PERIPHERAL NEUROPATHY IN TROPICAL PANCREATIC DIABETES

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Tropical pancreatic diabetes (TPD) is a form of diabetes seen in tropical countries which is secondary to chronic calcific, non-alcoholic pancreatitis. We have earlier reported on the clinical profile of this type of diabetes[7, 9, 10]. There are very few data on vascular complications in TPD[1]. We have recently shown that retinopathy, sometimes in a severe form, can occur in this condition[6]. OSUNTOKUN[8] reported the pattern of neuropathy of non-alcoholic pancreatic diabetes in Nigerians[8]. In this paper we report on peripheral neuropathy in TPD. To our knowledge this is the first report of combined electromyographic and biothesiometer studies in this form of diabetes.

PATIENTS AND METHODS

Sixteen consecutive TPD patients seen during the period 1st April 1984 to 30th November 1984 were studied. The criteria for diagnosis of TPD were those of MOHAN et al.[7] and consisted of the following:

1. diabetes mellitus;
2. history of recurrent abdominal pain from an early age;
3. presence of pancreatic calculi seen on plain X-ray of abdomen and confirmed on ultrasonography;
4. absence of alcoholism, gall stones or hyperparathyroidism.

An oral glucose tolerance test was carried out using a 75-g glucose load in those who did not exhibit unequivocal hyperglycemia. The criteria for diagnosis of diabetes were those of the WHO Expert Committee[11]. In all patients,

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pancreatitis had preceded diabetes by several years. Three patients had a family history of diabetes. Twelve patients were treated with insulin, the dose of which ranged from 20-75 U/day. Four were treated with oral hypoglycemic agents. The clinical and biochemical characteristics are given in tab. 1. Body mass index (BMI) was calculated according to the formula: weight in kg/height in $(m)^2$.

Identificaton of retinopathy was done as described earlier[6]. Proteinuria of ≥ 500 mg/day was taken to indicate nephropathy. Serum cholesterol, triglyceride and glycosylated hemoglobin estimations were carried out in all patients by previously described methods[7]. Serum C-peptide levels were assayed by the radioimmunoassay method of HEDING[4] using M1230 antiserum (Novo, Denmark). The serum samples were extracted with 30% polyethylene glycol to remove insulin antibodies and proinsulin according to the method of KUZUYA et al.[5].

Sixteen age, sex and weight matched NIDDM patients and an equal number of similarly matched healthy non-diabetic control subjects were also studied. All study subjects had normal renal function tests as assessed by normal blood urea and creatinine levels.

Neurological evaluation · The neurological evaluation was performed in all diabetic patients after control of hyperglycemia in order to eliminate the effects of uncontrolled hyperglycemia on the neurological studies.

Clinical neuropathy was defined as absence of ankle jerks and/or objective evidence of sensory impairment. Vibratory sensory threshold was measured by biothesiometer (Medasonics, CA, U.S.A.) on the great toe and ankle.

Nerve conduction studies were done by Medelac 7 Model machine at 27-29 °C room temperature. Motor conduction velocity (MCV) was measured in the right ulnar and right lateral popliteal nerve. An earth electrode was placed between stimulating and recording electrode. For stimulation of the ulnar nerve, the recording electrodes were placed over the *abductor digiti minimi* and stimulation was done at the wrist and above the elbow. For the lateral popliteal nerve, stimuli were applied at the ankle and neck of the *fibula* and the recording electrodes were placed over the *extensor digitorum*.

The distal and proximal latencies were taken, and nerve conduction velocity was calculated and expressed as m/sec.

Sensory potentials were obtained as follows.

The ring electrodes were applied over the little finger and used as stimulating electrode. The recording electrodes were placed over the ulnar nerve at the wrist. Thirty two potentials were averaged, using averaging computer. The latency to peak was measured. Peak to peak amplitude was measured.

For sural nerve potential, the reading electrode was placed behind the lateral malleolus and the stimulating electrode was placed over the sural nerve 14 cm above the malleolus. Antidromic stimulation was done and thirty two potentials were averaged.

