Electrophysiological Changes of Sensory Nerves In Patients with Type-2 Diabetes Mellitus of Different Duration

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Abstract :

Background: Peripheral neuropathy is a common complication of diabetes mellitus. Among the diabetic neuropathies symmetrical sensory polyneuropathy is the most common one. Abnormalities of sensory nerve conduction are features of diabetic nerve damage. Significant association has been found between electrophysiological parameters of sensory nerves and duration of metabolic derangement in patients with diabetic neuropathy. **Objectives:** The present study was designed to characterize nerve conduction abnormalities of sensory nerves in subjects with type 2 diabetes mellitus of different duration and also to assess whether duration of diabetes has any influence on the sensory nerve function. **Methods:** Forty-four type 2 diabetic subjects were included in two groups:- Group B_1 consisted of 23 diabetic subjects having duration of diabetes for 5-10 years (shorter duration) and Group B_2 consisted of 21 diabetic subjects having duration of diabetes for 10-15 years (longer duration). Twenty-five age and BMI matched healthy subjects without family history of diabetes were included as Group A (control) subjects. Sensory nerve conduction velocities, action potential amplitudes and latencies of ulnar and sural nerves were measured by a standard NCV-EMG equipment. **Result:** No significant changes in sensory nerve conduction parameters were observed in the group of diabetic subjects having shorter duration of diabetes. In the diabetic group with relatively longer duration of diabetes some of the sensory nerve conduction parameters were affected. Among them S SNAP and S NCV were significantly ($P<0.01$ and <0.05 respectively) reduced in diabetic group with relatively longer duration of diabetes. **Conclusion:** The results of the study indicated that neuronal dysfunction for sensory nerves appears after a prolonged exposure to hyperglycemia; there may also be some genetic and biochemical basis (other than hyperglycemia) for early sensory sparing in type 2 diabetic population of Bangladesh.

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Introduction:

Peripheral neuropathy is a common and disabling complication of diabetic mellitus. Although the exact etiology and pathogenesis of neuropathy is still uncertain, many investigators reported that metabolic changes contribute to diabetic neuropathy[1]. Symmetrical sensory polyneuropathy, the most common of the diabetic neuropathy is considered to have a metabolic cause[2]. There is evidence that the duration of impaired diabetic control, in particular, contributes to disturbed nerve function[3].

In diabetic neuropathic disorder, sensory, motor and autonomic functions are affected in varying degrees with sensory function predominating[4]. In diabetic polyneuropathy, sensory nerve conduction is believed to be more impaired than motor nerve conduction; sensory nerve conduction velocity is diminished and amplitude potentials are reduced early in diabetic neuropathy[5].

Electro diagnostic studies used in proper setting are a valuable tool for the evaluation of diabetic neuropathy as they are sensitive, specific, reproducible and easily standardized[6]. To observe the functional status of sensory nerves in diabetic neuropathic patients, sensory nerve conduction velocities (SNCV), distal latencies (DL), sensory nerve action potential (SNAP) are assessed.

The present study was designed to observe the effects of duration of diabetes on electrophysiological study of sensory nerves in patients having type –2 diabetes mellitus. The findings of the study may be helpful as background information for better management of the patients with different duration of diabetes suffering from neuropathy.

Methods:

The study was carried out in the Biomedical Research Group laboratory in BIRDEM and in the Department of

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Physiology BSMMU during the period of January 2002 to January 2003. Total 69 persons of both sexes with age range from 41 to 55 yrs were included in the study. The study was carried out on 44 diagnosed type-2 diabetic patients with different duration of diabetes suffering from neuropathy (Group B); 25 age and BMI matched apparently healthy subjects were also included in the study as control (Group A) Group B was further divided into Group B_1 which consisted of 23 diabetic subjects with duration of diabetes from 5 to 10 years(shorter duration) and Group B_2 which consisted of 21 diabetic subjects with duration of diabetes for more than 10 years (longer duration).

