RESEARCH ARTICLE

Study on electrophysiological changes of peripheral nerves in type 2 diabetes mellitus

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ABSTRACT

Background: Peripheral neuropathy is a common and disabling complication due to diabetes mellitus. In such neuropathy, the function of sensory neurons, motor neurons, and autonomic functions are affected. The involvement of sensory function predominates in majority of cases. The neuropathy when develops is not reversible and also can not be stopped with any modality of treatment. Aim and Objectives: The objective is to evaluate diabetic neuropathy using the electrodiagnostic studies which are considered as a valuable tool. These studies are sensitive, specific, reproducible, and easily standardized. Material and Methods: Forty patients were subjected to electrodiagnostic study to evaluate the status of peripheral nerves in type-2 diabetic patients. The different conduction velocities (motor nerve conduction velocity [MNCV], sensory nerve conduction velocity [SNCV]), distal latency (DL), nerve action potential (sensory nerve action potential [SNAP], and combined muscle action potential [CMAP]) are studied. All the cases were divided into two groups based on normal and abnormal diabetic neuropathy score. Sex, body mass index matched thirty numbers of healthy adults of both sexes were included in the control group. Nerve conduction study (NCS) of all the three groups were compared. Result: Neuropathy mostly peripheral was observed in 15 (37.5%) cases. The age of majority of cases was from 50–60 (45%) with mean age of 52.42 ± 7.39, having predominance of male (66.67%) in cases with symptoms of neuropathy. Fourteen (93.33%) cases out of the above cases had abnormal NCS. Abnormal NCS was also found in cases without clinical neuropathy, i.e. 14 (56%). The mean values of CMAP, SNAP, MNCV, and SNCV with prolonged DL are observed which was statistically significant. The conduction defect was observed more in lower limbs than in upper limbs. In the category of the motor nerve (common peroneal) is the most affected whereas the most affected sensory nerve was Sural nerve. Conclusion: Affection of nerves with neuropathies due to diabetes was in Sensory nerve than motor nerve. Early screening for neuropathy in clinical practice with NCSs can help in early diagnosis and their management.

KEY WORDS: Common Peroneal Nerve; Sural Nerve; Electrophysiological Studies; Nerve Conduction Studies; Diabetic Neuropathy

INTRODUCTION

The various forms of neuropathy in diabetes include peripheral neuropathy, third nerve palsy, mononeuropathy, mononeuropathy multiplex, diabetic autonomic neuropathy, and thoracoabdominal neuropathy. Neuropathy is one of the earliest and most commonly reported long-term complications
diabetic patients. Patients with type 2 diabetes mellitus (T2DM) usually present with distal polyneuropathy after only a few years of known poor glycemic control. Sometimes, these patients already have neuropathy at the time of diagnosis. Clinical and subclinical neuropathy has been estimated to occur in majority of diabetic patients, depending upon the diagnostic criteria and the patient examined. Diabetic neuropathy is a complex disorder, as it is associated with a large spectrum of clinical abnormalities showing damage of small and large nerves. Diabetic peripheral neuropathy (DPN) is more common in people who have poor control of their blood glucose, and also who have problem with controlling their lipid profile, blood pressure, and body weight within normal range. Neuropathy can go undetected and may manifest with clinical symptoms and signs of many other diseases. Foot problems are one of the most common complications in diabetes because of more vulnerability for neuropathy, peripheral vascular disease, abnormal pressure on the foot, and poor resistance to infection. These factors together result in ulceration and infection, leading to gangrene, and requiring amputation. The annual population-based incidence in diabetics with foot ulcer ranges from 1.0–4.1 percent and the prevalence ranges from 4–10 percent, suggesting that the lifetime incidence can go as high as 25 percent. Active management of glycemic status by screening and early detection of neuropathy and foot care can prevent morbidity significantly. Nerve conduction studies (NCS) are the most objective non-invasive measures of nerve function. Studies suggest that in T2DM, even at the time of diagnosis 45–60% were diagnosed with diabetic neuropathy. NCSs strongly reflect the underlying changes and are the most reliable standard. Although NCS has a lot of merits when compared with other screening tools of DPN, the main drawbacks are for the requirement of sophisticated instrument and exclusive neurology laboratory. Moreover, the recording is cumbersome and needs to be done only by trained personnel. The procedure is relatively costly. Therefore the present study was undertaken to study the electrophysiological properties of peripheral nerves in patients suffering from T2DM and to observe the effect of different determinants of DPN on nerve conduction study considering NCS as gold standard for screening DPN.

