Polyneuropathy is inadequately treated despite increasing symptom intensity in individuals with and without diabetes (PROTECT follow-up study)

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At a glance:

- 2.5 years after baseline examination 122 and 85 participants with and without diabetes, respectively, completed a questionnaire on the course of distal symmetric polyneuropathy (DSPN) and its management.
- In half of the follow-up participants, the intensity of neuropathic symptoms increased (paresthesia (49%) and/or numbness in the feet (48%)).
- More than one third of subjects with neuropathic symptoms at follow-up, did not receive any pharmacotherapy: 32.7% of type 2 diabetes patients and 40% of patients with no diabetes, respectively.

Introduction & Background

About one third of diabetic patients suffer from DSPN. DSPN is often undiagnosed and undertreated in clinical practice, despite its enormous clinical impact. It is defined as the presence of symptoms and/or signs of peripheral nerve dysfunction in patients with diabetes after other causes have been ruled out. The PROTECT study reported that painful and painless DSPN remained undetected in 57% and 82% of type 2 diabetes patients, respectively. This follow-up study aimed to collect information on the further course of the disease and its management after 2.5 years.

Materials & Methods

In the PROTECT study, the feet of 1850 subjects with or without diabetes were examined. DSPN was present if pressure, temperature and/or vibration perception were abnormal. The present follow-up study was conducted 2.5 ± 0.7 years after the baseline examination using a standardized

questionnaire, in which 85 subjects without a history of diabetes and 119 type 2 diabetes patients participated.

Respondents were asked, amongst other things, whether they had non-painful neuropathic symptoms such as tingling or numbness and painful neuropathic symptoms such as burning or pain, and if these symptoms were stronger, weaker or unchanged compared to baseline. Also, respondents had to tick a box if they received any medication against nerve damage (neuropathy) or complaints in the feet (tingling, burning, pain and/or numbness). The following answer options were available: acetylsalicylic acid, ibuprofen, diclofenac, paracetamol, metamizol, pregabalin, gabapentin, other anti-epileptics (such as carbamazepine), duloxetine, tricyclic antidepressants (such as amitriptyline), weak opioids (tramadol, tilidine), strong opioids (tapentadol, oxycodone, fentanyl), a-lipoic acid, benfotiamine, vitamin B complex, other preparations, capsaicin cream or patch, electrical therapy, acupuncture and miscellaneous.

Results

Compared to the group without diabetes, in the group of patients with type 2 diabetes more men than women were included, respondents were older and had higher body mass index and weight ($P < 0.05$). Moreover, type 2 diabetes patients were more likely to have an DSPN treatment accompanied by a doctor, more likely to have a daily foot inspection and more likely to have their feet examined by a physician ($P < 0.05$). According to Table 1 the percentage of respondents with paresthesias and/or numbness in the feet did not change from baseline to follow up. Moreover, burning and numbness decreased in the group without diabetes ($P < 0.05$) but not in patients with type 2 diabetes. Majority of the respondents reported that neuropathic symptoms became more severe (48-61%). In addition, 26-54% of the respondents who had no neuropathic symptoms at baseline, reported that they had developed symptoms at follow-up. None of the respondents reported an improvement in burning or pain, while 2-3% reported less paresthesia and/or numbness at follow-up (see Table 1).

About 33 and 40% of the respondents with type 2 diabetes and without diabetes, respectively, reporting neuropathic symptoms did not receive any pharmacotherapy. Diabetes type 2 patients most often received α2δ-ligands, miscellaneous treatments, vitamin B complex and benfotiamine, and participants without diabetes most often received vitamin B complex, non-steroidal anti-inflammatory drugs (NSAID) and α2δ-ligands. Type 2 diabetes patients and the group without diabetes reported using WHO step 1 analgesics (except acetylsalicylic acid) in 17.4% and 17.1% of cases, respectively, and opioids 7.2% and 12.2% of cases, respectively.

Table 1 | Respondents' reporting of neuropathic symptoms in the feet at baseline and follow up in percent.

	No diabetes (n = 85)		Type 2 diabetes (n = 119)	
	Baseline (%)	Follow up (%)	Baseline (%)	Follow up (%)
Paresthesia/ numbness	83.5	75.3	78.2	82.4
Stronger	–	56.3	–	51.5
Unchanged	–	39.1	–	40.4
Wealer	–	3.1	–	20
Resolved	–	17.2	–	9.1
Newly developed	–	28.6	–	53.8
Burning/pain	79.8	64.3*	68.1	60.5
Stronger	–	48.4	–	53.7
Unchanged	–	46.8	–	45.1
Wealer	–	0	–	0
Resolved	–	22.6	–	14.6
Newly developed	–	35.3	–	26.3

*P < 0.05 versus baseline.

Discussion & Conclusions

The intensity of neuropathic symptoms in the feet increased in 2.5 years in about half of the respondents. Despite this, more than one-third did not receive any pharmacotherapy for their symptoms. In addition, few respondents were treated with NSAID which are not recommended for neuropathic pain by guidelines. In summary, results indicate inadequate care, poor treatment adherence or limited effectiveness of treatments in patients with DSPN. Therefore, future educational programs, for diabetes patients and physicians, as well as following an evidence-based guideline-recommended approach should close the gaps arising from underestimating DSPN in diagnosis and management in primary care.

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