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ELECTROPHYSIOLOGICAL EVALUATION OF SUBCLINICAL NEUROPATHY IN DIABETES PATIENTS

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ABSTRACT

Introduction: Diabetic neuropathy is defined as the presence of symptoms and signs of peripheral nerve dysfunction in diabetes after exclusion of the other causes. Diabetes is the leading cause of peripheral Polyneuropathy in developed countries. In general, to define diabetic neuropathy, should be based on symptoms, objective signs and EDX confirmation. Nerve conduction study is widely used for the diagnosis of diabetic neuropathy. Nerve conduction abnormalities exist in subclinical stages of neuropathy that can be detected at an early asymptomatic stage by various electrodiagnostic test. Hence aim of this study is to study the effect of diabetes in motor and sensory nerve conduction velocity of peripheral nerves in diabetes patients and to observe the functional status of peripheral nerve in asymptomatic diabetes patient. **Methodology:** Thirty Patients diagnosed as diabetes, who were asymptomatic regarding neuropathy, attending the diabetology outpatient department, at government Rajaji Hospital, Madurai from April 2013 to April 2016 were included in this study. Patient diagnosed as diabetes who are asymptomatic regarding neuropathy, Age group of 20 to 60 years and both male and female were included in this study. **Results:** A total of 30 patients were included in this study. Electrophysiological study was conducted in all the patients. Four of the patients had normal NCS .Out of the remaining 26 cases, majority of the patients had sensorimotor Polyneuropathy. The next common type of neuropathy noted in our study was Predominant sensory neuropathy was noted in 3 patients and one of the patient had isolated sensory nerve involvement (both ulnar sensory, median and sural sensory). In our study, out of 26 cases with abnormal NCS, the nerves that are most commonly affected in the decreasing order are as follows- Median SNAP, Sural SNAP, Median CMAP, peroneal CMAP, tibial CMAP, ulnar CMAP and Ulnar SNAP. Most common nerve affected in upper limb is Median Nerve while in lower limb is sural nerve. **Conclusion:** The results of the present study done in diabetics without complications with duration of diabetes, indicate that there is a significant impairment of motor and sensory nerve parameters even though they are asymptomatic. We conclude the study with the observation that nerve conduction study can be used as a screening tool to diagnose neuropathy in subclinical stages and should be considered at risk category for aggressive glycemic control by diet, drugs and life style modification to prevent progression of neuropathy.

KEYWORDS: Diabetes, neuropathy, nerve study.

INTRODUCTION

Diabetes mellitus is estimated to affect 23.6 million people in the united states and this number is much larger in India. This trend is largely attributed to the increased prevalence of overweight and obesity. The microvascular complications of diabetes includes Retinopathy, Nephropathy and Neuropathy. Patients with sufficient duration of diabetes are vulnerable to the above complications.

Diabetic neuropathy is defined as the presence of symptoms and signs of peripheral nerve dysfunction in diabetes after exclusion of the other causes. Diabetes is the leading cause of peripheral Polyneuropathy in developed countries. In general, to define diabetic neuropathy, should be based on symptoms, objective signs and EDX confirmation.

The risk of developing symptomatic neuropathy in patients without neuropathic symptoms or signs at the time of diagnosis is estimated to be 4% to 10% by 5 years and up to 50% by 25 years. Longer duration of diabetes and male sex predispose to the development of neuropathy over time in TYPE 1 DM. In type 2 DIABETES, the risk is increased with the duration of the disease. The prevalence of neuropathy is significantly higher among the diabetics who consume excessive amounts of alcohol. Tobacco use predispose to early development and more severe symptom of neuropathy, presumably by inducing vasoconstriction and nerve

ischemia.

Nerve conduction study is widely used for the diagnosis of diabetic neuropathy. Nerve conduction abnormalities exist in subclinical stages of neuropathy that can be detected at an early asymptomatic stage by various electrodiagnostic test. Because peripheral nerves have the capability to regenerate, early diagnosis and timely intervention will reduce the morbidity in diabetes.

This study was undertaken to evaluate the electrophysiological profile in type 2 diabetes patients for the identification of subclinical neuropathy. Hence aim of this study is to study the effect of diabetes in motor and sensory nerve conduction velocity of peripheral nerves in diabetes patients and to observe the functional status of peripheral nerve in asymptomatic diabetes patient.

