Pharmacological Management of Fibromyalgia

Failure to recognise FM often leads to over-investigation, inappropriate referrals and unnecessary interventions. Current international guidelines emphasise that FM should be diagnosed and managed in the primary care setting without unnecessary investigations and referrals.

Fibromyalgia (FM) is a valid and common disorder of chronic widespread musculo-skeletal pain. Individuals with FM often complain of chronic fatigue, recurrent headaches, sleep disturbance, cognitive symptoms (relating mainly to short term memory and concentration) and symptoms of irritable bowel syndrome. Depression and anxiety disorders are also common in FM patients.

PREVALENCE
The prevalence is estimated to be 3%-5% of the adult population (three to six times more common in women) and it is the third most common chronic musculo-skeletal pain disorder after osteoarthritis and low back pain.

Patients with FM have a high rate of utilisation of medical services leading to a significant economic burden for healthcare funders. It has been shown that up to 40% of patients referred to a tertiary pain clinic meet diagnostic criteria for FM.

DEFINITION
FM is currently regarded as a disorder of central sensitisation and a deficient pain inhibitory system. This loss of pain modulation in FM patients causes pain amplification and functional magnetic resonance imaging (f-MRI) studies have confirmed abnormal pain processing in FM patients. These (and other) neurophysiological abnormalities have been identified in the research setting but are not yet available in clinical practice.

DIAGNOSIS
Diagnosis is based on a comprehensive history, physical examination and limited diagnostic blood tests, also to exclude other disorders which may mimic FM. The two key components of the original 1990 American College of Rheumatology (ACR) classification criteria of FM are widespread pain and widespread tender points with palpation, which are clustered mainly around the neck, inner scapular region, low back and buttck regions. The subsequent 2010 ACR diagnostic criteria for FM are focussed on core symptoms (widespread pain, insomnia and cognitive dysfunction) and assess both the widespread pain index and symptom severity.

MANAGEMENT
Pharmacological strategies are more effective when utilised as part of a multimodal approach which integrates an individualized exercise programme, ongoing patient education, cognitive behavioural therapy and attention to sleep hygiene. With our increased understanding of the mechanisms which contribute to the symptoms of FM, the treating practitioner can now target specific mechanisms with medications and can also use medication combinations synergistically. Initial medication choice is individualised and influenced by severity of symptoms, presence of comorbidities and adverse effects of

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medication. FM patients can often only tolerate lower dosages of medications and it is mostly appropriate to start with a lower dose and then to titrate slowly to the most effective dosage with the fewest side-effects for the individual patient.

Older randomised placebo-controlled trials (RCTs) demonstrated efficacy of the tricyclics (e.g. amitriptyline) in 30-35% of FM patients resulting in improvement in pain, sleep and fatigue symptoms.

As with tricyclics, serotonin and norepinephrine re-uptake inhibitors (SNRIs e.g. duloxetine) also inhibit the re-uptake of both serotonin and norepinephrine. They differ from the tricyclics in not having significant activity at other receptor systems with fewer side effects and improved tolerability. The pain-modulating effects of antidepressants should be explained to FM patients and these benefits are independent of their effects on mood.

Alpha-2-delta ligands (such as pregabalin and gabapentin) bind to subunits of the calcium channels and reduce the synaptic release of several neurotransmitters, resulting in a reduced neuronal excitability. Several placebo-controlled clinical trials have demonstrated the efficacy of pregabalin on key symptom domains in FM patients and it became the first drug to be approved by the FDA for FM in the USA in 2007.

Analgesics such as paracetamol are often trialled in doses of up to three to four grams a day. No appropriate trials have been performed on non-steroidal anti-inflammatory drugs (NSAIDs) in FM but they may reduce inflammation in peripheral pain generators.

The only opiate that has been shown to provide safe and effective pain relief in FM patients is the weak-opioid receptor ligand, tramadol. This drug is also an inhibitor of norepinephrine and serotonin re-uptake and has been shown in placebo controlled trials to be effective, safe and well tolerated in FM patients - both as a single drug or in a fixed combination with paracetamol. It is important not to prescribe tramadol in patients with seizure disorders, because it lowers the seizure threshold.

Current guidelines recommend the use of combination therapy in patients unresponsive to mono-therapy. This approach has the advantage of combining multiple mechanisms of action for reducing pain and targeting other symptoms and comorbidities. Strong opiates are not recommended in FM. There is evidence that strong opiates might worsen FM-related symptoms such as pain and hyperalgesia (opioid-induced hyperalgesia). There is furthermore evidence of reduced opioid receptor availability in FM patients which may explain the weak efficacy of strong opiates which is often seen clinically in FM patients.

Cortico-steroids and benzodiazepines are not recommended for FM patients. There is accumulating evidence which supports the role of peripheral pain generators (e.g. tendonitis, degenerative joint disease and myofascial trigger points) in driving central sensitization and pain in FM patients. Appropriate treatment of these concomitant peripheral pain disorders has been shown to improve the FM related pain symptoms.

Current genetic studies and identification of clinical subgroups may in future be useful to optimise the pharmacological treatment of FM.

CONCLUSION
Prompt recognition and an active patient-centred approach in primary care which integrates biomedical and behavioural aspects, is mostly a successful management strategy. Current genetic studies and identification of clinical subgroups may in future be useful to optimise the pharmacological treatment of FM. References available on request.