

Getting on with fibromyalgia



**Serena F Carville[†] &
Ernest HS Choy**

[†] Author for correspondence
King's College London School
of Medicine,
Department of Academic
Rheumatology,
Weston Education Centre,
Cutcombe Road,
London SE5 9RJ, UK
Tel.: +44 207 239 1887
Serena.Carville@hta.org.uk

'Treating each patient according to their specific symptoms and needs is a vital factor in fibromyalgia.'

For a number of years, fibromyalgia (FM) has been an under-researched and under-recognized condition. Much of the problem is attributable to the lack of acceptable diagnostic criteria. Over the years, a number of names have been used to describe the condition. The publication of the American College of Rheumatology (ACR) classification criteria in 1990 was a major advance in getting the condition recognized [1]. Although initially these criteria were intended as a means of providing a homogenous group for clinical research, they became widely used in clinical practice. Whilst the ACR criteria have received criticism, and undoubtedly require modification, using the diagnosis constructively has been shown to be beneficial in the UK. Using the General Practice Research Database, Hughes *et al.* have shown that healthcare utilization in patients with FM was already high compared with controls up to 10 years prior to diagnosis. Interestingly, healthcare costs were reduced after diagnosis, with less investigations, patient visits and secondary-care referrals [2]. Given that FM is a common condition, affecting 2% of the population, Professor Liam Donaldson, the UK's Chief Medical Officer, emphasized the need for more information for both doctors and patients in a letter written to all UK doctors in 2003.

The variety of names and difficulty in producing specific criteria result from the fact that FM comprises a range of diverse symptoms [3]. Physical and laboratory examinations are unremarkable, so patients' journeys through the healthcare system have often followed a long course of referrals to a variety of specialists before the diagnosis of FM is made. With conditions such as FM, and other multifaceted syndromes, there is a lot of skepticism regarding the condition and whether it actually exists. Patients will undoubtedly be confronted with this and will be frustrated by the need to 'prove to doctors that they

are ill'. However, recent research has revealed some abnormal pathophysiology findings in FM. These include responses to painful stimuli characterized by allodynia and hyperalgesia; elevated levels of substance P in the cerebrospinal fluid [4]; and altered hypothalamic-pituitary-adrenal (HPA) axis response to stress [5,6]. In addition, more recently, neuroimaging has demonstrated abnormal central pain processing [7,8]. It is most likely that a variety of mechanisms are involved in the pathophysiology of FM, in conjunction with environmental, psychosocial and genetic factors. Advances in our understanding of the pathophysiology should help to develop more tailored treatment for patients.

With under-recognition of the condition, many patients, in desperation, seek information on the internet and suggest the diagnosis of FM to their doctors. Delayed diagnosis increases healthcare costs, as well as increasing patient frustration and stress, which is detrimental to their management. Whilst management options have been limited in the past, increasing interest in research into the pathogenesis and pathophysiology of FM, as well as the development of new therapies, offers hope for better treatment in the future. Indeed, the first licensed medicine for treatment of FM, pregabalin, was approved by the US FDA last year [9].

The management of FM requires a multidisciplinary approach. A multidisciplinary task force of experts in the field of FM convened to produce guidelines for its management. This was done with the endorsement of EULAR, who have produced management guidelines for other conditions in rheumatology (for example, see Zhang *et al.* [10] and Zochling *et al.* [11]). The intention was to produce evidence-based recommendations that would primarily help to inform doctors regarding the treatments that were available for FM, as well as to give some guidelines on how to best manage patients, given that prognosis is poor and complete remission is unlikely. A systematic review of the literature revealed over 180 clinical trials involving more than 60 different treatments. Data were extracted with predefined criteria. A summary was synthesized and presented to the expert task force. The poorest-quality studies were

excluded. The inclusion of expert opinion in the formation of these recommendations was important to ensure that a balanced and fair view of treatment options was given. Importantly, a patient representative was included in the task force to make sure that patients' interests and concerns were taken into account.

An important aspect of the EULAR recommendations was to highlight that effective medical and non-medical treatments are available for FM. The review identified a large number of clinical trials of both nonpharmacological and pharmacological interventions, and both in combination. Support from expert opinion elicited using the Delphi technique lends further support to their use in FM.

Treating each patient according to their specific symptoms and needs is a vital factor in FM. The diverse symptom profile compounds the individuality of each patient and demands an individualistic approach to management rather than a 'one-size-fits-all' approach. The management strategy must be tailor-made according to the primary symptoms of concern to that particular patient, bearing in mind the range of treatments that have been shown to be effective.

