

# Can Fibromyalgia Syndrome Be Treated?

## Fibromyalgia Syndrome

Fibromyalgia Syndrome (FMS) is a chronic, painful, and sometimes disabling condition commonly encountered by primary care physicians. Recent research has provided information about the pathophysiology of FMS that has implications for treatment. For example, it now seems most likely that the major pathophysiologic mechanisms of FMS involve central sensitization in the CNS, although a peripheral source of nociception may initiate and/or perpetuate this sensitization.



Thus, drugs that act through the CNS (such as tricyclic agents, selective serotonin reuptake inhibitors [SSRIs], and tramadol) are more likely to be effective than those that act primarily at a peripheral level—for example, NSAIDs. The same CNS mechanism may also explain why hypnotherapy or meditation may be beneficial in Fibromyalgia syndrome.

Understanding pathophysiologic mechanisms, as discussed in our article in the September 1, 2003, issue 1, is important for treating disease. Although the mechanisms in Fibromyalgia syndrome are incompletely understood at this time, the relevant factors for treatment purposes include central sensitization (Amplified or Perpetuated by Poor Sleep); Psychological Distress; Peripheral Pain Generators (eg, Overuse of Body Parts, Repetitive Trauma, and Arthritis);

Deconditioning; and other aggravating factors (eg, Weather, Noise, and Comorbid Conditions).

The management of Fibromyalgia syndrome has been reviewed in detail. Key components of treatment are shown in Table 1. [See the original article.] We will describe each of these below.

## **Positive and Empathetic Attitude of the Physician:**

The management of Fibromyalgia syndrome begins with the very first contact with the patient. Many patients with aches and pains have had an unhelpful or even unpleasant experience with their previous health care providers, or heard of such experiences from their friends. Greeting a patient in a friendly and positive manner goes a long way to assure that you are a kind and interested physician. Maintain such an attitude of caring throughout the period of consultation and subsequent follow-ups.

## **Making a Firm Diagnosis:**

As we emphasized in our previous article, Fibromyalgia syndrome should be diagnosed by its own characteristic features of widespread pain and multiple tender points, and not by "Ruling out" other conditions, as stated in the American College of Rheumatology (ACR) criteria. Ordering one more test to exclude such and such disease may cause anxiety, since such an approach is not only unnecessary, it may also indicate uncertainty on the part of the physician, and thus erode a patient's confidence in him or her.

## **Patient Education, Reassurance, and Individualization of Treatment:**

After the diagnosis is made, patient education is a most important step. Provide information to patients with

Fibromyalgia syndrome, in a simple, understandable way regarding the diagnosis and probable cause, aggravating factors (Table 2), and prognosis, and then use Table 1 to discuss various elements of management. Emphasize that a patient's pain and other symptoms are "Real" and based on a "Chemical Imbalance," Such as excessive substance P and decreased serotonin.

However, reassure your patient that Fibromyalgia syndrome is not life-threatening (despite much pain), and that it does not cause tissue damage. (We avoid using the term "benign" because patients who are suffering may resent it.) Advise on general healthy behavior, including weight loss, smoking cessation, good sleep habits, and regular exercise. Also emphasize the need for both nonpharmacologic and pharmacologic therapy. A recent study has found an association between overweight and several important FMS features, such as fatigue, decreased physical function, and increased number of tender points. Smoking is positively associated with pain, global severity, and functional difficulties.

Tailor your management according to each patient's symptom profile. For example, some patients may have significant psychological distress, while others have a predominant sleep problem, and yet others have specific aggravating factors, such as poor sleep, repetitive trauma (vocational and recreational), and mental stress. Some patients cope with their symptoms fairly well, while others do not. Although Fibromyalgia syndrome is a chronic painful condition, emphasize that most patients find relief with appropriate treatment for a period of time, and that during this time they can be meaningfully functional.

## **Addressing Aggravating Factors:**

Aggravating factors that should be addressed are listed in Table 2. The importance of physical fitness (in the context of deconditioning) will be described in detail under

“Nonpharmacologic Intervention.” Other important factors will be discussed here. Note that treatment of concomitant hypothyroidism does not eliminate Fibromyalgia syndrome symptoms, but it may help relieve fatigue and low energy.

**Psychological Factors.** Psychological distress is correlated with pain, including pain in FMS. Thus, psychological factors, such as anxiety, stress, depression, and poor coping, should always be addressed. Stress is an important factor in both triggering and perpetuating Fibromyalgia syndrome symptoms. Besides counseling for psychological difficulties, anxiolytics and antidepressants in appropriate doses may be required. SSRIs are as effective as tricyclic agents for depression and have fewer side effects. If necessary, refer patients to a psychologist for stress reduction or to a psychiatrist for refractory anxiety and depression.

