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Evidence of Nerve Conduction Defects in Type-II Diabetic Patients without Neuropathic Symptoms

Authors
Dr Suneetha. G[1], Dr Satyanarayana Prasad. A[2]
[1]Assistant Professor of Physiology, NRI MC & GH, Chinakakani, Guntur (Dt), AP, INDIA-522503
[2]Senior Resident, Department of General Surgery, NRI MC & GH, Chinakakani, Guntur (Dt), AP, INDIA

Abstract
Diabetic neuropathy is the most dreadful complication of poorly controlled long standing diabetes mellitus, ending up in amputation in worst cases. This underscores the value of early detection and intervention of diabetic neuropathy. The objective of present study is to look for early changes in nerve conduction in patients not exhibiting symptoms of diabetic neuropathy as compared to the symptomatic patients.
Materials & Methods: *In a group of 34 patients with mean age of 59 years and asymptomatic for diabetic peripheral neuropathy, nerve conduction studies were conducted along with FBS, HbA_1c and compared the same parameters with a group of 52 patients with mean age of 56 years and symptomatic for diabetic neuropathy patients. Results of nerve conduction studies in both the groups are statistically compared with normal established reference values as well as between them. The number of cases demonstrating abnormal test parameters in the given groups is statistically analyzed using chi-square test.*
Results: *Results of the study confirmed that there is a decline in conduction velocity to an extent of 6m/sec on the average mostly in lower limb sensory nerves in symptomatic diabetic neuropathy patients. Even in diabetic subjects not reporting any symptoms of neuropathies, in 30% of cases there is decline in lower limb sensory conduction velocities to varying extents compared to the normal reference values.*
Conclusion: *Nerve conduction studies even in asymptomatic cases may prove to be valuable indices of progression to full blown diabetic neuropathy in due course and help initiate prophylactic measures to retard its progress.*
Keywords: *Type II Diabetes mellitus, DN, DPN, NCS, NCV, HbA_1c, ADA.*

Introduction

Diabetes mellitus is a major public health problem worldwide. India leads the world with largest number of diabetic subjects earning the dubious distinction of being termed the "diabetes capital of the world"[1]. Genetic predisposition combined with life style changes, associated with urbanization and globalization, contribute to this rapid rise of diabetes in India[1]. It is known that almost 50% of people with diabetes remain undetected and hence some may even present with micro vascular and macro vascular complications at the time of diagnosis[2, 3].

Diabetic neuropathy (DN) is the most common and troublesome complication of diabetes mellitus leading to great morbidity and resulting in a huge economic burden for diabetes care[4]. Diabetic Neuropathies constitute a heterogeneous group, the most common being diabetic polyneuropathy more often presenting as Diabetic Peripheral Neuropathy (DPN).

Chronic peripheral sensory motor symmetrical neuropathy (DPN) accounts for approximately 75% of the diabetic neuropathies[5]. It is defined as the presence of symptoms and/or signs of peripheral nerve dysfunction in people with diabetes mellitus, after exclusion of other causes[6]. The primary symptom of DPN is loss of sensation in the toes, which extends to involve the feet and leg in a stocking distribution. Some patients complain about numbness and pain, but the disease progresses most frequently insidiously and undetected. If no action is taken, foot callus, ulceration and infection might develop and further turn into distressing and painful impairment. The foot ulcers of diabetic patients mostly are neuropathic in origin, and therefore eminently preventable. Age, duration of diabetes and poor glycaemic control are recognised as risk factors for DPN, while cigarette smoking, hypertension, obesity, hyperlipidaemia and microalbuminuria has been pointed as potential risk indicators[5]. Yearly evaluation for DM complications, including neuropathy, is recommended by ADA[7].