The criteria for selection of diabetic subjects were (i) diagnosed type-2 diabetes mellitus (fasting blood glucose level> 7.0 mmol[7]) with neuropathy (WHO-1999) (ii) having pain, paraesthesia, numbness & burning sensation in the limbs. Diabetic subjects having acute diabetic complications, pregnancy and other acute or chronic illnesses were excluded from the study. The subjects were selected from the Out Patient Department (OPD) of BIRDEM and BSMMU. Healthy control subjects were selected from the friends and relatives of the investigator and also from the friends of the patients. Persons having history of diabetes up to second degree relations were also excluded from the control group.

Detailed socio-demographic data, family history and medical history were taken from all the subjects and their physical and clinical examinations were done on the very first day of the visit to OPD. Informed consent was taken from each of the subjects. On the day of experiment, fasting blood sample was collected and the nerve conduction study was carried out.

Anthropometric measurements were taken by using scales on bare foot (Detect-Medic, Detect Scales INC USA). Serum glucose was estimated by glucose oxidase (GOD/PAP) method[8] (Randox laboratories ltd UK; Berham and Trinder 1972). Percentage of HbA_{1c} was measured in whole blood by a variant heamoglobin testing system (Bio-Rad model) using a modified HPLC method[9] (Ellis-1984). Neurological parameters of ulnar and sural nerves were measured by a standard EMG machine[10] . Nerve conduction parameters were included according to the protocol recommended by San Antonio conference on diabetic neuropathy. All statistical analysis were performed using statistical package for social science (SPSS) version10 for windows.All parametric variables were expressed as mean ± SD and median (range). One way ANOVA with Bonferroni test was performed as the test of significance. The Mannwhitney U-test was used to compare between medians.

Results:

Glycaemic status (FSG, HbA_1C) of the study subjects are shown in Table-I. Glycamic status among the control group and diabetic groups of shorter & longer duration differed significantly. Fasting serum glucose and HbA_{1c} levels were found to be significantly higher ($P<0.001$) in both the diabetic groups than those of control group. But the differences of these values between the diabetic groups of different duration were not statistically significant.

Table-I

General Characteristics & Glycaemic Status of the Study Subjects (n = 69)

Group	Age (Years)	BMI (kg/m^2)	FSG(mmol/L)	HbA_{1c} (%)
A(n=25)	45.72 ± 4.72	25.19 ± 4.58	5.12 ± 0.80	5.68 ± 0.34
B_1 (n=23)	49.13 ± 6.10	25.41 ± 2.99	9.32 ± 3.76	8.52 ± 1.91
B_2 (n=21)	48.48 ± 4.83	23.21 ± 2.97	8.81 ± 3.31	8.66 ± 1.78

Statistical Analysis :

Groups	P value			
Avs B_1	0.168 ^{ns}	2.00 ^{ns}	0.001 * * *	0.001 * * *
Avs B_2	0.486 ^{ns}	0.424 ^{ns}	0.001 * * *	0.001 * * *
B_1vs B_2	2.000 ^{ns}	0.300 ^{ns}	2.000 ^{ns}	2.000 ^{ns}

Results are expressed as mean ± SD. One way ANOVA with Bonferroni test was performed as the test of significance.

A- control group

B_1- shorter duration of diabetes

B_2- longer duration of diabetes

*** Significant at the $p<0.001$

^{ns} - not significant

P- probability

FSG- fasting serum glucose

HbA_{1c} - glycosylated haemoglobin

n-number of subjects

Table-II

Nerve Conduction Parameters of Sensory Nerves in Different Groups (n = 69)

Group	Ulnar			Sural		
	SNCV(m/sec)	DL(msec)	SNAP(mv)	SNCV(m/sec)	DL(msec)	SNAP(mv)
Gp A(n=25)	52.40	2.16	20.36	47.60	2.18	16.21
Gp B_1(n=23)	51.00	2.08	18.46	48.20	2.10	19.82
Gp C(n=21)	48.20	2.28	18.85	43.90	2.28	10.55

Statistical Analysis

Groups	P value					
Grp A vs B_1	0.657 ns	0.071 ns	0.628 ns	0.844 ns	0.080 ns	0.375 ns
Grp A vs B_2	0.360 ns	0.860 ns	0.604 ns	<0.05*	0.651 ns	<0.01**
Grp B_1 vs B_2	0.488 ns	<0.05*	0.925 ns	0.061 ns	0.067 ns	<0.01**

Results are expressed as median. The Mannwhitney U-test was used to compare between medians.

