ADA position statement on diabetic neuropathy

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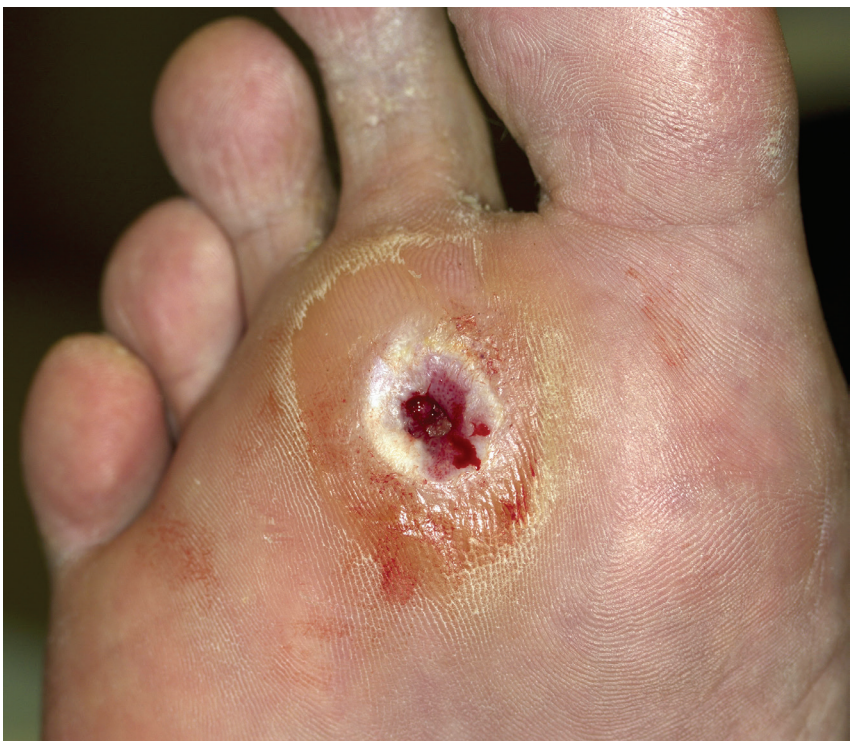
The American Diabetes Association (ADA)'s recent position statement provides a useful summary of the current evidence on the prevention and management of diabetic neuropathy.



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The American Diabetes Association (ADA) recently published a position statement on the prevention and management of diabetic neuropathy.[1] Drawing on recent reviews, it focuses on distal symmetrical polyneuropathy (DSPN) and cardiovascular autonomic neuropathy (CAN). This reflects the strength of evidence for these most common of the neuropathies but emphasises the lack of clinical research into its many other manifestations.

Prevention

Clinical trials have shown that tight glycaemic control – HbA1c ≤45.4mmol/mol (≤6.3%) – reduces the risk of DSPN by 78% in type 1 diabetes but a similar ambition in people with type 2 diabetes delivers a risk reduction of only 5–9%. It is not clear why this is so, but contributory factors probably include the attenuation of glycaemic control by multiple co-morbidities, polypharmacy, weight gain and hypoglycaemia, plus the cumulative effects of several years of asymptomatic hyperglycaemia.

Likewise, tight glycaemic control reduces the risk of CAN by almost a third after 14 years in people with type 1 diabetes whereas most clinical trials have not shown a comparable benefit in type 2 diabetes. Several trials suggest that intensive lifestyle change is also helpful, though how this is best delivered is unclear.

Chronic distal symmetrical polyneuropathy

Defined as "the presence of symptoms and/or signs of peripheral nerve dysfunction in people with diabetes after the exclusion of other causes," DSPN accounts for 75% of all diabetic neuropathies. The estimated prevalence in people with type 1 diabetes is 20% after 20 years but the outlook is worse in type 2 diabetes: 10–15% may be affected at the time they are diagnosed and around half may have developed DSPN after 10 years. Of those with impaired glucose tolerance, prediabetes or metabolic syndrome, 10–30% may already have DSPN, "especially the painful small-fibre neuropathy subtype."

