Painful Neuropathy and Foot Ulceration in Diabetic Patients

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OBJECTIVE — To examine the prevalence of painful symptoms in neuropathic patients with or without foot ulceration. It has been suggested that there are two clinical presentations of sensory diabetic neuropathy with little overlap: painful (acute or chronic) and painless with recurrent foot ulceration.

RESEARCH DESIGN AND METHODS — We examined three groups of diabetic patients matched for age and duration of diabetes—24 without neuropathy on clinical grounds (mean age 56.1 yr [range 38–76 yr], diabetes duration 12.6 yr [0.4–40 yr]), 30 with neuropathy (mean age 55.3 yr [range 21–73 yr], diabetes duration 17.3 yr [range 0.2–61 yr]), and 40 with neuropathic foot ulceration (mean age 58.1 yr [range 41–72 yr], diabetes duration 18.5 yr [range 1–46 yr])—and compared them with 20 healthy subjects (mean age 50 yr [range 37–69 yr]). For evaluation of neuropathy, the neuropathy sympton score, neuropathy disability score, and vibration perception threshold were measured.

RESULTS — No difference existed between the neuropathic and foot ulcer groups in the neuropathy symptom score (4.2 ± 3.9 [mean ± SD] vs. 2.5 ± 2.1, NS) and neuropathy disability score (15.1 ± 5.7 vs. 16.8 ± 6.1, NS), but the vibration perception threshold was lower in the neuropathic group (30.1 ± 13.4 vs. 40.5 ± 13.8 V, $P < 0.001$). Painful symptoms (neuropathy symptom score > 3), either in the past or during the time the study was conducted, had been experienced by none of the control subjects, 7 (29%) of the nonneuropathic group, 18 (60%) of the neuropathic group, and 17 (43%) of the foot ulcer group (NS for the last two groups), and were present at the time of examination in 13 (43%) of the neuropathic group and in 13 (33%) of the foot ulcer group (NS in all groups). Duration of symptoms was <12 mo in 12 (40%) neuropathic and 15 (38%) foot ulcer patients (NS).

CONCLUSIONS — We conclude that painful symptoms are frequent in diabetic neuropathy, irrespective of the presence or absence of foot ulceration and that these symptoms can occur at any stage of the disease. These results suggest that there is a spectrum of neuropathic syndromes from the painful to the patients with foot ulceration, and that much overlap exists.

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RECEIVED FOR PUBLICATION 19 NOVEMBER 1992 AND ACCEPTED IN REVISED FORM 15 APRIL 1993.

NSS, NEUROPATHY SYMPTOM SCORE; NDS, NEUROPATHY DISABILITY SCORE; VPT, VIBRATION PERCEPTION THRESHOLD; TYPE I DIABETES, INSULIN-DEPENDENT DIABETES MELLITUS; TYPE II DIABETES, NON-INSULIN-DEPENDENT DIABETES MELLITUS; API, ANKLE PRESSURE INDEX.

Painful symptoms such as paresthesiae, lancinating or aching pain, and/or burning sensation in the feet with a typical nocturnal exacerbation are common in diabetic neuropathy (1). Etiopathogenesis and natural history of painful diabetic neuropathy are not well established (2). It has been suggested that painful and painless diabetic neuropathy are two separate clinical conditions with little overlap (3,4). According to this suggestion, patients with painful neuropathy do not usually develop foot ulcers, whereas in patients with recurrent foot ulceration painful symptoms are rare. The aim of this study is to examine the prevalence of painful symptoms, either past or present, in diabetic patients with and without foot ulceration.

RESEARCH DESIGN AND METHODS

We studied three groups of patients with type I or type II diabetes and one group of healthy subjects. All diabetic groups were matched for age and known duration of diabetes. The first group included 24 diabetic patients (15 men, 6 type I) without neuropathy, according to the criteria described. Mean age was 56.1 yr (range 38–76 yr), and mean duration of diabetes was 12.6 yr (range 0.4–40 yr). The second group included 30 neuropathic diabetic patients (23 men, 13 type I). Mean age was 55.3 yr (range 21–73 yr), and mean duration of diabetes was 17.3 yr (range 0.2–61 yr). The third group included 40 patients with neuropathic foot ulceration (30 men, 14 type I). Mean age was 58.1 yr (range 41–72 yr), and mean duration of diabetes was 18.5 yr (range 1–46 yr). The nonneuropathic and neuropathic patients were randomly selected from the diabetes outpatient clinic, whereas the foot ulcer patients were randomly selected from the diabetic foot clinic where patients with active foot ulcers receive treatment. Two patients from the neuropathic group and one with a foot ulcer were treated with tricyclic antidepres-