MATERIALS AND METHODS

Thirty Patients diagnosed as diabetes, who were asymptomatic regarding neuropathy, attending the diabetology outpatient department, at government Rajaji Hospital, Madurai from April 2013 to April 2016 were included in this study. Patient diagnosed as iabetes who are asymptomatic regarding neuropathy, Age group of 20 to 60 years and both male and female were included in this study. Whereas patients who had diabetes with neuropathic symptoms, Peripheral neuropathy due to other cause- liver dysfunction, renal dysfunction, Radiculopathy due to cervical spondylosis, History of long term alcohol consumption and prolonged contact with poisonous substance, hypothyroidism, age group less than 20 years and above 60 years were excluded.

A detailed medical history, family history and clinical examination was done. Those patients who satisfied the inclusion criteria were then selected for further evaluation. Serum fasting blood sugar and postprandial blood sugar was done on the day of nerve conduction study HbAlC was also done simultaneously. Other blood investigations such as blood urea, serum creatinine, liver function test, complete hemogram and thyroid profile was also done

Nerve conduction studies were performed using standard techniques. Both motor nerve conduction and sensory nerve conduction were done in each patients. Autonomic function testing is not included in our study. Motor NCS was done in both median, ulnar, peroneal and tibial nerves. CMAP latency, amplitude and conduction velocity were recorded.

Regarding median nerve motor NCS recording, the nerve was stimulated at two sites, one at the level of wrist, between the tendons of flexor carpi radialis and Palmaris longus, while recording in Abductor pollicis brevis muscle. Ulnar motor NCS — nerve was stimulated distally at medial wrist, adjacent to flexor carpi ulnaris and proximally below the elbow about 3-4 cm distal to the medial epicondyle and recording site was Abductor digiti minimi.

Regarding peroneal nerve motor NCS, the nerve was stimulated at two sites, distally at the level of anterior ankle, slightly lateral to tibialis anterior tendon and proximally at below the fibular head about one to two finger breaths below, and the recording was done at Extensor digitorum brevis.

Regarding tibial motor NCS, distal stimulation was done at medial ankle- above and posterior to the medial malleolus and proximal stimulation was done at popliteal fossa- mid posterior knee over the popliteal pulse and the recording was done at Abductor hallucis brevis.

Sensory nerve conduction studies were done using the standard antidromic techniques, on the median, ulnar and sural nerves. SNAP latency, amplitude and conduction velocity were recorded. Median sensory NCS was recorded using the ring electrodes which were placed over the index finger and the stimulation site was middle of the wrist between the tendons of flexor carpi radialis and Palmaris longus. Ulnar sensory NCS was recorded by placing the ring electrodes over the little finger and stimulated at medial wrist, adjacent to flexor carpi ulnaris tendon. Sural sensory NCS was done using the surface electrodes. The recording electrodes were placed posterior to the lateral malleolus and the stimulation site was the posterior lateral calf. The values were compared with the reference values form our laboratory

The nerve conduction result is defined as axonal loss when,1) amplitudes decrease, 2) conduction velocities are normal or slightly decreased but never below 75% of the lower limit of normal, and 3) distal latencies are normal or slightly prolonged, but never greater than 130% of the upper limit of the normal. The nerve conduction result is defined as demyelinating when 1) amplitudes are normal or slightly decreased 2) Conduction velocities are slower than 75% of lower limit of normal, and 3) marked prolongation of distal latency by 130% of upper limit of normal. The nerve conduction result is defined as both if both the above findings are present.

RESULTS

A Total of 30 patients were studied. Out of 30 cases, 7 cases (23.3%) were below 38yrs of age, l6cases (53.3%) were between 39 to 50 years of age and 7 cases (23.3%) were above 50 years of age. Out of 30 cases, 16 were female (53.3%) and 14 were male (46.7%). Regarding the duration of diabetes, majority of the patient were between 2 to 5 years (50%). The next group to follow is 2years duration (33.3%) and finally 5 years duration (16.7%). Out of 30 cases, 25 patients (83.3%) were on oral hypoglycaemic therapy and 5 cases (16.7%) were on both OHA & Insulin therapy.

CMAP- MEDIAN NERVE

Table 6: Cmap Median Nerve.

CMAP MEDIAN	No.of cases	Percentage
NORMAL	18	60
AXONAL	5	16.7
EMYELINATING	7	23.3
Total	30	100
CMAP – MEDIAN SIDE	No.of cases	Percentage
NORMAL	18	60
LEFT	5	16.7
RIGHT	7	23.3
Total	30	100

Out of the 30 cases, 40% of cases showed abnormal Median CMAP- Out of the above abnormal cases, majority of them had involvement of right median nerve(23.3%).

