

A Study on the Utility of Nerve Conduction Studies in the Diagnosis of Subclinical Diabetic Peripheral Neuropathy

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ABSTRACT

Introduction: Peripheral neuropathy is the commonest incapacitating complication of diabetes mellitus. Many of the patients are asymptomatic for neuropathy thus developing diabetic foot and ulceration, ultimately leading to amputation. Study aimed to detect subclinical diabetic peripheral neuropathy in early stages by using nerve conduction studies.

Material and methods: Cases consisted of one hundred patients of Type 2 Diabetes Mellitus but asymptomatic for peripheral neuropathy. Twenty – five normal, healthy individuals served as controls. The studies of distal latency, amplitude and conduction velocity of motor fibers of right and left peroneal and tibial nerves were performed.

Results: There was a statistically significant decrease in motor nerve conduction velocity and prolongation of distal latency for both peroneal and tibial nerves on either side in cases versus controls. The CMAP (compound muscle action potential) amplitude in right and left peroneal nerves was less in cases as compared to controls, which was statistically significant for left side but not for right side. CMAP amplitude was statistically significantly less in cases versus controls for right tibial nerve, but for left tibial nerve there was a statistically insignificant increase. Data are presented as mean \pm SD. Results were evaluated by unpaired t-test. A level of $P < 0.05$ was accepted as statistically significant.

Conclusion: Nerve conduction studies (NCS) being simple and non-invasive technique can be used routinely to diagnose diabetic neuropathy in early stages so that proper treatment can be instituted to obtain good outcome.

Keywords: Diabetic Polyneuropathy, Nerve Conduction Study, Peroneal Nerve, Tibial Nerve

INTRODUCTION

Diabetes mellitus is one of the most common chronic diseases globally. It was estimated that in 2017 there were 451 million (age 18–99 years) people with diabetes worldwide which are expected to increase to 693 million by 2045. The high prevalence of diabetes has important social, financial and development implications especially in low and middle - income countries.¹ WHO studies reported that the total number of diabetics in India in 2000 was 31.7 million, which is likely to increase to 79.4 million by 2030.²

Diabetic neuropathy is the commonest complication of diabetes mellitus leading to high morbidity.³ It is defined as a disorder, either clinically evident or sub clinical that occurs in the setting of diabetes mellitus without other causes for peripheral neuropathy.⁴

It is estimated that 35% to 45% of diabetic patients suffer

from diabetic Polyneuropathy (DPN). The high prevalence of diabetic neuropathy is associated with significant morbidity including poor quality of life, recurrent foot infections and ulcerations.⁵ It has a long asymptomatic stage and progresses to diabetic foot resulting from infection and ulceration and finally leading to amputation.⁶ Diabetic foot is the commonest, costly and severe complications of diabetes mellitus. Amputation in diabetics is 10 to 30 times more common in diabetics than in non diabetics and it is estimated that every 30 seconds a lower limb or part of a lower limb is lost somewhere in the world due to diabetes.⁷ Symptoms of diabetic neuropathy (DN) usually develop at any degree of neuropathic dysfunction or may not develop at all. Therefore, there is a need to conduct Nerve conduction studies (NCS) whenever DN is suspected⁸, as early and precise detection will facilitate early intervention and prevent permanent and irreversible nerve damage.⁹

Electrophysiological studies help to localize lesions and describe the type and severity of the pathophysiologic process. Nerve conduction studies are non invasive, most sensitive and specific for the detection of peripheral neuropathy.¹⁰

Hence we undertook to conduct this study with a view to perform a comparative analysis of electrophysiological parameters of peripheral motor nerve function among normal subjects and diabetic patients with no symptoms of peripheral neuropathy. The findings will be helpful for early diagnosis of diabetic peripheral neuropathy, thus decreasing patient morbidity by allowing for therapeutic interventions including patient education and regular foot surveillance.

MATERIAL AND METHODS

The study was conducted in the department of Physiology in collaboration with department of Neurology after approval from institutional research and ethics committee. One

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hundred patients diagnosed to have Type 2 Diabetes Mellitus (DM 2) but without symptoms suggestive of peripheral neuropathy attending the Diabetic clinic of Department of Medicine were inducted into the study (cases). The control group consisted of twenty – five normal, healthy, age and sex matched individuals. Patients with symptoms of peripheral neuropathy, or of diseases likely to cause neuropathy, recent trauma to limbs, patients with amputated extremity and with pacemaker implantation were excluded from the study.