**Improving Sleep Quality.** Nonrestorative sleep exacerbates pain and fatigue. Poor sleep at night predicts pain the next day. Take a good sleep history and offer suggestions for improved sleep quality (Table 3). Morning fatigue is a sensitive indicator of nonrestorative sleep. Restless legs syndrome and/or periodic limb movement disorder is an important cause of sleep disturbance and is treatable with medications (see “Pharmacologic Management”).

**Environmental Factors.** Depending on individual sensitivity to specific weather factors, advise your patients to avoid unnecessary outside trips in the winter and to stay in comfortable temperature in an air-conditioned room in the summer as much as possible. Many patients are also sensitive to noise, smell, and light. Hyperresponsiveness to many of these environmental stimuli, as well as to many medications, is thought to be attributable to central sensitization.

**Occupational Factors.** Prolonged sitting or standing at work, adverse ergonomic factors that cause muscle or other soft

tissue strain, repetitive motion, and job stress and dissatisfaction may all contribute to Fibromyalgia syndrome symptoms. Based on current knowledge of pain physiology, repetitive motions are likely to cause central sensitization and subsequent amplification and intensification of pain. Because an important goal of treatment of FMS is to keep the patient employed, both for psychological and economic reasons, these work-related aggravating factors should be discussed with the employer, along with appropriate recommendations, such as change of duties and improvement of adverse ergonomic conditions.

**Comorbid Conditions.** Although this theory has not been directly proved in patients with Fibromyalgia syndrome, current knowledge of central sensitization operative in Fibromyalgia syndrome suggests that any continued source of peripheral nociception enhances this sensitization and worsens pain. Thus, arthritis of any kind, neuropathy, or headaches should be treated. Restless legs syndrome disturbs sleep (Table 2).

**Family and Social Factors.** Adverse family circumstances, such as a stressful marriage, demanding children, and a lack of empathy and understanding by family members, can add significant distress. This, in turn, may aggravate pain, fatigue, and other associated symptoms, such as headaches and migraine. However, excessive attention from a solicitous spouse may also adversely affect a patient's pain. Refer your patient to a psychologist for assistance with coping skills, if needed. Encourage patients to have a hobby and a network of support.

## **Nonpharmacologic Approach:**

When primary care physicians inquire about Fibromyalgia syndrome treatment, they commonly ask, "I have used such and such medications without success. What should I try next?" This is unfortunate, since nonpharmacologic approaches,

including patient support and education (Table 1), are an essential component of Fibromyalgia syndrome therapy and should be used in parallel with drug treatment with equal emphasis. Often physicians do not optimally utilize nonpharmacologic therapies. Patients who use both nonpharmacologic and pharmacologic therapies have better results than with either modality alone.

**Physical Fitness.** Many patients with FMS are deconditioned. Several controlled studies have shown the benefits of regular exercise in ameliorating Fibromyalgia syndrome symptoms, including pain. However, randomized, controlled studies that did not preselect patients based on their ability to engage in exercises did not demonstrate such benefit. I think the reason is obvious: it is difficult for most Fibromyalgia syndrome patients to exercise vigorously enough to achieve cardiovascular fitness.

But some exercise is better than none for overall health benefit, and it is important to be persistent in encouraging and monitoring a patient's exercise at every office visit. We emphasize that in the phrase "Regular Exercise," Regular is more important than exercise. It is the habit of initiating an exercise every day that is crucial.

We insist that patients keep a daily diary of their physical activities, preferably in graphic form (how much time spent and the peak pulse rate) and bring the weekly graphs for our inspection during the next visit. We encourage our patients by saying that everyone can exercise. The key is to start slowly – for example, only 2 to 3 minutes of exercise a day, if need be.

Ask patients to gradually increase the exercise time, say by 2 to 3 minutes each week, to the ideal 20 to 30 minutes of brisk exercise every day. Treadmill or outdoor walking, aerobic dancing, and swimming are excellent forms of exercise, depending on patient preference. Muscle strengthening

exercises, started gradually as above, is useful in reducing the effort needed to do a given task, and is likely to lessen fatigue.

