The rational management of fibromyalgia patients

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The rational management of fibromyalgia (FM) calls for a holistic approach based upon a bio–psycho–social approach to management. The biologic component of this approach requires an understanding of the physiology and biochemistry of chronic pain in terms of different levels of targeted intervention, and strategies for managing dysfunctional sleep, fatigue, deconditioning, psychologic distress, cognitive dysfunction and FM associated disorders [1]. The physician treating FM patients must have a wide-ranging interdisciplinary knowledge base coupled with an understanding and empathy for the existential crisis experienced by many FM patients. A structured multidisciplinary approach to managing FM patients requires an appreciation of the parts that make up the whole. One cannot successfully manage FM patients if one treats the diagnosis of FM as a unified entity. There are 12 separate management issues that usually require attention in most FM patients seeking medical help [Table 1]. The remainder of this article provides an overview of relevant management issues, which are then covered in depth in the following articles.

Table 1. The components of a structured fibromyalgia treatment program
1. Diagnosis
2. Education
3. Pain
4. Fatigue
5. Sleep
6. Psychologic disorders
7. Endocrine dysfunction
8. Dysautonomia
9. Deconditioning
10. Cognitive dysfunction
11. The existential crisis
12. Associated syndromes
Diagnosis and evaluation

The diagnosis of FM is usually based on 1990 recommendations of the American College of Rheumatology classification criteria. However, it is increasingly evident that many patients with widespread pain have less than the recommended 11 out of 18 tender points. It should be remembered that there are over 600 muscles in the human body, each of which theoretically might contain a tender point. Thus the 18 tender points to be routinely sampled in arriving at diagnosis FM represent only about 3% of the total available tender points. If a patient has widespread pain and tenderness in many other areas, he or she is unlikely to have a different neurophysiologic basis for their pain than patients with strictly ACR defined FM. Thus it is important to look at other sites that commonly harbor myofascial trigger points. The reason for this more extensive evaluation is two-fold: (1) to establish a probable diagnosis of FM in patients with less than 11 tender points, and (2) find pain generators relevant to myofascial peripheral pain that would benefit from trigger point therapy. The article by Yunus in this issue for in-depth coverage.

Taking a general medical history and performing a routine physical examination is unlikely to pick up many of the issues that are critical to formulating a rational structured treatment plan. Rather, a FM focused history and examination is an important requisite in structuring an effective management program. The history and examination will probably suggest certain problems that need further evaluation in terms of specialist referral or investigations. The particulars are discussed in depth in the articles by Yunus, Turk, and Borg-Stein.

FM is not a diagnosis of exclusion and thus laboratory tests and imaging studies play no role in establishing the diagnosis according to the 1990 ACR criteria. However, FM patients may have other painful conditions, indeed FM is a common accompaniment of lupus, rheumatoid arthritis and osteoarthritis. The role for further investigations in FM patients has not been well established, but there are clearly some associated and/or concomitant problems that will only be elucidated by an investigational approach. These ancillary problems and the usual investigations are shown in Table 2. Whether to proceed with any of these investigations is based on taking a FM-focused history and the findings on an attentive examination.

Table 2. Possible investigations

<table>
<thead>
<tr>
<th>Suspected problem</th>
<th>Initial investigation</th>
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<td>Endocrine</td>
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<td>Thyroid disorder</td>
<td>TSH</td>
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<td>Growth hormone status</td>
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<td>DHEA status</td>
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Table 2. Possible investigations

Sleep disorder
- Sleep apnea
- Narcolepsy
- Sleep phase disorder
- α-δ Sleep pattern
- Periodic limb movement
  Sleep study

Infectious diseases
- Hepatitis C
  Hepatitis C antibody
- HIV infection
  HIV screening test
- Lyme disease
  Lyme ELISA / Western blot

Psychologic stress
- Depression
  Beck depression inventory
- Anxiety
  Beck anxiety inventory
- Coping style
  Coping strategies questionnaire
- Overall impact on life activities
  Quality of life questionnaire

Peripheral pain generators
- Osteoarthritis
  Radiographs
- Peripheral neuropathy
  NCV / EMG
- Spinal stenosis
  MRI spine
- Disc herniation
  MRI spine
- Chiari I malformation
  MRI foramen magnum
- Endometriosis
  Gynecologic referral
- Migraine
  Response to 5HT₁D blocker