'F' wave was obtained by the following methods: the recording electrode was placed over the *abductor digiti minimi* and *extensor digitorum brevis*. Super maximal stimulation was applied to the ulnar nerve, at the wrist and to the lateral popliteal nerve at the ankle. Six pairs of potentials were obtained and the average of these was taken.

The latency of an 'F' wave indicated the time required for the evoked action potential to ascend antidromically to anterior horn cells and time required for the resultant action potential to descend orthodromically from anterior horn cell to muscle to produce muscle action potential.

Statistical analysis. - All values are expressed as mean ± SD. The unpaired *t*-test was used for statistical analysis.

RESULTS

The clinical characteristics of the study subjects and controls are shown in tab. 1.

Peripheral neuropathy was detected clinically in 5 NIDDM and 6 TPD patients. The results of the electrophysiological studies are shown in tab. 2 and figs 1 and 2. Abnormal MCV in the lateral popliteal nerve was seen in 9 patients with TPD and 8 patients with NIDDM. Biothesiometer readings were abnormal in the lower limb in 7 TPD patients and 7 NIDDM patients. Abnormal F wave was recorded in the lower limb in one patient with TPD who had clinical neuropathy. Abnormal sensory potentials were recorded in the sural nerve in 6 TPD and 8 NIDDM patients. None had an abnormal sensory potential in the ulnar nerve.

DISCUSSION

This paper presents a study of neuropathy in patients with TPD. Occurrence of peripheral neuropathy in TPD is similar to that found in a group of matched NIDDM patients, using motor conduction velocity, sensory potentials, F wave and biothesiometry.

groups M:F	controls (n = 15) 10:5	NIDDM (n = 16) 12:4	TPD (n = 16) 13:3
age (years)	40 ± 8	47 ± 12	48 ± 8
duration of diabetes (years)	–	9.6 ± 5	10 ± 5
BMI	21 ± 2.8	20.4 ± 2	19.4 ± 2.4
plasma glucose (mmol/l)			
initial			
fasting	5.6 ± 0.6	10.3 ± 1.6	10.7 ± 1.9
post-prandial	7.9 ± 0.9	16.4 ± 2.5	17.3 ± 2.3
follow-up			
fasting	–	5.9 ± 1.0	6.1 ± 0.8
post-prandial	–	9.3 ± 0.9	9.9 ± 1.2
HbA, (%)			
initial	7.2 ± 1.0	12.6 ± 3.2	12.2 ± 2.2
time of study	–	8.7 ± 1.0	8.6 ± 1.1
serum cholesterol (mmol/l)	4.8 ± 0.3	5.2 ± 0.8	4.0 ± 0.8
serum triglycerides (mmol/l)	1.1 ± 0.9	1.2 ± 0.4	1.1 ± 0.3
clinical neuropathy	–	5/15	6/16
nephropathy	–	1/16	1/16
retinopathy	–	5/16	4/16

All values are means ± SD

Tab. 1 - Clinical characteristics of the study groups.

subjects No.	age/sex	duration of diabetes (years)	complications			BM (V)		MCV (m/sec)		F wave (msec)		sensory potentials (msec)	
			DR	Nephr.	CN	GT (7 ± 1.5)	ankle (8 ± 3)	ulnar (52 ± 7)	LP (50 ± 6)	UL (31 ± 1)	LL (32 ± 2)	ulnar (2.8 ± 0.2)	sural (3.1 ± 0.4)
1	56/M	1	–	–	+	11.5*	15.5*	52	41*	29	30	2.2	5.2*
2	38/M	12	–	–	–	10*	12*	54	45*	30	34	1.8	2.3
3	30/F	10	–	–	–	8.5	10	55	63	26	33	2.2	2.4
4	55/M	12	–	–	+	10	10	41*	43*	30	36*	–	7.8*
5	35/M	3	–	–	–	8	9	50	52	23	30	2.9	2.4
6	30/M	6/12	–	–	–	8	9	67	66	29	31	2.2	2.8
7	26/F	5	–	–	–	9	9	66	52	26	28	2	3.3
8	35/F	4	–	–	–	8	12*	61	43*	28	24	–	7.0*
9	43/M	5	+	–	+	8	14*	51	42*	–	–	2.2	4.2
10	40/M	8	–	–	+	9	9.5	58	38	30	35	2	8.0*
11	44/M	10	–	–	–	8	9	59	50	28	30	2.4	2.6
12	36/M	3	–	–	–	8	8	59	42*	30	30	–	8.2*
13	32/M	5	+	–	–	6	8	47	54	31	31	2.8	2.6
14	41/M	12	+	–	+	11*	15*	47	40*	25	25	2.8	3.9
15	33/M	5	+	+	+	18*	23*	40*	40*	30	31	2.8	2.9
16	36/M	6/12	–	–	–	11.5*	13.5*	66	43*	25	26	–	4.8*