DSPN is associated with diabetic foot, Charcot neuroarthropathy, and falls and fractures. Pain and dysaesthesia due to small fibre damage are often the first symptoms. Neuropathic pain, typically burning, lancinating, tingling or shooting and worse at night, occurs in a quarter of people with DSPN. This, and the associated paraesthesia, hyperalgesia and allodynia, have a significant impact on wellbeing and quality of life. By contrast, loss of large fibre function causes numbness resulting in the loss of protective sensation, a risk factor for foot ulceration.

The evidence for drug treatment of pain associated with DSPN comes largely from trials that included all types of neuropathic pain. The ADA recommends pregabalin or duloxetine as initial therapy, with gabapentin a secondary option. (NICE recommends a choice between amitriptyline, duloxetine, gabapentin or pregabalin as initial treatment for neuropathic pain and, if one option fails, sequential trials of the others.)[2] If first-line therapy fails, alternative options such as a tricyclic antidepressant or venlafaxine, or combination therapy, should be tried. Opioids are not recommended as first- or second-line therapies: patients with pain despite one of the recommended treatments should be referred to a pain specialist before a strong opioid is prescribed.

DSPN compromises balance through loss of proprioception and weakness, leading to unsteady gait. Physical difficulty due to neuropathic pain and the adverse effects of its treatment on cognitive function, combined with polypharmacy, can cause drowsiness, dizziness and blurred vision and add to the impairments associated with older age. It is therefore important to assess gait and balance to determine the risk of falls and ensure proper foot care.

Cardiovascular autonomic neuropathy

CAN is uncommon in people with newly diagnosed type 1 diabetes but affects at least 30% after 20 years; in type 2 diabetes, it is present in 60% of people after 15 years. Although prevalence increases with age, 20% of young people with diabetes may have CAN, with young women and individuals with poor glycaemic control particularly at risk. CAN also occurs in people with impaired glucose tolerance, insulin resistance or metabolic syndrome.

CAN is an independent risk factor for cardiovascular mortality, arrhythmia, silent ischaemia, any major cardiovascular event and myocardial dysfunction. After adjusting for other cardiovascular risk factors, it is associated with more than a two-fold increased risk of all-cause and cardiovascular death. Paradoxically, some evidence suggests that intensifying control of blood glucose and blood pressure in people with CAN may increase the risk of a cardiovascular event.

CAN may be asymptomatic, detectable only by decreased heart rate variability with deep breathing. Symptoms, late manifestations that correlate poorly with the degree of neuropathy, include light-headedness, weakness, palpitations, faintness and syncope, all of which occur on standing.

Patients with microvascular and neuropathic complications, possibly including those with hypoglycaemia unawareness, should be screened for CAN. Other causes (co-morbidities, drug therapy) should be excluded. Treatment involves nonspecific measures to optimise management and hopefully slow progression.

Symptomatic treatment of orthostatic hypotension includes physical activity (to avoid deconditioning) and volume repletion. If this is insufficient, pharmacological options include low-dose fludrocortisone and the alpha-1 agonist midodrine, though there is a risk of supine hypertension with both.

Summary

The ADA statement provides a fuller description of diabetic neuropathy and its management than the relevant NICE guidance and, though some details differ from UK practice, it is a useful summary of current evidence.

References

1. Pop-Busui R, *et al*. Diabetic neuropathy: a position statement by the American Diabetes Association. *Diabetes Care* 2017;40:136–54. Available from: http://care.diabetesjournals.org/content/diacare/40/1/136.full.pdf

2. National Institute for Health and Care Excellence. *Neuropathic pain in adults: pharmacological management in non-specialist settings*. CG173. November 2013 (updated February 2017). Available from: https://www.nice.org.uk/guidance/cg173

Declaration of interests

None to declare.

Steve Chaplin is a medical writer specialising in therapeutics