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RESEARCH ARTICLE

Electrophysiological study of the palmar cutaneous nerves in diabetics

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ABSTRACT

Background: Polyneuropathy in diabetics which may be asymptomatic, targets particularly sensory neurons and their axons, starting in their distal terminals. **Aims and Objectives:** Aim of the present study was to identify the presence of subclinical neuropathy in Type 2 diabetic patients with the help of sensory nerve conduction studies (NCS). **Material and Methods:** Diabetic and control groups underwent standard antidromic technique of sensory NCS and recording of sensory nerve action potentials (SNAPs) of the palmar digital branches of the median and ulnar nerves using Neuro perfect software on windows based computerized electromyographic/nerve conduction velocity/evoked response Mark II system and surface electrodes. **Results:** On comparing the parameters of NCS it was found that distal latency of both the nerves was higher in diabetics than controls with a statistically significant difference. Results also showed a statistically significant decrease in conduction velocities of both nerves in diabetics. The mean SNAP amplitudes for all tested nerves were found to be decreased significantly in diabetics. **Conclusions:** Sensory nerves are found affected in diabetics with no clinical sign and symptoms of neuropathy. NCS is a sensitive test which can be used to identify subclinical cases.

KEY WORDS: Type 2 Diabetes Mellitus; Peripheral Neuropathy; Sensory Nerve Conduction Study; Median Nerve; Ulnar Nerve; Distal Latency; Conduction Velocity

INTRODUCTION

Diabetes mellitus is becoming a major cause of premature disability worldwide and has a high prevalence in India. The prognosis of the diabetic patients largely depends on the complications seen in the natural course of illness. Diabetic Peripheral Neuropathy (DPN) is a common complication of diabetes which may go undetected. It usually proceeds in a gradual, subtle way, but with very harmful effects. It may be presenting feature in many patients. Patients are asymptomatic and neurological deficit may be discovered by chance during a routine neurological examinations.[1]

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It occurs in both Types 1 and 2 diabetes and is more common with increasing age and duration of diabetes. Advanced DPN causes serious complications and worsen the quality of life in diabetic patients. As it progresses, it results into painful neuropathy. Painful paresthesia of the fingers may progress into a deep-seated ache, which may radiate up to the whole arm. This occurs primarily at night but maybe later initiated during the day also due to flexion and extension of the wrist. Sensory neuropathy may also result in troubled proprioception and abnormal muscle sensory function.[2-5]

Several theories have been proposed to explain the pain related to the diabetic neuropathy, such as metabolic and autoimmune mechanisms associated with glial cell activation, changes in the blood vessels that supply the peripheral nerves, changes in sodium and calcium channels expression and in central pain mechanisms. In spite of several pharmacological interventions, pain relief is unsatisfactory for most patients.[6]

The early and precise detection can help in better understanding the pattern of pathophysiological changes as well as in controlling the progression of neuropathy. Although there are multiple methods for detecting and monitoring DPN, nerve conduction studies (NCS) are generally considered to be most sensitive and reproducible.[7]

The present study was designed to test the hypothesis that metabolic derangement is associated with alteration in electrophysiological parameters of peripheral nerves before actual manifestations of neuropathy in Type 2 diabetic patients. It has been established that electrodiagnostic assessments are sensitive, specific, and reproducible measures of the presence and severity of peripheral neuropathy.[8]

Hence, a sensory NCS was carried out to identify the presence of subclinical neuropathy in Type 2 diabetic patients. Progression of neuropathy can be reduced by early detection and intervention.

MATERIALS AND METHODS

The study was conducted in the Department of Physiology of Dr. D. Y. Patil Medical College, Hospital, and Research Center, Pune, India, on patients of Type 2 diabetes mellitus attending the diabetic clinic. Design of the study was cross-sectional. In this study sensory nerve conduction of median and ulnar nerves were performed on 50 Type 2 diabetic male patients with age ranged 40–65 years. Mean duration of disease was 6 ± 2.5 years. The age recorded was that at the time of examination and the duration is the interval between the diagnosis of non-insulin-dependent diabetes mellitus and the time of examination. These patients were compared with 50 apparently healthy males, age and anthropometrically matched. All the patients with chronic musculoskeletal disorders, retinopathy, nephropathy or chronic disease, alcoholics, and smokers were excluded from the study. Detailed sociodemographic data, family history, and medical history were taken from all the subjects, and their physical and clinical examinations were done on the very 1st day of a visit to out-patient department. None of the subjects had any clinical sign and symptoms of neuropathy. The details of the study were explained in the language they understood, and informed consent was taken from each of the subjects. On the day of the test, blood samples were collected for blood sugar estimation which was following NCS. Anthropometric measurements (height and weight) were taken using scales on barefoot. Both fasting and postprandial blood glucose levels were estimated by glucose oxidase (Glucose Oxidase/Peroxidase) method lipid profile was estimated by an autoanalyzer, enzymatic method.[9]