Autonomic dysfunction
- Neurally mediated hypotension
  Tilt table test
- Postural orthostatic tachycardia syndrome
  Tilt table test

**Education**

There is a wealth of evidence that higher educational attainments are associated with a better prognosis in many chronic diseases. There are several studies that support the value of education in FM patients. Indeed, education has several components common to cognitive behavioral techniques, such as goal setting and reassessment of priorities. The major elements of an educational program are shown in Table 3 and covered in the articles by Burckhardt and Goldenberg in this issue.

Table 3. The components of a fibromyalgia educational program
Table 3. The components of a fibromyalgia educational program
1. Validate symptoms
2. Emphasize nondestructive (not necessarily benign) nature of FM
3. Focus on improving function, not complete eradication of symptoms
4. Discuss importance of mind–body relationships—teach meditation and relaxation techniques
5. Discuss drug and nondrug therapy options
6. Discuss “touted cures” for FM
7. Explain the importance of gentle life-long exercise
8. Inform about principles of sleep hygiene
9. Discuss pacing of activities, feeling of guilt, and improved assertiveness
10. Emphasize patient's active role in any treatment

Pain

It is increasingly evident that pain perception in FM is due in part to changes in the central nervous system (CNS) that result in amplification of nociceptive impulses. This is generally referred to as “central sensitization” and is thought to result from the plasticity of neuronal synapses in response to past pain experiences. There are presumably different levels of central sensitization, accounting for the wide experience of pain in FM. A prominent psychologic input often “colors” the suffering component of the pain experience. There is now an extensive literature describing the neurophysiology and biochemistry of pain perception and amplification. Based on this contemporary scientific background, it is now possible to formulate a rational approach to managing FM related pain. The four major sites in the pain system that are potentially amenable to modification are shown in Fig. 1. In considering the rational management of pain in FM it is logical to focus on each of these four areas, namely peripheral pain generation, dorsal horn sensitization, psychologic influences, and the modulating influences of the descending pain pathway. An overview of this approach to managing FM related pain is given in the article by Rao in this issue.

Fig. 1. Neural impulses destined to result in the sensation of pain arise in peripheral nociceptors and travel in unmyelinated type C fibers to the dorsal horn of the spinal cord. After crossing the midline, ascending impulses travel to the thalamus. A projection from the lateral thalamus goes to the somatosensory cortex. A second projection from the medial hypothalamus travels to several subcortical nuclei—especially those making up the limbic system. The cognitive activity of the prefrontal cortex and the subconscious activation of subcortical nuclei influence the activity of structures in the midbrain (the PAQ and RVM), which, in turn, modulate the activity at the dorsal horn by way of the descending tract.

The periphery

There is no specific tissue pathology, at least in peripheral tissues, that can be said to be characteristic of FM. However, this fact should not be taken as negating the importance
of peripheral nociceptive mechanisms. Once the CNS is sensitized, peripheral pain
generators will not only be perceived as being more painful, but a persistent barrage of
nociceptive impulses will prolong and amplify the biochemical machinery of central
sensitization. The most common peripheral pain generators in FM are myofascial trigger
points. Although trigger points can be discerned with precision clinically, their underlying
pathology is still not well established. Common peripheral pain generators are shown in
Table 4

Table 4. Common peripheral pain generators
Myofascial trigger points
Degenerative joint disease
Inflammatory joint disease
Bursitis
Tendinitis
Developmental defects (eg, scoliosis)
Hypermobility syndrome
Neuropathic pain
Injuries / trauma
Repetitive strain
Visceral pain (eg, IBS, endometriosis)
Herniated discs
Spinal stenosis / Chiari malformation.
Recurrent headaches (eg, migraine)

Although some peripheral pain generators, notably arthritic disorders, may be helped by
nonsteroidal anti-inflammatory drugs (NSAIDs), central pain is not usually very responsive
to these agents. Thus the use of NSAIDs is usually adjunctive to the use of centrally acting
analgesics. Specific treatments for other pain generators would include, for example,
gabapentin in neuropathic pain and 5-HT1D antagonists in vascular headaches. Some pain
generators, such as osteoarthritis of the knees or the hips, and endometriosis, may be
helped by surgery. As the most common pain generator in most FM patients is myofascial
trigger points, it is imperative that these be identified and effectively managed by pacing,
stretching, improved physical conditioning, self help techniques such as acupressure and
spray and stretch, and by physician intervention with procaine or botulinum toxin injections.
The search for these pain generators is a critically important and often neglected aspect of
treating FM. This topic is covered in depth in the article by Borg-Stein in this issue.

