SOMATIC NEUROPATHY IN DIABETES MELLITUS

Brig AS KASTHURI, ^{VSM}*, Maj S SOFAT ⁺, Col N KUMAR [#]

ABSTRACT

One hundred patients of Diabetes Mellitus (70 with and 30 without clinical somatic neuropathy) were studied to correlate clinical severity with the magnitude of nerve conduction abnormalities. Age range was 10-79 years (mean 49) with equal number of males and females. Incidence of neuropathy was more in patients over 40 years of age (60 out of 70 patients) with duration of disease over two years (78.33%). The grades of severity were mild in 22 (31.33%), moderate in 25 (35.71%) and severe in 23 (32.86%) patients. Nerve conduction studies were carried out in 48 (27 with and 21 without clinical neuropathy) patients, using the apparatus Dantec (Cantata TM). The nerves (median, peroneal and sural) were stimulated at two points and the recording of latency; amplitude (micro V) and motor and sensory nerve conduction velocities (m/s) were done under identical environmental conditions. Sensory nerve conduction velocity was more affected than motor velocity. In the 21 patients without clinical neuropathy, 14 showed abnormalities indicating early involvement of peripheral nerves. Reduction of motor nerve conduction velocity was more in patients with moderate and severe grades. The reduction was more in lower than in upper limbs. Nerve conduction abnormality helps in diagnosis in diabetic neuropathy even in preclinical state and correlates with severity, in clinical neuropathy.

MJAFI 2000; 56 : 33-36

KEYWORDS: Diabetic neuropathy; Nerve conduction abnormality; Peripheral neuropathy.

Introduction

Diabetic neuropathy is probably the most common complication of diabetes mellitus (DM). Two-thirds of diabetic patients have one or more forms of neuropathies. Any and all of the diabetic neuropathies may be the clinical manifestations of DM in the absence of other overt manifestations. Peripheral nerves can be stimulated and conduction velocities of motor and sensory fibers can be measured separately. Velocity and amplitude measurements of nerve conduction help gauge the type and severity of neuropathy. The present work attempts to correlate the clinical severity with the magnitude of nerve conduction abnormalities in our service population, using Dantec computerized equipment.

Material and Methods

One hundred patients of DM from a service hospital were included in this study. Diagnosis was as per WHO [1]. A detailed history for symptoms of DM and somatic neuropathy were enquired into. Clinical examination laid stress on somatic neurological manifestations to divide patients with and without neuropathy. Somatic peripheral neuropathy was arbitrarily classified into the following group [modified from 2].

a) *Mild neuropathy* Sensory deficit over the feet, with or without diminution or loss of ankle jerk.

b) *Moderate neuropathy* Absent ankle jerk, plus diminished sensation upto knee, with or without sensory deficit in upper limbs.

c) *Severe neuropathy* Sensory loss atleast upto knees in lower extremities, with varying sensory deficit in upper limbs, absent tendon jerks and motor weakness.

Only 48 patients consented to undergo nerve conduction studies. Both motor and sensory nerve conduction was studied in these 48 patients (27 with and 21 without neuropathy) and in an equal number of controls using apparatus Dantec (Cantata TM). The median, peroneal and sural nerves on both sides were studied. All measurements were taken, in the same room with the patient in supine position, limbs fully extended and after 30 minutes of rest. Temperature of the extremities was not recorded, but tests were carried out in almost identical conditions. The stimulus frequency of 1 Hz with duration 200 msec was employed for motor and sensory conduction. Surface electrodes to stimulate the nerves were placed at elbow and wrist for median nerve, popliteal fossa and ankle for peroneal nerve and at 120 mm proximal to lateral malleolus for sural nerve. The patient was grounded by means of a grounding electrode (soaked in saline) and the surface of the skin over the stimulation points was prepared (cleaning with spirit). Initial stimulus intensity was 0 mA and it was then gradually increased, till a supramaximal stimulus was obtained. The surface electrode picked up the action potential from the muscle activated by the same nerve from the first point. The procedure was repeated at a second point. The graph was automatically projected onto the monitor and both the traces were frozen. The difference in the latency was measured by adjusting the time markers. The distance between the two points of stimulation was measured. This data was then fed into the apparatus and the instrument automatically displayed the nerve conduction velocity (NCV) in m/s and a print out of this was obtained.

