Fibromyalgia

In fibromyalgia, the most effective TCA appears to be amitriptyline (number needed to treat [NNT] 4.9).[249,266]

In practice

Amitriptyline probably provides very good pain relief to some patients with neuropathic pain or fibromyalgia, but in a minority; amitriptyline will not work for most people. When initiating a therapeutic trial, start at the lowest recommended dose (eg amitriptyline 5–10 mg at night) and assess the patient for benefit and harm at one week.[100] If needed, increase the dose slowly to minimise adverse effects; the maximum dose is approximately 75–100 mg at night.

In older patients, TCAs should be used with caution. Medications with anticholinergic activity increases risk of cognitive impairment, risk of falls and even mortality.[267,268]

5.2.2 Serotonin noradrenaline reuptake inhibitors

Musculoskeletal pain

Duloxetine is a recommended treatment in updated guidelines for osteoarthritis.[269] It is as effective as other first-line treatments (eg NSAIDs) for pain and disability of osteoarthritis.[270,271] Duloxetine appears to be well tolerated in older patients with osteoarthritis pain (of the knee).[270]

Neuropathic pain

There is evidence that some antidepressants, in particular duloxetine and venlafaxine, may be effective first-line treatments for neuropathic pain, including diabetic polyneuropathy.[96,255,256,263] Duloxetine has been shown to be effective and safe for the treatment of painful diabetic peripheral neuropathy in older patients.[272]

Chemotherapy-induced peripheral neuropathy (CIPN) is poorly understood and is resistant to treatment. However, duloxetine (30 mg titrated to 60 mg/day over five weeks) has resulted in a modest reduction in pain severity relative to placebo.[273] Additional benefits included reduced numbness and tingling of the feet, and improved quality of life.[273]

Fibromyalgia

The serotonin noradrenaline reuptake inhibitor (SNRI) duloxetine is effective in reducing pain and improving quality of life in fibromyalgia.[249,274] The NNT is approximately six.[256,275] However, it is not effective at improving sleep or fatigue.[274]

In practice

SNRIs are regarded as a first-line therapy for managing neuropathic pain.[96] The NNT is approximately seven for 50% pain relief.[96] When initiating a therapeutic trial, start at the lowest recommended dose (eg duloxetine 30 mg) and assess the patient for benefit and harm at one week. If insufficient but partial pain relief is achieved, increase the dose and reassess within one week; this may be repeated. Modest reduction in pain severity may be achieved with duloxetine dose titrated to 60 mg/day over five weeks. Duloxetine 60–120 mg/day provides analgesia for diabetic neuropathy, with lower efficacy for fibromyalgia.

Use the lowest individualised effective dose to minimise adverse effects, the most common of which is intolerable drowsiness. If the benefit–harm ratio is unacceptable, consider stopping the drug.