A COMPARATIVE STUDY OF ELECTROPHYSIOLOGICAL FINDINGS OF SENSORY NERVES IN PATIENTS WITH DIABETES MELLITUS AND HEALTHY CONTROLS IN AND AROUND DIBRUGARH TOWN.

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Abstract

Diabetes mellitus is now considered a major health problem worldwide, with serious socio-economic impacts. The metabolic dysregulation associated with diabetes causes secondary pathophysiologic changes in multiple organ systems. Both microvascular and macrovascular complications predominate the scenario of diabetes mainly due to delayed diagnosis and late presentation of the disease. Diabetic neuropathy is the most common and troublesome complication of diabetes, leading to great mortality and morbidity. Diabetic polyneuropathy worsens gradually without clinical symptoms until the condition is fairly advanced, hence the need for early diagnosis. Electrophysiological studies are the most sensitive and specific methods for detecting diabetic polyneuropathy. The present study was designed to evaluate and compare nerve conduction study parameters in sensory nerves in patients of diabetes mellitus and in normal healthy controls in and around Dibrugarh.

The study included 30 healthy controls and 60 known cases of diabetes, all aged 40-60 years. Of the 60 diabetics, 30 presented with symptoms of neuropathy and 30 presented without symptoms of neuropathy. Nerve conduction studies were performed using the equipment Neuro Perfect 4-channel EMG NCV EP and latencies, amplitudes and conduction velocities were evaluated. The latency, amplitude and velocity of sensory nerves in cases differed highly significantly from those in controls. The mean latencies, mean amplitudes and mean velocities of median and ulnar nerves of cases differed highly significantly as compared to controls.

Introduction:

Mankind has been afflicted by diabetes mellitus for a very long time. Although the scientific knowledge about diabetes has increased exponentially over the years, yet there are massive gaps in the understanding of many aspects of diabetes. Current statistics project diabetes mellitus as the third most common cause of morbidity and mortality, after cardiovascular diseases and malignancies (Textbook of diabetes, 4th edition).
According to recent WHO estimates, presently India has 32 million diabetic subjects, and this is projected to increase to 100 million, i.e., a rise by 25% by the year 2035 (Wild, Roglic et al., 2004).

The metabolic dysregulation associated with diabetes causes secondary pathophysiologic changes in multiple organ systems (Harrison’s Principles of Internal Medicine, 17th edition). Microvascular as well as macrovascular complications predominate the features of Indian diabetics, mainly due to delayed diagnosis and late presentation of the disease. Diabetic neuropathy is the most common and troublesome complication of diabetes mellitus, involving both peripheral and autonomic nerve functions (Dyck P J et al., 1999). Distal peripheral neuropathy, also known as diabetic polyneuropathy, is by far the most common type of neuropathy seen in diabetes mellitus (Melton LJ et al., 1999). The prevalence of diabetic polyneuropathy varies in the literature from 5%-100% (Vinik A I et al., 2004).

The routine evaluation of DPN is based on patient symptoms and a physical examination. However, simple screening methods are of limited value in early neuropathy. Nerve conduction studies (NCS) are the most sensitive and specific diabetic polyneuropathy detection method (Perkins B A et al., 2001).

NCS assess the ability of peripheral nerve to conduct electrical impulses. A representative waveform is generated by nerve stimulation and its parameters are evaluated to monitor neuronal function (NCBI Bookshelf, 2004). NCS help to:

- Localize the site or level of the lesion, determining if the pathology involves the peripheral nerve, neuromuscular junction, plexus, nerve root or anterior horn cells.
- Identify the pathophysiology, in particular, distinguishing axonal loss from demyelination.
- Diagnose mononeuropathies
- Diagnose more diffuse processes (eg. generalized peripheral neuropathy due to diabetes or GBS) (Huynh W et al., 2011).

In electrodiagnostic studies, three electrodes are used: active, reference and ground. The action potential is measured between active and reference electrodes and the ground electrode serves as a zero voltage reference point. The electrodes are made up of a variety of metals and alloys such as stainless steel, platinum, silver chloride, nickel, chromium, silver and gold. A metal electrode when interacts with an electrolyte such as sweat, electrode paste or fluid, an electrochemical reaction occurs which results in an electrode polarization potential. Both surface and needle electrodes can be used (Textbook of Diabetes, 4th edition; Cornblath DR, 2004; Mishra and Kalita, 2nd edition).