**MATERIALS AND METHODS**

The sample used in this study comprised 70 patients. The cases were divided into three groups. Group I comprising 15 cases with symptoms of peripheral neuropathy. Group II comprised 25 cases without symptoms of peripheral neuropathy and Group III comprised 30 age, and body mass index (BMI) matched healthy subjects as control group. The 40 cases in Group I and II were in the age group of 40–70 Years with established type 2 diabetes (American Diabetic Association [ADA] criteria) attending a tertiary care hospital of Odisha the Group III cases (healthy controls) were taken by history, questionnaire and by clinical examination from general population. Informed consent was obtained from all patients. The ADA criteria for diagnosis of DM includes: (1). Symptoms of DM with a random glucose concentration ≥200 mg/dl. The classic symptoms of DM being polyuria, polydipsia, and weight loss. (2). Fasting blood glucose ≥126 mg/dl (7.0 mmol/l). Fasting is defined as no calorie intake for at least 8 h. (3). HbA1C >6.5% 4. Two-hour plasma glucose ≥200 mg/dl (11.1 mmol/l) during an oral glucose tolerance test. The inclusion criteria are age group of 40–70 years, suffering from T2DM as per ADA criteria, positive diabetic neuropathy score (DNS) score (score of 2 or more), and nonsmokers. The exclusion criteria are cases suffering from hypertension, chronic renal failure, previous spinal injury, Type 1 DM, history of cervical or lumbar discopathies, alcohol abuse, Vitamin B12 or folate deficiency, age above 70 years, and smokers. For controls, the inclusion criteria are fasting blood sugar (FBS) <126 mg/dl and DNS score of zero. The DNS was adopted from the neuropathy symptom score of Dyck. was used, i.e., if the symptoms occurred more than twice in the previous two weeks shall be answered as yes and is taken as positive point1. For “no” answer no point is awarded. The questionnaire is for symptoms of unsteadiness in walking, tenderness of legs or feet, a burning, aching pain or, pricking sensations at legs or feet, and numbness on legs or feet. Score of zero was taken as absent of polyneuropathy and score of 1–4 as the presence of polyneuropathy. The nerve was stimulated by placing electrodes on the skin. The 1st set of electrodes was used to send small pulses of the electrical signal to stimulate the nerve. The 2nd set of electrodes placed at 7 cms away from the 1st set which receives and transmits the corresponding electrical signal generated in the nerve to the recording machine, i.e., the Neurostim NS-2 by Medicaid. The room temperature was maintained at 21–23°C and the skin temperature was maintained at 32°C. The stimulation of the nerve is detected and displayed in a monitor in form of waves. Different nerves tested were median nerve, ulnar nerve, posterior tibial nerve, common peroneal nerve, and sural nerve. The nerve conduction velocity (NCV) of different nerves is shown in Table 1. In case of the common peroneal nerve, the surface recordings were taken from extensor digitorum brevis and stimulation was given at three places.

### Table 1: Nerve conduction velocity in different nerves

| Nerve            | NCV     | CMAP/SNAP |
|------------------|---------|-----------|
| Median           | 59.83±3.56 ms |  |
| Ulnar            | 56.2±3.38 ms |  |
| Posterior tibial | 48.3±4.5 ms |  |
| Common peroneal  |         |           |
| Above knee       | 49.67±8.77 ms | 4.23±1.6 mv |
| Below knee       | 46.54±4.4 ms |  |
| Sural            | 50.9±5.4 ms | 18±10.5 μV |
i.e. at the ankle 2 cm distal to the fibular neck, at the neck of fibula, and 5-8 cm above the fibular neck. The sural nerve is stimulated distal to lower border of gastrocnemius at the junction of the middle and lower third of the leg, 10–15 cm proximal to recording electrode. Data analysis was done using SPSS 16 statistical package. Results were compared by mean ± standard deviation and paired t-test. \( P < 0.05 \) was considered statistically significant. The work has been recommended by the Institutional Ethics Committee.