The American Diabetes Association recommends that glycosylated haemoglobin (HbA1c) should be less than 7%. Most previous studies, which reported HbA1c correlation with polyneuropathy, used higher HbA1c cut points and focused on neurologically symptomatic patients[8, 9]. Diabetic patients have a 12 times higher risk of amputations when compared with non-diabetic subjects, due to diabetic neuropathy[10]. However the progression of neuropathy can be reduced by early detection and intervention[11]. Nerve conduction studies, primarily nerve conduction velocities are considered one of the most sensitive indices of the severity of neuropathy[12]. Nerve conduction tests are used to localise lesions and to describe the type and severity of pathophysiologic process, including alterations in functions that are not recognised clinically.

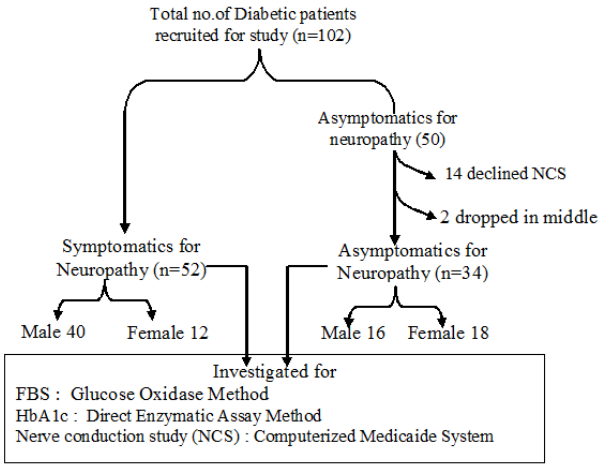
Some people with diabetes may not report neuropathic symptoms. But there is a possibility of subclinical involvement of nerves, which can be detected by electrophysiological study of nerve conduction. Defective nerve conduction is also believed to precede progression to symptomatic diabetic neuropathy at a later stage[13].

This underscores the value of early detection and intervention of diabetic neuropathy. The objective of present study is to look for early changes in nerve conduction in patients not exhibiting symptoms of diabetic neuropathy as compared to the symptomatic patients.

Materials & Methods

Electrophysiological studies of nerve conduction as well as other relevant laboratory parameters as shown in the flow chart were finally done in 52 diabetic subjects with symptoms and signs of neuropathy and 34 subjects without such symptoms and signs. The procedure was explained to all the subjects and written consent was obtained and was cleared by the institutional ethics committee. Clinical examination was performed in all the subjects to detect signs of neuropathy. Standard test procedures were employed to collect the following laboratory data.

Flow Chart Summarizing study Design



Results of nerve conduction studies, Fasting Blood Sugar (FBS), and HbA_1C are statistically compared between the two groups using student 't'- test.

Results

Comparative picture of biochemical parameters between the two groups under study is presented in table-1. The table-2 presents NCV between two study groups.

- In both groups the velocities are effected, more so in symptomatic subjects. However there is a greater statistically significant decline in conduction velocity in symptomatic subjects.
- Even in diabetic subjects not reporting any symptoms of neuropathies, in 30% of cases there is decline in lower limb sensory conduction velocities to varying extents compared to the normal reference values.

Table 1 : Comparison of biochemical parameters as mean values between asymptomatic and symptomatic groups.

Biochemical parameters	Asymptomatic diabetes patients (n = 34)	Symptomatic diabetes patients (n=52)	'p' value
HbA_1C (%)	7.82 ± 0.81	7.60 ± 0.90	>0.05
FBS (mg/ dl)	186.62±36.14	184.87±35.99	>0.05

p value <0.05 significant

Table 2 : Comparison of mean values of NCV (m/sec) between two groups with P values

Nerve	Conduction velocity (m/sec)		
	Asymptomatic Mean±S.D (n=34)	Symptomatic Mean±S.D (n=52)	'p' value
Median (motor)	53.5±8.57	50.4±6.71	<0.05
Median (sensory)	51±8.18	43.71±7.69	0.0001
Ulnar (motor)	54.4±9.12	50.92±6.30	>0.05
Ulnar (sensory)	53.76±8.34	50.21±5.96	0.025
Peroneal	46.19±8.74	42.71±5.33	0.025
Tibial	44.19±8.63	42.02±4.47	>0.05
Sural	49.32±8.43	34.98±20.03	0.00005

p value <0.05 significant

Table 3 : Comparison of mean values of latencies (m.sec) between two groups with 'p' values