Table 1—*Clinical characteristics of studied groups*

	Study groups			
	Control	Nonneuropathic	Neuropathic	Foot ulcer
n	20	24	30	40
Age (yr)	50.0 (37–69)*†	56.1 (38–76)	55.3 (21–73)*	58.1 (41–72)†
Diabetes duration (yr)	—	12.6 (0.4–40)	17.3 (0.2–61)	18.5 (1–46)
API	1.4 ± 1.1*	0.9 ± 0.4*	1.1 ± 0.3	1.1 ± 0.3

Data are means ± SD (range) and means ± SD for API.
*P<0.05.
†P<0.01

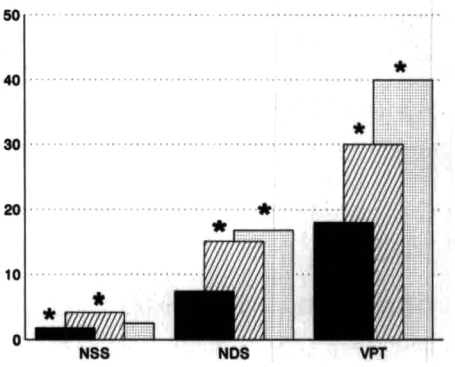

Figure 1—*Results of NSS, NDS, and VPT in the diabetic groups. (■), Nonneuropathic group; (▨), neuropathic group; (▩), foot ulcer group. *P < 0.05.*

sants for painful neuropathy. The control group included 20 healthy nondiabetic subjects (16 men), with a mean age of 50.0 yr (range 37–69 yr). Clinical details of the groups studied are shown in Table 1.

Painful symptoms of neuropathy were assessed using a modified NSS based on the original one proposed by Dyck (5). More specifically, the patients were asked if they had experienced at any time in the past or during the time the study was conducted the following symptoms: pins and needles, abnormal cold or hot sensations in their feet, lancinating or aching pain, burning pain of the feet (causalgia), and/or irritation in their feet and legs by the bedclothes at night (paresthesiae). The patients were also asked if the duration of symptoms was > or <1 yr. Each symptom was scored as the following: *1*) unpleasant but not affecting work or recreational activities; 2) reducing ability for work or recreational activities; 3) incapacitating—disabled for work or recreational activities.

For the first five symptoms, 1 extra point was added if nocturnal exacerbation was present (maximum score of 23 points). The NSS was considered abnormal if it was ≥3 points. When equal to 3 points, it was considered abnormal only if more than one symptom was present in this particular patient.

The NDS was used to quantify the severity of diabetic neuropathy on clinical examination as has been described previously (6). In summary, the sensations of pain, touch, cold, and vibration were tested in both legs of all patients and were scored according to the level up to which the sensation was impaired. An NDS >5 (maximum 28) was considered abnormal.

The VPT was measured at the great toe of the dominant side of each patient using a biothesiometer (Biomedical Instruments, Newbury, OH). The age-related upper normal limits were derived from previously published data (6). Peripheral neuropathy was diagnosed when at least two of the quantitative measurements (i.e., NSS, NDS, and VPT) were abnormal.

API was calculated with the help of a hand-held doppler apparatus. Patients had API measurements taken in both legs. The lowest of the two measurements was entered for the analysis. The study was explained to all patients and was approved by the Central Manchester Health Authority Ethical Committee. Nonparametric statistical analysis with the Mann-Whitney *U* test was performed using the Minitab statistical software (Minitab, State College, PA).

RESULTS — The mean NSS was similar in the neuropathic (4.2 ± 3.9) and foot ulcer groups (2.5 ± 2.1), but was higher in the neuropathic group when compared with the nonneuropathic group (1.8 ± 2.3, $P < 0.05$). No difference existed between the nonneuropathic and the foot ulcer groups (Fig. 1). None of the patients in the control group complained of painful symptoms, either in the present or in the past, and therefore the mean NSS was 0.

Painful symptoms (NSS >3), at any time, either past or present, had been experienced by 7 (29%) patients in the nonneuropathic group, 18 (60%) in the neuropathic group, and 17 (43%) in the foot ulcer group (NS between the last two groups). No statistical difference existed between the foot ulcer group and the nonneuropathic and neuropathic groups, but a significant difference existed between the last two groups ($P < 0.05$, Fig. 2). Symptoms had been present for >12 mo in 4 (17%) nonneuropathic, 12 (40%) neuropathic, and 15 (38%) foot ulcer patients (NS for all groups). At the time of examination painful symptoms were present in 5 (21%) patients in the nonneuropathic group, 13 (43%) in the neuropathic group, and 13 (33%) in the foot ulcer group (NS for all groups). Two patients with painful symptoms, one of recent onset and one of long duration (>10 yr), also had Charcot arthropathy with gross deformity of their feet.

