Fibromyalgia syndrome – current concepts

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Abstract

Fibromyalgia (FM) is a recognised chronic pain syndrome that is diagnosed without any special investigations. This syndrome constitutes widespread pain in a specific distribution, for a specific period of time, as well as tenderness over at least 11 out of 18 clearly defined tender points. This syndrome is a common cause of other conditions commonly encountered in general practice and this article provides a practical and clinical approach to diagnosis and treatment.

( SA Fam Pract 2006;48(3): 20-28)

Introduction

Fibromyalgia (FM) is the most common cause of widespread musculoskeletal pain and most patients also complain of chronic fatigue, non-restorative sleep, gastrointestinal symptoms and widespread joint pain.1,2 FM is a clinical diagnosis and therefore, according to the 1990 American College of Rheumatology (ACR) criteria for diagnosis (see later), laboratory tests and imaging studies play no role in establishing the diagnosis.3 Failure to recognize FM by primary care doctors often leads to over-investigation, over-treatment and inappropriate referrals because of the multiple symptoms of the disorder.

There is now convincing evidence that abnormal central pain mechanisms and amplification of nociceptive input (“central sensitisation”) may be the reasons for the augmented pain experience of FM patients.4 The primary care doctor, having a better understanding of the biopsychosocial background of the patient, is in the best position to optimally manage patients with FM.5

The term “fibrositis” was first used by Sir William Gowers in 1904 in a lecture on lumbago, but only in the 1960s was fibrositis described as a syndrome of general pain, multiple tender points, poor sleep and fatigue.5 Moldofsky described an objective sleep abnormality on the sleep electroencephalogram (EEG) in “fibrositis” patients in 1975 and it became evident soon afterwards that this was a common clinical disorder.5 This led to the ACR requesting a scientific committee to provide diagnostic guidelines, which were published in 1990, now using the term fibromyalgia.8

Diagnosis

The ACR classification criteria for FM consist of:8

1. Widespread pain for three months or longer in an axial distribution plus pain on both sides of the body, as well as above and below the waist.
2. The presence of 11 or more out of 18 specified tender points with moderate digital pressure of 4 kg (roughly the force required to blanch the examining nail when pressing against a hard surface). The location of the 18 tender points is shown in Figure 1.9

For a tender point to be considered “positive”, the patient must state that the palpation was painful (“tender” is not considered “painful”).10 Unlike myofascial pain syndrome (MPS), which is a regional pain disorder, the pain in FM is widespread and many patients “hurt all over”. In clinical practice the characteristics of MPS and FM often overlap.9,10 The principal diagnostic feature of MPS is the presence of myofascial trigger points – a trigger point is considered to be different from a tender point because

Figure 1: Location of the 18 tender points (ACR definition)9

1. Suboccipital muscle insertion
2. Anterior aspects of the C5-7 intertransverse spaces
3. Midpoint upper border of trapezius
4. Supraspinatus origin
5. Second rib, lateral to costochondral junction
6. 2 cm distal to lateral epicondyle
7. Upper outer quadrant of gluteal muscles
8. Posterior to trochanteric prominence
9. Medial fat pad of knee proximal to joint line.
Table I: Red flags that may indicate other disease

- Weight loss
- Fever
- Malaise
- Neurological signs
- Constant progressive pain
- History of cancer
- Sedimentation rate >25 mm/hr

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of the presence of a taut band in the involved muscle and a distinct pattern of referred pain with palpation (the trigger point is an area of exquisite local tenderness in the taut band).\textsuperscript{11} It has been demonstrated that up to 70% of patients with FM may have myofascial trigger-points.\textsuperscript{11,12,13}

Clinical features

Pain

The essential features of FM are widespread musculoskeletal pain in the presence of multiple painful tender point sites. There are a number of red flags, which may indicate other abnormalities. These are listed in Table I.\textsuperscript{14}

The widespread pain of FM may originate from a soft tissue injury such as whiplash or surgery with a delay in onset after the precipitating event.\textsuperscript{15} Chest pain and shortness of breath are often experienced, with tenderness over the costochondral tender points (commonly referred to as “atypical chest pain”).\textsuperscript{5,10} A subset of patients predominantly complain of peripheral arthralgia without joint swelling.\textsuperscript{9} Low back pain is common and there may be concomitant myofascial pain that may shoot down the leg, simulating sciatica.\textsuperscript{10,11} Chronic tension-type headache and migraine are common in FM patients and could possibly be considered as a “continuum” with a temporal sequence of migraine, chronic daily headache, and fibromyalgia in a subgroup of patients.\textsuperscript{16}

The pain and generalised stiffness of FM are often aggravated by weather factors, poor sleep, over-use, trauma and mental stress.\textsuperscript{9}