The sensory conduction can be measured orthodromically or antidromically. In orthodromic conduction, a distal portion of the nerve e.g. digital nerve is stimulated and sensory nerve action potential (SNAP) is recorded at a proximal point along the nerve. In antidromic conduction, the nerve is stimulated at a proximal point and SNAP is recorded distally. For orthodromic conduction, ring electrodes are preferred to stimulate the digital nerve; whereas surface electrodes are commonly used for antidromic stimulation (Mishra and Kalita, 2nd edition).

Normal values for sensory NCS (mean ± SD): (Kimura J, 1986)

| Nerve  | Recording site | Stimulation site | Latency (ms) | Amplitude (µv) | Conduction velocity (m/s) |
|--------|----------------|-----------------|--------------|----------------|--------------------------|
| Median | 2nd digit      | Wrist           | 2.84 ± 0.34  | 38.5 ± 15.6    | 56.2 ± 5.8               |
| Ulnar  | 5th digit      | Wrist           | 2.54 ± 0.29  | 35.0 ± 14.7    | 54.8 ± 5.3               |

In the light of the above facts, the present study was conducted to evaluate and compare the findings of nerve conduction studies of sensory nerves of diabetic patients and normal apparently healthy controls in and around Dibrugarh town.

**Material and Methods:**-

The present study was carried out in the Department of Physiology, in collaboration with the Department of Neurology, Assam Medical College and Hospitals, Dibrugarh after due permission from the ethics committee of Assam Medical College and Hospitals, Dibrugarh. The study was undertaken for a duration of one year. 90 subjects were enrolled which included 30 apparently healthy controls, 30 diabetic patients with symptoms of neuropathy and 30 diabetic patients without symptoms of neuropathy. Diagnosed cases of diabetes mellitus between the age-group of 40-60 years, of both sexes, attending the diabetes clinic in AMCH, Dibrugarh were included. Patients with history
of earlier cranial nerve lesion, stroke, alcohol abuse, chronic renal failure, hereditary neuromuscular disease and those taking drugs with the potential to cause neuropathy were excluded from the study. The equipment used was Neuro Perfect 4-channel EMG NCV EP. A detailed history was taken. Patients were questioned regarding the duration of diabetes, chief complaint at presentation, present symptoms of neuropathy and the limbs involved. Details of the treatment history was also taken. Any history regarding conditions that could lead to neuropathy was taken, like drug history, previous history of trauma or stroke, family history of any neuromuscular disease and history of smoking or alcoholism. Prior to the test, the patient was explained that he/she would experience a ‘tingling’ or ‘tapping’ sensation. Sensory nerve conduction studies were done on median and ulnar nerves. The parameters tested were amplitude, latency and conduction velocity.

The NCS was performed according to standard protocols and settings. Surface electrodes and surface stimulators were used. Three types of electrodes were used: active, reference and ground. The electrodes were coated with electroconductive gel and placed with adhesive tapes. The concerned nerves were tested bilaterally in all subjects. Data was analyzed using GraphPad Prism 6 for Windows version 6.05. The statistical methods used were Chi square test, Fisher’s exact test and Student t-test as and where applicable. A p-value < 0.05 was considered statistically significant, a p-value < 0.001 was considered statistically highly significant, while a p-value > 0.05 was considered statistically non-significant.

**Result and Discussion:**
In our study, 60 diabetic cases and 30 healthy controls were enrolled. Among the cases, 30 were diabetics with symptoms of neuropathy and 30 were diabetics without symptoms of neuropathy. Table 1 shows the sex distribution of cases and controls.

| Sex       | Diabetes cases with symptoms of neuropathy | Diabetes cases without symptoms of neuropathy | Controls |
|-----------|------------------------------------------|---------------------------------------------|----------|
|           | No. | %   | No. | %   | No. | %   |
| Male      | 15  | 50  | 15  | 50  | 15  | 50  |
| Female    | 15  | 50  | 15  | 50  | 15  | 50  |
| Total     | 30  | 100 | 30  | 100 | 30  | 100 |

**Table 1:** Table showing sex distribution of diabetes cases and controls

The mean age of the diabetes cases was 49.92 ± 6.75 years while the mean age of the healthy controls was 47.30 ± 5.40 years. There was no significant difference between the mean ages of the cases and controls as shown in Table 2.

| Mean age | Case         | Control     | p-value |
|----------|--------------|-------------|---------|
|          | 49.92 ± 6.75 | 47.30 ± 5.40| p= 0.068|

