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SHORT COMMUNICATIONS

Diabetic Neuropathy – Clinical and Electrophysiological Study in Synalbumin Positive and Synalbumin Negative Subjects

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Summary. Clinical examination and nerve conduction in the median and lateral popliteal nerves were carried out in nine synalbumin positive and ten synalbumin negative subjects. There was no evidence of any abnormal neurological signs in either group and the results of the nerve conduction in the two groups showed no significant difference. — The role of an underlying hereditary error is discussed with respect to the aetiology of diabetic neuropathy.

La neuropathie diabétique. Etude clinique et électrophysiologique chez des sujets synalbumine-positifs et synalbumine-négatifs

Résumé. On a étudié le tableau clinique et la conduction nerveuse dans les nerfs médian et latéral poplité, chez neuf sujets synalbumine-positifs et dix sujets synalbumine-négatifs. On n'a trouvé de signes neurologiques anormaux dans aucun des groupes, et les résultats de l'étude de la conduction nerveuse dans les deux groupes n'a pas montré de différence significative. — Le rôle d'une tare héréditaire à la base est discutée en ce qui concerne l'étiologie de la neuropathie diabétique.

Diabetische Neuropathie — Klinische und elektrophysiologische Untersuchungen bei Synalbumin-positiven und Synalbumin-negativen Personen

Zusammenfassung. Bei der klinischen Untersuchung und der Messung der Leitgeschwindigkeit im N. medianus und N. popl. lat. von 9 Synalbumin-positiven und 10 Synalbumin-negativen Vp. fanden sich in beiden Gruppen keine abnormen neurologischen Befunde und keine signifikanten Unterschiede der Nervenleitgeschwindigkeit. — Die Bedeutung des zugrundeliegenden hereditären Defektes für die Ätiologie der diabetischen Neuropathie wird diskutiert.

Key-words: Nerve conduction, synalbumin positive, synalbumin negative, diabetic neuropathy, hereditary error.

Introduction

In recent years there has been growing speculation that diabetic neuropathy is dependent on an underlying hereditary error, like other conditions associated with diabetes, such as retinopathy, nephropathy and, angiopathy (BARTELS and RULLO, 1958; POMERZANE 1959; ARING, 1960; CALVERLY and MULDER, 1960; DOBSON and BRENNAN, 1961; ELLENBERG, 1961; 1962; HOLT, 1962). That diabetes mellitus is a hereditary disorder and the prediabetic state a definite entity is well documented (COLWELL, 1942; JACKSON and WOOLF, 1957; MATHEWS, 1958; POMERZANE, 1959; BEST, 1962).

However, a major difficulty in studying prediabetic disorders has been the lack of any means of identifying the prediabetic patient except retrospectively when diabetes has become clinically manifest or by genetic inference. Recently it has been shown that diabetics possess increased insulin antagonism in their plasma in association with the albumin fraction. Subjects with this increased antagonism have been called "synalbumin positive" and those without increased antagonism "synalbumin negative". The insulin antagonist had also been demonstrated in relatives of diabetics and the evidence suggests that it is inherited as an autosomal dominant characteristic, and that all constituted diabetics are synalbumin positive. The potential diabetic state may therefore be recognised by assaying the plasma of suspects for increased synalbumin activity (VALLANCE-OWEN and LILLEY, 1961; VALLANCE-Owen, 1966), without reference to carbohydrate-intolerance.

Material and Methods

There were nine synalbumin-positive men and women and ten synalbumin-negative men and women, all having normal oral glucose tolerance. Most of the patients were women subjects who had had unexplained foetal deaths (15 women and 4 men). The age range in the nine synalbumin-positive subjects was 21—53 years (mean 36.9 years) and in the ten synalbumin-negative subjects 26—38 years (mean 29.4 years). None of the female subjects from either group gave a history of paraesthesia or of entrapment neuropathy during their pregnancies. There was no history of entrapment neuropathy, paraesthesia or any foot deformity in the family from either group.

Albumin was extracted from fasting venous blood by the method of DEBRO, TARVER and KORNER (1957) as modified by VALLANCE-OWEN (1958). Insulin antagonism was then assessed by measuring the glucose uptake of the rat hemidiaphragm in, a) GEY and GEY (1936) buffer plus 1000 μU crystalline insulin/ml, and b) GEY and GEY buffer plus 1000 μU insulin/ml plus 1.25% albumin. The experimental procedure was as described by VALLANCE-OWEN, HURLOCK and PLEASE

(1955). Increased insulin antagonism (ie, synalbumin positivity) was present if the glucose uptake in the presence of albumin was significantly less than in the buffer.

After these two groups had been separated by the above procedure, they were examined by two of us on a 'blind' basis for any evidence of nervous system involvement. Motor and sensory nerve conduction was performed in the median and lateral popliteal nerves of all subjects. A detailed account of the method has been given elsewhere (CHOPRA, 1967; CHOPRA and HURWITZ, 1969).

