUBJECTS AND METHODS

Subjects

Subjects examined were 10 male adult patients with DM admitted to a medical school hospital. They had suffered from DM for 2 months to 30 years (mean 11 years). Concentrations of fasting blood sugar (FBS) in the patients were 105–363 (mean 219) mg/100 ml at the time of examination. Their ages ranged from 35 to 58 (mean 50) years. One of the patients was insulin dependent and all others were non-insulin dependent; four patients had mild symptoms owing to diabetic neuropathy. Control subjects, matched with each patient by age (same 4-year span), were selected randomly from 41 male healthy adults in the same residential area as the patients. Neither the patients nor the controls suffered from other neurological or other endocrinological disorders. None of them had occupational exposure to heavy metals or solvents. There were no significant differences in age, skin temperature, consumption of alcohol and height between the patients and the controls (paired sample *t*-test, $t = -0.17, -0.23, 0.95$ and 0.84 , respectively; $p > 0.05$).

Methods

The nature of the procedures used in the present study was fully explained to all subjects, and the study was carried out with their informed consent. The DCV was measured by the method reported by us previously (Araki et al. 1986a, 1988; Yokoyama et al. 1987), a modified method of Barker et al. (1979). The

measurement was conducted in a warm laboratory (26–30°C) using a two-channel electromyograph (Medelec MS-92, Surrey, England). Skin temperature was in the range of 30–34°C for all subjects. The right median nerve was stimulated repeatedly with a 70–100 V square-wave pulse of 0.2 msec duration, with stainless ring electrodes tied around the proximal and distal interphalangeal joints of the second finger. The compound action potential (CAP) was recorded at the wrist and the elbow. The responses were averaged 50 to 150 times (bandpass, 20–2,000 Hz). The DCV was calculated by the double conduction distance method (Barker et al. 1979) between the velocities of 30.0 and 77.5 m/sec with an interval of 2.5 m/sec from the two CAPs, using a NEC PC-9801 microcomputer. The calculated DCV was expressed by the conduction velocities below which 10, 20, 30, 40, 50, 60, 70, 80, and 90% of active nerve fibers lie (V10, V20, V30, V40, V50, V60, V70, V80 and V90 velocities, respectively). When the measurement was made over a period of 15 days in a 24-year-old healthy student, the daily variations (coefficients of variation) ranged from 2.0 to 4.7% for the V10 to V90 velocities (Araki et al. 1986a).

Fig. 1. Distribution of conduction velocities in 10 DM patients and the same number of age-matched controls (average and standard error).

Conventional median SCVs in the forearm (wrist to elbow) and palm (second finger to wrist) segments were calculated from the two CAPs. Daily variations in the SCVs were below 3.6% (Araki et al. 1986b).

Statistical analysis

The paired *t*-test was conducted to compare the V10 to V90 velocities of the DCV and SCVs between DM patients and controls. Relations of FBS, duration of DM, age and skin temperature (explanatory variables) to DCV parameters and SCVs were analyzed by multiple regression analysis as well as simple correlation coefficient in the 10 DM patients. In these analyses, the four explanatory variables were chosen from the following reasons: (1) Manifestation of diabetic neuropathy increases in parallel to aging and duration of DM (Pirart 1978). (2) Skin temperature and age are considered confounding factors in measurement of DCV (Cummins and Dorfman 1981; Sax et al. 1981). (3) FBS is related to MCV in DM patients (Graf et al. 1979, 1981; Porte et al. 1981). The statistical analyses were performed using the Statistical Packages for the Biosciences (SPBS) (Uni-Science Co., Murata et al. 1991a).

RESULTS

The DCV in diabetic patients and in control subjects is shown in Fig. 1 and

TABLE 1. *Differences in distribution of nerve conduction velocities (DCV) and sensory nerve conduction velocities (SCV) in the median nerve between 10 diabetes mellitus (DM) patients and 10 healthy controls*

	Patients ^a	Controls ^a	Matched differences ^b
DCV (m/sec):			
V10	37.8 (30.8–50.4)	43.2 (32.0–53.6)	-5.4 ± 9.3
V20	41.7 (31.8–51.8)	46.3 (35.5–55.0)	-4.6 ± 8.0
V30	44.4 (33.3–53.1)	50.6 (42.4–56.2)	$-6.2 \pm 7.1^*$
V40	46.0 (34.8–54.3)	53.1 (44.2–58.9)	$-7.1 \pm 6.7^{**}$
V50	47.7 (36.5–55.6)	54.3 (45.7–59.4)	$-6.6 \pm 6.5^*$
V60	49.3 (38.3–56.9)	56.2 (47.0–60.9)	$-6.9 \pm 6.8^*$
V70	51.0 (39.9–61.4)	57.6 (48.1–62.6)	$-6.6 \pm 7.4^*$
V80	53.2 (44.1–64.6)	59.2 (49.6–66.3)	$-6.0 \pm 6.9^*$
V90	55.4 (46.0–67.1)	61.3 (51.2–72.5)	$-5.9 \pm 7.3^*$
Nerve conduction velocity (m/sec):			
SCV, palm	39.9 (32.4–47.6)	49.0 (44.07–55.4)	$-9.1 \pm 6.7^{**}$
SCV, forearm	53.2 (47.0–65.3)	59.0 (50.9–63.8)	$-5.8 \pm 5.8^*$

^aMeans with ranges in parentheses.