The dorsal horn

The synapse of first and second order neurons in the spinal cord is the site of dynamic
state-dependent modulation of nociceptive impulses leading to central sensitization.
The critical pathophysiologic event leading to sensitization of the dorsal horn WDR neurons is “wind-up.” This term refers to the fact that repetitious activation of C fibers results in an exponential increase in the magnitude of the response recorded in the second order neurons in the dorsal horn. An important molecular event in the initiation and maintenance of central sensitization is activation of NMDA receptors (N-methyl-D-aspartate). Activation of NMDA receptors induces a long lasting activation potential in the stimulated neuron that results in functional neuroplasticity. With more persistent activation of NMDA receptors, structural reorganization of the dorsal horn synapse may occur; this leads to long lasting changes that result in amplified efferent sensory activity in the spinothalamic tracts. The release of excitatory amino acids such as glutamate and their interaction with cognate receptors is enhanced by neuropeptides such as substance P (SP) and nerve growth factor (NGF). This mechanism may be relevant to abnormal sensory processing in FM, as the CSF levels of both SP and NGF have been reported to be elevated in FM. It is also important to note that the activity of dorsal horn neurons is modified by the descending pain system. The concept that the somatosensory system can operate at several different levels of activity, which are dependent upon the variation of afferent input, is important in the rational pharmacotherapy of chronic pain states.

Reducing “nociceptive amplification” that occurs at the first synapse is mainly accomplished through pharmacologic means. Currently the only FDA approved drugs that modulate dorsal horn cell reactivity are those that activate or amplify the descending pain system.

The descending system originates in the midbrain and terminates at the level of dorsal horn neurons; thus influencing spinal cord sensitization. It is now increasingly appreciated that this descending system is responsible for such diverse events such as the placebo effect, fear induced hypoalgesia, anticipatory hyperalgesia, the benefits of cognitive behavioral therapy, the action of opioids and inflammation-induced hyperalgesia. Much of the research on the descending modulatory system has focused on the reduction of dorsal horn activity. Most of the drugs used to treat pain act at the level of the descending inhibitory system, working to modulate the activity of the dorsal horn. These include opioids, tramadol, GABA agonists, antidepressants, α2 adrenergic agonists and 5-HT3 antagonists. These medications are discussed in the articles by Rao, Barkhuizen, and Spaeth in this issue.

The ascending system would logically be targeted by inhibition of substance P release or blocking its interaction with the NK1 receptors. However, clinical trials of a first generation substance P antagonist have been disappointing in chronic pain states. To date NGF antagonists have not been used in human clinical trials. There is good experimental evidence that blocking NMDA receptors ameliorates pain in FM subjects. Most of this work has been performed using ketamine—a dissociative anesthetic. Dextromethorphan is a weak NMDA receptor antagonist that has been successfully used in neuropathic pain and more recently as an adjunct to tramadol and treatment of FM. These topics are discussed in depth in the articles by Rao, Barkhuizen, Russell, and Henriksson in this issue.

*The brain*
FM patients are sometimes told, but more often given subliminal cues, that their problem is “all in your head.” There is now overwhelming scientific evidence that the higher cortical centers do in fact influence the experience of pain [36][37][38][39]. However, there is no conclusive evidence, to date, that a pain experience can be exclusively generated by activity of the higher cortical centers. The critical role of the central nervous system in modulating the subjective experience of pain can now be described in terms of abnormal brain scans, the neurophysiology of central sensitization, disorders of neurotransmitters and their receptors and the remarkable clinical efficacy of drugs that target and transmitters and their receptors. This molecular pharmacologic approach to etiology is well exemplified by the success of serotonergic agents in diseases such as depression and migraine. Targeting the brain in this new era of understanding “symptoms without pathology” is now seen as one part of a multimodal approach to management [40]. Drug therapy, transcranial magnetic stimulation, hypnotherapy and cognitive behavioral therapy are some of the current tools commonly used to target the brain in the management of chronic pain problems. A detailed discussion of the psychologic aspects of managing FM patients is found in the articles by Turk and Burckhardt in this issue.