* = abnormal values

Tab. 2 - Results of neurological evaluation in TPD. Figures in brackets = normal control values. BM = biothesiometer; DR = diabetic retinopathy; Nephr. = nephropathy; CN = clinical neuropathy; GT = great toe; LP = lateral popliteal; UL = upper limb; LL = lower limb.

We have reported that retinopathy is common in TPD patients and its prevalence is similar to that in the NIDDM patients[7]. There is only one report on peripheral neuropathy in TPD patients using electrophysiological studies. OSUNTOKUN[8] in a review of the neurology of non-alcoholic pancreatic diabetes in Nigerians noted that there was no difference in the pattern of neuropathy compared to primary forms of diabetes mellitus. In a large series of TPD described by GEEVARGHESE[2] from India, there was no mention of neuropathic complications.

All TPD patients with clinical neuropathy showed abnormal MCV and biothesiometer readings while three patients without clinical evidence of neuropathy also exhibited abnormal readings. This supports the existence of subclinical neuropathy in TPD similar to that reported in the primary form of diabetes.

TPD is an example of acquired insulin deficiency in man. The B-cell secretory defect in this disorder is variable[7]. Thus this clinical syndrome provides a valuable model for investigating the effects of hyperglycemia due to pure insulinopenia. Many biochemical aberrations arising from chronic hyperglycemia and leading to metabolic changes in nerves which interfere with their normal function have been described[3]. The two groups of diabetic patients compared in this study had different etiology and clinical features, the common feature being hyperglycemia. The TPD patients had a similar degree of hyperglycemia as the NIDDM patients as evidenced by their comparable mean HbA_1 before and after therapy. The similarity in the occurrence of neurological complications in the two groups indicates that the causation of nerve conduction

