

Chronic widespread pain and the fibromyalgia syndrome

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Abstract

Chronic pain syndromes are characterized by pain that is present every day and is not explicable by any specific physical injury or disease. The pain is related to central sensitization of the central nervous system pain mechanisms such that pain is amplified. The term 'chronic widespread pain' (CWP) means that the pain is present on both sides of the body, both above and below the waist and in the spinal region. Fibromyalgia is a subgroup of CWP in which, as well as pain, patients suffer from typical symptoms including fatigue, unrefreshing sleep and 'fibro-fog'. It is estimated that 11% of the population suffer from CWP and 2–6% have fibromyalgia. CWP and fibromyalgia are clinical diagnoses based primarily on the history. Investigations are only useful to exclude other diagnoses or to look at specific areas where the pain is out of proportion to the rest of the body. There is no cure for CWP or fibromyalgia, and treatments are designed to improve quality of life rather than remove the symptoms. Patient education and encouragement of exercise are key. There is only weak evidence for any medications. However, amitriptyline, tramadol, duloxetine and pregabalin are all useful in some patients.

Keywords

Central sensitization; chronic widespread pain; fibromyalgia; pain; pain management

Key points

- Chronic widespread pain syndromes are characterized by widespread pain every day that cannot be ascribed to a specific medical diagnosis
- Fibromyalgia is a subset of chronic widespread pain in which there are other symptoms such as fatigue, non-refreshing sleep and 'fibro-fog' The diagnosis of fibromyalgia is clinical, and investigations are generally normal
- The population prevalence of chronic widespread pain is 11% and of fibromyalgia is 2–6%
- There is no cure for fibromyalgia and the symptoms are likely to persist, so the key goal of management is to educate and inform the patient and to improve quality of life
- Non-pharmacological methods such as exercise should be tried first. Drugs such as amitriptyline, pregabalin, duloxetine and tramadol can be used but have limited effect

Introduction

Chronic pain syndromes are those in which patients suffer every day from pain that cannot be ascribed to a specific diagnosis such as cancer or inflammatory arthritis. The pain is often very distressing and combined with other physical and psychological symptoms. Blood tests and imaging are typically either normal or non-contributory and this can lead to a sense of frustration for patients who feel that they are being given the message that nothing is wrong despite their symptoms being very real.

Definition and epidemiology

Chronic pain is generally defined as pain every day for at least 3 months.¹ Chronic widespread pain (CWP) implies that this pain is present on both sides of the body, both above and below the waist and in the spine. Using these definitions, researchers in a number of different countries have carried out postal questionnaire studies to determine the prevalence of chronic pain and CWP. One of the largest

studies, from Wichita, Kansas, USA, reported on results from questionnaires sent to >3000 households chosen randomly from the telephone directory. The prevalence of chronic pain overall was 30% and of CWP 11%.² Prevalence figures for CWP are remarkably similar in similar studies done in different countries and the prevalence of CWP remained constant over a 2-year period in a study in West Sweden. However, within those 2 years some people found that their pain improved or resolved whereas others had a new onset of CWP.

Fibromyalgia syndrome is a subset of CWP. It was originally defined in American College of Rheumatology (ACR) classification criteria of 1990, which specified that patients had to describe CWP and also to report tenderness to pressure applied to at least 10 of 18 specific points on the body (the 'tender point test'). These criteria allowed epidemiological studies to be carried out, giving a population prevalence of 2% for fibromyalgia. The tender point test was, however, difficult to standardize and required the patient to be examined. Therefore, in 2010 the ACR produced alternative criteria specifying that the patient must have CWP as well as other typical fibromyalgia symptoms including fatigue, unrefreshing sleep and 'fibro-fog' but not requiring demonstration of tender points.³

Since the new criteria do not require physical examination, it was possible to determine the population prevalence of fibromyalgia by means of large questionnaire studies. Prevalence figures of 2.1% in Germany and 6.4% in Minnesota, USA have been reported.¹ Fibromyalgia occurs in both sexes but is more common in women. The Minnesota questionnaire study reported a prevalence of 7.7% in women and 4.9% in men – although only a quarter of these people had actually been diagnosed medically.

