



The Role of Electrodiagnosis in The Evaluation of Subclinical Diabetic Neuropathy

KEYWORDS

Diabetes mellitus, Subclinical neuropathy, Nerve Conduction Studies

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ABSTRACT *Introduction.* Diabetic neuropathy is now the most common neuropathy in the developed and developing world. The clinical course of neuropathy parallels the duration and severity of hyperglycemia. Glycemic control is directly related to the progression of diabetic neuropathy in both type 1 and type 2 diabetes. Diabetic neuropathy can be classified into two stages or classes, subclinical (class I) and clinical (class II). The subclinical neuropathy is diagnosed by electrodiagnostic tests, quantitative sensory tests, and autonomic function tests. The nerve conduction studies are well accepted for the evaluation of diabetic neuropathy. *Methods.* The present study was conducted from October, 2014 to May, 2015 at Sri Satya Sai Neuro Centre, Vijayawada, Andhra Pradesh, in collaboration with Neurologist. A total of 41 patients including both male and female subjects in the age range of 40 years to 55 years were selected for the study with the duration of diabetes ranging from 2 to 2½ years. Since the median nerve is the most common peripheral nerve involved in the diabetes, motor nerve conduction study of the median nerve is chosen for the present study. *Results.* Out of the total 82 hands, 73 hands revealed prolonged median distal motor latency and 9 hands revealed normal values. Out of the total 41 patients, abnormal median distal motor latencies are observed in both the hands of 32 patients and in at least one hand of all the remaining 9 patients indicating that all the patients under study are having abnormal parameters. It is to be reiterated that all the 41 subjects are asymptomatic in so far as neuropathy is concerned. *Discussion.* The present study reveals alteration in the electrophysiological parameters of median nerves in the diabetics who are not having any symptoms suggestive of overt neuropathy. *Conclusions.* This present study revealed that the nerve conduction studies are invaluable aids to diagnose the presence or otherwise of the subclinical neuropathy in diabetics and thereby suggesting the fact that the aggressive management of hyperglycemia might suggest an important strategy to control the occurrence of manifest neuropathy in the diabetic populations.

Introduction

Diabetic neuropathy, first identified as a clinical entity more than 200 years ago, is now the most common neuropathy in the developed and developing world¹. The prevalence of diabetes is rapidly rising at alarming rate all over the globe². Diabetic neuropathy is actually composed of several distinct syndromes with differing anatomic distributions, clinical courses, and probably underlying pathogenetic mechanisms. The overall prevalence of diabetic neuropathy is approximately 45% to 50%, with a clinical course that parallels the duration and severity of hyperglycemia¹. Glycemic control is directly related to the progression of diabetic neuropathy in both type 1 and type 2 diabetes. The International Diabetes Federation (IDF) estimated the total number of diabetic subjects to be around 40.9 million in India and this is further set to rise to 69.9 million by the year 2025³.

Diabetic neuropathy can be classified into two stages or classes, *subclinical (class I)* and *clinical (class II)*⁴. Subclinical diabetic neuropathy consists of evidence of peripheral nerve dysfunction such as *slowed motor and sensory conduction, elevated sensory perception thresholds that occur in the absence of clinical signs, and/or symptoms of diabetic neuropathy*. Clinical diabetic neuropathy consists of the superposition of symptoms and/or clinically detectable neurologic deficits. Clinically overt diabetic neuropathy manifests itself as the presence of one or more of the individual clinical syndromes, representing either *diffuse or focal neuropathy*. Advanced neuropathy causes serious complications, such as diabetic foot ulcers, gangrene, and charcot arthropathy, all of which worsen the quality of life in diabetic patients⁴. Therefore, early detection of nerve dysfunction is important to provide appropriate care for patients with diabetic polyneuropathy⁵.

Neurologic complications are not reserved for a specific type of diabetes but occur equally in type 1 and type 2 diabetes mellitus⁶. Diabetic neuropathy affects the sensory, motor and autonomic neurons of the peripheral nervous system. The early and precise detection of neuropathy can help in the better understanding of the pattern of pathophysiological changes as well as in controlling the crippling illness like peripheral neuropathy⁷.

The subclinical neuropathy is diagnosed by electrodiagnostic tests, quantitative sensory tests, and autonomic function tests. The nerve conduction studies are well accepted for the evaluation of diabetic neuropathy⁸. These are sensitive measures, able to detect abnormalities in diabetic patients that may not be clinically apparent. Nerve conduction studies are used to evaluate sensory and motor nerves. Electrodiagnostic studies are a valuable component of the overall evaluation of patients with known or suspected diabetes. The whole-nerve electrophysiologic procedures have emerged as an important method of tracing the onset and progression of diabetic neuropathy. These are objective, parametric, non-invasive, and highly reliable measures. The diagnosis of subclinical diabetic neuropathy requires the demonstration in a diabetic patient of objective measurement of peripheral neural impairment not attributable to a nondiabetic etiology in the absence of detectable signs or symptoms of neuropathy. It has been established that electrodiagnostic assessments are sensitive, specific, and reproducible measures of the presence or otherwise and severity of the peripheral neuropathy and they also correlate with the morphological findings of nerve biopsy and thus define quantitative nerve dysfunction⁹.