CMAP-ULNAR NERVE

Table 8: Cmap Ulnar Nerve.

CMAP - ULNAR	No.of cases	Percentage
NORMAL	22	73.3
AXONAL	4	13.3
DEMYELINATING	2	6.7
BOTH	2	6.7
Total	30	100
CMAP - ULNAR SIDE	No.of cases	Percentage
NORMAL	22	73.3
LEFT	3	10
BOTH	5	16.7
Total	30	100

Out of 30 cases, 27.7% cases showed abnormal ulnar CMAP.Out of these, axonal type is the commonest one(13.3%). Out of the 8 cases showing abnormal CMAP in ulnar nerve, majority of them had involvement on both sides(16.7%).

CMAP- PERONEAL NERVE

Table: Cmap-Peroneal Nerve.

CMAP - PERONEAL	No.of cases	Percentage
NORMAL	21	70
AXONAL	5	16.7
DEMYELINATING	4	13.3
Total	30	100
CMAP - PERONEAL SIDE	No.of cases	Percentage
NORMAL	21	70
RIGHT	1	3.3
BOTH	8	26.7
Total	30	100

Out of 30 cases, 9 cases (30%) showed involvement of peroneal nerve. Among the affected cases (9 cases), majority of them (26.7%) had involvement of both sides.

CMAP TIBIAL NERVE

Table 12: cmap tibial nerve.

CMAP – TIBIAL	No.of cases	Percentage
NORMAL	22	73.3
AXONAL	3	10
DEMYELINATING	4	13.3
BOTH	1	3.3
Total	30	100
CMAP — TIBIAL SIDE	No.of cases	Percentage
NORMAL	22	73.3
BOTH	8	26.7
Total	30	100

Out of the 30 cases,8 cases (26.6%) had tibial nerve involvement. Among the cases showing abnormal Tibial nerve CMAP, all the cases showed involvement on both sides

SNAP

In median nerve out of 30 cases, nearly 20 cases (66.6%) showed abnormal median nerve SNAP. Out of the affected case, both sides (56.7%) are affected in majority of cases. In ulnar nerve, Out of the 30 cases, only 4 cases (13.3%) showed abnormal ulnar SNAP. In sural nerve out of the 30 cases, 22 cases (70%) showed sural nerve abnormality .All of the involved cases showed both right and left sural nerve involvement.

FINAL INTERPRETATION

Out of the 30 cases, only 4 patients had normal Nerve conduction study (13.3%). Remaining 26 patients (86.7%) had involvement of any of the above nerves.

Final interpretation	No.of cases	Percentage
NORMAL	4	13.3
BOTH	26	86.7
Total	30	100

DISCUSSION

Diabetic peripheral neuropathy is one of the complications that contribute to the morbidity of such diabetes patients. There are evidence stating that earlier subclinical diabetic neuropathy diagnosis can result in fewer diabetic foot ulcers and amputations. There is a also a strong association between polyneuropathy, duration of diabetes, and the level of HbAlc, thereby indicating that near normal glycemic control should be precautions to delay the beginning or progression of Polyneuropathy.[33]

An extensive study conducted by Pitrat J.et al[1] of nearly 4400 clinical patients, reported a prevalence rate of diabetic neuropathy ranging from7% of individuals within one year of diagnosis to 50% for those with diabetes for more than 25 years. The risk for complications of neuropathy increases with increasing duration and severity of hyperglycemia. The present study is done to study the effect of diabetes in motor and sensory nerve

conduction parameters in diabetes patients and to observe the functional status of peripheral nerve in asymptomatic diabetes patients.

A total of 30 patients were included in this study. Abida Farheen et al[2] studied sixty cases of asymptomatic diabetes Most of the patients are between 39 — 50 years of age(53.3%). The age group studied by Abida et al[2] was between 40- 50 years of age. Among the 30 cases in our study, 14 of them were male(46.7%) and 16 of them were female(53.3%)- hence our study had a slight female preponderance. But Abida et al study had male preponderance.

Out of 30 cases, most of our patients had duration of diabetes being 2-5 years (50%). Most of the studies done in diabetes had duration over a period of 1 to 10 years. Regarding treatment received, out of 30 cases, 25 patients were on OHA alone (83.3%) and 5 of the remaining patients were on both insulin and OHAs(16.7%). Regarding diabetic control in our population it has been found that 16 patients of our study had an HbAlC levels more than 8(53.33%) and 14 patients had HbAlC levels less than 8(46.66%).