Research evidence strongly suggests that FM is a heterogeneous condition, with patients falling into different subgroups according to their symptom profile [12,13]. Three subgroups have been proposed. The first is those with moderate levels of anxiety, depression and catastrophizing, poor pain control but the highest pain thresholds and low tenderness. This group was suggested to represent 'typical' FM, as it was the largest group identified. Group two is those with high levels of anxiety, depression and catastrophizing, low pain control and considerable tenderness, whereas group three has low levels of anxiety, depression and catastrophizing, good pain control, but very low pain thresholds and the most tenderness [13]. These subgroups of patients would therefore be expected to respond to different management approaches [14]. Classification of these subgroups and the ability to identify patients within each at diagnosis would aid practitioners in choosing a more effective treatment regime for the patient concerned. For those patients with the highest levels of mood disturbances, it is important that this factor should be managed first through antidepressant therapy irrespective of their pain levels. The EULAR recommendations included the use of antidepressant therapy, which is beneficial for FM independent of its antidepressant effects; however, groups with high levels of depression

may require targeted antidepressant therapy. Although the cause and effect relationship between pain, mood and other symptoms is not known in FM, managing the dominating factor first should aid the treatment of other symptoms.

There has been a number of reviews on fibromyalgia treatments either focusing on nonpharmacological treatments, pharmacological treatments alone, or more specific treatments, involving exercise or antidepressants for example [15–19]. Some reviews have also been carried out with the intention of providing guidelines in the management of this condition [19]. The EULAR recommendations largely agree with previous reviews.

It has been suggested that no effective treatment exists for FM. This may be true if the intention is to cure all symptoms with one single treatment. However, with a combination of both nonpharmacological and pharmacological treatments, including patient education, current and ongoing research suggests that a good management strategy for patients could be obtained. It is hoped that these recommendations will assist practitioners in managing patients with FM constructively.

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Patient education is an important factor, as patients frequently do not understand the condition. For many patients, knowing that it is unlikely that FM symptoms will ever completely resolve, but equally that it is not progressive, helps patients to manage the pain and means that they will be less likely to have unrealistic treatment goals. Exercise is beneficial in FM, particularly aerobic exercise, but needs to be tailored to the individual patient's ability level. Although the pain levels may be increased initially, physical function, quality of life, sleep and fatigue improve with sustained exercise. Patients should be made aware of this factor so that they do not worry that they have made themselves worse or caused an injury, which is frequently reported.

Other nonpharmacological treatments that can be beneficial include hydrotherapy or balneotherapy. With or without exercise, the therapeutic effect of warm water provides improvements in pain, function and mood. While the effects may be short-lived once treatment ceases, there are no safety effects in the

long term, so if facilities are available, treatment can continue. In addition, some patients may benefit from cognitive–behavioral therapy and physiotherapy.

Pharmacological treatment can be useful in combination with nonpharmacological interventions. However, not all are effective. NSAIDs are commonly prescribed for FM to help improve pain. In clinical trials, NSAIDs appear to be ineffective, and their use in FM is not recommended. The most widely used class of medication is antidepressants, used independently of their antidepressant effects. There is a wide range of antidepressants available that are effective in FM, including: SSRIs, such as amitriptyline and fluoxetine; dual re-uptake inhibitors, such as duloxetine and milnacipran; and mono-amine oxidase (MAO) inhibitors, such as moclobemid and pirlindole. Tramadol can be considered for its analgesic effects. More recently, pregabalin, tropisetron and pramipexole have become available, which can also be of benefit, and pregabalin is now licensed by the FDA for FM. With all of these treatments, the individual patient should be considered to determine which will suit them best, and patients should be monitored throughout treatment, as long-term treatment effects are uncertain.

Since the completion of the EULAR recommendations, more trials have been published reporting promising treatments for FM, such as gabapentin [20], which showed improvements in pain, function and other symptoms, and paroxetine [21], which was beneficial for function but not pain. Equally, numerous new studies have been published for nonpharmacological interventions, which, amongst other additions, add support to the use of cognitive–behavioral therapy and related treatments [22,23].

Currently, most of these interventions have only been tested in the short term, and this needs to be considered when managing patients' long-term

care. Nonpharmacological interventions, such as cognitive–behavioral therapy, hydrotherapy and exercise, have no side effects, and are therefore safe in the long term, although with exercise the program should be graded and individualized. With the pharmaceutical treatments, it is likely that as research increases in the area of FM, more knowledge will be gained on their long-term efficacy, and a review of recommendations in 5 years' time should provide more information in this respect. Patients should therefore be monitored throughout their management, particularly as this is a condition in which patients report 'good' and 'bad' periods, which may then require modifications in their care.

Some may view the benefit of current treatment for FM as limited, producing neither a cure nor a drastic improvement, such as observed with TNF antagonists in rheumatoid arthritis. Nonetheless, current treatments have led to clinically meaningful improvements. In combination, they can make a sufficient impact on symptoms and signs, allowing patients to cope with this chronic debilitating illness. One should not underestimate the impact of this in improving the quality of life of FM patients. For funders of healthcare and society, the reduction in healthcare utilization is of equal importance.

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Affiliations

- *Serena F Carville*
King's College London School of Medicine,
Department of Academic Rheumatology,
Weston Education Centre,
Cutcombe Road, London SE5 9RJ, UK
Tel.:+44 207 239 1887
Serena.Carville@hta.org.uk
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