**Physical Therapy.** No controlled data exist to show that physical therapy by itself helps patients with Fibromyalgia syndrome. However, clinical observation suggests that a subgroup of patients report significant benefit from such therapy for a few days. Physical therapy modalities include local heat (moist or dry), ultrasound, stretching, range of motion exercises, muscle strengthening exercises, manipulation, and correction of posture. After initial demonstration by a therapist, many of these modalities may be used by a patient at home regularly.

**Electromyographic Biofeedback.** Current data on the efficacy of electromyographic (EMG) biofeedback alone are contradictory. However, if facilities are available, this modality may be prescribed along with other important forms of therapy, such as education, exercise, and medication. Some patients may benefit if they can be persuaded to try EMG biofeedback for at least 4 months or longer.

**Acupuncture and Transcutaneous Electrical Nerve Stimulation (TENS).** One double-blind controlled study has shown the benefit of electroacupuncture in Fibromyalgia syndrome over 3-week period. Long-term studies is needed. Appropriate studies showing the efficacy of conventional acupuncture or TENS are lacking. Some patients report benefit, but others report aggravation of pain from acupuncture or TENS therapy.

Cognitive behavioral therapy and multidisciplinary treatment. Cognitive behavioral therapy(CBT) involves training patients in coping skills, healthy behavior patterns, and restructuring of maladaptive beliefs, such as catastrophizing ("I have a serious disease like cancer, and I may die of it") or significant pessimism ("My symptoms are killing me and I will never get better. I cannot do exercise; I cannot do

anything”).

Although a few nonrandomized studies using waiting list controls demonstrated the benefit of CBT in Fibromyalgia syndrome, two well-designed randomized investigations using attention controls (who received adequate patient education regarding Fibromyalgia syndrome and its management, but without structured comprehensive CBT) demonstrated no benefit in the group that used CBT (Which is Time-Consuming and Expensive) compared with the control group.

We have found that some – but not all – “Difficult” Fibromyalgia syndrome patients (those who did not respond to usual treatment) whom we referred to a competent psychologist for CBT derived some benefit. However, one may argue that CBT should be started early (particularly in those showing poor coping skills during the initial consultation) rather than late, before maladaptive behaviors become ingrained.

Instead of recommending multidisciplinary treatment in a group setting under one umbrella, we individualize care and refer patients to an appropriate facility (Physical Therapy, Exercise, CBT, etc) as needed. Multidisciplinary treatment is expensive and often not covered by insurance and, because of the group setting, does not focus on an individual patient’s concerns. Its value is yet to be determined by randomized, double-blind controlled studies.

**Hypnotherapy.** One controlled study has shown the benefit of hypnotherapy in “Refractory” Fibromyalgia syndrome. we believe hypnotherapy is worth trying in an otherwise nonresponsive patient if a competent therapist is available.

**Meditation.** In an open but otherwise well-designed study, weekly supervised meditation for 10 weeks was impressively beneficial in more than half of patients. Patients were also required to meditate daily for 50 minutes at home. In practice, however, patients may not be willing to comply with



such a time-consuming regimen.

## **Pharmacologic Treatment:**

Drug treatment is as important as nonpharmacologic therapy. Randomized, double-blind, controlled studies have shown the efficacy of several drugs in FMS; however, long-term data are not available. Because evidence-based medicine is appropriately emphasized in current medical practice, agents with clinically demonstrated efficacy should be tried first.

We then use other drugs in the same class (e.g., Tricyclic agents other than amitriptyline) that have a similar mode of action, despite the fact that these drugs may not have been studied in controlled trials. Like any treatment modality, Drug therapy needs to be individualized, Depending on symptom severity, Comorbid psychiatric or "Organic" Diseases, Sleep Difficulties, and history of side effects. Drug treatment in Fibromyalgia syndrome has been reviewed.

**Simple Analgesics.** Simple analgesics, such as acetaminophen, may be prescribed for patients with mild or mild to moderate pain. NSAIDs were ineffective in several studies of patients with FMS. However, these agents may be used for concomitant conditions, Such as arthritis and dysmenorrhea, with the usual precautions.

Table 4 lists the centrally acting drugs that have been found useful or effective in Fibromyalgia syndrome, including those that were studied in controlled trials. Their dosages and common side effects are also listed.

**Tricyclic Agents.** These drugs are reuptake blockers of both serotonin and norepinephrine, neurotransmitters that are implicated in the inhibitory pathway of pain physiology. Amitriptyline 2,16 and cyclobenzaprine 2,17 are the most widely used, based on their demonstrated efficacy in several studies. A lower dose of amitriptyline than that used in

depression is effective in Fibromyalgia syndrome. The usual dose is 25 to 50 mg at bedtime. In patients who have side effects at 25 mg, start with a lower dose, i.e., 10 mg, and gradually titrate to 50 to 75 mg at bedtime.

