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Complaints of neuropathy related to the clinical and neurophysiological assessment of nerve function in patients with diabetes mellitus

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Abstract

To determine the value of a detailed evaluation of neuropathic sensory complaints in assessing diabetic polyneuropathy, a questionnaire listing different sensory symptoms was compared with a clinical and neurophysiological examination of the peripheral nerves. Thirty-seven insulin dependent and thirty-one non-insulin dependent diabetic patients who were consecutively referred because of suspected polyneuropathy were investigated. In all patients both clinical and neurophysiological examination confirmed the diagnosis of polyneuropathy. Only the scores of the clinical examination were significantly correlated with the scores of the sensory symptoms ($r = 0.31$, $P < 0.01$). Using a factor analysis, a dimension of complaints of sensory alteration could be distinguished from a dimension of complaints of neuropathic pain (alpha coefficients 0.88 and 0.86, respectively). Tingling sensations turned out to be an expression of the dimension of complaints of sensory alteration. The scores of clinical and neurophysiological examinations were only significantly correlated with the dimension of sensory alteration ($r = 0.38$, $P < 0.002$; $r = 0.37$, $P < 0.02$, respectively). We conclude that only symptoms of numbness and tingling sensations in hand and feet are associated with objectively assessed diabetic polyneuropathy.

Keywords: Diabetic polyneuropathy; Neuropathic sensory complaints; Neuropathic pain; Sensory alteration

1. Introduction

Neuropathy is a common long-term complication of diabetes mellitus. The course of diabetic neuropathy can be asymptomatic but can also lead to severe complaints [1]. In the variety of disturbances accompanying diabetic polyneuropathy,

complaints related to the autonomic nervous system are often mild and non-specific [2,3]. However, sensory complaints which frequently accompany diabetic polyneuropathy can be very distressful [4]. Several terms have been used to describe neuropathic sensory disturbances [5–8]. Descriptions such as burning, stabbing, lancinating and toothache pain and tingling sensations are used in addition to contact hyperaesthesia, dysaesthesia and numbness. Usually, positive sensory symptoms (pain and tingling sensations) are

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discriminated from symptoms of sensory loss (numbness) [7,9,10].

Controversy exists about the relationships between neuropathic symptoms and disturbances found in clinical and neurophysiological examination. Dyck et al. found an association between complaints of diabetic polyneuropathy, abnormalities of the clinical examination and abnormalities of nerve conduction [11]. This association was not confirmed in studies of other investigators [12,13].

The aim of this study was to investigate the relationship between a detailed evaluation of neuropathic sensory complaints with objectively assessed nerve functions. For this purpose we used a questionnaire in which different neuropathic sensory symptoms were described. During the development of this questionnaire, the Diabetes Symptom Checklist-type 2 (DSC-type 2), there was some evidence for the existence of two dimensions in the variety of neuropathic sensory symptoms [14]. We investigated if this division could be confirmed in patients with diabetic polyneuropathy. Moreover, we studied the association between different neuropathic sensory complaints and the clinical and neurophysiological examinations. In this manner we tried to estimate the value of different sensory symptoms for the assessment of diabetic polyneuropathy.

2. Materials and methods

2.1. Patients

A total of 68 patients participated in the study. All patients were consecutively referred to the neurologist with suspected polyneuropathy. All eligible patients consented to participate in the study. Patients were excluded from the study when neuropathy other than of diabetic origin was suspected and when there was evidence of peripheral vascular disease.

2.2. Clinical and neurophysiological assessment of severity of polyneuropathy

All patients underwent a clinical and a neurophysiological examination. The outcome of both forms of examination was scored as a measure of the severity of polyneuropathy.

The clinical examination included the assessment of sensory functions, muscle strength of the feet and ankle reflexes. Pinprick sense, light touch sense (cotton wool), vibration sense (128 Hz tuning fork) and position sense were scored separately as 0: normal, 2: impaired, 4: absent. Moreover, light touch sense was related to the anatomic level below which it was impaired and scored as 0: normal, 1: toe, 2: mid-foot, 3: ankle, 4: mid-calf and 5: knee. Ankle jerks were scored as 0: normal, 2: impaired and 4: absent. Strength of extensor hallucis longus and gastrocnemius muscles were scored as 0: normal, 2: impaired and 4: absent. The total score of the clinical examination could vary between 0 and 33. A total score of 0 was graded as no polyneuropathy, 1–9 as mild, 10–18 as moderate and 19–33 as severe polyneuropathy.

