

ELECTROPHYSIOLOGICAL CHANGES OF MOTOR NERVES IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Abstract

Peripheral neuropathy is a common disabling complication in patients with diabetes and this complication is related to the duration of the disease process. Nerve conduction study is widely used for the assessment of diabetic polyneuropathy not only to evaluate the degree of abnormality but also to document serial changes in the clinical course of the disease. This study was designed to characterize motor nerve conduction abnormalities in subjects having relatively shorter and longer duration of type 2 diabetes mellitus and also to assess whether time related variable like duration of diabetes has any influence on motor nerve function of the subjects. Forty-four type 2 diabetic subjects were included in two groups:- Group B consisted of 23 diabetic subjects having duration of diabetes for 5-10 years (shorter duration) and Group C 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 (non-diabetic) subjects. Motor nerve conduction velocities, action potential amplitudes and latencies of ulnar and peroneal nerves were measured by standard Nerve Conduction Velocity- Electromyography (NCV-EMG) equipment. Motor conduction parameters like ulnar compound muscle action potential (U CMAP), peroneal compound muscle action potential (P CMAP) and peroneal nerve conduction velocity (P NCV) were found to be significantly reduced ($p < 0.001$, < 0.01 , < 0.01 respectively) in diabetic group with shorter duration of diabetes (Group B) in comparison to non-diabetic control group (Group A). In the diabetic group with relatively longer duration of diabetes (Group C) motor nerve conduction parameters like U CMAP and P NCV were significantly reduced ($p < 0.001$, < 0.01 respectively). The results showed that in the type 2 diabetic population, motor nerve conduction parameters were affected early and there was gradual deterioration of motor function as duration of diabetes increased. Though previous studies on diabetic neuropathy suggest that abnormalities of sensory nerve conduction are early features of diabetic nerve damage and sensory nerves are more susceptible to fall prey to metabolic assaults,

the present study indicates that motor nerves are also involved and the neuropathic changes assessed by electro diagnostic methods in motor nerves may occur early in patients with type 2 diabetes mellitus. So, there may be some genetic and biochemical basis (other than hyperglycaemia) for early motor involvement in type 2 diabetic population of Bangladesh.

Key words: Diabetic neuropathy, electrophysiology, nerve conduction, electromyography.

Introduction

Peripheral neuropathy is one of the important late complications of diabetes mellitus. The prevalence of diabetic neuropathy appears to parallel with duration and severity of hyperglycaemia in both type I and type 2 diabetes¹. Several studies suggested that, there may be a relationship between degree of hyperglycaemia and impairment of nerve conduction in diabetic patients. Recent studies have shown that intensified metabolic control can prevent or delay the development of diabetic neuropathy; also near normal gluco-regulation results in improvement of peripheral nerve function in these patients².

Though people with diabetes can develop neurological problems at any time, the risk of developing diabetic neuropathy increases with the duration of diabetes³⁻⁵. Gregersen found that motor conduction may get reduced in diabetes and positive correlation was demonstrated between neglected diabetes control and slowing of motor conduction velocity⁶. Fagerberg et al also demonstrated that motor conduction velocity decreases with duration of diabetes mellitus⁷.

Evaluation of neuropathy is generally undertaken by electrophysiological measurements⁸. According to San Antonio convention for neuropathy, to label a patient as a case of diabetic neuropathy, the patient must have a minimum of a sign or a symptom and an abnormal electrodiagnostic test⁹. Electrophysiological studies are more sensitive than clinical examinations as clinical examinations fail to offer quantitative results and the electrodiagnostic tests are also the least variable non-invasive measures of neuropathy. To observe the

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functional status of peripheral nerves in diabetic neuropathic patients, motor nerve conduction velocities (NCV), distal latencies (DL), compound muscle action potential (CMAP)) are assessed.

It has been established that Electrodiagnostic assessments are sensitive, specific and reproducible measures of the presence and severity of peripheral neuropathy and they also correlate with the morphologic findings of nerve biopsy and thus define quantitative nerve dysfunction¹⁰. Franklin et al stated that prevalence of peripheral neuropathy is specific to the population tested, so it is important to study nerve conduction parameters in different racial groups taking into consideration that various factors like environmental and nutritional heterogeneity may influence the parameters¹¹. Consensus statement 1992 suggested that all aspects of nerve conduction studies should be standardized and every laboratory should have population based reference values¹².