Fatigue

Tiredness is a major complaint in most FM patients and may even be the predominant symptom.\textsuperscript{17} The etiology of fatigue in FM is multifactorial and may include non-restorative sleep, deconditioning, depression, and hypothalamic-pituitary-adrenal axis dysfunction with growth hormone deficiency.\textsuperscript{18} It has also been demonstrated that a substantial percentage of patients with FM also meet criteria for Chronic Fatigue Syndrome (CFS) and vice versa.\textsuperscript{19}

Sleep disturbance

Most FM patients are light sleepers, being easily aroused by low-level noises or intrusive thoughts.\textsuperscript{3,20} They therefore have a higher number of arousals at night and this correlates with sleep EEG findings of an increase in stage 1 alpha waves (representing arousal) and decreased delta waves in stages 3 and 4 non-REM sleep (representing restorative sleep), with intrusion of alpha waves and “disruption” of the slow delta waves (known as alpha-delta sleep anomaly, which is not specific for FM)\textsuperscript{20} (see Figures 2a and 2b).\textsuperscript{21}

Slow-wave sleep has been linked with serotonin synthesis and growth hormone secretion and is associated with conservation of energy.\textsuperscript{22} There is a relationship between poor sleep and pain intensity, and non-restorative sleep in the previous night may predict pain the next day in FM patients.\textsuperscript{23}

Figure 2a: Typical sleep stage cycle of a healthy adult\textsuperscript{21}

Figure 2b: Typical sleep stage cycle of a healthy adult\textsuperscript{21}

Neurocognitive dysfunction

Cognitive dysfunction is more severe in patients who also meet criteria for CFS and is often a major problem.\textsuperscript{10} Defects have been described in short-term memory and concentration, word retrieval and verbal fluency.\textsuperscript{24,25} A possible explanation for these symptoms could be related to the role of serotonin in the processing of sensory information.

Associated symptoms\textsuperscript{3,10,24,26,27}

Patients with FM often have a variety of overlapping conditions or syndromes that include irritable bowel syndrome, restless legs syndrome, irritable bladder, chronic fatigue syndrome, regional myofascial pain, multiple chemical sensitivities, non-cardiac chest pain, chronic pelvic pain, tension-type headaches and migraine. Autonomic dysfunctions may include neurally-mediated hypotension, dizziness and vertigo. Persistent hyperactivity of the sympathetic nervous system could link the widespread pain and associated symptoms.\textsuperscript{3} All too often the primary care doctor fails to link the associated disorders with the patient’s primary pain problem, and this may lead to unnecessary investigations, referrals and even inappropriate surgical interventions.

Psychosocial factors are an important determinant of pain in any disease, and FM is no exception.\textsuperscript{9} These may include maladaptive coping, such as fear avoidance and catastrophising, sick role behaviour, deterioration of social or support network.\textsuperscript{28} The emotional component of pain is complex and is influenced by past experiences, beliefs and fears, as well as by genetic factors.\textsuperscript{29}

Approximately 20 to 40% of FM patients have an identifiable current mood disorder, mostly a depressive disorder, and there is also an overlap with posttraumatic stress disorder and somatoform disorders.\textsuperscript{28} The current growth of knowledge regarding the neurobiology of the amplification of sensory input in patients with FM
sensitisation may follow soft tissue response to painful stimuli. Hyperalgesia, i.e. an exaggerated clinical phenomenon of FM patients. This process leads to the wide spectrum of symptoms in central processing of pain generates pain generators and the abnormal system, which causes pain regulation in the central nervous spinal cord. There is a loss of pain sensitisation, with disordered sensory central problem in FM is "anti-pain system" could possibly be genetic and explain the striking familial prevalence of fibromyalgia. Serotonin modulates incoming pain impulses and has been demonstrated to be low in the cerebrospinal fluid of FM patients, while substance P levels have been shown to be high and appear to be a biological marker for the presence of chronic pain. Functional magnetic resonance imaging studies have demonstrated that the amount of pain stimuli required to cause activation of pain processing in the brain is much lower in FM patients than in healthy controls.

It is interesting to again note the high co-occurrence rates of FM, CFS, migraine headaches, irritable bowel and bladder syndromes and restless legs syndrome – these disorders possibly share a common pathogenesis and management (the term "central sensitivity syndromes" has been used to describe this group of disorders). Numerous studies have been performed to evaluate the hypothalamic-pituitary-adrenal axis in FM patients and many abnormalities have been documented, including relative adrenal insufficiency, low levels of growth hormone and a relative inability for stress events (such as infection or physical and emotional stress) to activate the HPA-axis. FM seldom presents spontaneously. Most patients relate an acute injury, infection or emotional stressor as a precipitating event. It seems that the start of FM symptoms may occur when a genetically predisposed individual is exposed to certain environmental triggers. Repeated exposure to stressors over a period of time may also precipitate FM.