The neurophysiological examination of the peripheral nerves included the assessment of sensory and motor nerve conduction velocities, amplitudes of sensory and motor nerve action potentials and the Hoffmann reflex of the soleus muscle. Conduction velocities and amplitudes of action potentials were scored as 0: within normal range (mean of normal value $\pm$ 2 S.D.), 1: 10% or less below lower limit of normal range and 2: more than 10% below the lower limit of normal range. The H-M interval of the Hoffmann reflex was scored as 0: within normal range (mean of normal value $\pm$ 2 S.D.), 1: 10% or less above the upper limit of the normal range and 2: more than 10% above the upper limit of the normal range. The HM ratio was scored as 0, 1 or 2 according to the method mentioned for the scoring of conduction velocities and amplitudes. The total score of the neurophysiological examination could vary between 0 and 20. A total score of 0 was graded as no polyneuropathy, 1–8 as mild, 9–15 as moderate and 16–20 as severe polyneuropathy. The way these examinations were carried out and the manner of scoring the severity of disturbances were described in detail in an earlier report [12].

2.3. Assessment of severity of symptoms

For measuring the severity of neuropathic sensory complaints we used the DSC-type 2 [14]. This instrument consists of 34 questions about diabetes related symptoms. Ten of these questions concern

Fig. 1. Correlation between the scores of neuropathic sensory complaints and the scores of the clinical examination in 68 diabetic patients. The line represents the regression line.

omplaints which are related to sensory polyneuropathy (Table 1).

In this checklist the patients were asked how often the complaints occurred in the past month. The possible answers were scored as 0: no, not at all; 1: yes, once or more times per month; 2: yes, once or more times per week; 3: yes, daily. The sum of the scores of the neuropathic sensory complaints was counted as the measure of severity and varied between 0 (no complaints) and 30 (severe complaints).

2.4. Statistical analysis

Pearson's correlation coefficient was used to measure the agreement between the severity of neuropathic sensory complaints and the outcome of the clinical and neurophysiological examinations of the peripheral nerves.

Principal components factor analysis with varimax rotation was used to study the structure of responses to the neuropathic sensory complaints section of the DSC-type 2 for the population studied. Reliability was assessed using Cronbach's alpha coefficient of internal consistency.

3. Results

Sixty-eight diabetic patients, (37 type 1, 31 type 2; 36 males, 32 females) participated in the study. Their mean age $\pm$ S.D. was 51.7 ± 8.5 years, the mean duration of diabetes was 21.3 ± 11.2 years. Diabetic polyneuropathy was diagnosed in all patients according to both the clinical and the neurophysiological examination. The individual total scores of the clinical examination of the patients varied from 2 to 25 (mean $\pm$ S.D., 13.0 ± 6.11). The total scores of the neurophysiological examination varied from 2 to 19 (mean $\pm$ S.D., 10.0 ± 4.0). The individual total scores of the neuropathic sensory complaints section of the DSC-type 2 varied from 0 to 10 (mean $\pm$ S.D., 1.9 ± 2.7).

Table 1
Factor analysis of neuropathic sensory complaints in 68 diabetic patients

	Factor loadings	
	Factor 1, (Sensory alteration dimension)	Factor 2 (Neuropathic pain dimension)
1. Tingling or prickling in hands or fingers	0.829	—
2. Numbness of the hands	0.813	—
3. Queer feeling in legs or feet when touching	0.812	—
4. Tingling or prickling in legs or feet	0.691	0.548
5. Numbness of the feet	0.689	0.344
6. Tingling in the limbs at night	0.627	0.578
7. Shooting pains in the legs	0.309	0.847
8. Burning pain in the legs during the day	—	0.823
9. Aching calves when walking	—	0.814
10. Burning pain in the calves at night	—	0.766

The magnitude of factor loading indicates the degree of relationship to each factor; loadings below 0.3 are not shown.

Fig. 2. Correlation between the dimension of complaints of sensory alteration and the scores of the clinical examination in 68 diabetic patients. The line represents the regression line.

The scores of the clinical examination were significantly correlated with the scores of the neuropathic sensory complaints (correlation coefficient 0.31, $P < 0.01$) (Fig. 1). There was no significant correlation between the scores of the neurophysiological examination and the scores of the neuropathic sensory complaints (correlation coefficient 0.29, $P > 0.05$).

Responses to the ten questions of the DSC-type 2 concerning complaints of sensory polyneuropathy were factor analyzed. The analysis produced two factors (dimensions) accounting for a total of

Fig. 3. Correlation between the dimension of complaints of sensory alteration and the scores of the neurophysiological examination in 68 diabetic patients. The line represents the regression line.