A- control group
B_1- shorter duration of diabetes
B_2- longer duration of diabetes
** Significant at the p<0.01
* Significant at the p<0.05
ns - not significant (p>0.05)
SNCV-sensory nerve conduction velocity
DL- distal latency
SNAP- sensory nerve action potential
m/sec-metre/second
msec-milisecond, mv-milivolt
n-number of subjects

In diabetic group with shorter duration of diabetes (Group B_1) no significant changes in all the sensory conduction parameters were observed when compared to those of control group (Group A). In the diabetic group with relatively longer duration of diabetes, sensory nerve conduction parameters were affected, among them S SNAP & S NCV were significantly (P<0.01 and <0.05 respectively) lower in diabetic group with longer duration (Group B_2) when compared to those of control group (Group A). Ud latency was significantly (P<0.05) higher and S SNAP was significantly (P<0.01) lower in Group B_2 when compared to those of Group B_1 No significant changes in other nerve conduction parameters were however observed when comparison was done between those of Group B_1 and Group B_2 (Table II).

Discussion:

The diabetic subjects were of comparable age and similar BMI to that of non-diabetic control. The glycemic status in two diabetic groups under study was not different from each other, so there occured a unique opportunity to observe the effect of duration of diabetes on peripheral nerve function of these diabetic subjects.

Significant sensory nerve dysfunction in diabetic group with relatively longer duration of diabetes was observed in this study; this finding is consistent with the previous findings of Vinik et al , Gregersen , Valensi et al[11-13] .. Knuiman et al[14] also reported that sensory neuropathy is more common in long standing diabetic subjects especially in those who develop the disease late in life.

No significant sensory nerve dysfunction was found in diabetic group with relatively shorter duration of diabetes when compared to that of non-diabetic group. This finding of early sensory sparing goes against the anticipated notion that diabetic polyneurophathy may start very early in diabetic patients and frequently involves sensory fibers.[15,16]. Biswash[17] also observed deterioration of motor nerve function without sensory nerve dysfunction in fairly controlled type 2 diabetic subjects with shorter duration. So early sensory sparing may be taken to be a finding which is characteristic of the Bangladeshi population with type 2 diabetes.

The finding of early sensory sparing also indicated that factors other than glycemia may be important to maintain normal sensory nerve function. There may be genetic and other biochemical basis for early sensory sparing in type 2 diabetic subjects under the present study[18]. Though genetic predisposition for development of neuropathy has been suggested, at least 2 studies failed to find an association between signs of peripheral neuropathy and

family history of NIDDM suggesting a single gene is not responsible for both NIDDM and peripheral neuropathy[12]. The possibility also remains that neuronal dysfunction may appear at a specific cut - off level of glycemia and that level may be much higher for sensory nerve dysfunction.

Conclusion:

In the present study significant impairment was observed in some parameters of sensory nerve function in diabetic group with longer duration of diabetes; all these changes indicate that duration of hyperglycemia plays a detrimental role on sensory nerve function. Again, the findings of early sensory sparing indicate that other metabolic, vascular and genetic factors may be involved or this finding may be a characteristic feature of diabetic population of Bangladesh only with relatively shorter duration of the disease. For more assurance further research on newly diagnosed diabetics and on subjects with more prolonged duration of diabetes and also on poorly controlled diabetic individuals in order to observe the effects of severity and duration of hyperglycemia on nerve conduction parameters are recommended.

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