Sensory nerve conduction was recorded by placing two surface electrodes over the distribution of the sensory nerve. The nerve was then stimulated, e/g., median nerve at the wrist and the sural nerve 120 mm proximal to the lateral malleolus. Once the graph was obtained, the averager was used to eliminate the muscle action potentials and the latency was measured with the time marker at the first positive peak. The distance from the stimulation electrode to the proximal electrode (recording) was measured manually and fed into the apparatus. The apparatus calculates the nerve conduc-

* Commandant, 158 Base Hospital, C/o 56 APO, ⁺ Graded Specialist (Medicine), Command Hospital (CC), Lucknow 226 002, [#] Senior Adviser (Medicine and Neurology), Command Hospital, Air Force, Bangalore 500 007.

TABLE 1
Duration from diagnosis of diabetes mellitus to detection of neuropathy

Duration (years)	Grades of neuropathy No (%)			Total	Without neuropathy	Total
	Mild	Moderate	Severe			
< 2	13 (56.52)	06 (26.09)	04 (17.39)	23 (100)	17	40
2-4	02 (11.11)	11 (61.11)	05 (27.78)	18 (100)	06	24
> 4	07 (24.14)	08 (27.58)	14 (48.28)	29 (100)	07	36
Total	22 (31.43)	25 (35.71)	23 (32.86)	70	30	100

$\chi^2 = 15.76$, $df = 4$, $p < 0.01$. A significant relationship exists between the duration from the date of diagnosis (in years) and the grades of neuropathy ($p < 0.01$). The severity increased from 17.39% to 48.28% as the duration increased. * Figures in the parenthesis indicate percentages

TABLE 2
Symptoms and signs of somatic neuropathy

Symptoms	No (%)
Paraesthesia (Pins and Needles 31, Tingling and numbness 25, Burning 4).	60 (85.71)
Pain	21 (30.00)
Weakness	05 (07.14)
Swelling of foot, diplopia, ulcer foot	1 each
Signs	
Sensory abnormality	
(a) Glove and Stocking hypoaesthesia	40 (57.14)
(b) Loss of vibration sense	25 (35.71)
(c) Sensory loss confined to lower limb	14 (20.00)
Tendon reflex abnormalities	
(a) Absent ankle jerk	19 (27.14)
(b) Generalized hyporeflexia	13 (18.57)
(c) Absent ankle and Knee jerk	09 (12.85)
Miscellaneous	
Weakness of anterior thigh muscles	4
Weakness of dorsiflexor of ankle	3
Foot drop, third nerve palsy and non-healing ulcer	one each

tion velocity and it was flashed on the right hand side of the oscilloscope and a printout was taken.

Nine patients with neuropathy consented for sural nerve biopsy. About 30 mm of sural nerve was removed; proximal to lateral malleolus and fixed in 2% buffered glutaraldehyde. Transverse and longitudinal sections were stained with hemotoxylin and eosin to look for fiber loss (axonopathy) and stained with special sialochrome stains for evidence of demyelination.

Results

A total of 100 patients completed the study (age range 10-79); (male 50, female 50). Out of the 100 patients, 70 had clinical evidence of neuropathy and 30 had no neuropathy. The mean age in years $\pm$ standard deviation (SD) for the total population was 48.49 ± 19.93 . The mean age $\pm$ SD for diabetics with neuropathy was 50.36 ± 13.06 and for diabetics without neuropathy was 33.91 ± 12.65 . Among the 70 patients with neuropathy the maximum number (60) was in the sixth decade. The difference in incidence of neuropathy between the sexes is insignificant.

Duration from diagnosis of DM to detection of grades of somatic neuropathy is as per Table 1. The incidence of somatic neuropathy in diabetics of less than two years duration was 23 out of 40 (57.50%), between 2 to 4 years duration was 18 out of 24 (75.00%) and in more than four years duration was 29 out of 36 (80.55%) patients. A significant relationship existed between duration of the disease and the grade of neuropathy ($p < 0.01$).