The present study was designed to observe the effects of increasing duration of diabetes on electrophysiological study of peripheral nerves (motor) in patients having type 2 diabetes mellitus and also to find out a base line data in healthy Bangladeshi adults. The findings will be helpful as background information for better management of the patients suffering from diabetic neuropathy.

Materials and Methods

The study was carried out in Biomedical Research Group Laboratory of Bangladesh Institute of Research & Rehabilitation in Diabetes, Endocrine & Metabolic Disorder (BIRDEM) and in the Department of Physiology Bangabandhu Sheikh Mujib Medical University (BSMMU) during the period of January 2002 to January 2003. Sixty nine persons of both sexes were included in the study (Table-I). The study was carried out on diagnosed type-2 diabetic patients suffering from neuropathy. Age and body mass index (BMI) were matched with apparently healthy subjects. Diabetic subjects were selected basing on the following criteria : (i) diagnosed type 2 diabetes mellitus with neuropathy, (ii) fasting blood glucose level > 7.0 mmol/dL¹³, (iii) having pain, paraesthesia, numbness and burning sensation in the limbs. Diabetic subjects having acute diabetic complications, pregnancy and other acute or chronic illnesses were excluded from the study. Diabetic subjects were selected from the out patient department (OPD) of BIRDEM and BSMMU. Healthy controls 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 excluded.

Detailed socio-demographic data, family history and medical history were taken from all the subjects and their physical and clinical examinations were done on 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 (Randox Laboratories Ltd)¹⁴. Percentage of HbA_{1c} was measured in whole blood by a variant haemoglobin testing system (Bio-Rad model) using a modified HPLC method¹⁵. Neurological parameters of ulnar and peroneal nerves were measured by a standard EMG machine. Nerve conduction parameters were included according to the protocol recommended by San Antonio Conference on diabetic neuropathy. All statistical analyses were performed using statistical package for social science (SPSS) version-10 for windows.

All parametric variables were expressed as mean \pm SD and median (range). One way ANOVA with Bonferroni test was performed as the test of significance. The Mannhitney U-test was used to compare between medians; p values of less than 0.05 were considered as statistically significant.

Twenty five (11 male and 14 female) non-diabetic apparently healthy controls were included in the study in group A. Twenty three (2 male and 21 female) diabetic subjects with duration of diabetes for more than 05 years (5-10 years) were included in the study group B. Twenty one (5 male and 16 female) diabetic subjects with duration of diabetes for more than 10 years (10-15 years) were included in the study group-C.

Results

Characteristics (age, BMI) and glycaemic status of the study subjects are shown in Table-I. The subjects were of similar age and BMI. Glycaemic status among the control group and diabetic groups of shorter and longer duration of diabetes differed significantly. Fasting serum glucose levels were found to be significantly ($p < 0.001$) higher in both the diabetic groups than that of control group. HbA_{1c} levels were also found to be significantly ($p < 0.001$) higher in both the diabetic groups in comparison to that of control group. Differences in fasting serum glucose and glycosylated haemoglobin values between the diabetic groups were not significant.

Nerve conduction parameters of motor nerves in controls (group A) and diabetic groups with shorter (group B) and longer duration (group C) are shown in table-II. Statistical analysis for significance of difference has been shown in Table III. Nerve conduction velocity (NCV), distal latency (DL) & compound muscle action potentials (CMAP) were expressed in meter/second (m/sec), in mili second (m sec) & in milivolt (mv) respectively. Motor conduction

Table-I: Characteristics and glycaemic status of the study subjects. diabetes on nerve conduction parameters of diabetic subjects.

Groups	Age (years) Mean ± SD	BMI (kg/m ²) Mean ± SD	FSG(mmol/L) Mean ± SD
A (n=25)	45.72 ± 4.72	25.19 ± 4.58	5.12 ± 0.80
B (n=23)	49.13 ± 6.10	25.41 ± 2.99	9.32 ± 3.76
C (n=21)	48.48 ± 4.83	23.21 ± 2.97	8.81 ± 3.31
Statistical Analysis : p value			
A vs B	0.168 NS	2.000 NS	<0.001 ***
A vs C	0.486 NS	0.424 NS	<0.001 ***
B vs C	2.000 NS	0.300 NS	2.000 NS
A = Control group		FSG = Fasting serum glucose	
B = Duration of diabetes for 5 to 10 years		HbA1c = Glycosylated haemoglobin	
C = Duration of diabetes for 10 to 15 years.		p = probability	
n = Number of subjects		NS = Not significant	
*** = Significant			

In the present study significant motor function deterioration was found in the diabetic groups with both shorter and longer duration of diabetes in comparison to non diabetic group. This finding is consistent with the observation of Fagerberg et al, Gregersen and Brill who reported that motor defects are common in diabetes with neuropathy and increase in frequency with the duration of the disease^{7,16,17}.