Materials and Methods

The present study was conducted from October, 2014 to May, 2015 at Sri Satya Sai Neuro Centre, Vijayawada in collaboration with Neurologist. A total of 41 patients including both male and female subjects in the age range of 40 years to 55 years were selected for the study. Among the 41 patients, 23 are male subjects and 18 are female subjects. All the patients belong to the type 2 diabetes mellitus and the duration of the diabetes from the initial diagnosis to the present study period is ranging from 2 to 2½ years. All the patients are not having any symptoms suggestive of neuropathy. 40 healthy volunteers, non-diabetic, served as controls for obtaining the normative data. All the patients and controls were age, sex, height, weight and BMI matched. The details of the study were explained and informed consent was taken from each of the individual. Since there are no distinguishing features unique to diabetic neuropathy, all other likely causes of peripheral neuropathy or disorders that mimic peripheral neuropathy were excluded by careful history and physical examination and appropriate diagnostic tests. Diabetic neuropathy affects the sensory, motor and autonomic neurons of the peripheral nervous system. Since the median nerve is the most common peripheral nerve involved in the diabetes, motor nerve conduction study of the median nerve is chosen for the present study. Median motor nerve conduction was performed on both sides in each patient in the environment with room temperatures ranging from 22°C to 25°C using the computerized RMS EMG EP MK II machine and the surface electrodes. The Recording (active) electrode was placed close to the motor point of the abductor pollicis brevis muscle and the Reference electrode was placed about 3 cm distal to the active electrode at the first metacarpophalangeal joint. The Ground electrode was placed between stimulating and recording electrodes¹⁰. The CMAP amplitudes, the distal latencies, and the motor nerve conduction velocities (MNCVs) were obtained with supramaximal stimulation first given at the wrist and later at elbow.

Results

In the present study, 41 patients including 23 male subjects and 18 female subjects, with relatively short duration of diabetes (2 to 2½ years) and without any symptoms suggestive of neuropathy, were compared with 40 healthy controls from which the normative data was obtained and depicted in **Table 1**. Motor nerve conduction study was performed in 82 hands of 41 patients. The CMAP amplitude, the distal motor latency and the MNCV of the subjects under study are compared with those of healthy controls and are summarized in **Table 2**. Out of the total 82 hands, 73 hands revealed prolonged median distal motor latency and 9 hands revealed normal values. Out of the total 41 patients, abnormal median distal motor latencies are observed in both the hands of 32 patients and in at least one hand of all the remaining 9 patients indicating that all the patients under study are having abnormal parameters. The Motor Nerve Conduction Velocity was diminished in 69 hands and the Compound Muscle Action Potential is diminished in 65 hands. It is to be reiterated that all the 41 subjects are asymptomatic in so far as neuropathy is concerned. All the results are correlated with the blood sugar levels.

Table 1. Median Motor Conduction Study (MNCS) – Normative Data

Distal Motor Latency – DML (msec)	CMAP amplitude (mV)	Motor Nerve Conduction Velocity – MNCV (m/sec)
< 4.2	> 4.4	> 49

Table 2. Parameters of median nerve MNCS in diabetics and in controls – comparison

Nerve	Parameters	Diabetics Mean	Non-diabetics Mean (2 SD)
Median Nerve (Right and Left)	Distal Motor Latency (mSec)	4.89	< 4.2 (0.21)
	Amplitude (mV)	3.1	> 4.4 (1.0)
	Conduction Velocity (m/s)	44.85	> 49 (2.5)

Discussion

Carpal Tunnel Syndrome and diabetic polyneuropathy (DPN) are common conditions in patients with type 1 and type 2 diabetes. The prevalence of CTS is thought to be higher in patients with DPN than in the general population. Hence, the median nerve is chosen to know the presence or otherwise of the abnormalities of the nerve conduction studies in the present study of subclinical diabetic neuropathy. The present study reveals alteration in the electrophysiological parameters of median nerves in the diabetics who are not having any symptoms suggestive of overt neuropathy. Hyperglycemia leads to elevated intracellular glucose and cellular toxicity in the endothelial cells of the vasa nervorum. It is also postulated that hyperglycemia induces decreased formation of neurotrophin like nerve growth factor (NGF) and contributes to neuropathy by preventing normal axonal repair and regeneration¹¹. Added to this intracellular glucose can be converted to the so called Amadori product, and these in turn can form advanced glycosylated end products (AGEs), which cross-link matrix proteins. This damages the blood vessels¹². This results in ischemia of the nerves, which in turn leads to neuropathy. Many studies^{13, 14}, have also found alteration in the nerve conduction studies of median nerve suggestive of neuropathy in diabetic subjects. Early in the disease, these processes may not be manifest with clinical features suggestive of neuropathy. These biochemical alterations start long before the clinically overt neuropathy is appreciated. In the present study, the most sensitive neurophysiological indicator, the distal motor latency is prolonged beyond the upper normal limit and the compound muscle action potentials and the motor nerve conduction velocities are diminished much below the normative data. Thus, the present study clearly revealed the substantive use of electrophysiological studies in documenting the subclinical neuropathy in the otherwise clinically asymptomatic diabetics.

Conclusions

This present study revealed that the nerve conduction studies are invaluable aids to diagnose the presence or otherwise of the subclinical neuropathy in diabetics and thereby suggesting the fact that the aggressive management of hyperglycemia might suggest an important strategy to control the occurrence of manifest neuropathy in the diabetic populations.

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