A detailed history with special regard to symptoms of peripheral neuropathy and various diseases which can cause neuropathy was taken. For diabetic patients duration of diabetes and drugs used for treatment was enquired into and recorded. Careful assessment of clinical status including temperature, height, and weight and body mass index was done and a detailed neurological examination was performed. Nerve conduction studies were performed in Neurophysiology Laboratory of the hospital. The NICOLET Viking IV (Model: JN 440BX550-F3/128) machine manufactured by Biomedical, Madison, Wisconsin, USA was used for these studies.

The studies of distal latency, amplitude and conduction velocity of motor fibers of right and left peroneal and tibial nerves were done (during the study we lost 2 patients for right peroneal nerve, 3 patients for left peroneal nerve and 1 patient for left tibial nerve studies). Limb temperature was

maintained between 34 °C and 35 °C at the time of conduction studies. Amplifier settings for motor nerve conduction were - sweep speed: 2ms/div, sensitivity; 5mv/div and filter setting: 20 Hz to 10 kHz.

For peroneal nerve G₁ recording electrode was placed over extensor digitorum brevis, G₂ over the fifth toe and 'Ground' close to the recording electrodes.

For tibial nerve G₁ was placed over the abductor hallucis to test the medial plantar branch, G₂ over great toe or over the fifth toe and 'Ground' was placed close to the recording electrodes.

STATISTICAL ANALYSIS

Data are presented as mean ± SD. Results of the nerve conduction studies were evaluated by unpaired t-test. A level of *P* < 0.05 was accepted as statistically significant.

RESULTS

Table 1 shows baseline data of cases and controls. The mean age of diabetic patients (cases) was 52.81 years (± 6.31). The mean age of the controls was 49.68 years (±12.01). The ages of cases and controls were compared by unpaired student 't' test and difference was not statistically significant. The cases and controls were height and weight matched.

In our study, there was a decrease in MNCV and prolongation of distal latency of peroneal nerve on both sides (right and left) in diabetic patients as compared to controls which were statistically significant. The CMAP amplitude in both right and left peroneal nerves was less in cases versus controls but the difference was not statistically significant on right side. (Summarized in table 2)

It was found that mean MNCV of right and left tibial nerves was statistically significantly less in cases than in controls. Results also showed statistically significant prolonged

Parameters	Cases (n=100) Mean ± SD	Controls (n=25) Mean ± SD	P value
Age (years)	52.81 ± 6.31	49.68 ± 12.01	0.07
Height (cm)	162.31 ± 7.97	163.80 ± 7.13	0.39
Weight (kg)	72.56 ± 10.71	71.84 ± 6.39	0.76
BMI (kg/m ²)	27.53 ± 3.32	26.90 ± 3.35	0.43

Table-1: Base line data of cases and controls

Nerve	Parameters	Cases(n=98) Mean ± SD	Controls(n=25) Mean ± SD	P value
Right Peroneal Nerve	Distal latency (ms)	3.57 ± 0.72	3.20 ± 0.63	0.0214
	Amplitude (mv)	5.33 ± 2.48	5.45 ± 2.01	0.823
	Conduction velocity (m/s)	40.30 ± 4.43	45.76 ± 4.83	0.0001
Left Peroneal Nerve	Distal latency (ms)	Cases (n=97) Mean ± S D	Controls (n=25) Mean ± SD	P value
	Amplitude (mv)	4.15 ± 0.79	3.72 ± 0.84	0.0188
	Conduction velocity (m/s)	3.77 ± 1.86	4.85 ± 1.55	0.0083
		43.38 ± 5.35	46.96 ± 3.70	0.0021

Table-2: Parameters of motor nerve conduction study in peroneal nerves of cases and controls.