Fatigue

Tiredness is a major complaint of nearly all FM patients. Indeed if it is the predominant complaint, these patients may be diagnosed as having chronic fatigue syndrome (CFS). There are many potential causes for excessive fatigue in FM patients (see Table 5). Many of these causative factors are most amenable to nonpharmacologic interventions. However, sleep problems, depression and other psychologic stressors, some features of dysautonomia, and endocrine dysfunction are appropriately treated with drugs. The pharmacologic treatment of these problems is dealt with in the other sections of this review. Recent studies using the 5-HT3 receptor antagonist tropisetron reported benefits both in FM related fatigue and in chronic fatigue syndrome [41][42][43]. There are increasing anecdotal reports that modafinal (Provigil), a nonamphetamine drug used in narcolepsy and sleep deprivation situations, is of some benefit in improving nonspecific fatigue [43][44][45][46]. See the article by Guymer and Clauw in this issue for more in-depth coverage of managing fatigue.

Table 5. Common causes of fatigue

- Anemia
- Nonrestorative sleep
- Concurrent disease
- Dysautonomia
- Endocrine dysfunction
- Inappropriate workload
- Chronic inflammation
- Medication side-effects
- Hemochromatosis
- Deconditioning
Table 5. Common causes of fatigue

Primary sleep disorders
Major depression
Anxiety states
Chronic stressors

Sleep

Most FM patients report being light sleepers, being easily aroused by low-level noises or intrusive thoughts. Many exhibit an α–δ EEG pattern, which would explain why they never get into the restorative stages 3 and 4 of non-REM sleep \(^{47}\) \(^{48}\). The experimental induction of α–δ sleep in healthy individuals has been reported to induce musculoskeletal aching and/or stiffness as well as increased muscle tenderness \(^{49}\). A poor night's sleep is often followed a worsening of FM symptoms the next day \(^{50}\). Poor sleep is a major contributor to fatigue. Management of disturbed sleep in FM patients involves a careful analysis of causative factors, including primary sleep disorders such as sleep apnea and periodic limb movement disorder. Important nonpharmacologic aspects of sleep management include ensuring an adherence to the basic rules of sleep hygiene and regular low-grade exercise. The use of low dose tricyclic antidepressants (amitriptyline, trazadone, doxepin, imipramine, etc.) \(^{51}\) has been the mainstay of sleep pharmacotherapy in FM patients \(^{52}\) \(^{53}\). Cyclobenzaprine, a TCA analog, has also been used in some success in some FM patients, with positive effects on sleep more than on other features of FM \(^{52}\) \(^{54}\). However, some FM patients cannot tolerate TCAs due to unacceptable levels of daytime drowsiness or weight gain. In these patients benzodiazepine-like medications such as alprazolam \(^{55}\), zolpidem \(^{56}\) and zopiclone \(^{57}\) have been shown to be beneficial in a few trials. γ-Hydroxybutyrate (GHB) was used in a one-month polysomnographic study in 11 FM patients. There was a significant improvement in both fatigue and pain, with an increase in slow wave sleep and a decrease in the severity of the α anomaly \(^{58}\). A subset of FM patients suffer from a primary sleep disorder, which requires specialized management. About 25% of male and 15% of female FM patients have sleep apnea. Unless specific questions about this possibility are asked, sleep apnea will often be missed. Patients with sleep apnea usually require treatment with positive airway pressure (CPAP) or surgery. By far the commonest sleep disorder in FM patients is restless leg syndrome/periodic limb movement disorder. Treatment is usually with L-Dopa/carbidopa (Sinemet 10/100 mg at suppertime) or clonazepam (Klonopin 0.5 or 1.0 mg at bedtime) \(^{59}\). More recently other dopamine agonists such as pergolide, tolazepole and pramixepole have been proven to be effective \(^{59}\) \(^{60}\) \(^{61}\) \(^{62}\). In recalcitrant cases of restless legs, methadone (10–30 mg/hs) usually provides relief. The management of sleep problems in FM is covered in depth in the article by Moldofsky in this issue.

