

Fibromyalgia

Documentation & Treatment

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Fibromyalgia syndrome is a relatively new name for an old medical problem. Why do people chronically hurt all over, feel fatigued, and wake up feeling non-rested despite getting adequate sleep? Why do these symptoms often appear to coexist with painful bowel, bladder, and jaw (TMJ) symptoms, as well as symptoms of anxiety and cognitive impairment? The term fibromyalgia (FM) was only defined in 1990 by the American College of Rheumatology. Since then, the National Institutes of Health (NIH) and other institutions have dramatically increased their funding for FM research, and there has been a significant increase in published articles on fibromyalgia and medical conferences that include FM research and treatment in the curriculum.

The major purpose of this article is to provide information that FM patients can take to their doctors to help them make diagnoses earlier. It can also be used as a tool to provide objective scientific evidence for skeptical doctors who don't believe that FM is a real medical entity. Finally, it will provide some basic FM treatments that primary care doctors can initiate.

FM is not a new medical problem, it is just better understood recently. It used to be called by different names. There are medical articles on "neurasthenia" and "muscular rheumatism" which date back to the mid-1800's that describe illnesses similar to FM. Dr. Gowers created the term "fibrositis" in 1904, but it wasn't until 1978 that Drs. Smythe and Moldofsky published research on the associated

sleep pathology and the peripheral and central nervous system (CNS) pain sensitization that appears to be essential to the development of FM.¹

Rheumatologists have taken the lead in diagnosing and treating FM, which makes sense since rheumatology was the medical specialty that defined the syndrome. In addition, many fibromyalgia patients have joint pain and other forms of musculoskeletal pain in addition to their FM, as well as elevated levels of inflammatory chemicals that cause pain called cytokines (anti-TNF and Il6) in their central nervous systems—abnormalities shared by many other rheumatology patients. There is also a strong association between FM and many of the diseases rheumatologists treat (rheumatoid arthritis, Sjögren's syndrome and systemic lupus). It has been estimated that 10-20% of patients in a rheumatologist's office practice have FM.²

Despite all of the recent advances in the understanding of FM, the problem many FM patients still experience is a long, time delay between the onset of their symptoms and the diagnosis of FM. Since FM patients often have multiple symptoms, and there are no objective lab tests or imaging studies that are readily available to make the diagnosis, they often face years of multiple medical evaluations, multiple specialists, a lot of frustration and suffering, and no answers. It would benefit the FM patient if more primary care doctors considered FM in their differential diagnosis when a patient presented with chronic pain and fatigue since FM is a relatively common illness estimated to affect 4-10 million Americans. Demographic studies show that FM has a prevalence in the U.S. of 3½ % of all women and ½ % of all men over the age of 18 years. These figures are similar to the prevalence of FM

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in other countries.³ Many of my patients have reported having symptoms for over five years and consulting more than five doctors before being referred to me for diagnosis.

If FM is such a relatively common illness, why do so many patients complain about delays in diagnosis and about doctors who still don't believe that FM even exists? My impression is that many doctors practicing today who were trained before 1990 when FM was defined may be reluctant to accept new diagnoses that were not known at the time they were trained. I teach doctors in training at the George Washington University Hospital, and I find their knowledge regarding FM to be generally good. A careful history and complete physical examination are necessary to make the diagnosis. Unfortunately, with the pressures of managed care, doctors are sometimes pushed to spend less face-to-face time with their patients, thus making FM more difficult to diagnose.

FM is not an easy diagnosis to make. It is essential for a doctor to do an adequate medical evaluation to "rule out" other diseases that can mimic FM. Once a patient is diagnosed with FM, it is important not to attribute all existing symptoms to FM without considering other possible causes. FM patients can get sick with other illnesses just like any other patient, but their symptoms may be more severe and the anxiety relating to their illness may be greater than other patients with the same illness, injury, or infection. It is also important to reassure doctors that FM patients get better from infections and surgical procedures just like other patients. When the diagnosis of a patient with chronic musculoskeletal pain and fatigue is unclear or resistant to treatment, rheumatologists are available for consultation and treatment.

Scientific Findings That Support Fibromyalgia As A Medical Entity

Tender Point Exam and Pain Threshold Studies

The definition of FM includes identification of at least 11 of a possible 18 tender points and widespread pain for at least three months duration as described in the 1990 ACR definition of FM. These tender points can be assessed by pressing on specific locations of the body with a pressure of 4 kg/m² (enough pressure to blanch the skin under

the thumb nail). Pressing on these painful points usually creates an involuntary painful response, and the doctor usually doesn't have to ask if it hurts. The tender points exam includes good diagnostic criteria (82% sensitive and 87% specific to FM), but tender points are not the only tender areas FM patients have. They also demonstrate generalized hyperalgesia that gets better and worse consistent with other FM symptoms.⁴ It is important to note that successfully treated FM patients may have fewer than 11 positive of the 18 tender points, and this just means they are doing well.