It is important to stress that fibromyalgia and chronic pain syndromes are not diagnoses of exclusion. For example, patients can have rheumatoid arthritis as well as CWP. This can make it difficult to interpret whether current treatment of the inflammatory arthritis is working as patients may complain of pain and tenderness even if the inflammation is suppressed.

Pathology and pathogenesis

In the chronic pain syndromes, the tissues in which the pain is felt are morphologically normal. There is no structural correlate of the pain. The biopsychosocial model of chronic pain syndromes emphasizes the fact that they typically arise from a complex interplay of psychological stressors and adverse social factors combined with abnormalities of the pain-processing mechanisms. Sleep disturbance is a key determinant of this type of pain. In fibromyalgia, for example, disrupted, unrefreshing sleep leads to chronic fatigue and muscular tension. The pain and tension in the muscles disturbs sleep further, leading to a vicious cycle.

Biologically, the key element in the pathogenesis of chronic pain syndromes is central sensitization, which can be defined as amplification of neural signalling within the central nervous system that elicits pain hypersensitivity.⁴ Research methods such as quantitative sensory testing have been used to demonstrate central sensitization and there have been reports of altered findings on functional magnetic resonance imaging in patients with fibromyalgia.¹

Diagnosis and investigation

The diagnosis is a clinical one. For fibromyalgia, the key features in the history are widespread pain that has been present every day for at least 3 months, sleep disturbance and a feeling that sleep is unrefreshing. Some patients describe a situation where they seem to sleep through the night but wake in the morning feeling as though they have not slept at all. It is believed that this is probably a very light sleep insufficient to allow muscle relaxation. In addition to this a feeling of so-called 'fibro-fog' is common. Patients feel that they do not think as clearly as they used to and can have difficulty remembering things. Very often, patients have already undergone a series of blood tests and imaging studies that are normal.

On examination there are typically no localizing signs such as joint inflammation or neurological deficits. However, for many individuals, the chronic pain and muscle tension are such that they have reduced mobility, particularly in the shoulders, lumbar spine and hips. The tender point test can be helpful in demonstrating to patients that they fulfil diagnostic criteria for fibromyalgia but it does not alter management. It is important to be on the lookout for pain in one area of the body that is out of proportion to the rest. Just because an individual has a chronic pain syndrome does not mean that every pain is caused by that syndrome. For example, where one shoulder is clearly more painful and limited than the other, there could be an underlying bursitis or tendinopathy. The clinical features of fibromyalgia are summarized in Table 1.

Investigations are designed to exclude other possible causes of the symptoms. Typically, baseline urea and electrolytes, full blood count, liver function and C-reactive protein tests are

requested. Vitamin D concentration and thyroid function tests can be helpful. Imaging studies are unlikely to help unless there is reason to suppose that a particularly painful area of the body is being affected by a specific problem outwith the chronic pain syndrome.

Prognosis and explanation to the patient

Many patients with CWP have suffered symptoms for many years and have undergone multiple consultations and investigations without a diagnosis. It can therefore be helpful and a relief to be given an explanation that makes sense. It is, however, important to spend time showing why this is the correct diagnosis. Patient information resources such as the leaflet produced by the charity Versus Arthritis are very helpful in this regard.

It is important to give a fair and balanced indication of prognosis. Chronic pain syndromes do not damage joints or internal organs so are not dangerous in that way, but they cannot be cured by physicians. Some patients improve as a result of changes in psychological and social factors (e.g. leaving a difficult employment or personal situation). In most cases, however, the patient continues to live with the symptoms long term. The aim of treatment is to reduce the symptoms if possible and to maximize the quality of life that the individual experiences, despite these symptoms.

Management

A number of reviews and guidelines have assessed the clinical trial evidence for the different therapies used in fibromyalgia. These include a British Medical Association Clinical Review¹ and European League Against Rheumatism (EULAR) Guidelines.⁵ Much of the literature is of limited quality as trial follow-up periods are typically relatively short for this chronic condition, many participants drop out of trials and many others are excluded because of co-morbidities such as depression. The EULAR Guidelines of 2017 are very useful in that they describe and grade the evidence relating to multiple pharmacological and non-pharmacological therapies. The key findings are summarized in Table 2.