Sensory NCS of palmar cutaneous branch of the right ulnar and right median nerves were performed in an environment with room temperature ranging from 23°C to 25°C using Neuro perfect software on windows based computerized electromyographic/nerve conduction velocity/evoked response Mark II system supplied by Recorders and Medicare Systems, Chandigarh, India, and surface electrodes. By standard surface stimulating and recording techniques, peripheral nerves were electrically stimulated, and antidromic recording of sensory nerve action potentials (SNAPs) was obtained from a purely sensory portion of the nerves, such as on a finger. The SNAP is the summation of the action potentials in sensory nerve axons evoked by the stimulus.[10] Sensory NCS included the measurements of latency and amplitude of SNAP with distal stimulation and calculation of conduction velocity.

With the help of stimulating electrodes single distal stimulation of 20–30 milliampere (mA) was given to obtain SNAP. The bipolar stimulator had a production current ability of 50 mA. The pulse duration was 0.1–0.2ms. Supramaximal stimulation was ensured. Signal averaging was applied. The time it takes for the electrical impulse to travel from the stimulation to the recording site was measured. This value was called as distal latency and was measured in milliseconds (ms). Amplitude of SNAP was measured in microvolt (μV).

For median sensory study, ring electrodes were used over index finger for recording SNAP where the active electrode (G1) was placed at metacarpophalangeal (MCP) joint and a reference electrode (G2), 3–4 cm distal to it. The single stimulation was given at middle of the wrist. For ulnar sensory study, ring electrodes were used over little finger where G1 was placed over MCP joint, and G2, 3–4 cm distal to it and stimulation was given at medial aspect of wrist. Ground electrode was placed between stimulating electrode and recording electrode for both the nerves. Distance between active electrode and stimulating electrode was measured in millimeter by measuring tape for both the nerves for calculation of conduction velocity. Latency, amplitude, and conduction velocity were measured. Conduction velocity of nerve was calculated based on the latency and the distance between the stimulating and recording electrodes. It was expressed in meter/second (m/s).[11] Recordings were obtained at following instrument setting: Sensitivity: 10–20 μV mm–1, low-frequency filter: 20–30 Hz, high-frequency filter: 3 KHz, and sweep speed: 2–7 ms mm^{-1}.

Statistical Analysis

All the test results obtained were expressed as a mean ± standard deviation. Statistical analysis of data was done using *t*-test and Microsoft office Excel 2010. For all the analysis probability values $P < 0.05$ were considered as statistically significant and $P < 0.001$ was considered as statistically highly significant. The study was approved by the Ethics Committee of our institution.

RESULTS

In the present study, 50 male diabetic subjects with a mean duration of disease 6 ± 2.5 years were compared with 50

non-diabetic (control) subjects of same age group and sex. The baseline characteristics of all the subjects are summarized in Table 1. On comparing the parameters of sensory nerve conduction of nerves between both the groups summarized in Table 2 it was observed that the latency of both the nerves was significantly more and conduction velocities were significantly less in diabetics as compared to control subjects. The amplitudes of SNAP of both the nerves were significantly less in diabetics.

DISCUSSION

In the present study, it was observed that the latency of median and ulnar nerves was significantly more and conduction velocities were significantly less in diabetics as compared to control subjects. The amplitudes of SNAP of both the nerves were significantly less in diabetics.

Conduction velocity of the nerve is determined by the velocity of fast fibers and amplitude of SNAP is determined by the numbers of large sensory fibers activated. Decreased conduction velocity and increased distal latency of median sensory nerve were also observed by Leventoglu *et al*. in diabetics.[12] Tendency for reduction of median sensory velocity was also found in patients of diabetes without neuropathy when compared with non-diabetic healthy controls by Gauhar *et al.*, however, their results were not statistically significant.[13] Metabolic Schwann cell lesion was suggested as the primary defect in diabetic neuropathy by Bischoff. Friedrich Behse *et al*. found that axonal degeneration and Schwann cell damage seems to proceed independently of each other.[14,15] Decreased in SNAP amplitudes were also observed by Rota *et al*. and Leventoglu *et al.* in their studies. Rota *et al.*[16] reported reduced SNAP amplitude of median nerve in 70% and ulnar nerve in 69% of the diabetic patients. Decreased amplitude of median sensory nerve was also observed by Leventoglu *et al*. in diabetics.[12] Bischoff in his study also found that neuropathy that occurs early in the course of diabetes is associated with axonal degeneration.