Nerve	Parameters	Cases (n=100) Mean ± SD	Controls(n=25) Mean ± SD	P value
Right Tibial Nerve	Distal latency (ms)	4.14 ± 1.03	3.49 ± 0.51	0.0027
	Amplitude (mv)	7.25 ± 3.92	9.44 ± 4.16	0.0151
	Conduction velocity (m/s)	41.77 ± 6.13	45.12 ± 4.10	0.0108
Left Tibial Nerve	Distal latency (ms)	Cases(n=99) Mean ± S D	Controls(n=25) Mean ± SD	P value
	Amplitude (mv)	3.95 ± 0.74	3.23 ± 0.42	0.0001
	Conduction velocity (m/s)	8.61 ± 4.00	8.43 ± 3.41	0.8327
		41.09 ± 5.43	44.64 ± 3.43	0.0023

Table-3: Parameters of motor nerve conduction study in tibial nerves of cases and controls.

mean distal latency in tibial nerves on both sides in cases as compared to controls. The CMAP amplitude in right tibial nerve was less in cases as compared to controls which was statistically significant. Increase in CMAP amplitude of tibial nerve on left side in cases as compared to controls was not statistically significant. (Summarized in table 3)

DISCUSSION

The present study reveals alterations in electrophysiological parameters of peroneal and tibial nerves in diabetics. Observation that motor nerves of the lower extremities are most often affected in adult diabetic patients is supported by the previous data. Results of our study are similar to that of Kimura J et al¹¹ and Prasad Neelambala et al¹² as they also found increased latency and decreased conduction velocity in lower limb nerves in diabetics as compared to normal subjects. Finding of Meerwaldt et al¹³ and Sonawne PP et al¹⁴ that peroneal MNCV is less in diabetic as compared to controls is also in accordance with our study. Fall in motor amplitude of peroneal nerve in diabetics with no symptoms of neuropathy as reported by Baba M¹⁵ and sonawne PP¹⁴ also supports our data.

For tibial nerve amplitude, Prasad Neelambala et al¹² and Aruna et al¹⁶ have found decrease in amplitude on both sides in diabetics but in our study on left side there was an increase but it was not statistically significant.

Decreased Nerve Conduction Velocity (NCV) is probably one of the earliest neurological impairment in Type 2 diabetic patients and is often present even at the time of diagnosis. Thereafter, slowing of NCV generally progresses at a rate of approximately 1 m/s/year.¹⁷

Hyperglycemia causes nerve damage by various mechanisms. It causes cellular toxicity in the endothelial cells of capillaries associated with peripheral nerves, leading to decreased capillary blood flow which in turn causes endoneural hypoxia resulting in death of the neural cells and so nerve conduction parameters are altered. Another proposed mechanism is that due to hyperglycemia there is decreased formation of neurotrophin like nerve growth factor (NGF) thus contributing to neuropathy by preventing normal axonal repair and regeneration.¹⁸

In addition intracellular glucose can be converted to so called Amadori product, and these in turn can form advanced glycosylated end products (AGEs), which cross-link matrix proteins. This damages the blood vessels, resulting in ischemia to the nerves which may be responsible for neuropathy.¹⁹

Though blood sugar level estimation and cardiovascular checkups are done regularly in diabetic patients but other possibly affected systems such as peripheral nervous system is often neglected. They are referred to neurology clinic only when neuropathy symptoms have already worsened and difficult to manage.²⁰

As up to half of the diabetic patients may be asymptomatic for neuropathy, so absence of symptoms should never be assumed as absence of disease process. Diagnosis should be made in asymptomatic stage with a careful clinical

examination of the lower limbs as these patients are known to be at high risk of foot complications like foot ulceration, infections which may require amputation. Early diagnosis and glycemic control are important factors for preventing diabetic neuropathy.¹⁷

Electrophysiological techniques can diagnose diabetic neuropathy at subclinical level. Impairment of sensory motor axons and the myelin sheath at the distal end already exists in the initial stages of diabetic peripheral neuropathy, before symptoms arise.²¹ Ongoing damage to myelin sheath is depicted by slowing of nerve conduction velocities and decrease in amplitude occurs with the loss of neurons which indicates rising HbA1c levels.²²

CONCLUSION

Diabetic neuropathy is the most common and disabling complication of diabetes. Nerve conduction studies are very useful in early detection of peripheral neuropathy and stopping the progression of the disease thus preventing permanent and irreversible damage. All newly diagnosed diabetic patients should undergo electrophysiological evaluation for screening of neuropathy, especially of lower limbs.

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