**RESULTS**

A total number of 70 patients were available for study. The sex distribution is given in Figure 1. The mean age in Group I cases was 56.68 ± 5.04, in Group II 0.43 ± 8.28, and in Group III 49.6 ± 6.19. Table 1 depicts the nerve conduction velocity in different nerves and Table 2 describes the observed parameters in three groups. The nerve conduction in sensory and motor in upper limb and lower limb in different groups are shown in Table 3 and 4, respectively. In Group I (15) cases 26.66% (4) were having distal symmetrical polyneuropathy and 73.33% (11) were having distal sensory-motor polyneuropathy. The relation of nerve conduction velocity and duration of diabetes is shown in Table 5.

**DISCUSSION**

The mean age in the present study of the diabetic cases were 52.42 ± 7.39 years with highest incidence of cases in the age of 40–50 (45%) of which mean age of cases in Group-I and Group-II were 56.68 ± 5.04 and 50.43 ± 8.28 respectively as compared to 49.06 ± 6.19 in Group-III. This shows that symptoms of neuropathy appear more as the age progresses and duration of disease advances. Study by Shaw et al.\[11\] Found mean age of development of diabetic neuropathy is 50 years. This study showed cases suffering with T2DM having male predominance of 57.5% as well as the appearance of symptoms of neuropathy with male

| Parameters | Group I | Group II | Group III | Sex |
|------------|---------|----------|-----------|-----|
| Male       | 10 (66.67%) | 13 (52%) | 18 (60%) | |
| Female     | 05 (33.33%) | 12 (48%) | 12 (40%) | |
| Average Age| 56.68±5.04 | 50.43±8.28 | 49.06±6.19 | |
| BMI        | 26.25±2.09 | 25.27±2 | 22.51±2.25 | |
| Mean FBS   | 202±54.06 | 149±43.65 | 87.06±11.07 | |
| HbA1C      | 8.96±1.97 | 7.24±0.92 | 5.3±0.57 | |

**Table 3: Motor and Sensory nerve conduction study in the upper limb in different groups**

| Variables | Group I | Group II | Group III | \( P \)-value |
|-----------|---------|----------|-----------|--------------|
| Median Nerve (Motor) | | | | |
| DML       | 3.99±0.86 | 3.78±0.99 | 3.36±0.66 | <0.128 |
| CMAP      | 7.84±2.11 | 8.04±3.42 | 10.67±2.0 | <0.056 |
| MNCV      | 49.01±9.1 | 54.74±3.71 | 56.42±6.3 | <0.05 |
| Ulnar nerve (Motor) | | | | |
| DML       | 3.13±0.84 | 2.87±0.5 | 2.43±0.52 | <0.23 |
| CMAP      | 7.89±3.12 | 8.81±2.27 | 9.89±2.63 | <0.092 |
| MNCV      | 52.77±7.2 | 55.91±9.1 | 56.93±4.2 | <0.05 |
| Median Nerve (Sensory) | | | | |
| DL        | 3.8±1.49 | 3.43±1.21 | 2.89±0.46 | <0.05 |
| SNAP      | 20.52±5.34 | 23.72±6.8 | 25.04±5.63 | <0.05 |
| SNCV      | 52.14±5.64 | 53.31±5.41 | 57.04±3.17 | <0.099 |
| Ulnar nerve (Sensory) | | | | |
| DL        | 3.71±0.46 | 2.83±0.58 | 2.33±0.51 | <0.05 |
| SNAP      | 14.32±5.10 | 16.03±5.18 | 18.4±5.36 | <0.05 |
| SNCV      | 51.87±5.52 | 54.57±4.56 | 55.34±2.96 | <0.05 |