Common adverse reactions include grogginess, dry mouth, daytime sleepiness, weight gain, and paradoxical insomnia. Cardiac arrhythmias, mostly associated with tricyclic antidepressants, occur rarely; use caution in prescribing these agents in patients with heart disease and in elderly persons. Cyclobenzaprine, a drug related to the tricyclics but without antidepressant properties, is as effective as amitriptyline and has similar side effects. The Long-Term efficacy of tricyclic agents in Fibromyalgia syndrome is not known.

**SSRIs.** Fluoxetine alone at an average dose of 55 mg/d was effective in most outcome measures in a double-blind, randomized, controlled study of women with Fibromyalgia syndrome. A similarly controlled study of a combination of fluoxetine, 20 mg in the morning, and amitriptyline, 10 to 25 mg at bedtime, found that this combination was significantly more effective than either drug alone in relieving both pain and poor sleep. Studies have shown that a drug with both serotonergic and noradrenergic properties works better in chronic pain.

Remember, the dose of a tricyclic drug, when used in combination with an SSRI (particularly fluoxetine), should be kept low to avoid serious drug interactions resulting in tricyclic overdose; blood tricyclic level should be checked if such an interaction is suspected. Other SSRIs shown in Table 4 have not been studied in Fibromyalgia syndrome, but anecdotal observation supports their benefit, particularly in combination with a low-dose tricyclic agent (10 to 50 mg at bedtime).

Other antidepressant medications. Many patients in our clinic

have reported benefit from venlafaxine, trazodone, and nefazodone, but controlled studies are lacking.

### **Other Centrally Acting Drugs:**

Tramadol, like cyclobenzaprine, is a centrally acting drug without antidepressant properties. It is a reuptake inhibitor of serotonin and norepinephrine, but it also binds weakly with  $\mu$ -opioid receptors. Although reports of addiction are rare, tramadol should not be prescribed in patients with a history of drug (including alcohol) abuse. Tramadol was effective in a randomized, double-blind controlled trial of patients with Fibromyalgia syndrome. In our practice, we prescribe 400 to 800 mg/d in divided doses with food. Smaller doses should be tried first and increased to the optimal dose, because adverse reactions (Such as GI Effects, Dizziness, and Somnolence) are common.

Note that drugs with demonstrated efficacy in randomized, double-blind studies are not all antidepressants, which suggests that depression is not synonymous with Fibromyalgia syndrome. Moreover, tricyclic antidepressants have a direct central analgesic effect in Fibromyalgia syndrome irrespective of their effect on depression.

Medications for associated symptoms. Hypnotic agents are useful for induction of sleep, but not for sleep maintenance or pain. Tricyclic agents are a better choice for restorative sleep in patients with Fibromyalgia syndrome. Associated significant anxiety and depression should be adequately treated with anxiolytic agents (such as alprazolam) and antidepressants; remember that a larger dose of antidepressants is required than the low dose prescribed for Fibromyalgia syndrome symptoms alone. For restless legs syndrome, there are several choices (all taken at bedtime):

- Clonazepam, 0.5 to 2 mg.
- Carbidopa-Levodopa, 25 to 100 mg, 1 or 2 tablets on an

empty stomach.

- Opioids (eg, Codeine (, 30 to 60 mg). Caveats include an increase in restless legs syndrome in the afternoon associated with Carbidopa-Levodopa and the potential abuse of codeine.

## **Tender Point Injections:**

In an open study, injections of tender point sites were useful, with a median relief period of 3 months. We ask our patients to localize their most symptomatic sites with their own fingertips first and then we confirm those sites by palpation for injection. We use a 27-gauge 1-inch long needle and 1% or 2% lidocaine, 0.25 to 0.50 mL, usually in no more than 4 or 5 (Typically 2 to 4) sites. Make sure that the needle does not penetrate tissues beyond the muscles, to avoid such complications as pneumothorax.

Studies of myofascial syndrome suggest that the addition of corticosteroids has no advantage over lidocaine alone. Even dry needling is useful, although it is more painful than injection of a local anesthetic. Such injections may work by stimulating the local pain inhibitory neurons, probably "Desensitizing" the state of central sensitization in FMS, which may explain why the benefit lasts beyond the local anesthetic effects. Remember, the success of a tender point injection depends not only on the injection itself, but also "Physician Effect" (Positive Attitude, Support, Encouragement).