^bMean and standard deviation of matched differences.

* $p < 0.05$ and ** $p < 0.01$ (paired *t*-test).

Table 1. The DCV in DM patients was shifted toward slower conduction velocities. The V30 to V90 velocities of the DCV and the SCVs of the palm and forearm segments for DM patients were significantly smaller than those for control subjects. Fig. 2 exemplifies the differences in V50 and V90 velocities between the two groups.

The results of the multiple regression analysis are shown in Table 2. FBS, age and skin temperature were significantly related to the V50 to V90 velocities; duration of DM was also significantly related to the V80 and V90 velocities. On the other hand, neither FBS nor duration of DM were significantly related to SCVs ($p > 0.05$). Fig. 3 illustrates the relationship between duration of DM and the V90 velocity in DM patients.

DISCUSSION

The V30 to V90 velocities of the DCV were significantly reduced in DM patients in the present study. This finding agrees with the data by Dorfman et al. (1983), who reported that faster fibers were earlier affected than the slower fibers in DM patients.

Also, the present result is in line with the histological data by Chopra and Hurwitz (1969) that larger ($11 \mu\text{m}$ and over in diameter) myelinated fibers in the

Fig. 2. Differences in distribution of conduction velocities (V50 and V90 velocities, m/sec) between 10 DM patients and the same number of matched controls (paired sample t -test).

Transverse lines indicate mean values.

TABLE 2. *Relations of fasting blood sugar (FBS), duration of diabetes mellitus (DM), age and skin temperature (explanatory variables) to distribution of nerve conduction velocities (DCV) and sensory nerve conduction velocities (SCV): multiple regression analysis*

DCV and SCV ^a	Multiple correlation coefficient (R)	Standardized regression coefficient			
		FBS	Duration of DM	Age	Skin temperature
DCV:					
V10	0.51	0.02	0.11	−0.63	0.56
V20	0.63	−0.38	−0.03	−0.72	0.52
V30	0.73	−0.44	−0.08	−0.78	0.63
V40	0.82	−0.50	−0.11	−0.82	0.75
V50	0.91*	−0.54*	−0.16	−0.83*	0.86*
V60	0.95*	−0.56*	−0.19	−0.79*	0.90**
V70	0.98**	−0.56**	−0.23	−0.73**	0.93**
V80	0.99**	−0.48**	−0.34**	−0.69**	0.89**
V90	0.99**	−0.48**	−0.34**	−0.62**	0.89**
Nerve conduction velocity:					
SCV, palm	0.79	−0.08	0.64	−1.00*	1.02
SCV, forearm	0.90	−0.48	−0.18	−0.69	0.89*

^aCriterion variables.

* $p < 0.05$ and ** $p < 0.01$.

Fig. 3. Relation of duration of DM to V90 velocity in 10 DM patients. Only duration of DM was significantly related to DCV, i.e. V80 and V90 velocities, by simple correlation. r indicates the Pearson's product moment correlation.

sural nerves of DM patients with or without mild clinical symptoms of neuropathy were more affected than the smaller (6 to 10 μm) fibers; using the conversion coefficient of 6 m/sec per the fiber diameter of 1 μm (Buchthal and Rosenfalck 1966), the conduction velocities of the larger and smaller fibers are assumed to be approximately above 60 m/sec and 36 to 60 m/sec, respectively. It is thus suggested that faster fibers are more vulnerable than slower fibers in early stage of DM.

Furthermore, the results of the present study indicated that conduction velocities of faster fibers depend on FBS and duration of DM in DM patients. Similarly, age and skin temperature were considered to be major confounding factors for conduction velocities of the faster nerve fibers.

Finally, conventional SCVs were significantly related neither to FBS nor to duration of DM. This is consistent with the previous observations that neither FBS (Graf et al. 1979, 1981; Porte et al. 1981) nor severity of diabetic neuropathy (Lamontagne and Buchthal 1970) were significantly related to the SCVs. It is suggested that conduction velocities of faster nerve fibers are more sensitive to changes in FBS and duration of DM than conventional SCVs in DM patients.

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