NB: <0.05-significant, <0.001-highly significant

Figure 1: Distribution of sex in study groups
Peripheral neuropathy due to diabetes, commonly develops insidiously, with various clinical manifestations contributing to morbidity. Early detection of DPN leads to lesser numbers of foot ulcers and amputations. Many advances have been made in electrophysiological techniques and quantitative sensory testing for the detection of DPN. To identify asymptomatic individuals American Diabetes Association and clinical practice guidelines recommend annual screening for neuropathy who are likely to develop complications. It is difficult to diagnose at the early stages as there are no symptoms. It has become possible for identification of sub-clinical pathological changes by the increasing use of electrophysiological techniques. The main abnormality in NCS is seen as reduced amplitude, slowed conduction velocity, or prolonged latent period. Combined muscle action potential (CMAP) and motor nerve conduction velocity (MNCV) were significantly diminished in both the nerves of the upper and lower limbs of asymptomatic group as compared to the control group, though tendency of reduction in ulnar nerve conduction velocity was not significant. In the present study, out of 40 cases, 15 (37.5%) were with predictive value of 99.79%. Out of 15 cases of clinical neuropathy 11 (73.33%), cases showed distal symmetrical sensory-motor polyneuropathy whereas distal symmetrical sensory polyneuropathy was found in 4 (26.67%) as was observed by Zachodne DW et al. Zhang et al.[17] Studied on 500 diabetic patients in china with 221 in symptomatic group and 279 in asymptomatic group and found abnormal nerve conduction in 71.6%. Mohsen Janghorbani et al.[18] studied with 810 Type 2 diabetic patients in Iran and found the prevalence of peripheral neuropathy in 75.1%. In the present study, distal motor and sensory latency in the median nerve, posterior tibial nerve, and common peroneal nerves except ulnar nerve was seen in the asymptomatic group and were prolonged significantly compared to the control group.

### Table 4: Motor and sensory nerve conduction study in lower limb in different groups

| Variables | Group I | Group II | Group III | P-value |
|-----------|---------|---------|-----------|---------|
| Common Peroneal Nerve (Motor) | | | | |
| DML | 5.79±0.79 | 3.69±1.03 | 4.64±0.69 | <0.05 |
| CMAP | 4.69±1.02 | 6.71±1.74 | 8.17±1.32 | <0.05 |
| MNCV | 42.54±0.03 | 47.19±6.29 | 50.39±3.35 | <0.05 |
| Posterior Tibial Nerve (Motor) | | | | |
| DML | 4.83±1.2 | 4.57±1.24 | 4.02±0.52 | <0.021 |
| CMAP | 5.76±2.45 | 7.5±2.63 | 8.48±1.97 | <0.05 |
| MNCV | 40.64±7.82 | 48.38±5.47 | 50.79±3.61 | <0.05 |
| Sural Nerve (Sensory) | | | | |
| DL | 4.63±1.11 | 2.89±0.95 | 2.05±0.45 | <0.05 |
| SNAP | 7.82±0.95 | 16.03±5.18 | 11.07±2.18 | <0.001 |
| SNCV | 42.35±6.95 | 47.13±4.98 | 53.69±3.31 | <0.05 |

NB: <0.05-significant, <0.001-highly significant

### Table 5: Nerve conduction study in relation to duration of diabetes and HbA1C

| Variables | Group I | Group II | Group III | P-value |
|-----------|---------|---------|-----------|---------|
| Duration of diabetes (years) | Normal NCS | Abnormal NCS | Normal NCS | Abnormal NCS |
| 0-5 | 1 | 3 | 6 | 3 |
| 6-10 | 0 | 4 | 5 | 8 |
| >10 | 0 | 7 | 0 | 3 |
| HbA1C | | | | |
| <7 | 1 | 2 | 5 | 3 |
| 7-10 | 0 | 7 | 6 | 11 |
| >10 | 0 | 5 | 0 | 0 |