Psychologic distress

Increased levels of psychologic distress resulting in psychiatric syndromes are a common accompaniment of many painful chronic illnesses \(^{63}\) \(^{64}\) \(^{65}\). Approximately 30 percent of FM patients have significant current depression and about 60% have a lifetime prevalence of depressive illness \(^{65}\) \(^{66}\) \(^{67}\). Primary depressive illness can be helped by psychotherapeutic techniques as well as pharmacotherapy. In that FM patients often develop stressors...
related to psychosocial/economic issues, therapy focusing on problem solving techniques and cognitive restructuring may be beneficial in addition to drug therapy. Patients with very severe depression and suicidal ideation, bipolar disorder, and psychotic features should be referred to a psychiatrist. Although antidepressant medications are commonly used in the treatment of pain and sleep in FM patients, the doses used are usually suboptimal for treating depressive illness. There has not been a single trial to specifically address the issue of treating depression in FM patients, although one recent article addressed this issue in a useful review. It is generally assumed that treating depression in these patients is no different than treating primary depressive illness. This may be correct, but it must be born in mind that FM patients may be taking many other medications with the potential for adverse interactions and are more sensitive to medication side-effects. For instance, most of the antidepressant drugs lower the epileptogenic threshold and this theoretically could result in problems with other agents, such as tramadol, that also lower this threshold. Single doses of more than 200 mg of bupropion or a total daily dose of more than 450 mg poses an increased risk of seizures. Selective serotonin–reuptake inhibitors may cause drug interactions because of their inhibition of the cytochrome P-450 system. Since the cardiovascular effects of tricyclic antidepressants include postural hypotension (a common problem in FM patients with dysautonomia), cardiac conduction abnormalities, and arrhythmias, the use of these drugs should be avoided in patients with symptomatic hypotension, ischemic heart disease and known arrhythmias. Nearly all antidepressant medications are eliminated through the liver, so they should be used with caution in patients with hepatic dysfunction. The evaluation and management of psychologic issues are covered in the articles by Turk, Burckhardt, and Goldenberg in this issue.

Endocrine dysfunction

There is no good evidence that FM is primarily due to endocrine dysfunction. However common problems such as hypothyroidism and menopausal symptoms will often aggravate pain and fatigue and appropriate replacement therapy is usually indicated. There has been much interest in abnormalities of the hypothalamic–pituitary–adrenal axis (HPA) in FM patients. The general impression is that FM patients have a somewhat reduced HPA responsiveness. However, replacement therapy with Prednisone 15 mg/day was not shown to be therapeutically useful. About one third of FM patients are growth hormone deficient and replacement therapy is of benefit to many growth hormone deficient FM patients. See the article by Genen et al in this issue for in-depth coverage.

Dysautonomia

Abnormalities of autonomic function appear to be associated with both FM and chronic fatigue syndrome. The most common presentation of dysautonomia in FM patients is the finding of neurally mediated hypotension in about one third of patients. Another manifestation of dysautonomia is the postural orthostatic tachycardia syndrome (POTS). These patients have an exaggerated increase in their heart rate, rather than a pronounced fall in blood pressure, in response to standing and exercise. Dysautonomia is often associated with severe fatigue. Treatment involves: (1) education as to the triggering factors and their avoidance, (2) increasing plasma volume (increased salt intake, prescription of Florinef), (3) avoidance of drugs that aggravate hypotension (eg, TCA’s, antihypertensives), (4) preventing the ventricle–baroreceptor–reflex (α-adrenergic antagonists or disopyramide), and (5) minimizing the efferent limb of the baroreceptor...
Deconditioning