Nerve	Latency (m sec)		
	Asymptomatic Mean±S.D (n=34)	Symptomatic Mean±S.D (n=52)	'p' value
Median (motor)	3.42±0.99	4.34±1.06	0.0001
Median (sensory)	3.06±0.82	3.55±0.83	>0.05
Ulnar (motor)	2.62±0.69	2.78±0.79	>0.05
Ulnar (sensory)	2.26±0.54	2.35±0.75	0.005
Peroneal	4.38±1.34	4.13±0.99	>0.05
Tibial	4.29±0.76	4.76±1.56	0.025
Sural	3.18±0.69	2.51±1.48	0.025

p value <0.05 significant

Table 4 : Comparison of mean values of F – latencies (m.sec) between two groups with P values for motor nerves

Nerve	F – wave Latency (m sec)		
	Asymptomatic Mean±S.D (n=34)	Symptomatic Mean±S.D (n=52)	P value
Median (motor)	27.65±4.53	28.83±4.55	>0.05
Ulnar (motor)	28.59±5.58	28.86±5.31	>0.05
Peroneal	49.42±11.17	47.83±8.53	>0.05
Tibial	46.86±5.17	49.98±8.50	<0.05

p value <0.05 significant

Table 5 : Comparison of mean values of Amplitudes (mV or µV) between two groups with 'p' values

Nerve	Amplitude (mV or µV)		
	Asymptomatic Mean±S.D (n=34)	Symptomatic Mean±S.D (n=52)	'p' value
Median (motor)	10.09±3.39	8.49±2.75	0.001
Median (sensory)	33.42±21.58	18.40±11.44	0.0001
Ulnar (motor)	8.73±2.36	8.22±2.08	>0.05
Ulnar (sensory)	29.11±24.30	20.81±10.62	0.025
Peroneal	5.28±2.50	4.50±2.94	>0.05
Tibial	11.55±5.43	8.25±4.89	0.025
Sural	22.00±14.65	11.13±9.41	0.00001

p value <0.05 significant

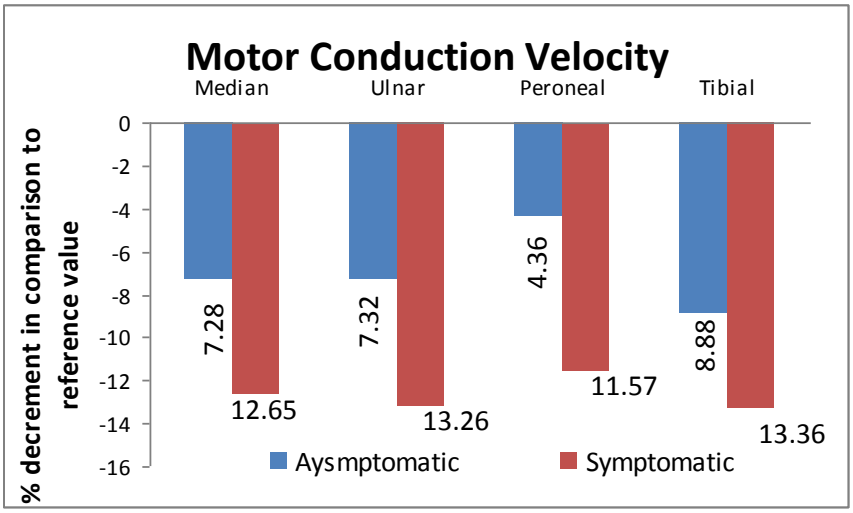


Chart 1 : Comparison of decline in motor nerve conduction velocities between two study groups