FM is also commonly found as an accompaniment to disorders with longstanding musculoskeletal pain, including rheumatoid arthritis, osteoarthritis, low back pain and systemic lupus erythematosus. These have been referred to as secondary fibromyalgia and it is assumed that these conditions may act as inducers of central sensitisation.

According to the International Association for the Study of Pain (IASP) definition, pain is not only a sensory but also an emotional experience and may be present in the absence of tissue damage. FM is a pain disorder in which the interplay between the psyche and the body and its effect on the altered physiology produces pain – it is thus a complex interaction between disordered pain processing, genetic predisposition, cognitive patterns and exposure to stressors that forms the basis for the pain and other symptoms. An individual's interpretation of pain may be influenced by many psychosocial factors, e.g. childhood events and conditioning, and family environment. Psychosocial factors are also important in the development and maintenance of "organic" disorders such as hypertension, asthma and diabetes mellitus – it is therefore inappropriate to classify illnesses as either "organic and real" or "psychological and all in the mind" – chronic illnesses mostly have a component of both.

**Management**

The management of FM patients is often time-consuming and the clinical spectrum of symptoms shows considerable individual variation. The biopsychosocial approach with a patient-centred doctor-patient relationship is an integral part of the management and should include a supportive attitude and knowledge of current pain physiology. The goal is to decrease pain and increase function while patients develop a self-management programme to improve self-efficacy. The primary care doctor is in the most favourable position to manage patients with FM.

**Education**

The role of education is to validate the patient's symptoms and to explain the nature of the disorder. It is accepted as a critical feature in FM management and has been proven to be effective. Patients should be encouraged to take an active role in
the management, to focus on appropriate self-management and to accept that there is no “instant cure” for the disorder. Other components of education include drug and non-drug therapy, the importance of low-intensity life-long exercise and the principles of sleep hygiene. 3, 24, 42

FM is a non-destructive disorder and the patient should focus on improving health and wellness rather than focussing on illness and disability. 14 The focus is on improvement in function and not a complete eradication of symptoms – patients should be warned against untested “remedies and magical cures” available on some internet sites and from some health shops.

Exercise
It is rare for patients to improve if they do not engage in a programme of low-impact aerobic and stretching exercises. It is advisable to start gently and to avoid high-impact exercises that aggravate the pain. Walking for 30 minutes a day or regular water exercises for deconditioned patients is recommended as a first line of therapy. It is advisable to gradually build up to 3-4 times per week for 20-30 minutes, and strengthening exercises may be performed during the later stages of conditioning. 3, 42 Exercise is more beneficial if some degree of pain control has been achieved. Active tender or trigger points may inhibit effective stretching and should be treated before the programme is initiated. 14, 43, 44

Various studies have provided evidence that exercise produces significant improvement in FM patients. 24, 42, 43 All components of a fitness programme (aerobics, stretching and strengthening) appear potentially safe and beneficial if individually adjusted. 44 An important aspect in FM exercise prescription is to avoid muscle micro-trauma and “overtraining” (which may worsen the central sensitisation) by keeping the exercise intensity low and appropriate. 44 Passive physical therapy and electrotherapy are only regarded as an adjunct to the overall exercise programme. 14

Sleep and mood disorder
The majority of FM patients have disturbed sleep – usually perceived to be light, with easy and frequent arousals and a “non-restorative” character. Although FM patients may have a primary sleep disorder (e.g. restless legs syndrome and sleep apnoea syndrome) that requires specific treatment, no obvious “cause” will be found for the sleep disruption in most patients. 9, 45

A significant problem for some patients is simply inadequate time allowed for sleeping due to a lifestyle that is too busy and hectic. Other sleep hygiene measures include going to bed earlier and at the same time each night, no daytime naps, avoiding stimulants such as caffeine and nicotine, not “taking worries to bed”, with a relaxation routine before sleeping that includes progressive muscle relaxation and imaging a pleasant scene. 38

Low-dose tricyclic antidepressants (TCAs), e.g. amitriptyline and dothiepin, have been studied best and are the most commonly prescribed drugs for FM-associated sleep disturbances. 46 The key is to use very low dosages (e.g. 10-20 mg two hours before retiring), increasing these gradually if appropriate. Tricyclics increase the concentration of serotonin and/or norepinephrine by blocking their re-uptake, but also have the ability to block the N-methyl-D-aspartate (NMDA)-mediated neurotransmission. 47 (NMDA-neurotransmission has been implicated in the pathogenesis of various chronic pain disorders.)