Most FM patients are aerobically unfit and have suboptimal strength and poor flexibility. The notion that “exercise is good for FM patients” is an accepted contemporary truth. There is evidence that acute exercise is associated with reduced pain perception \[82\] and a lowered pain threshold \[83\] . Although endorphins are secreted in response to acute exercise \[84\] , they are probably not the sole mechanism of exercise-induced analgesia \[85\] . During graded exercise, endorphins only start to increase at the anaerobic threshold (ie, lactate production), and in moderate steady state exercise they do not increase until exercise duration exceeds one hour \[86\] . The benefits of exercise are based on reasonable scientific evidence, but exercise may also be deleterious. Whether it is good or bad for FM patients probably depends upon many variables, such as age, current level of conditioning, rate of increase of exercise intensity, frequency of exercise, ratio of eccentric to concentric muscle use, hormonal anabolic status and negative factors such as obesity, arthritis and concomitant muscle disease. FM introduces an important factor into the equation of postexertional pain, that is, amplification of sensory processing (ie, central sensitization). It is hypothesized that for a given intensity of exercise, FM patients will experience more postexertional pain than non-FM patients \[87\] . The message is that exercise is a double-edged sword in the management of FM patients. It’s just too easy to blame a patient’s lack of progress on their poor adherence to a too rigorous exercise regime. A carefully planned individual exercise program is always needed; this is best supervised by an exercise physiologist or a physiotherapist. A structured approach to prescribing exercise in FM patients is given in the article by Jones and Clark in this issue.

Cognitive dysfunction

Cognitive dysfunction is a major problem, according to self-reports, for many FM patients \[88\] . Patients commonly describe difficulties with short-term memory, concentration, logical analysis and motivation. Problems with cognitive function are being increasingly recognized in FM patients and are the subject of increasing research efforts \[89\] . Currently, defects have been described in terms of working memory, episodic memory and verbal fluency. These decreases in cognitive performance and has been estimated to be equivalent to 20 years of aging \[90\] . Cognitive dysfunction adversely affects the ability to be competitively employed and may cause concern as to an early dementing type of neurodegenerative disease. In practice the latter concern has never been a problem and patients can be reassured. The cause of poor memory and problems with concentration is, in most patients, related to the distracting effects of chronic pain and mental fatigue. Thus the effective treatment of cognitive dysfunction in FM is dependent on the successful management of the other symptoms.

The existential crisis

There is a universal human need for understanding bothersome symptoms in terms of a definitive diagnosis and plans for a cure. Everyone expects a cure until confronted with a chronic and currently incurable disorder. Despite being a common disorder, the term FM does not have widespread public recognition. One might expect that the concept of
chronicity without degeneration would bring sighs of relief, but this is seldom the case. As rheumatologist I am often struck by the fact that most patients would prefer a diagnosis of lupus or rheumatoid arthritis rather than a diagnosis of FM. And, it is not just the patient who would prefer these diagnoses, so too would many rheumatologists! Having a chronic painful disease, which there is currently no cure, often produces a cascade of emotional reactions that can be likened to an existential crisis. Needless to say, this crisis is made all the more worse if there is doubt cast on the legitimacy of a diagnosis. Many patients have not heard of FM. Those who are acquainted with this diagnosis are often more medically sophisticated and aware of the apathy and skepticism surrounding the diagnosis of FM; thus they are often reluctant to accept this diagnosis. It often takes many patients a year or more to come to terms with a diagnosis of FM. During this time they typically go through stages of disbelief, anger and frustration, anxiety and depression, before they accept the reality of having such a frustrating and life altering the condition. It is only when they fully accept this diagnosis that much progress can be made in terms of a structured approach to management in which the patient themselves becomes an integral part of the treatment team. It's important for physicians treating FM patients to understand that there is a time lag in acceptance, and that during this period little progress may be made. This is time when patience, perseverance, listening, education and empathy are most needed. See the articles by Turk, Burckhardt, and Goldenberg in this issue for further coverage.

Associated disorders

FM has been associated with several distinct syndromes (see Table 6). In some cases, these syndromes are a significant contributor to the overall symptom morbidity of FM patients. Furthermore, some may aggravate central sensitization by providing peripherally generated nociceptive input.