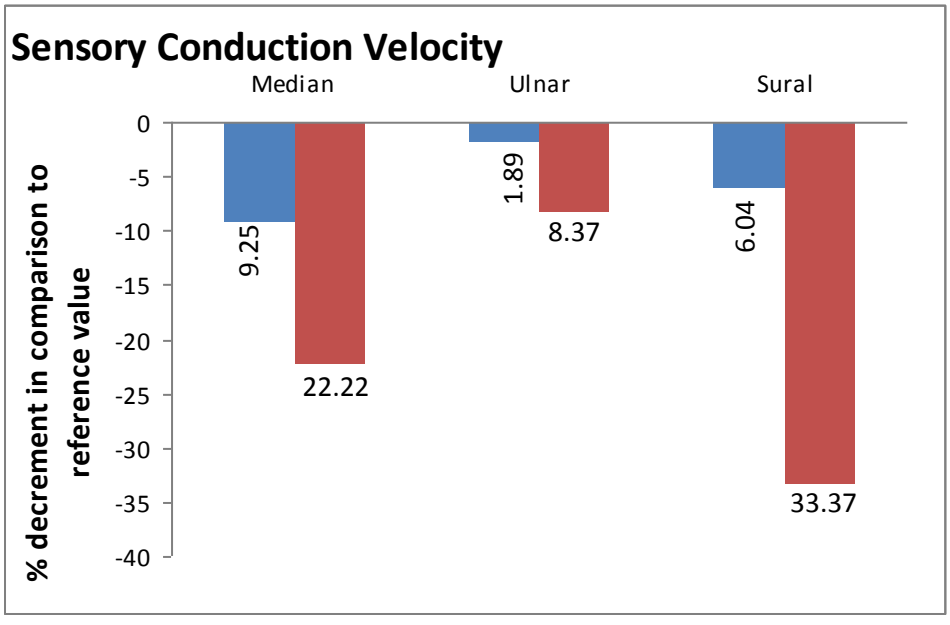


Chart 2 : Comparison of decline in motor nerve conduction velocities between two study groups

Discussion

The main focus of the study is to investigate the electrophysiological measures of sensory and motor nerve conduction in two groups of diabetic patients. One group presenting with symptoms of neuropathy (symptomatic) and other group without symptoms of neuropathy (asymptomatic). The idea is to find out the possibility of sub-

clinical nerve conduction defects in diabetic patients.

Mostly nerve conduction studies have been accepted as an essential part of diagnosis for DPN as it has many benefits[14, 15]. Discordance between nerve conduction velocity and symptoms and signs of DN has been reported before[16, 17]. We found that nearly 8% of our patients with symptomatic DN had normal NCS, which is lower than that reported by Sangiorgio et al[16] and Fedele et al[17]. Also nearly 57% of patients who did not have symptoms of neuropathy showed some abnormality in NCS. This discordance between symptoms and NCS means that we cannot rely on patient's symptoms for the diagnosis of DN and we need NCS for better assessment and diagnosis of DN[18]. Electrophysiological parameters such as nerve conduction velocity (NCV), latency, F-wave latency and amplitudes of action potentials were recorded in both the asymptomatic and symptomatic subjects and results were tabulated. Table – 2 compares conduction velocity in both upper and lower limbs, in sensory and motor nerves between the two groups under study.

In the table –2 shown, there is over all declines in the conduction velocities of both motor and sensory nerves in both groups, i.e. symptomatic and asymptomatic subjects. Greater decline is observed in symptomatic subjects in relation to both motor and sensory conduction velocities. In symptomatic subjects particularly the sensory conduction velocities of upper limb nerves i.e. median and ulnar nerves, are significantly affected, 'p' values being 0.0001 for median sensory nerve and 0.025 for ulnar sensory nerve. Regarding the lower limb nerves in symptomatic subjects the greatest decline is observed in relation to the sensory conduction velocity of Sural nerve. The 'p' value being 0.00005. Severe decline in conduction velocity is most often detected in sural nerve. This is in accordance with the well-known fact that DPN mostly involves lower limb sensory nerves[19]. Relating to the conduction velocities of motor nerves, the statistically significant difference between asymptomatic and symptomatic groups is observed for median nerve in the upper limb with a 'p' value of <0.05 and peroneal nerve in the lower limb with a 'p' value of 0.025. The results are in coordination with a study conducted in Kufa University[20].