Though not significant, tendency for reduction in UNCV & PNCV and increase in Ulnar & Peroneal distal latency were observed in diabetic group with longer duration of the disease in comparison to non diabetic group. No significant changes were observed regarding these parameters between non diabetic & diabetic group having shorter duration of diabetes.

Table-II: Nerve conduction parameters of motor nerves in controls (Gp A) and Diabetic Groups (Gp B & Gp C).

Parameters	Ulnar nerve			Peroneal nerve		
	Gp A (n = 25)	Gp B (n = 23)	Gp C (n = 21)	Gp A (n = 25)	Gp B (n = 23)	Gp C (n = 21)
MNCV (m/sec)	54.20	54.50	50.50	47.00	44.00	44.20
DL (m sec)	2.68	2.44	2.70	4.08	4.00	4.16
CMAP (mv)	8.86	3.99	6.57	7.53	2.31	6.24

m/sec = meter/second : m sec = mili second, mv = mili volt

Table-III: Test of significance to show differences in motor nerve parameters of various groups.

Group	Ulnar nerve			Peroneal nerve		
	NCV (m/sec)	DL (m sec)	CMAP (mv)	NCV (m/sec)	DL (m sec)	CMAP (mv)
Gp A vs B	0.901 NS	0.103 NS	<0.001***	<0.01***	0.327	<0.001***
Gp A vs C	0.110 NS	0.912 NS	<0.05*	<0.01**	0.982 NS	0.197 NS
Gp B vs C	0.136 NS	0.107 NS	0.107 NS	0.488 NS	0.417 NS	<0.01**

parameters namely U CMAP, P CMAP and P NCV were significantly reduced ($p < 0.001$, < 0.001 , < 0.01) in group-B in comparison to group A. In group C subjects, motor nerve conduction parameters were affected; among the parameters U CMAP, P NCV were significantly reduced ($p < 0.001$, $p < 0.01$) in group C diabetic subjects when compared to group A.

Discussion

In the present study, data from healthy control subjects have given the idea about normal range of nerve conduction parameters in healthy adults of Bangladesh. The diabetic subjects were of comparable age and similar BMI to that of non-diabetic controls. The relatively well controlled glycaemic status of the study group provided a unique opportunity to observe the influence of duration of

duration of the disease.

In this study, deterioration of nerve conduction parameters that is, peripheral nerve dysfunction was found to be more in the nerves of the lower limb (peroneal) in comparison to the nerves of upper limb (ulnar). Mulder et al and Halar et al also informed that nerves of the lower limbs are more susceptible to diabetic assault than the nerves of the upper limb^{18,21}.

The present study also showed significant reduction in amplitude and conduction velocity in motor nerves of diabetic group with shorter duration of diabetes which were more pronounced in peroneal nerve. This finding supports the observation of Greene et al and Bishwas^{22,19}. On the contrary, in diabetic group with relatively longer

duration of diabetes CMAP amplitude and conduction velocity were found to be variably affected in motor nerves. Greene et al, Dyck et al and Boulton et al also observed the same²²⁻²⁴.

The glycaemic status in two diabetic groups under study is not different from each other, so there occurs a unique opportunity to observe the effect of duration of diabetes on peripheral nerve function of these diabetic subjects. Significant deterioration in some of the motor conduction parameters were observed in diabetic group with shorter duration of diabetes. Progressive deterioration of some motor conduction parameters were observed in diabetic group with longer duration of diabetes. This significant motor dysfunction in diabetic group with prolonged duration of diabetes in the present study is consistent with the previous findings of Vinik et al, Gregersen, Valensi et al, Zochodne and Pirart^{4,9,16,25,26}.

Conclusion

The present finding of predominant motor nerve involvement in diabetic patients may be uncommon as sensory polyneuropathy has been found to be the most common of the diabetic neuropathies, but it is not unusual as several reports gave consistent indication of motor nerve involvement in diabetes. So predominant motor involvement may be taken to be a finding which is characteristic of the Bangladeshi population in both type 1 and type 2 diabetes. Also there may be a genetic and other biochemical basis for motor involvement in type 2 diabetic subjects under the present study. Though genetic predisposition for further 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 neuropathy⁹. The possibility also remains that neuronal dysfunction may appear at a specific cut-off level of glycaemia which may be much lower for motor nerve dysfunction.

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