Initial management of all patients with fibromyalgia should focus on education and information for the patient and a non-pharmacological approach. Exercise was the only form of treatment that was graded by EULAR as having strong evidence for efficacy. It may be fair to consider, however, that patients who considered themselves able to enlist in a trial of exercise might be a somewhat self-selected group. In the real world, many individuals with chronic pain syndromes maintain that their pain is too severe to allow them to exercise.

The EULAR guidelines went on to delineate additional forms of treatment, for which evidence was weak but extant, that could be used in individual patients. Psychological support using a cognitive behavioural approach has been shown to help, particularly where chronic pain is associated with mood disorders or difficulty coping. Drugs including pregabalin, tramadol and duloxetine can help reduce severe pain. Pregabalin and amitriptyline may improve sleep quality. All these drugs, however, can have significant adverse effects, especially when used long-term (Table 2).

Multidisciplinary pain management programmes including both physiotherapy and psychology can be helpful for some individuals but require an acceptance by them that the pain will not be cured or reduced by the programme; the aim is to learn how to cope with the pain.

A recent review⁴ raised the interesting prospect that patients with chronic pain syndromes could be stratified for different types of treatment depending on the presence and magnitude of central sensitization.⁴

Long-term follow-up in secondary care is not necessary for individuals with fibromyalgia. Since the symptoms are chronic and often distressing, however, it is not uncommon for patients to be referred back repeatedly to different clinics such as rheumatology and pain management in the hope of a new approach. Under these circumstances, it is important to reassess to ensure that no new cause of pain has developed. Patients with chronic pain syndromes can develop other conditions, just like everyone else.

Table 1 -

Clinical features to consider in diagnosing fibromyalgia	
History	<ul style="list-style-type: none"> • Pain has been present every day for at least 3 months • Pain is widespread – typically all four limbs and the spine • Pain is usually not associated with any visual change in the painful area (swelling or redness) • Sleep is usually disrupted and/or unrefreshing • The patient feels fatigued • The patient describes increased difficulty in thinking, reasoning or remembering ('fibro-fog') • There is often a history of depression and/or anxiety • Some patients describe increased sensitivity to touch, heat or cold
Examination	<ul style="list-style-type: none"> • The extent of limitation of movement is variable • Some patients have almost full range of movement at all joints, and this is a good prognostic feature • Other patients have limited movement because of pain and tenderness in the muscles. They can resist passive movement • The shoulders, lumbar spine and hips are most commonly affected by limitation caused by pain • There are no signs of joint inflammation or specific nerve root compression • Patients often describe widespread tenderness to palpation • Tenderness at the specific points specified in the ACR 1990 criteria does not alter management but can be helpful in validating the diagnosis for the patient • Look out for a particular area where the pain and limitation are out of proportion to the rest of the body: there could be a separate localized problem there
Investigations	<ul style="list-style-type: none"> • There are no diagnostic investigations in fibromyalgia • Investigations are typically normal • If not done previously, baseline blood tests (urea and electrolytes, liver function tests, calcium, phosphate, full blood count, C-reactive protein) are useful to ensure that other diagnoses have not been missed • Thyroid function and vitamin D concentrations can be useful as they identify easily treatable causes of pain and fatigue • Autoantibody tests such as antinuclear antibody and rheumatoid factor are best avoided unless specific features of history and/or examination suggest an autoimmune rheumatic disease • Imaging tests are generally normal • Imaging of a particular region where the pain is out of proportion to the rest of the body can help to identify or exclude a localized problem in that area • Where the patient expresses particular concern about a specific area of the body, imaging that area can help to reassure them that fibromyalgia rather than a specific structural problem is causing the pain there