In the clinical neuropathy group 64 patients had distal symmetrical neuropathies (59 with sensory involvement, 4 with motor and

one had neuropathic ulcer). The remaining six patients had asymmetrical neuropathy (4 diabetic amyotrophy and one each of femoral mononeuritis and cranial neuropathy). The symptoms and signs of somatic neuropathy are given in Table-2. Glove and stocking hypoaesthesia was the dominant sensory abnormality in 40 (57.14%) patients. Sensory loss (touch and pain) confined to lower limbs was seen in 14 (20%) patients. Ankle jerk was absent in 19 (27.14%) patients. Some of the cases had more than one abnormality.

The value of MNCV in diabetics with and without neuropathy is given in Table-3. MNCV was considerably reduced in diabetics as compared to controls. Those with clinical evidence of neuropathy are affected more than those without neuropathy. Lower limb nerves are affected more often than upper limb. Correlation of grades of severity in 48 patients of MNCV and SNCV are given in Table-4. MNCV was reduced in moderate and severe grades of somatic neuropathy as compared to the mild grade when patients with and without neuropathy were compared and this is statistically significant ($p < 0.01$). The reduction in sensory action potential (SAP) was more than that of MNCV. The motor and sensory nerve conduction velocities are reduced in diabetics of longer duration as compared to lesser duration (Table-5).

Sural nerve biopsy could be performed in 9 patients with DM. All these patients had evidence of axon loss, which correlated, with low amplitude of evoked nerve and muscle action potentials with reduced recruitment on EMG. Segmental demyelination and remyelination was detected in three of them. This limited number of cases does not permit any statistical analysis.

Discussion

In one series of 150 patients of diabetic neuropathy, 85% were over the age of 40 years [3]. Sixty of our 70 patients (85.42%) were also over the age of 40 years. The mean age (50.36 ± 13.06) of those with neuropathy was higher than those (33.91 ± 12.65) without neuropathy, indicating higher incidence at later age group. The prevalence of neuropathy also increased with the duration of disease: 7.50% at the time of diagnosis of DM to 66.33% after 25 years of disease [4]. In this study it was observed that severity of neuropathy increased from 17.39% to 48.28% as the duration increased ($p < 0.01$). (Table 1).

Distal symmetrical sensory or sensori-motor polyneuropathies with predominant involvement of the distal lower limbs are the most common forms seen. In small-fiber neuropathy pain and paraesthesia predomi-

TABLE 3
Values of MNCV and SNCV*

Age (years)	Type of patients	No	Sural Nerve		Median Nerve		Peroneal nerve VEL m/s
			AMP micro V	VEL m/s	AMP micro V	VEL m/s	
≤ 15	Control	5	11.93 ± 2.4	52.16 ± 7.9	17.32 ± 5.07	68.01 ± 4.00	48.02 ± 3.11
	With neuropathy	2	02.19 ± 1.86	36.81 ± 3.84	08.90 ± 1.07	56.00 ± 3.89	42.13 ± 7.96
	No neuropathy	6	06.74 ± 2.13	49.11 ± 2.84	13.01 ± 1.45	60.00 ± 4.87	44.11 ± 5.0
16-30	Control	10	11.90 ± 3.6	51.97 ± 8.1	19.35 ± 5.88	65.73 ± 3.92	47.58 ± 3.00
	With neuropathy	2	01.89 ± 0.44	28.29 ± 3.9	13.04 ± 1.22	52.58 ± 9.73	15.57 ± 7.54
	No neuropathy	12	03.86 ± 0.17	40.74 ± 7.8	15.01 ± 1.00	57.81 ± 4.01	43.82 ± 2.11
31-45	Control	15	11.89 ± 2.6	51.03 ± 8.0	17.00 ± 6.4	65.0 ± 4.03	47.65 ± 3.92
	With neuropathy	14	02.76 ± 2.2	16.08 ± 3.0	12.66 ± 0.36	58.55 ± 6.22	38.97 ± 9.58
	No neuropathy	04	08.46 ± 2.7	41.00 ± 7.1	14.75 ± 0.25	61.00 ± 5.01	40.00 ± 3.68
46-60	Control	30	10.90 ± 2.32	50.89 ± 7.6	16.97 ± 5.82	65.74 ± 5.99	47.05 ± 4.11
	With neuropathy	29	03.99 ± 0.13	27.00 ± 1.75	06.00 ± 1.74	49.77 ± 9.05	39.12 ± 8.02
	No neuropathy	05	08.14 ± 0.17	42.00 ± 3.08	13.00 ± 1.02	58.00 ± 6.62	42.66 ± 3.11
> 60	Control	20	10.81 ± 1.96	49.96 ± 6.2	15.36 ± 4.98	65.01 ± 4.84	46.0 ± 2.66
	With neuropathy	23	01.76 ± 0.14	23.11 ± 0.11	05.84 ± 1.21	57.07 ± 7.99	39.00 ± 8.00
	No neuropathy	3	03.84 ± 0.72	25.70 ± 1.03	07.89 ± 1.01	59.00 ± 2.0	42.00 ± 4.84