The NDS was lower in the nonneuropathic group (7.4 ± 6.4) when it was compared with the neuropathic (15.1 ± 5.7) and foot ulcer group (16.8 ± 6.1), but no difference existed between the last two groups. The VPT

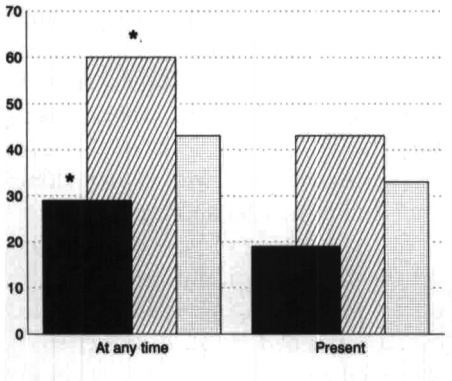

Figure 2—*Prevalence of painful symptoms either at any time or currently present in the diabetic groups. No difference was found between the neuropathic and foot ulcer groups. (■), Nonneuropathic group; (▨), neuropathic group; (▩), foot ulcer group.* *P < *0.05.*

was significantly higher in the foot ulcer group (40.5 ± 13.8 V) compared with the neuropathic (30.1 ± 13.4, $P < 0.001$), nonneuropathic (18.5 ± 12.0, $P < 0.0001$), and control (11.8 ± 8.2, $P < 0.0001$) groups. The VPT in the neuropathic group was also higher compared with the nonneuropathic ($P < 0.002$) and control ($P < 0.0001$) groups, whereas it was higher in the nonneuropathic group when compared with the control group ($P < 0.05$).

No difference was found in the API among the diabetic groups. API was lower in the nonneuropathic group when compared with the control group, but no difference existed between the control, neuropathic, and foot ulcer groups (Table 1). API was >0.60 in all subjects except in 2 patients with a foot ulcer, both asymptomatic, in whom it was 0.40.

CONCLUSIONS— In this study we have shown that painful symptoms can be present in diabetic patients irrespective of the existence of foot ulceration. A similar percentage of neuropathic patients with and without foot ulceration complained of painful symptoms of comparable severity and duration. These results confirm our clinical experience that painful symptoms can be present at any stage of diabetic neuropathy, from subclinical to very late neuropathy even with severe Charcot arthropathy and foot ulceration.

Recent studies that have examined the differences between painful neuropathy and painless neuropathy with recurrent foot ulceration have shown that, in the former group, there is a significant uniform dysfunction of small fibers and a wide range of large fiber abnormalities, whereas in the latter group the main characteristic is severe dysfunction of both large and small fibers (3,4). These findings led to the hypothesis that painful and painless neuropathy are two distinct clinical syndromes with minimal overlap. Our results cannot support this hypothesis. Painful symptoms were similarly present in patients with and without foot ulceration, suggesting that painless and painful neuropathy represent extreme forms of the same syndrome. Therefore, the presence or absence of symptoms cannot predict foot ulceration, and the painful-painless foot at risk of ulceration, as described by Ward (7), is often observed in diabetic neuropathic patients. However, the VPT was higher in the foot ulcer group and, as recent studies have shown, it can predict foot ulceration (8).

Peripheral vascular disease can also cause pain in the lower limbs, but the different clinical presentation, namely pain induced by exercise and relieved by resting the leg and the absence of pain, makes the confusion with the neuropathic pain unlikely. In this study the API was similar in the neuropathic and foot ulcer groups. No electrophysiological measurements were used for the diagnosis and quantification of diabetic neuropathy, but we believe that clinical examination and quantitative sensory testing are satisfactory in evaluating painful symptoms of diabetic neuropathy in patients with or without foot ulceration. Although a statistical difference was observed in the age of the control group, we do not think that this difference was of any significant clinical importance. Finally, the fact that 3 patients were on medication for the painful symptoms does not seem to have influenced the results of this study.

In summary, we have shown that positive symptoms are frequent in diabetic neuropathy, irrespective of the presence or absence of foot ulceration, and these symptoms can occur at any stage of the disease. Results suggest that there is a spectrum of neuropathic syndromes from the painful to the patients with foot ulceration, and that much overlap exists.

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