<table>
<thead>
<tr>
<th>Table 6. Commonly associated problems</th>
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<tr>
<td>Irritable bowel syndrome</td>
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<td>Irritable bladder syndrome</td>
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<td>Restless leg syndrome</td>
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<td>Cognitive dysfunction</td>
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<td>Dizziness</td>
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<td>Cold intolerance</td>
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**Irritable bowel syndrome**

Irritable bowel syndrome is a very common associated condition, affecting 30–50% of FM patients. Treatment involves (1) elimination of foods that aggravate symptoms, (2) minimizing psychologic distress, (3) adhering to basic rules for maintaining a regular bowel
habit, (4) prescribing medications for specific symptoms: constipation (stool softener, fiber supplementation and gentle laxatives such as bisacodyl), diarrhea (loperamide or diphenoxylate) and antispasmodics (dicyclomine or anticholinergic/sedative preparations such as Donnatal). There is currently interest in using 5-HT₃ antagonists to help visceral spasm and diarrhea \[^{100}\]. However, the recently introduced 5-HT₃ antagonist, Alosetron, was withdrawn from the market in the United States after some patients developed severe ileus, with several deaths.

**Irritable bladder syndrome**

Irritable bladder syndrome is increasingly being recognized as a problem for FM patients \[^{(213)(1756)}\]. Treatment involves (1) increasing intake of water, (2) avoiding bladder irritants such as fruit juices (especially cranberry), (3) pelvic floor exercises (e.g., Kegel exercises) and the prescription of antispasmodic medications (e.g., oxybutinin, flavoxate, and hyoscamine).

**Dizziness**

Dizziness is a common complaint of FM patients, but has only been formally studied sporadically. Treatable causes related to FM include: (1) proprioceptive dysfunction secondary to muscle deconditioning, (2) proprioceptive dysfunction secondary to myofascial trigger points in the sterno–cleido–mastoids and other neck muscles, (3) neurally mediated hypotension and (4) medication side effects. Treatment is dependent on making an accurate diagnosis.

**Cold intolerance**

Many FM patients complain of being colder than their partners; indeed, a significant subset of FM patients have cold induced vasospasm \[^{(101)}\]. Treatment involves: (1) keeping warm, (2) low-grade aerobic exercise (which improves peripheral circulation), (3) treatment of dysautonomia (see above), and (4) the prescription of vasodilators such as the calcium channel blockers (but these may aggravate the problem in patients with hypotension).

**Multiple sensitivities**

This condition is thought to be a manifestation of central sensitization. Several recent reports have suggested multiple sensitivity is a common accompaniment of FM \[^{(102)(103)}\]. The major management strategy is to avoid the offending agents. There have been no studies of pharmacotherapy of this condition in FM patients. In general, FM patients are unduly sensitive to drug side effects, so new medications should be started at low doses.

**Evaluating response to treatment**

The primary aim of therapy in chronic incurable disorders is to enable the patient to live as full and productive life as possible. Thus palliation of symptoms combined with improved physical and emotional well-being are the essential goals of effective treatment. Assessing
Improvement or worsening in FM has to take into account the plurality of relevant problems as given in Table 1. In general, questionnaires that provide details about quality of life probably give the best overall self-assessment of change, as quality of life is severely impaired in FM patients \[104\] \[105\]. However, there is not necessarily a linear relationship between quality of life and health status. Improved coping, as occurs longer the duration, the older the individual, the more likely the person will report a relatively good quality of life. The short form 36 (SF 36) is a commonly used health questionnaire that has been applied to many chronic disorders and thus has the advantage of enabling comparisons with other disorders. Pain can be assessed with regular use of pain diagrams and visual analog scales (pain VAS) as well as its effect on function. Interestingly, measurement of tender point scores has been reported to bear little relationship to self-reported pain \[106\]. The 6-minute walk distance has proved useful in assessing improved conditioning in FM \[107\] \[108\]. If the patient’s main current problem is depression, it would be appropriate to monitor this with a daily diary and/or Beck Depression Inventory. It is evident that the priorities of management will change over time, for instance, an initial focus on pain relief may later be replaced with a focus on fatigue or cognitive dysfunction. A questionnaire that provides an overall view of the plurality of problems in FM is the Fibromyalgia Impact Questionnaire (FIQ) \[109\]. The FIQ has shown a good sensitivity to change \[107\] \[110\] \[111\] and is currently the most widely used FM questionnaire and by one assessment the most useful \[112\]. See the articles by Yunus, Turk, and Goldenberg in this issue for more information.

References

Abstract


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