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RELATIONS AMONG DIABETIC POLYNEUROPATHY, HbAıc, ALBUMINURIA AND DURATION OF DISEASE IN NON-INSULIN DEPENDENT DIABETES MELLITUS*

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Summary: Relation between regulation of diabetes and diabetic peripheral polyneuropathy remains controversial. Previous reports on this relations included relatively few. For this reason we planned to investigate the subject on a larger group of patients (80 diabetics and 23 control) Motor conduction velocities of the patients were compared with control subjects and sensory-neural conduction velocities were compared with the literature. Both motor and sensory-neural Conduction velocities were significantly lower in the diabetic group. HbAıc concentrations were in significant correlation with slowing of motor conduction but sensorial conduction velocity showed no correlation with HbAıc concentration. Slowing of motor and sensorial conduction velocities were also correlated with both albuminuria and duration of diabetes. Our findings suggest that proper regulation of diabetes may have some beneficial effect on abnormalities of neural function.

Key Words: Diabetes mellitus, neuropathy, HbAıc, albuminuria

Polyneuropathy is a frequent complication of diabetes mellitus. The role of hyperglycemia in the pathogenesis and progression of diabetic polyneuropathy is unclear but prior studies have suggested a possible metabolic cause (2). Greene and Sima's studies revealed that long-lasting hyperglycemia activates the polyol pathway via aldose reductase which results in sorbitol deposition and decrease of myoiinositol in the nerve tissue (11). As a result of these alterations, reductions in axolemmal sodium-potassium ATPase activity and nerve conduction delay with constructional abnormalities occur (11,16). Some authors suggested the role of

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nonenzymatic glycosylation due to hyperglycemia in the pathogenesis of diabetic polyneuropathy (3). Graf and coworkers observed a relation between hyperglycemia and slowing of motor conduction velocity, but a similar relation between hyperglycemia and sensorial conduction velocity was not found (8). These findings support the hypothesis of a metabolic component to diabetic polyneuropathy and suggest that optimal glycemic control may be beneficial to the patients with this disorder (9,14).

Although relations among the diabetic complications are not clear, a significant correlation between diabetic nephropathy and polyneuropathy has been reported (1,15). Improvement of diabetic polyneuropathy with optimal glycemic control has been observed, mostly in type-1 diabetes mellitus. Our study is performed in a larger group of patients with type-2 diabetes mellitus to evaluate the relations among diabetic polyneuropathy. HbAıc, albuminuria and duration of the disease.

Patients and Methods

This study is performed on 80 type-2 diabetic patients who accepted the study protocol admitted to the Department of Internal Medicine in Erciyes University between 1988 and 1989. None of these patients had been treated for diabetic polyneuropathy prior to the study. Patients who had a history of chronic alcoholism or a disease resulting in polyneuropathy other than diabetes mellitus are excluded.

Fifty-six female and 24 male diabetic patients ranged in age from 42 to 78 years (56±9.1). Duration of known diabetes was 36±72 months (ranged between 1 to 312 months). Twelve patients had been treated with insulin and 54 patients with oral antidiabetics and 14 patients were receiving diabetic diet only. A group of 23 healthy volunteers (12 male and 11 female) were selected as a control group. Control subjects ranged in age from 41 to 67 years (46±9.4). In this group motor conduction velocities were measured and compared to the diabetic patients. Sensorial conduction velocities of the patient group were compared with a previous study with a 23 patient control group ranged in age from 33 to 73 years (51±2) (8).

Conduction velocities were measured bilaterally in motor (peroneal) and sensory (sural) nerves. To measure motor nerve conduction velocity, surface electrodes were placed on the extensor digitorum brevis muscle. Sensory nerve conduction velocity was recorded behind the lateral malleolus after an electrical stimulus had beed given between two heads of the gastrocnemius muscle (8,9).

HbAıc concentrations were detected with colorimetric thiobarbituric acid method (Biotrol, Paris). Values lower than 7.2 percent were considered normal.

Albuminuria was detected in random urine with radioimmunassay using commercial kits (Diagnostic products Co., California): 0-29 miligrams of albumin excretion in 24 hrs urine was considered normal and 30-300 miligrams of albumin excretion as mikroalbuminuria. Albumin excretion greater than 300 miligrams/24 hours, detected by conventional methods, was accepted as macroalbuminuria.

Nerve conduction velocities of diabetic patients and control subjects were compared and relations among nerve conduction velocities of the diabetic patients, HbAıc, albuminuria and duration of diabetes were also investigated.

Student's (t) test was used for statistical analyses. Values in the tables are given as mean ±SD.