**Table 2:** Table showing age distribution of cases and controls

Figure 1 shows that of the 60 cases of diabetes that included diabetics with symptoms of neuropathy as well as diabetics without symptoms of neuropathy, all 60 (100%) showed abnormal changes in nerve conduction studies.
Figure 2 shows the type of nerve involvement. All the 30 diabetics presenting with symptoms of neuropathy showed motor nerve involvement while 27 showed sensory nerve involvement. Of the 30 cases presenting without symptoms of neuropathy, all 30 (100%) showed motor nerve involvement while 27 (90%) showed sensory nerve involvement. The difference between the two groups was not significant.

Figure 3 shows the distribution of cases according to the involvement of sensory nerves. Among the 60 diabetics, sensory median involvement was found in 47 while sensory ulnar involvement was also found in 47.
As shown in Figure 4, the mean latency, amplitude and velocity were respectively 2.42 ± 1.45, 18.10 ± 12.17 and 38.11 ± 20.16 among the cases. While the same parameters for the controls were respectively 2.18 ± 0.31, 39.75 ± 13.30 and 57.94 ± 5.43. The difference of association between the two groups was statistically highly significant.

Figure 5 shows that the mean latencies of sensory median and sensory ulnar nerves in diabetics were respectively 2.59 ± 1.55 and 2.24 ± 1.33. In the controls, the same were 2.25 ± 0.33 and 2.12 ± 0.27. The difference in association between the two groups was found to be statistically highly significant.
Figure 6 shows that the mean amplitudes of sensory median and sensory ulnar nerves were respectively 18.51 ± 13.31 and 17.70 ± 11. While the same in controls were 36.42 ± 13.78 and 43.08 ± 12.13 respectively. The difference in association between the two groups was statistically highly significant.

Figure 7 shows that the mean conduction velocities of sensory median and sensory ulnar nerves in diabetic cases were respectively 37.78 ± 20.51 and 38.44 ± 19.97. While the same in controls were respectively 59.83 ± 6.16 and 56.05 ± 3.83. On comparing the two groups the difference was statistically highly significant.
Discussion :-
The mean age of the diabetes cases was 49.92 ± 6.75 years while the mean age of the healthy controls was 47.30 ± 5.40 years. The difference of mean ages between the two groups was not statistically significant, implying that the two groups were homogenous in nature. Sultana S et al. in their study from January 2002 to January 2003 evaluated 69 cases of diabetes and found the mean age to be 49.13 ± 6.10 in cases with shorter duration of diabetes and 48.48 ± 4.83 in cases with longer duration of diabetes, which is comparable to our study.

All the 60 cases that were studied, irrespective of presence or absence of symptoms of neuropathy, showed abnormal NCS results. The finding is comparable to findings of the studies by Ambreen Asad et al. in 2009. 60 diabetics were evaluated, 30 with symptoms of neuropathy and 30 without symptoms of neuropathy. The results of the study showed that both clinical assessment and NCS are valuable in detecting cases of peripheral neuropathy. However, NCS is a more powerful tool for detection of neuropathy as it is helpful for detecting subclinical neuropathies as well. In the study by Loseth S et al. in 2007, out of the 50 patients 44% presented with symptoms of distal neuropathy predominantly in the legs. Abnormal NCS was observed in 52% of the cases. In the study by J Parvej in 2011 in 40 diabetics, NCS abnormalities were found in 75% of the cases and it was inferred that the prevalence of neuropathy was higher if electro-physiological methods were used. Among the cases without symptoms of neuropathy, 60% showed abnormal NCS findings. It was concluded that in diabetics without symptoms of neuropathy, electrophysiological abnormalities were present even at the time of diagnosis. Lamontagne A et al. (1970) observed abnormalities of sensory action potentials in median nerve of patients without corresponding clinical symptoms and signs, which made it possible to diagnose latent involvement of the nerves.