Table 2

Summary of main treatment methods considered in the EULAR 2017 guidelines			
Treatment	EULAR recommendation	Advantages	Disadvantages
Patient education	Strongly recommended	It is essential to ensure that the patient understands the diagnosis, that it is a complex chronic condition that cannot be completely cured, and the aims of treatment	None
Exercise	Strong for	Review of trials of exercise showed significant benefit in pain reduction. In comparison to medication, no significant adverse effects	Many patients say that their pain is so bad that they cannot do exercise. These patients may not have been represented in studies reviewed by EULAR
Pregabalin	Weak for	Much more evidence for pregabalin than gabapentin EULAR suggested that it could be considered as a potential treatment to reduce pain or sleep disturbance	Common adverse effects include memory loss, drowsiness, dizziness, headache and weight gain
Amitriptyline	Weak for	Used in low doses (up to 30 mg at night) it can improve sleep quality and reduce tiredness and pain	Common adverse effects include drowsiness, dry mouth, constipation and headache Should be used with caution in patients with a history of arrhythmia, epilepsy or liver disease Not recommended in pregnancy or breastfeeding
Duloxetine	Weak for	EULAR suggested that this drug can be used to try to reduce severe pain	Common adverse effects include difficulty sleeping, nausea, dizziness, dry mouth, tiredness, headache, blurred vision and constipation
Tramadol	Weak for	Tramadol is an opioid drug with some selective noradrenaline (norepinephrine) reuptake inhibitor activity EULAR found some evidence that it can help reduce pain in some patients. In contrast there was no evidence to support the use of other opioids	Common adverse effects include drowsiness, dizziness, tiredness, dry mouth, constipation, nausea and headache Over time, the body can develop tolerance so that it is difficult to stop taking tramadol without suffering adverse withdrawal effects such as agitation, anxiety, shaking and sweating
Cognitive behavioural therapy	Weak for	EULAR felt that the quality of trials reviewed was generally poor but there was some evidence for efficacy in reducing pain In contrast to medication, there are no significant adverse effects so this is very safe option	Undertaking cognitive behavioural therapy requires a significant commitment of time and effort by the patient and an acceptance that the pain will not be cured
Multidisciplinary pain management programme	Weak for	Combining physiotherapy, psychology and educational approaches in a single programme may be very helpful, especially to improve coping strategies	Undertaking these programmes requires a significant commitment of time and effort by the patient and an acceptance that the pain will not be cured

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TEST YOURSELF

To test your knowledge based on the article you have just read, please complete the questions below. The answers can be found at the end of the issue or online [here](#).

Question 1

A 35-year-old woman presented with a history of aches and pains all over the body for many years. All blood tests and imaging organized previously had been normal. On clinical examination, she had limited movements at both shoulders because of pain but no swollen or inflamed joints.

According to the ACR 2010 diagnostic criteria for fibromyalgia, what extra symptom would support a diagnosis of fibromyalgia?

- A Palpitations
- B Joint hypermobility
- C Unrefreshing sleep
- D Weight gain
- E Depression

Correct answer: C. Although patients report a multiplicity of symptoms, the only ones used in the criteria for the diagnosis of fibromyalgia were fatigue, unrefreshing sleep and cognitive symptoms; therefore the other options are wrong.

Question 2

A 40-year-old man re-presented with unrelieved pain. He had been seen 4 years previously when a diagnosis of fibromyalgia had been made. He had not responded to a range of medications and a further review was sought. On clinical examination, there were no swollen or inflamed joints. There was full movement of all joints except that the right shoulder had limited abduction and external rotation compared with the left.

What would be the most appropriate next investigation?

- A Rheumatoid factor
- B Plain radiograph of the right shoulder
- C C-reactive protein
- D Thyroid function test
- E Ultrasound scan of the right shoulder

Correct answer: E. There are no features to suggest an inflammatory arthritis, so rheumatoid factor (A) and C-reactive protein results (C) are unlikely to be informative. The asymmetry of shoulder pain suggests that there is a different process causing the pain in the right shoulder. The most likely cause is a soft tissue problem such as tendinopathy or bursitis, which would be identified by ultrasound scan but not by plain radiograph (B). Abnormal thyroid function (D) would not cause shoulder pain.

Question 3

A 55-year-old woman presented for review. She had previously been found to have fibromyalgia and had been advised to try exercise. She had done this but continued to suffer from pain and poor sleep. She wanted to try a medication to reduce her symptoms. Her body mass index was 34 kg/m².

What would be the most appropriate medication?

- A Amitriptyline
- B Diclofenac
- C Pregabalin
- D Duloxetine
- E Tramadol

Correct answer: A. There is no evidence to support use of non-steroidal anti-inflammatory drugs (B) in fibromyalgia. Pregabalin (C) can commonly cause weight gain and it is better to avoid tramadol (E) because of the risk of tolerance. Amitriptyline is more likely to help her poor sleep than duloxetine (D).

Commented [CW1]: AQ: please add feedback for why option D is wrong.