Results

There was no evidence of any abnormal motor or sensory signs in the nervous system in any patient from either group. Normal tendon jerks were present in all, except one female subject aged 21 in the synalbumin-positive group, who had diminished ankle jerks.

diabetics with and without objective neuropathy (LAWRENCE and LOCKE, 1961; MULDER, LAMBERT, BASTRON and SPRAGUE, 1961; SKILLMAN, JOHNSON, HAMWI and DRISKILL, 1961; GILLIATT and WILLISON, 1962; MAYER, 1963; CHOPRA, 1967; CHOPRA and HURWITZ, 1968; 1969). Peripheral nerve conduction in such patients was found to be slower than in the normal subjects. Indeed, structural lesions of the peripheral nerves in association with abnormal electrophysiological findings have been demonstrated by histopathological studies in patients with and without neuropathy (THOMAS and LASCELLES, 1965; 1966; CHOPRA, 1967; CHOPRA, HURWITZ and MONTGOMERY, 1969).

Although electrophysiological tests may reveal abnormality in peripheral nerves before there are any clinical signs, the present study has not demonstrated any significant difference between the synalbumin-positive and synalbumin-negative patients. This may well

Table 1. *Median nerve*

Group	Motor nerve conduction			Sensory nerve conduction			
	Term. lat. ms	Conduction velocity m/s Elbow-wrist	Axilla-elbow	Digit-wrist Conduction vel. m/s	Amp. μV	Wrist-elbow Conduction vel. m/s	Amp.μV
Synalbumin positive	3.9±0.2	54.4±1.9	61.8±2.9	42.6±1.9	22.5±3.5	62.8±2.8	7.2±2.2
Synalbumin negative	3.6±0.2	52.6±1.8	64.3±2.8	45.2±1.8	28.2±3.3	60.5±2.6	7.9±2.1
Variance ratio	$P>0.2$	$P>0.2$	$P>0.2$	$P>0.2$	$P>0.2$	$P>0.2$	$P>0.2$

Term. lat. Terminal latency — wrist to abductor pollicis brevis
ms Millisecond m/s Metres per second
Amp. Amplitude μV microvolts.

Table 2. *Lateral popliteal nerve*

Group	Motor nerve conduction		Sensory nerve conduction	
	Term. lat. ms	Conduction velocity m/s Knee-ankle	Conduction velocity m/s Ankle-knee	Amp.μV
Synalbumin positive	5.3±0.2	52.5±2.7	50.3±1.6	7.0±1.4
Synalbumin negative	5.1±0.2	50.8±2.2	49.1±1.4	8.7±1.3
Variance ratio	$P>0.2$	$P>0.2$	$P>0.2$	$P>0.2$

Term. lat. Terminal latency ankle-extensor digitorum brevis
ms Millisecond m/s Metres per second
Amp. Amplitude μV Microvolts.

The mean values of motor and sensory nerve conduction in the median and lateral popliteal nerves are given in Tables 1 and 2. The analysis of variance between the two groups showed no significant difference in all the 11 parameters tested in each patient.

Discussion

Several authors have studied peripheral nerve conduction in diabetes mellitus, and have concluded that there is evidence of peripheral nerve involvement in suggest that the peripheral nerves are only affected when there is carbohydrate intolerance. Peripheral neuropathy has been reported as the first presenting symptom of diabetes (MARTIN, 1953), but it is very difficult to know how long such patients had been suffering from a mild asymptomatic diabetic state. However, in two patients with peripheral neuropathy reported by RUDY and EPSTEIN (1945), the diagnosis of diabetes mellitus was confirmed only some months after the onset of the neuropathy. Carbohydrate into-

lerance may be associated with a change in nerve metabolism, and so neuropathy in diabetics although occurring with carbohydrate intolerance need not be directly related to the level of hyperglycaemia. The findings in this study support those carried out by LAWRENCE and LOCKE (1961), who did not find any difference in nerve conduction between relatives of diabetics and control subjects.

There are no reports in the literature of pathological changes in the peripheral nerves of prediabetics as there is in diabetics without clinical neuropathy. However, nodular glomerulosclerosis in unsuspected or mild diabetics (GREENFIELD, BLACKWOOD, MCNENEMY, MAYER and NORMAN, 1958; ELLENBERG, 1962) and evidence of renal disease in the prediabetic state are documented (DAYSOG, DOBSON and BRENNAN, 1961).

It is concluded from a clinical and electrophysiological study that there is no evidence of involvement of peripheral nerves in subjects who are synalbumin positive. The peripheral nerves become particularly vulnerable with the onset of carbohydrate intolerance irrespective of the degree of hyperglycaemia. Although this study is against an herediatry error in the aetiology of diabetic neuropathy, it would not exclude a deviation from normal in metabolism in the prediabetic patient with increased susceptibility of the nerve when diabetes becomes overt. More sensitive biochemical and electrophysiological tests of peripheral nerve functions may help resolve this problem.

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