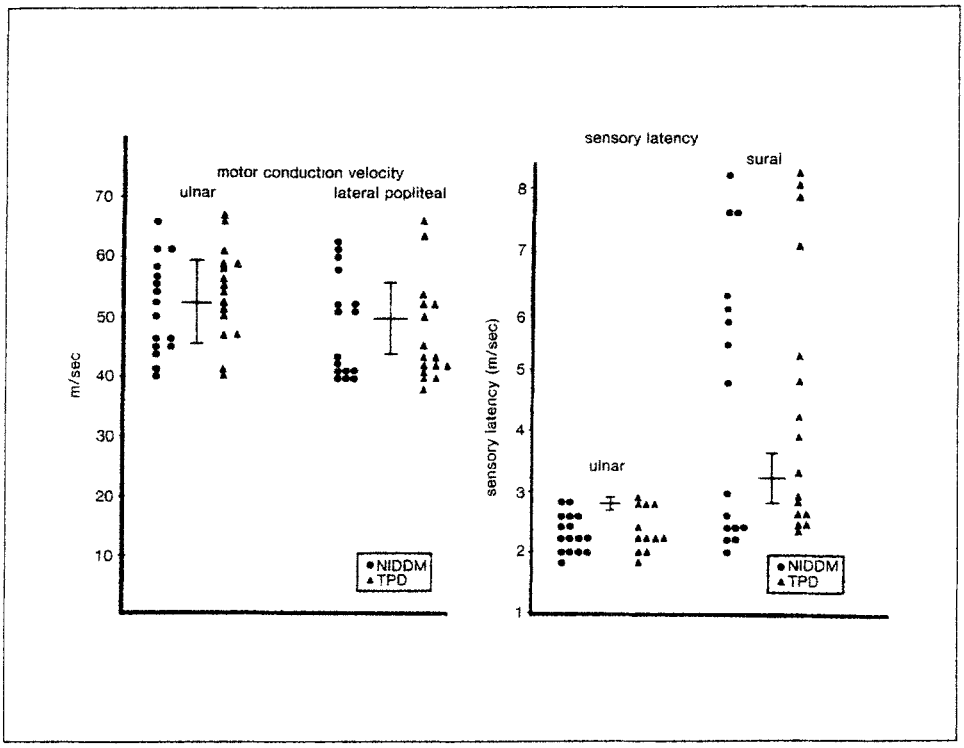

Fig. 1 - Motor conduction velocity and sensory latency in the study groups.

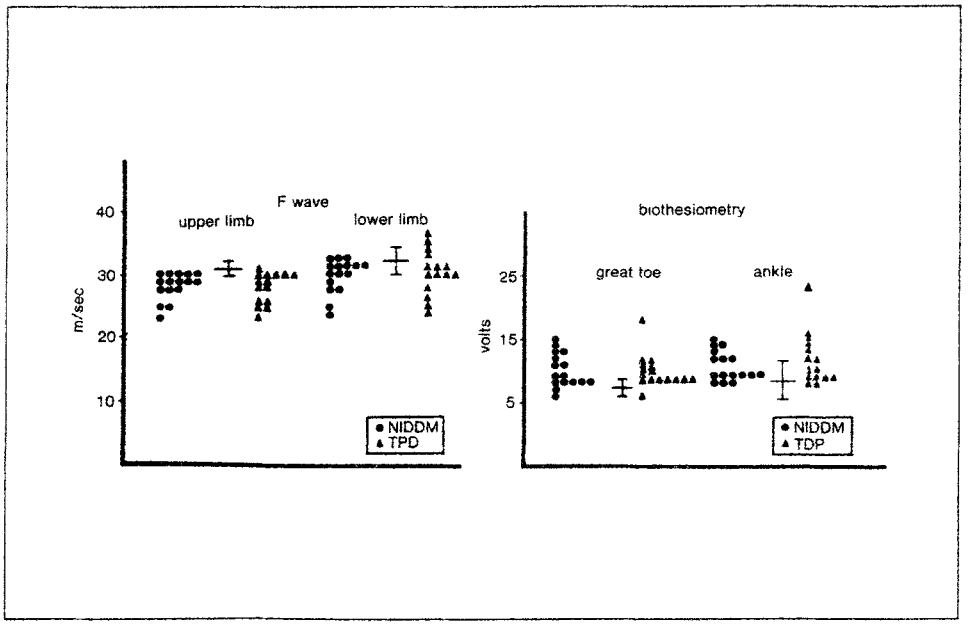

Fig. 2 - F wave and biothesiometry findings in the study groups.

defects is similar in different groups of diabetic patients, irrespective of the cause of hyperglycemia.

SUMMARY

Electrophysiological evaluation of peripheral neuropathy was done in 16 patients with tropical pancreatic diabetes (TPD) and the data compared with those of a matched group of 16 NIDDM patients. Peripheral neuropathy was present in 6 TPD and 5 NIDDM patients. Abnormal motor conduction velocity in the lateral popliteal nerve was seen in 9 TPD patients and in 8 NIDDM patients and biothesiometry was abnormal in 7 patients in each group. One TPD patient had an abnormal F wave in the lower limb. An abnormal sensory potential was recorded in the sural nerve in 6 TPD and 8 NIDDM patients. The study showed that occurrence of peripheral neuropathy in TPD was similar to that in NIDDM. Subclinical neuropathy could be detected by electromyographic recording in both groups of patients.

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