Other doctors have shown in studies that the tender point exam is reproducible in FM patients. Dr. Bradley has demonstrated that lower pain threshold responses to thermal stimuli consistently are present in FM patients compared to normal controls, and this scientific finding has been reproduced by Dr. Geisser. Drs. Gracely and Clauw have demonstrated on functional brain MRI's that FM patients' response to pressure stimuli consistently activates the areas of the brain associated with pain at a lower pressure threshold than in normal controls.⁵

Sleep Studies

Fatigue is an important FM symptom, and it is often multimodal in cause. Chronic pain, inflammation, sleep disturbances, chronic anxiety and depression, exercise deconditioning, sedative effects of prescribed medications, neurally mediated hypotension, and poor management of available energy can be involved in patients who are fatigued. While sleep medications such as zolpidem that preserve normal sleep architecture are effective in treating FM fatigue, they are not effective in treating FM pain for most patients.

The sleep abnormalities in FM are reproducible on overnight sleep EEG studies (this test may be ordered but is not necessary for the diagnosis of FM). One sees alpha wave intrusion in delta sleep and a decrease in delta (stage 3 and 4) sleep in many FM patients (though these findings may not be present in treated patients). Such findings are sensitive indicators of the classical non-restorative sleep often described in FM patients, but they can also be seen in patients with rheumatoid arthritis, osteoarthritis, and Sjögren's syndrome as well as other illnesses.⁶

Genetic Studies

There is scientific evidence that a subset of fibromyalgia patients have genetic factors that predispose them to vulnerability to FM. These patients tend to have primary FM. Primary FM usually has been present since childhood though the symptoms may not be clinically apparent until the patient is exposed to a significant physical or emotional stressor. Secondary FM is usually secondary to an overwhelming infection, injury, or a predisposing rheumatic disease. Genetic abnormalities in the functional polymorphism in the promoter region of the serotonin transporter gene have been noted in FM.⁷ Patients with adequate serotonin promoter genes seem to be less susceptible to the adverse effects of chronic stress and depressive events. Another gene, catecholamine-O-methyltransferase (COMT) has been shown to be associated with pain regulation and myofascial pain of the jaw, and there is an increased association of COMT in FM patients.⁸

Myofascial Pain and Muscle Biopsy Studies

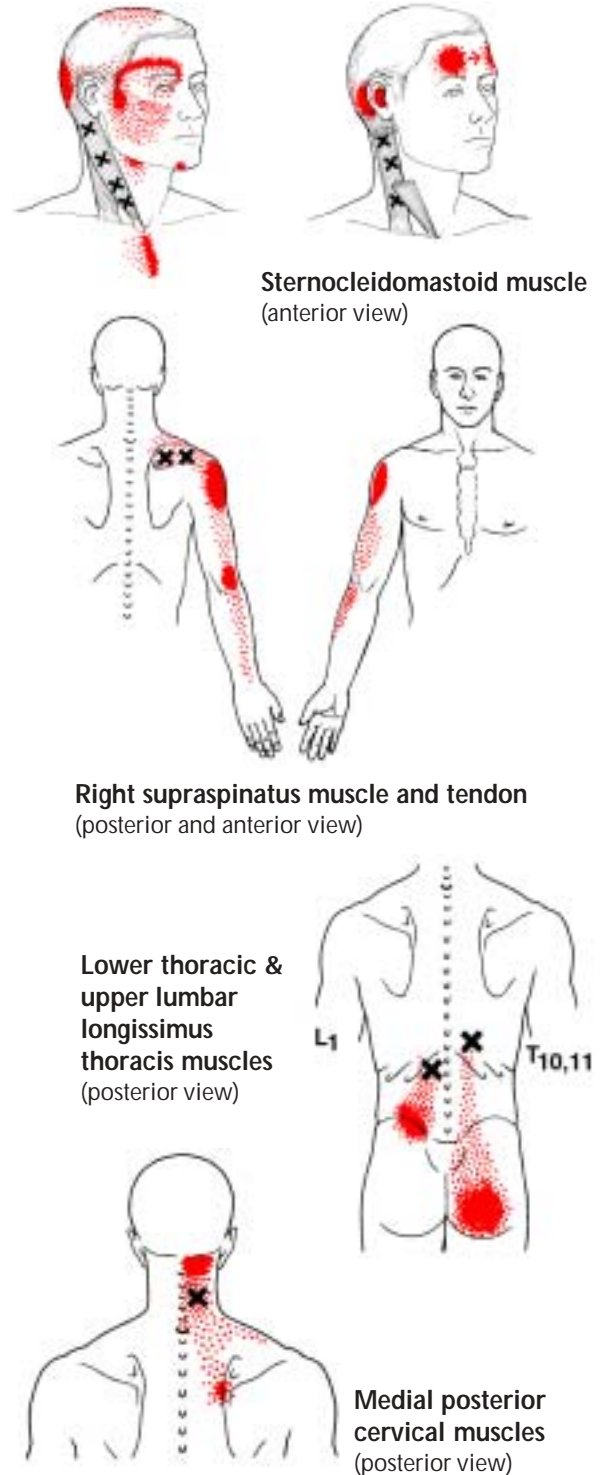
Myofascial pain is a big problem for many FM patients. Patients with this condition get palpable “knots” in their muscles and soft tissues that look and feel like painful muscle spasms. Doctors of physical medicine and rehabilitation often describe myofascial pain as originating in painful tissue which contains nodules associated with “trigger points”* in palpable, tense, or taut bands that may produce a twitch response upon palpation. These trigger points are often so painful that the patient is very uncomfortable. There can also be latent trigger points that are only painful upon palpation. Trigger points are typically associated with a referred pain pattern, sometimes at distant sites in the body. (See Figure 1) All trigger points are responsible for musculoskeletal stiffness, weakness, and limitation of motion.