69.4% of the variance (Table 1). Loading for both dimensions ranged between 0.83 and 0.63 and 0.85 and 0.77, respectively. Dimension 1 (items 1–6) appeared to represent complaints of sensory alteration, while dimension 2 (items 7–10) appeared to represent complaints of neuropathic pain.

Thirty-eight of the patients investigated had symptoms of both sensory alteration and neuropathic pain (scores > 0 on dimensions 1 and 2). A group of 20 patients had only complaints of sensory alteration (score > 0 on dimension 1 and 0 on dimension 2); no patients had only complaints of neuropathic pain (score > 0 on dimension 2 and 0 on dimension 1) and 10 patients had no neuropathic sensory complaints (score 0 on both dimensions). The individual scores of both the clinical and the neurophysiological examinations were compared with the total scores of the items representing the two dimensions of the neuropathic sensory symptoms section of the DSC-type 2 in all patients. Both clinical and neurophysiological examinations showed a significant correlation with the dimension complaints of sensory alteration. Correlation coefficients were 0.38, $P = 0.002$ and 0.37, $P = 0.02$, respectively (Figs. 2 and 3). Clinical and neurophysiological examinations were not related to the dimension neuropathic pain (correlation coefficients 0.08 and 0.04, respectively).

4. Discussion

The clinical manifestations of diabetic neuropathy vary considerably. The most common manifestation is the mixed sensory-motor-autonomic polyneuropathy that predominantly involves sensory functions [1]. Historically, sensory polyneuropathy is thought to be subdivided into two types. These are the 'pseudotabetic' type, which is manifested by painless, distal, sensory disturbances and impaired balance and the type in which disabling sensory symptoms (spontaneous pain and tingling sensations) are common [10]. Previous investigations indicated that pain in diabetic polyneuropathy might be caused by small fibre damage and painless sensory loss by large fibre damage [1,6,7,10,16,17]. However, in more recent studies it was shown that the severity of sen-

sory complaints was neither correlated with the extent of sensory disturbances found in clinical and neurophysiological examinations, nor with the extent and type of fibre involvement found in nerve biopsy specimens [12,13].

Only Dyck et al. showed that symptoms of polyneuropathy were significantly associated with scored neurological abnormality according to the Neurological Disability Score [11]. However, in the mentioned studies sensory symptoms were not described in detail and no division was made between different individual complaints [11–13].

In the present study a detailed questionnaire was used, which was originally developed for use in type 2 diabetic patients. We made no distinction between type 1 and type 2 diabetic patients, because polyneuropathy appears to be identical in both groups of patients [18].

Our results show that sensory complaints are significantly correlated with the results of the clinical examination and not with the results of the neurophysiological examination. In this study the existence of two separate dimensions of neuropathic symptoms, neuropathic pain and sensory alteration, among the manifestations of distal symmetrical polyneuropathy was confirmed. Tingling sensations turned out to be an expression of the dimension sensory alteration and not of the dimension neuropathic pain. This is interesting because, according to previous studies, pain and tingling sensations should be considered both as 'positive neuropathic symptoms' [6,10,11]. Our data show that in understanding the pathophysiology of sensory symptoms accompanying diabetic polyneuropathy, pain and tingling sensations have to be considered as part of two different dimensions of complaints.

Our study also points out that, in contrast to complaints of neuropathic pain, only complaints of sensory alteration are related to both the scored clinical and neurophysiological examinations. This result may implicate that complaints of numbness and tingling sensations in hands and feet are more important than complaints of pain in assessing diabetic polyneuropathy and in measuring the severity of the disease. Asking for complaints of sensory alteration appears to be a useful addition to complete the clinical assessment of diabetic

polyneuropathy and may, therefore, be helpful in predicting the patient's risk status for foot ulceration.

We conclude that the sensory neuropathy items of the DSC-type 2 are more useful than the symptom scoring systems that we and other investigators used in previous studies [11–13]. In future studies we will investigate whether the DSC-type 2 could also be used in following the course of diabetic polyneuropathy and in assessing the effects of treatment.

Neuropathic sensory complaints consist of two different dimensions, neuropathic pain and complaints of sensory alteration. In contrast to neuropathic pain, complaints of sensory alteration are correlated to the severity of polyneuropathy as measured clinically and neurophysiologically. Furthermore, tingling sensations are part of the sensory alteration dimension and should therefore be considered separately from neuropathic pain in the assessment of diabetic polyneuropathy.

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