HbA1C is 7.74 ± 1.48. In the present study, out of 40 cases, 15 (37.5%) were with predictive value of 99.79%. Out of 15 cases of clinical neuropathy 11 (73.33%), cases showed distal symmetrical sensory-motor polyneuropathy whereas distal symmetrical sensory polyneuropathy was found in 4 (26.67%) as was observed by Zachodne DW et al. Zhang et al.[17] Studied on 500 diabetic patients in china with 221 in symptomatic group and 279 in asymptomatic group and found abnormal nerve conduction in 71.6%. Mohsen Janghorbani et al.[18] studied with 810 Type 2 diabetic patients in Iran and found the prevalence of peripheral neuropathy in 75.1%. In the present study, distal motor and sensory latency in the median nerve, posterior tibial nerve, and common peroneal nerves except ulnar nerve was seen in the asymptomatic group and were prolonged significantly compared to the control group.
symptomatic group, MNCV and CMAP were significantly diminished in the nerves of the lower limb than in the upper limb in comparison to subjects of asymptomatic group. When symptomatic cases were compared with the control group all the parameters of NCS in both lower as well as upper limb were significantly altered. 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 in comparison to the nerves of the upper limb. Halar et al and Mulder et al also showed that nerves of the lower limb are more susceptible to diabetic injury than the nerves of the upper limb. Sensory nerve conduction velocity (SNCV) and amplitudes were markedly lower in both the limbs of asymptomatic group than in control except for some parameters of sensory components of the ulnar nerve. In the symptomatic group, SNCV was notably slower with diminished in amplitude and distal sensory latency was significantly prolonged in the sural nerve. As SNCV, sensory nerve action potential (SNAP), and CMAP were all remarkably lower in asymptomatic group compared to controls, indicating that impairment of motor and sensory axons and the myelin sheath at the distal end already exists in the early stage of DPN, before symptoms appear. These observations indicate that after symptomatic peripheral nerve impairment emerges in diabetic patients, lesions in the sensory nerves of the median nerve, ulnar nerve, and sural nerve and in the neuromaxis and myelinitis sheath of motor fibers of median, ulnar, common peroneal, and posterior tibial nerves are markedly aggravated compared with the asymptomatic group. In the diabetic groups, lesions in the lower extremities are more severe than that of the upper extremities. Moreover, among all patients with diabetes, the common peroneal nerve was the most common and severely affected. The sural nerve was found to be severely impaired from the sensory nerve tests showing highest rate of SNAP abnormality.

In the present study, the electrophysiological abnormalities observed may be due to nutritional deficiency and metabolic disorders resulting from the diabetes which lead to axoplasmic transport impairment in peripheral nerves, and prevent distal axons from getting sufficient nutrition and ultimately leading to their degeneration. Liu et al. studied 700 patients with DPN using NCS and found that longer the duration of the disease, the greater is the abnormal electrophysiology. Many studies indicate that both MNCV and SNCV are related to the degree of the control of blood sugar level. Slowing of nerve conduction velocity is a concomitant finding of aging. In this study, sural nerve SNCV slowed as the duration of disease advanced. The same is not seen with other sensory and motor nerves.

This study revealed peripheral nerve dysfunctions which were found mostly in the distal segments even without significant clinical diagnosis. The present work emphasizes on the NCS of peripheral nerve dysfunctions in diabetic patients without symptoms of peripheral neuropathy but is in risk of developing foot ulcers and related morbidity in future.

CONCLUSION

Neuropathy of peripheral nerves is a common complication of diabetic mellitus resulting in disability. The sensory, motor, and autonomic functions are affected in varying degrees with a predominance of sensory function. Such neuropathy is irreversible. The different available modalities of treatment are not effective. Hence, it is always better to have early screening and proper control. Evaluation of diabetic neuropathy by Electro-diagnostic studies are a valuable tool. These tools are specific, sensitive, and easily standardized.

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