*MNCV - motor nerve conduction velocity; SNCV - Sensory nerve conduction velocity

TABLE 4
Correlation of grades of severity of MNCV and SNCV

Grades (Clinical)	MNCV (No of patients)		SNCV (No of patients)	
	With neuropathy	Without neuropathy	With neuropathy	Without neuropathy
Normal	0	17	0	7
Mildly reduced	22	4	16	9
Moderate and severely reduced	5	0	11	5
Total	27	21	27	21

 $\chi^2 = 34.25, p < 0.01 (S)$ $\chi^2 = 10.71, p < 0.01 (S)$

nate. In large-fiber neuropathy patients have unsteadiness of gait, absent ankle jerk, diminished position and vibration sensations. In 40% of patients with somatic neuropathy, some degree of autonomic dysfunction can be detected [4]. Sensory-nerve action potentials, which reflect conduction in large myelinated fibers, may be remarkably normal in patients with selective loss of pain and temperature sensation [5]. In the clinical neuropathy group 64 had distal symmetrical peripheral neuropathy (59 with sensory involvement and 4 with motor and one neuropathic ulcer) and the rest

six had asymmetrical neuropathy (4 diabetic amyotrophy and one each of foot drop, third nerve palsy). The symptoms and signs observed are more or less similar to other studies [2,6].

MNCV was abnormally reduced in diabetics with symptoms than without symptoms. In five clinically symptomatic patients, MNCV could not be measured at all in any limb. In 31 patients, MNCV was reduced compared to controls out of which 27 were symptomatic. The reduction of MNCV were comparatively more severe in peroneals than in the median nerve. This was similar to other studies [2,7]. Sensory nerve conduction abnormalities (significant reduction in amplitude) were found in 40 out of 48 patients studied. The 8 patients in whom it was normal were all asymptomatic. This may be an early indication of involvement of peripheral nerves. Other studies also show, that the earliest sign of diabetic polyneuropathy on nerve conduction studies, is reduced amplitude of SAP [7]. Use of patient self-testing sensory kit using nylon-filament sensory testing tool with 10-g bending force helped in finding sensory loss previously undetected

TABLE 5
Value of nerve conduction velocity for controls and neuropathy cases

Age (yr.)	Type of patients	No	Median Nerve			Peroneal nerve		
			Mean $\pm$ SD	t	p-value	Mean $\pm$ SD	t	p-value
≤ 15	Control	5	68.01 $\pm$ 4.00	-	-	48.02 $\pm$ 3.11	-	-
	Neuropathy	2	56.00 $\pm$ 3.89	-	-	42.13 $\pm$ 7.96	-	-
16-30	Control	10	65.73 $\pm$ 3.92	3.66	< 0.01 (HS)	47.58 $\pm$ 3.00	0.73	> 0.05 (NS)
	Neuropathy	2	52.58 $\pm$ 9.73			45.57 $\pm$ 7.54		
31-45	Control	15	65.00 $\pm$ 4.03	3.34	< 0.01 (HS)	47.65 $\pm$ 3.92	3.23	< 0.01 (HS)
	Neuropathy	14	58.55 $\pm$ 6.22			38.97 $\pm$ 9.58		
46-60	Control	30	65.75 $\pm$ 5.99	8.03	< 0.01 (HS)	47.05 $\pm$ 4.11	4.80	< 0.01 (HS)
	Neuropathy	29	49.77 $\pm$ 9.05			39.12 $\pm$ 8.02		
> 60	Control	20	65.01 $\pm$ 4.84	3.86	< 0.01 (HS)	46.08 $\pm$ 2.66	3.78	< 0.01 (HS)
	Neuropathy	23	57.07 $\pm$ 7.99			39.00 $\pm$ 8.00		

In all the age groups, the median nerve velocity was found to be significantly higher in case of controls as compared to neuropathy cases ($p < 0.01$). However, no comparison could be made in case of age group less than 15 years due to non-availability of adequate number of cases.