Electrophysiological study was conducted in all the patients. Four of the patients had normal NCS. Out of the remaining 26 cases, majority of the patients had sensorimotor Polyneuropathy. The next common type of neuropathy noted in our study was Predominant sensory neuropathy was noted in three patients. One of the patient had isolated sensory nerve involvement (both ulnar sensory, median sensory and sural sensory).

The above findings are in concordance with many studies, starting from Abida et al which showed sensorimotor Polyneuropathy as the most common type in their group. Another study done by Balaji et al[3] who studied nerve conduction profile in type 2 diabetes, he concluded that "The most common pattern of neuropathy noted in our study was distal symmetrical sensory and motor Polyneuropathy"

Out of the 26 patients, with regard to neuropathy pattern in each nerve, axonal pattern predominated in ulnar and peroneal motor study. Demyelinating pattern predominated in median, tibial CMAP and median SNAP. Regarding ulnar nerve involvement, 2 patients had axonal with secondary demyelination pattern, four patients had axonal pattern and two patients had demyelinating pattern. Sural nerve pattern predominately showed axonal with secondary demyelination pattern.

In our study, out of 26 cases, the nerves that are most commonly affected in the decreasing order are as follows- median SNAP, sural SNAP, Median CMAP, peroneal CMAP, tibial CMAP, ulnar CMAP and Ulnar SNAP. Most common nerve affected in upper limb is Median Nerve while in lower limb is sural nerve. Thus our study results also correlates with the study done by Anitha varma et al[4], in which they found that sural& median are commonly affected.

Our study also showed that lower limb nerves are more affected compared to upper limb nerves which is in concordance with the findings of Zahed Ali et al.[5] In another study conducted by K.Munshiker et al[6], Conduction velocity of compound muscle action potential of motor nerves of lower limbs -common peroneal nerve and posterior tibial nerve were / significantly decreased The difference in sensory nerve conduction and motor nerve conduction may due to diameter and myelination of sensory and motor nerve. According to Erlanger and Gasser classification of motor nerve and large diameter nerves and groups under As. Most of sensory nerves are A§ and A6 Neurons whose diameter are less compare to motor neuron. In Diabetes mellitus sensory nerves are affected first.

In the present study, almost all patients (26 out of 30 cases) had shown electrophysiological changes indicating that they may had subclinical neuropathy which stresses the importance of the nerves conduction study (NCS) in the diagnosis of subclinical neuropathy particularly in sustained hyperglycemia. This result of our study is in accordance with the findings of I.W. Muflih et al study[7] and other studies.

In a study conducted by Weisman A, et al[8] it has been concluded that Individual NCS parameters or their simple combinations are sufficiently valid measures for identification and future prediction of DSP. It has also been said that simple combinations of nerve parameters may enhance the detection of incipient nerve injury which is characterized by more subtle electrophysiological abnormalities. Our study showed definite involvement of nerve fibres in nearly 26 out of 30 patients, which can predict the future occurrence of diabetic neuropathy.

In a study conducted by Xuan Kong et al[9] DPN was identified in 52.6% of patients; in another 19.3% of patients the electrodiagnostic encounter yielded normal results. our study showed evidence of neuropathy in nearly 86.7% (26 cases) and only 13.3% of individual yielded normal results (4 cases). With regarding to the duration of diabetes and neuropathy, our study didn't show any statistically significant association. This may be probably due to small population (30 cases).

In a study done by Abida Farheem et al[2], it has been concluded that Nerve conduction velocity progressively decreased from the controls to diabetics with good glycaemic control, to the diabetics with poor glycaemic control. There is negative correlation between sensory nerve conduction velocity & glycemic control. (HbAlc). In our study, it has been found that as HbAlC level increases, nerve conduction velocity decreases, On the contrary, DCCT trial and sosenko et al., found no

correlation between AIC levels and peripheral neuropathy.

CONCLUSION

The results of the present study done in diabetics without complications with duration of diabetes, indicate that there is a significant impairment of motor and sensory nerve parameters even though they are asymptomatic. We also found a negative correlation between HbA1c levels and nerve conduction parameters (Median and sural SNAP). This indicates that poor metabolic control causes early onset and rapid progression of neuropathy. We conclude the study with the observation that nerve conduction study can be used as a screening tool to diagnose neuropathy in subclinical stages and should be considered at risk category for aggressive glycemic control by diet, drugs and life style modification to prevent progression of neuropathy.

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