Table 1: Baseline anthropometric data, blood sugar, and lipid profiles of diabetics and controls

Characteristics	Mean±SD	
	Diabetics	controls
Participants (n)	50	50
Age (years)	56±6	51.7±6
Weight (Kg)	73±14	68±13
Height (Meters)	1.7±0.04	1.69±0.04
Fasting plasma glucose (mg%)	140±14.56	90±8.53
2-h plasma glucose (mg%)	227±23	126.55±11.63
Total cholesterol (mg%)	177.24±31	163.9±24.8
Triglyceride (mg%)	123.42±26	116±24
HDL (mg%)	41.4±10	48±15
LDL (mg%)	100±27	81±25

HDL: High-density lipoprotein, LDL: Low-density lipoprotein

Diabetes is characterized by hyperglycemia with abnormalities of utilization and production of glucose. In addition to this, there are abnormalities of fat and protein metabolism. The neurological manifestations have been noted to be related not only to the underlying metabolic defects but also vascular changes and complications arising from insulin hypoglycemia and acidosis. Recognizing the earliest alteration of nerves or blood vessels from diabetes may prove important information useful for understanding pathophysiologic derangement of its complications and developing preventive treatments.[17] A number of studies suggest some evidence of nerve abnormality that can occur relatively early in the course of diabetes. Studies have also shown once neuropathy is present, there is a tendency toward rapid pathological progression. In this scenario, it becomes important to diagnose it as early as possible so that suitable interventions can be taken to prevent its progression. In diabetic polyneuropathy, sensory nerve conduction is believed to be more impaired than motor nerve conduction.[18]

Multiple mechanisms have been suggested by which hyperglycemia causes nerve damage. Hyperglycemia leads to elevated intracellular glucose and cellular toxicity in the endothelial cells of the capillaries associated with peripheral nerves.[19] Hyperglycemia also induces oxidative stress and causes activation of Protein Kinase C (PKC). Activation

Table 2: Parameters of sensory nerve conduction of diabetics and controls

Parameters	Nerves	mean±SD		
		Diabetics	Controls	*P*
Distal latency (ms)	Median	2.4±0.3	2±0.2	0.000
	Ulnar	2.1±0.4	1.7±0.1	0.003
Amplitude (μV)	Median	39±25	82±22.7	0.000
	Ulnar	29±19	58.8±18.6	0.000
Conduction velocity (m/s)	Median	52±8	66.8±8.3	0.000
	Ulnar	48±8	55.4±5.1	0.003

*P<0.05 statistically significant **P<0.001 statistically highly significant. Units: Ms: Milliseconds; μV: Microvolt; m/s: Meters per second. SD: Standard deviation

of PKC has been linked to vascular damage in DPN.[20] The glucose-induced pathologic features of DPN are well characterized and include enhanced activity of the polyol pathway, the formation of advanced glycation end products, PKC activation, enhanced modification of proteins with *N*-acetyl glucosamine through the hexosamine pathway, increased inflammation, and a reduction in neurotrophic factors. Myelin is the major peripheral nerve component undergoing excessive glycosylation in diabetes.[21,22] Oxidative stress depletes nitric oxide within the peripheral nerves and endothelium of the microvasculature by reducing endothelial nitric oxide synthase, altering nerve perfusion.[23] Dyslipidemia is also found to be associated with nerve damage in diabetes. Many theories had been postulated to explain the possible relationship between lipid disorders and peripheral neuropathy. Abnormal serum lipids could mediate nerve infarction through fat embolism or lipid-induced platelet aggregation.[24] There is also a great possibility that serum lipid abnormalities have a direct effect on the cell membrane and might influence the structure of outer layers of myelin sheath.[25]

Our study has shown that simple non-invasive and objective tests like NCS are useful in recognizing the early alteration of nerves in asymptomatic diabetics and it could go a long way in early diagnosis of neuropathy. On the basis of the results obtained in the present study, nerve conduction tests are recommended at the time of diagnosis of diabetes which can be useful for setting preventive measures for diabetic neuropathy.

Our study has certain limitation. We did not attempt to correlate glycemic status and dyslipidemia with nerve conduction parameters. Further, a longitudinal study may be more helpful to monitor the progression of diabetic neuropathy.

CONCLUSION

Electrodiagnostic tests are sensitive and helpful in detecting subclinical abnormalities of nerve fibers. In diabetics, there are significant changes in sensory nerve conduction parameters as compared to non-diabetics, which is indicative of the development of neuropathy. Screening should be done on a regular basis to diagnose subclinical cases so as to avoid further complications.

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