Long-term treatment of insomnia with benzodiazepines has no place in FM management. 48 The intermittent use of non-benzodiazepine gaba-receptor agonists such as zopiclone and zolpidem improves sleep, but has no significant effect on pain. 49

Studies with the selective serotonin re-uptake inhibitors (SSRIs) fluoxetine, sertraline and citalopram have been disappointing and these drugs are less effective than TCAs for treating the pain in FM patients. 47, 49 Most studies however agree that SSRIs reduce depression when present in FM patients, making them valuable adjuncts to therapy.

Dual re-uptake inhibitors (DRIs) such as venlafaxine and duloxetine differ from TCAs in having no significant activity at other receptor systems and are therefore tolerated better. 47, 50 Clinical data have thus far demonstrated a benefit versus placebo when DRIs were used for the pain in FM patients. 51, 52 Future studies should compare efficacy with medications such as TCAs. DRIs are more expensive than TCAs, with no proven benefit for the pain in FM patients. 52

Pain
The pain in FM patients may have a very negative impact on the patient’s functional, emotional and socio-economic wellbeing. There is also growing evidence that persistent pain, regardless of its cause, may alter the nervous system (via the mechanism of central sensitisation and new gene expression), followed by increased pain sensitivity and hyperalgesia. 52, 53

Once the central nervous system has become sensitised, peripheral pain generators will be perceived as being more painful and will amplify the central sensitisation. 3, 24, 29 The management of peripheral pain generators is therefore of critical importance in the management of FM patients 14, 35 these include conditions such as visceral pain (e.g. irritable bowel syndrome and endometriosis), tendinitis and bursitis, neuropathic pain, and degenerative joint disease. Myofascial trigger points due to comorbid myofascial pain syndrome are the most common peripheral pain generators in FM patients 2, 3, 5 and the nociceptive afferent input from these trigger points may act as inducer of central sensitisation, with subsequent spreading of pain to other areas. 11

The non-pharmacological treatment of pain in FM patients includes education, physical therapy and exercise, cognitive behavioural therapy (CBT) and myofascial trigger point therapy as part of a multi-dimensional strategy. CBT has been shown to be beneficial in FM and other chronic illnesses and aims to increase coping strategies and eliminate maladaptive illness behaviour. 14 As in other chronic pain disorders, patients must take personal responsibility for effecting change (“internal locus of control”), develop optimistic attitudes and engage in
pain-distracting activities. Internalisation and denial of negative emotions, dysfunctional families, fear (which may be generated by physicians!) and the repeated drawing of the patient’s attention to his/her pain symptoms (e.g. in medico-legal proceedings) may amplify the pain symptoms.11 Cognitive strategies include restructuring of negative and catastrophic thinking patterns.

Suboptimal treatment of the biomedical aspects of chronic pain may worsen central sensitisation and the prognosis of FM patients and appropriate use of analgesics is mostly indicated. Pharmacological therapy for FM pain includes the central-acting analgesics paracetamol and tramadol. Tramadol is a weak opioid receptor agonist and has serotoninergic and nor-adrenergic properties. A tramadol-paracetamol combination has also been shown to be safe, effective and well tolerated for the treatment of FM pain.5,56 There is no current evidence to suggest that tissue inflammation is present in patients with FM, and anti-inflammatory medications are only regarded as useful adjuncts for some of the peripheral pain generators.57 FM patients have used many other drugs and supplements, such as 5-hydroxytryptophan, 5-adenosylmethionine, guaferasine, that are available in health shops with little or no scientific support and, in some cases, significant potential toxicity.58 The National Institutes of Health Consensus statement on accupuncture in 1998, concluded that accupuncture could be useful as an adjunct treatment in FM as part of a comprehensive management program. A few classes of agents that are not widely used clinically, but have shown promising results in recently controlled studies, include 5-HT3 antagonists (e.g. odansetron), NMDA-antagonists (e.g. ketamine) and pregabalin, a second-generation anticonvulsant.47,58

Conclusion

FM is a common but complex pain disorder that affects mostly middle-aged women and has been accepted as a distinct clinical disorder by the World Health Organisation and various other scientific bodies. It is a disorder of increased pain sensitivity and pain amplification due to a complex interaction between genetic predisposition, exposure stressors, cognitive factors and peripheral pain generators.

The primary care doctor is in an ideal position to manage these patients. Prompt recognition and optimal management will prevent iatrogenic harm and will mostly lead to substantial improvement in and even remission of the symptoms. A patient-centred approach that integrates biomedical and behavioural aspects is mostly successful, as long as it addresses the individual patient's unique set of problems.

Most clinical trials in the literature focus on single modality approaches, and more studies that combine medication and other modalities are needed to evaluate efficacy. Primary care physicians are ideally suited to participate in such a study. See CPD Questionnaire, page 54

References

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