The peroneal nerve velocity was significantly higher in case of controls as compared to neuropathy beyond the age 31 years ($p < 0.01$). However, the difference was found to be not significant in case of age group 16-30. No comparison could be made in case of age group less than 15 years.

in 23 out of 145 individuals studied. Loss of protective sensation was seen at plantar aspect of distal phalanx of great toe and first, third and fifth metatarsal heads [8]. Reduction in amplitude with normal velocity was observed in 65% of patients with abnormal sensory nerve conduction. Twelve out of 40 patients with abnormal sensory nerve conduction had both median and sural nerves (upper and lower limbs) affected and 28 had abnormalities only in the lower limbs. Various workers [7,9] have also observed this.

Severity of nerve conduction abnormalities correlated well with clinical and histopathological severity of neuropathy [2,10]. Distally accentuated axonal degeneration has been noticed to be the salient change in diabetic neuropathy and it affects both myelinated and unmyelinated fibers [3,9]. In the 9 patients who underwent sural nerve biopsy eight patients had clinically moderate neuropathy and one patient was asymptomatic. All of them showed evidence of axonal loss, while segmental demyelination and remyelination were observed in 22.2% of patients. Statistical significance could not be accorded to the correlation of these results in view of the small number of cases. No single satisfactory treatment for any of the neuropathic syndromes has been forthcoming. Early and intensive treatment of hyperglycemia reduces the occurrence of clinical neuropathy by 60%. Once neuropathy is established, significant recovery does not occur [11]. Hence early detection of neuropathy helps in aggressive treatment. This study did not include response to treatment.

Out of 100 patients studied, 70 had clinical neuropathy. Nerve conduction velocities (motor and sensory) were abnormally reduced in diabetics, than in non-diabetics and the reduction was more in patients with clinical neuropathy. There was significant correlation with age and duration of disease. The slowing of

conduction velocities occurs much earlier and is more severe in lower limbs than in upper limbs. The main type was distal symmetrical sensory neuropathy. Pins and needles sensation and numbness were the important symptoms and tendon reflex abnormalities by newer equipment give more accurate results and has a definite role in the diagnosis of diabetic neuropathy.

REFERENCES

1. Diabetes mellitus. WHO TRS No 727. WHO, Geneva 1985:10-2.
2. Vijayan G, Singh N, Roy S, Pathak SN. Diabetic neuropathy. A clinical, electrophysiological and histological study. *Ind J Med Research* 1971;59:1843-5.
3. Martin MM. Diabetic neuropathy. A clinical study of 150 cases. *Brain* 1953;76:594-8.
4. Harati Y. Diabetes and the nervous system. In: Browlee M, King GL, eds. *Endocrinology and Metabolism Clinics of North America*. Philadelphia, WB Saunders 1966;25:325-59.
5. Donaghy M. Disorders of peripheral nerves. In: Walton J, ed. *Brain's diseases of the nervous system*. Delhi, Oxford University Press 1994:613-5.
6. Viswanathan I, Bajpai HS, Katiyar BC. Neurological complications of diabetes mellitus. *J Ind Med Association* 1976;66(8):176-9.
7. Chopra JS, Hurowitz LJ. A comparative study of peripheral nerve conduction in diabetics and on-diabetics. *Brain* 1969;92:83-6.
8. Birke JA, Rolfsen RJ. Evaluation of a self-administered sensory testing tool to identify patients at risk of diabetes related foot problems. *Diabetes Care* 1998;21:23-5.
9. Behse F, Buchthal F, Carben I. Nerve biopsy and conduction studies in diabetes mellitus. *J Neurol Neurosurg Psych* 1977;40:1072-4.
10. Malik RA. The pathology of human diabetic neuropathy. *Diabetes* 1997;46(suppl 2):S50-3.
11. The diabetes control and complications trial research group. The effect of intensive diabetic therapy on the development and progression of neuropathy. *Ann Intern Med* 1995;122:561-8.