Corroborating with decline in conduction velocities corresponding increase in the latencies is observed in the nerves tested as shown in the table – 3. The most noticeable increase in latency is with median motor nerve in symptomatic group compared with asymptomatic group, with a 'p' value of 0.0001. There is also statistically significant difference in latencies between the two groups for sensory component of ulnar nerve in the upper limb ('p' value being 0.005) and for tibial and sural nerves in the lower limb (p value 0.025 for each nerve). Many patients with sensory motor neuropathy showed a prolongation in distal motor latency in our study which is in accordance with a study conducted by Moaz et al[18].

Most of the examined motor nerves show no prolongation of the F – wave latency as shown in table – 4, in symptomatic group compared to asymptomatic group, except tibial nerve, with a 'p' value being <0.05 and this is due to the affect of central root by diabetic neuropathy. This indicates that F – wave latency abnormalities are more frequently observed in lower extremities. This was also suggested through a study conducted by Moaz et al[18].

In the symptomatic subjects as shown in table – 5, the amplitudes of various nerve potentials are significantly decreased compared to asymptomatic individuals, except for ulnar motor and peroneal nerves. The decline in amplitudes of nerve action potentials of all sensory nerves in symptomatic group is observed compared to motor component. Regarding amplitudes of nerve action potentials, there is statistically significant difference observed between asymptomatic and symptomatic groups in median sensory nerve, the 'p' value being 0.0001; in ulnar sensory nerve, the 'p' value being 0.025 and in sural nerve the 'p' value being 0.00001. The reduction in mean amplitudes of motor nerves is not significant in both symptomatic and asymptomatic groups compared to reference values. Mean amplitudes of sensory

nerves action potentials are not reduced significantly compared to reference values in asymptomatic group. But in symptomatic group the reduction in mean amplitudes of sensory nerves is, 40.51% for median nerve, 8.48% for ulnar nerve and 38.57% for sural nerve compared to reference values. A more than 40% reduction in amplitude was assumed to be due to the loss of myelinated fibres. In our study reduced sensory nerve action potential (SNAP) amplitude for ulnar nerve is observed in about 90% of symptomatic patients and 23% of asymptomatic patients. Rota et al also concluded that upper limb sensory nerves conduction studies, letting exploration of more distal involvement as compared to sural and peroneal nerves, are highly sensitive in detecting early signs of neuropathy[21].

Chronic hyperglycemia is said to promote diabetic neuropathy by varied mechanisms such as increased oxidative stress, decreased nitric oxide, impaired endothelial function. The results of the present study suggest early subtle changes in nerve conduction velocity even in diabetic patients not presenting with symptoms of neuropathy. The significance of electrophysio-logical study of nerve conduction velocities in asymptomatic people is highlighted by Hoffman et al, who demonstrated abnormal nerve conduction even in prediabetic individuals with abnormal GTT[13]. They are also said to be more prone to development of Polyneuropathy. Neuropathy was diagnosed solely on the basis of electrophysiological study of nerve conduction in 44% of asymptomatic subjects by Moaz[18]. As per a "research group" report in 1993, improved glycaemic control has been shown to prevent and delay progression of diabetic neuropathy emphasizing the importance of early diagnosis and aggressive management in these patients. Decline in conduction velocity is most often detected in sural nerve. This is in accordance with the well known fact that DPN mostly involves lower limb sensory nerves.

Conclusion

The results of the present study suggest early subtle changes in nerve conduction velocity even in diabetic patients not presenting with symptoms of neuropathy.

Nerve conduction studies even in asymptomatic cases may prove to be valuable indices of progression to full blown diabetic neuropathy in due course and help initiate prophylactic measures to retard its progress. So there is a necessity for prospective follow up of patients with demonstrable nerve conduction defects to establish predictive value of subsequent development of overt neuropathy.

Hence screening for nerve conduction studies of border line diabetic patients or those with impaired glucose tolerance is desired.

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