Results

Nerve conduction velocities of diabetic patients and control subjects were shown in Table I. Motor conduction velocity was found 38.7±8.3 M /sec in control subjects, and was significantly lower in the diabetic group ($p<0.001$).

Table I. Comparison Between Conduction Velocities of Diabetic Patients and Control Subjects

Conduction Velocity (M/sec)	Patients (n:80)	Control Subjects (n:23)	p
Motor nerve	38.7±7.3	50.3±5.4*	<0.001
Sensorial nerve	28.5±10.3	40.1±0.7**	<0.001

* Our control group
** Graf and Cowarker's patients

Sensorial conduction velocity was 28.5±10.3 M/sec in diabetic subjects which was significantly lower than 40.1±0.7 M/sec of the control group in the literature ($p<0.0001$).

Slowing of nerve conduction velocity was correlated with duration of diabetes. Nerve conduction velocities in the patients with more than 10 years of known diabetes were lower than the patients with less than 10 years of disease ($p<0.01$), as shown in Table II.

Table II. Relation Between the Duration of Diabetes and Conduction Velocities

Conduction Velocity (M/sec)	Duration of diabetes Over 10 years (n:22)	Below 10 years (n:58)	p
Motor nerve	33.5±7.0	41.1±6.0	<0.01
Sensorial nerve	21.5±7.9	28.0±9.5	<0.01

Relation between HbAıc and nerve conduction velocities was also evaluated. Table III shows that slowing of motor conduction velocity was significant in the patients with high HbAıc concentration ($p<0.001$). No relation was observed with HbAıc and sensorial conduction velocity in the same group ($p>0.05$).

Table III. Relation Between HbAıc Concentration and Conduction Velocities

Conduction velocity (M/sec)	HbAıc Concentration High (n:59)	Normal (n:21)	P
Motor nerve	37.7±7.8	42.5±4.5	<0.01
Sensorial nerve	17.9±12.4	22.5±10.0	>0.05

Albuminuria, including both microalbuminuria and macroalbuminuria, was correlated with both motor and sensorial conduction velocities. Patients with albuminuria had a slower nerve conduction velocity than the patients without albuminuria ($p<0.01$). Relation between albuminuria and nerve conduction velocities are shown in Table IV.

Table IV. Relation Between Albuminuria and Conduction Velocities

Conduction velocity (M/sec)	Albuminuria Yes (n:32)	No(n:48)	P
Motor nerve	35.8±6.4	41.8±6.6	<0.01
Sensorial nerve	23.8±6.8	30.6±10.8	<0.01

Discussion

Previous studies have revealed that both motor and sensorial conduction velocities were significantly slower in the diabetic population (6,8,12). Our observations "showing the impairment of nerve conduction as a result of diabetes mellitus" support these reports which include experimental studies performed on diabetic animals and have shown that increase in glucose, fructose and sorbitol levels in the nerve tissue were correlated with slowing of nerve conduction velocities (7,17). A similar relation was found between nerve tissu myoinositol concentration and nerve conduction (4,10). Hyperglycemia enhances urinary excretion of myoinositol and also reduces the transport of myoinositol into the nerve cells, resulting in slowing of conduction velacities (4,10).

High levels of HbAıc, which is a good indicator of hyperglycemia in the previous 6-8 weeks, is correlated with slowing of motor coduction (6,8,12,13). This relation was not found between HbAıc and sensorial nerve conduction velocity (15). Some authors have shown that, by optimal glycemic control, impairment in motor conduction could be improved (9, 13,18). Fraser and covarkers studied the patients with diabetic polyneuropathy before and after insulin and sulfonylurea treatment and observed that, only after insulin treatment, motor nerve functions could be improved (6). In our study, we saw a relation between HbAıc and motor conduction velocity but there was not a similar relation between HbAıc and sensorial conduction velocity. All these observations support the hypothesis that motor and sensory nerve velocities are affected by different factors. There is insufficient knowledge about these factors at present. Adding myoinositol to diet improves sensorial nerve functions more than motor nerve functions(5).

In this study we found a correlation between duration of diabetes and impairment of nerve functions, which supports observations of Gregerson(12).

We also observed a significant correlation between albuminuria and slowing of nerve conduction. Impairment of motor and sensory nerve functions was more pronounced in patients with albuminuria. In their study. Parving and coworkers observed a significant relation between macroalbuminuria and slowing of nerve conduction velocity (15). Since diabetic microangiopathy has some role in the pothogenesis of both nephropathy and neuropathy, this significant correlation between these two diabetic complications is not surprising.

In conclusion, we suggest that there are correlations among diabetic polyneuropathy, HbAıc, albuminuria and duration of the disease. Diabetic regulations may have a beneficial effect on impaired neural functions.

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