Among the 30 cases presenting with symptoms of neuropathy, 30 (100%) showed motor nerve involvement while 27 (90%) showed sensory nerve involvement. Of the 30 cases presenting without symptoms of neuropathy, 30 (100%) showed motor nerve involvement while 27 (90%) showed sensory nerve involvement. The difference between the two groups was not significant. This finding of predominant motor involvement in diabetes is in stark contrast to the otherwise accepted view that sensory fibres are more commonly affected in diabetes. This disparity could well be due to the fact that sural sensory nerve, which is usually the most commonly affected nerve, could not be included in our study owing to some technical difficulties in our facility. The present study is consistent with the study by Biswas in 2003 who reported deterioration of motor nerve function without sensory dysfunction in type 2 diabetics with short duration of diabetes. This is also comparable to the finding of predominant motor abnormality in newly diagnosed diabetics by Bhowmik in 1999. In a study by Young R J et al. in 1983, among the 22 diabetics studied, 19% showed motor abnormalities without sensory abnormalities.

In the present study, sensory median nerve involvement was found in 47 (78.33%) cases and sensory ulnar nerve involvement was also found in 47 (78.33%) cases. Studies by Al-Muhammadi et al. and Karsidaga et al. showed
that the most common nerve involved by diabetic polyneuropathy is sural nerve followed by median sensory nerve and then ulnar sensory nerve. A study by Hendriksen et al. in 1993 revealed that nerve conduction abnormalities were most pronounced in motor nerves of the leg (Tibial), followed, in order of severity, by sensory nerves of the leg (sural) and then sensory nerves of the arm (ulnar).

In the present study, the mean latency of sensory nerves in cases is significantly increased as compared to controls. The mean amplitude and velocity of sensory nerves in cases is significantly reduced as compared to controls. Highly significant increase in the mean latencies of median sensory and ulnar sensory nerves were observed in cases when compared with those of controls. Statistically highly significant reduction in the mean amplitudes and mean velocities of sensory median and sensory ulnar nerves were observed in cases as compared to controls. The findings are consistent with established findings. Rota et al. (2005) evaluated 39 newly diagnosed diabetics and performed NCS of median, ulnar, peroneal, tibial and sural nerves. A reduced sensory nerve action potential (SNAP) amplitude was observed in the median nerve in 70% of the patients, in the ulnar in 69% and in the sural nerve only in 22%. In the cases showing a decrease in the SNAP amplitude of the ulnar or median nerve, the SNAP amplitude of the sural nerve was normal in 82 or 80% of the subjects respectively. Hidasi E (2008) evaluated 77 diabetics and studied if there were any statistically significant differences between controls and diabetics with regard to the latency, amplitude, area of sensory potentials, duration and conduction velocity of the median sensory nerve. Statistically significant differences were observed in almost all the measured parameters. The sensory latencies were longer in diabetics while sensory amplitudes and velocities were reduced in diabetics when compared with controls.

Lamontagne A et al. (1970) conducted electrophysiological assessment of 30 diabetic patients. SNAPs were recorded in the median nerve and conduction velocity, amplitude, duration and shape of the potentials were compared to those of normal subjects. Of the 30 patients, 24 showed abnormalities in sensory conduction, amplitude and shape. An average of 50% decrease in amplitude was noted in sensory potentials. In the study by Behse et al. (1977) twelve patients with diabetes mellitus, abnormal glucose tolerance tests, and signs and symptoms of neuropathy were examined. Sensory conduction was determined along the sural nerve, superficial peroneal nerve, saphenous nerve, distal portion of the posterior tibial nerve and the distal segments of the median nerve. In 76% of the sensory nerves examined in the lower extremities, and in 30% of branches of median nerves, conduction velocity was slowed. In 65% of the nerves examined in the upper and lower extremities, the amplitude of the sensory nerve action potentials was diminished.

**Conclusion :-**
The present study dealt with a total of 60 subjects of which 30 were diabetics with symptoms of neuropathy and 30 were diabetics without symptoms of neuropathy. Each group of diabetic consisted of 15 males and 15 females. 30 age and sex matched apparently healthy subjects were taken as controls, which included 15 males and 15 females. The difference of mean ages between the cases and controls was statistically non-significant, which could be attributed to the fact that the two groups were homogenous. Abnormal electrophysiological findings were observed in 60 (100%) cases, thereby agreeing with the views of previous studies that found NCS to be a sensitive tool for diagnosing subclinical neuropathy. 100% motor involvement and 90% sensory involvement was demonstrated in diabetics with symptoms of neuropathy as well as diabetics without symptoms of neuropathy. Ulnar sensory nerve involvement was found in 47 (78.33%) cases. Median sensory nerve involvement was also found in 47 (78.33%) cases. The mean latency of sensory nerves was significantly increased while mean amplitude and velocity of sensory nerves was significantly reduced in cases as compared to controls.

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