Microvascular complications: Diabetes-related neuropathy

Recommendations

Recommendation	Reference	Grade*
All patients should be screened for diabetic peripheral neuropathy, starting at diagnosis of type 2 diabetes and at least annually thereafter	1 American Diabetes Association, 2019	B
Screening for peripheral neuropathy should be conducted by assessing loss of sensitivity to the 10 g monofilament, or loss of sensitivity to vibration at the dorsum of the great toe	2 Diabetes Canada, 2018	A, level 1
The following agents may be used alone or in combination to relieve painful peripheral neuropathy: • anticonvulsants – pregabalin – gabapentin – valproate • antidepressants – amitriptyline – duloxetine – venlafaxine • topical nitrate spray • opioid analgesics	2 Diabetes Canada, 2018	 A, level 1 B, level 2 B, level 2 B, level 2 B, level 2 B, level 2
People with type 2 diabetes should be treated with intensified glycaemic control to prevent the onset and progression of neuropathy	2 Diabetes Canada, 2018	B, level 2
*Refer to 'Explanation and source of recommendations' for explanations of the levels and grades of evidence.		

Clinical context

Diabetic neuropathies increase with age, duration of diabetes and level of control of diabetes. They are heterogeneous, with diverse clinical manifestations, and may be focal or diffuse.

Symptoms include pain and paraesthesia, and if the autonomic nervous system is involved, gastrointestinal, bladder and sexual problems may arise. These increase the patient's burden of self-care and overall management. Foot ulceration and amputation are important and costly sequelae of diabetic neuropathy[2] (refer to the section 'Microvascular complications: Foot care').

Peripheral neuropathy

Manifestations of diabetes-related peripheral neuropathy include:

- polyneuropathy – diffuse and symmetrical neuropathy (most common)
- mononeuropathy
- polyradiculoneuropathy

- thoracic radiculopathy
- cranial neuropathy.

Autonomic neuropathy

Autonomic neuropathy may result in:

- orthostatic hypotension with >20 mmHg drop
- impaired and unpredictable gastric emptying (gastroparesis), which can cause a person's blood glucose levels to be erratic and difficult to control. Pro-kinetic agents such as metoclopramide, domperidone or erythromycin may improve symptoms
- diarrhoea, chronic constipation, reduced anal sphincter control
- delayed/incomplete bladder emptying, urinary incontinence
- erectile dysfunction and retrograde ejaculation in males
- reduced vaginal lubrication with arousal in women
- loss of cardiac pain, 'silent' ischaemia or myocardial infarction
- sudden, unexpected cardiorespiratory arrest, especially under anaesthetic or treatment with respiratory-depressant medications
- difficulty recognising hypoglycaemia (hypoglycaemic unawareness)
- unexplained ankle oedema.

In practice

Before any treatment is instigated, exclusion of non-diabetic causes of neuropathy is suggested. This includes assessment for vitamin B12 deficiency, hypothyroidism and renal disease, and a review of neurotoxic drugs, including excessive alcohol consumption.

The clinical focus is on prevention via optimising glycaemic management and early recognition, facilitated by good history and routine sensory testing.

Assessment

People with type 2 diabetes should be checked for diabetic peripheral neuropathy at diagnosis, and at least annually thereafter.[1]

Tests to assess for diabetic peripheral neuropathy are shown in Box 1. Combinations of more than one test have >87% sensitivity in detecting diabetic peripheral neuropathy. Loss of 10 g monofilament perception and reduced vibration perception predict foot ulcers.[3]

Several neuropathy scoring systems (diabetic neuropathy symptom score, neuropathy impairment score and Michigan neuropathy screening instrument) may be used with examination to confirm diagnosis and assess severity.[4–6]

Motor neuropathy sometimes occurs, with muscle wasting, weakness and abnormalities of gait. This can contribute to foot problems by altering the biomechanics of the ankle and foot.

Cardiovascular autonomic neuropathy should be suspected with resting tachycardia (>100 beats per minute) or orthostatic reduction in blood pressure (a fall in systolic blood pressure >20 mmHg on standing without an appropriate heart rate response). This applies to patients not currently on antihypertensive agents that may cause variations in blood pressure responsiveness, such as β-blockers. It is associated with increased cardiac event rates.

Box 1. Tests to assess for peripheral neuropathy[3]

- Small fibre:
  - pinprick sensation
- Large fibre:
  - vibration perception (using a 128 Hz tuning fork)
  - 10 g monofilament pressure sensation at the distal plantar aspect of both great toes and metatarsal joints
  - assessment of ankle reflexes
  - loss of protective sensation (10 g monofilament)

Management

Management of diabetes-related neuropathy mainly involves professional assessment and foot care to prevent diabetes-associated foot disease. The appearance of peripheral neuropathy should prompt review of glycaemic control and consideration of intensified management to prevent progression.[2]

The pain of peripheral neuropathy can be difficult to manage, although there is evidence that several agents can improve symptom control and quality of life.

- Tricyclic medications could be considered as a first-line treatment.
- Gabapentin provides pain relief of a high level in approximately one-third of people who take this medication for 'painful neuropathic pain'.[7]
- Pregabalin at daily oral doses of 300–600 mg provides high levels of benefit for some patients experiencing neuropathic pain, including painful diabetic neuropathy.[8]

For information about the Foot Forward program to prevent amputation, contact Diabetes Australia.

References

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