## **What About Narcotics?**

Whether narcotics may be used in benign pain conditions such as FMS or osteoarthritis (OA) is a contentious issue among physicians. A double-blind, randomized controlled study of oxycodone (10 to 20 mg every 12 hours) in OA demonstrated its efficacy and relative safety over a period of 12 months.

We use narcotics quite uncommonly, and only when other management components have failed. We have found oxycodone, 10 to 30 mg/d in divided doses every 12 hours, and acetaminophen, 300 mg, with codeine, 30 mg, 2 to 4 times a day, beneficial. We use opioids mostly during a Flare-up, but they may be continued long-term provided no side effects or abuse emerges.

Although, theoretically, short-acting opioids may have a greater potential to induce addiction, we have not encountered such a problem in our practice. The key is to select patients carefully. A history of addiction or alcohol or drug abuse is a contraindication, and patients must be monitored regularly for Drug-Seeking behavior. Another caveat based on recent studies is that opioids can paradoxically increase sensitivity to pain in some persons. A patient who seems to need higher doses after some time may benefit from a decreased dose.

## **Complementary and Alternative Medicine:**

Complementary and alternative medicine (CAM) in FMS has been reviewed. It remains, for the most part, unproved in Fibromyalgia syndrome. A large number of studies on St John's wort have yielded contradictory results. This herb product cannot be confidently recommended at this time because of a lack of standardization in various manufacturers' products; its potential serious interactions with other antidepressants, particularly SSRIs; and its ineffectiveness in severe depression.

S-adenosylmethionine (SAM-e) is a naturally occurring compound that, at a dose of 400 mg bid, significantly improved pain, fatigue, and mood in a randomized, double-blind controlled study involving 44 Fibromyalgia syndrome patients. GI symptoms are the most common side effects, and an interaction with other antidepressants may occur. We have found SAM-e beneficial in a few of our patients.

Static magnetic therapy also relieved pain over a period of 6

months in a randomized, Double-Blind controlled study. We have not used this therapy so far, but it is worth trying in consultation with an expert in this area.

There are limited studies on CAM in Fibromyalgia syndrome, but for general information, the review by Crofford and Appleton is useful.

The figure shows a general pyramidal approach to Fibromyalgia syndrome management. Note that tender point injections may be used at any stage of treatment and opioid therapy is kept at the top rung of the pyramid.

## **Prognosis:**

Although follow-up studies of patients with Fibromyalgia syndrome show no significant fluctuations over a period of several years, these studies have not evaluated symptoms frequently, for example, every 1 to 2 weeks. Our observations suggest that most patients experience significant relief with therapeutic interventions over a period of 2 to 12 weeks (sometimes longer), during which time they are also meaningfully functional. In a minority of patients, such relief may be sustained long-term. Thus, appropriate management is important.

## **Clinical Highlights:**

- ▶ Reassure patients that fibromyalgia syndrome (FMS) is not life-threatening and will not cause tissue damage, and that their symptoms are real and likely caused by a chemical imbalance. Educate patients about such healthy behaviors as weight loss, smoking cessation, and good sleep habits.
- ▶ Stress may trigger or perpetuate Fibromyalgia syndrome symptoms, including pain. Besides counseling, pharmacologic agents such as antidepressants may be required. For patients who are anxious, anxiolytics at bedtime may be useful.
- ▶ Regular exercise is an important component of therapy. Have

patients start gradually, if necessary, and encourage them to keep an exercise diary. Appropriate forms of exercise include walking, aerobic dancing, swimming, and muscle strengthening. Other nonpharmacologic modalities include physical therapy, electromyographic biofeedback, electroacupuncture, transcutaneous electrical nerve stimulation, cognitive behavioral therapy, hypnotherapy, and meditation.

▶ Simple analgesics, such as acetaminophen, may be prescribed for mild to moderate pain. NSAIDs are ineffective for FMS symptoms but may be helpful for concomitant conditions.

▶ Amitriptyline is an effective tricyclic antidepressant and the agent most extensively studied for Fibromyalgia syndrome. It is used in lower doses than those recommended for depression. Cyclobenzaprine has similar efficacy and side effects. Fluoxetine is effective alone at a higher dose and in combination with amitriptyline.

▶ Tender point injections generally relieve symptoms for 1 to 3 months. Ask the patient to localize the most symptomatic sites with his or her fingertips first, and then confirm those sites by palpation for injection. Use a 27-gauge 1-inch needle and 1% or 2% lidocaine, 0.25 to 0.50 mL, in no more than 5 (usually 2 to 4) sites.

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