There is scientific evidence that myofascial tissue on muscle biopsy has reduced blood flow, reduced oxygen receptors,⁹ increased levels of the pain neurotransmitter substance P,¹⁰ and reduced ATP receptors.¹¹ Muscle biopsies are not necessary for the diagnosis of myofascial pain, but they may be ordered if there is an abnormal EMG-nerve conduction study, and neuromuscular disease is suspected. Sympathetic nerve blockade reverses

*not to be confused with the diagnostic “tender points” of fibromyalgia

Figure 1: Examples of Referred Pain Patterns of Myofascial Trigger Points As Described by Travell & Simons

(X's show trigger points. Stippling shows pain referral patterns.)



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many of the abnormal findings in the muscle which accompanies myofascial tissue pain, and these findings appear to confirm a neuromuscular link and evidence of sympathetic nervous system dysfunction in myofascial pain.¹²

Central Sensitization, CNS “Windup” and Hyperalgesia

The central nervous system (CNS) is the major source of pain in FM, and treatment of CNS pain is essential in FM. FM patients get a phenomenon called central sensitization, the amplification of CNS pain transmission and processing that causes hyperalgesia. We now understand that increased afferent pain pathways in the CNS are associated with elevated levels of the neurotransmitters substance P and glutamine. There is also a reduction in the descending CNS pain pathways of inhibitory neurotransmitters (serotonin and norepinephrine) that dampen pain transmission. These findings in the dorsal horn of the spinal cord in FM contribute to the hyperalgesic state and are also associated with reactive depression and increased anxiety. Functional brain MRI studies consistently show increased brain activity in response to a noxious stimulus in FM. This finding is consistent with central sensitization.

Drs. Price and Staud have demonstrated that with increasing nociceptive input there is an increased temporal summation of CNS pain discharges or “windup.” Windup of the nociceptive neurons in the dorsal horn of the spinal cord involves increased NMDA receptor activity and neural plasticity of nociceptive spinal cord pathways, and it is an important factor in central sensitization.¹³ The increased brain activity in response to painful stimuli appears to be related to the increased pain processing in FM. This helps to explain why non-steroidal anti-inflammatory pain medications (NSAID’s) are not that effective in FM since they help reduce peripheral pain and not the CNS pain present in FM patients.

Autonomic Nervous System Abnormalities

FM patients commonly have autonomic nervous system abnormalities that make them vulnerable to coexistent conditions such as neurally-mediated hypotension, irritable bowel and bladder syndromes, vascular headaches, and reduced heart rate variability. These medical problems are partially due to neuroendocrine abnormalities including alter-

ations in the hypothalamic-pituitary-adrenal (HPA) axis. There are a number of studies showing dysregulation of the HPA in FM. Documented abnormalities include low AM cortisol and 24-hour urinary cortisol levels, inappropriately high levels of adrenocortical trophic hormones (ACTH), and failure to suppress normally with dexamethasone.¹⁴ The physician needs to be aware of the need to treat neurally-mediated hypotension in FM patients with adequate salt and fluids as well as stressing conservation of energy. If the hypotension is more severe, cardiac consultation and tilt table testing can be ordered.

Treatment of Fibromyalgia by the Patient’s Primary Care Doctor

I’ve listed below some of the most commonly used therapies in FM. I’ve tried to emphasize evidence-based, successful therapies. No one therapy is successful for all FM patients. It is very important to see a given FM patient on a regular basis and carefully determine which therapies are most successful for that particular patient. Since FM patients frequently have multiple symptoms, it is often necessary to titrate medication dosages and combine treatments to achieve a successful treatment program.

Medical Management for Fibromyalgia

In addition to a tender points exam and an assessment of myofascial pain, what other diagnostic criteria should the physician use to assess the status of the FM patient? First, see your patient often until his or her symptoms stabilize. Have the patient keep a pain and activity diary. By asking on a regular basis about his or her functional status (activities of daily living, exercise and work) and recording the visual analogue pain scores (0-10 score), you will have a good idea how the patient is doing. Also assess for adequate posture, muscle tone, and gait as part of the examination.

Important non-pain symptoms associated with FM usually include fatigue, nonrestorative sleep disturbances, cognitive dysfunction, increased anxiety, and reactive depression (which is clearly distinguished from major depressive disorder).¹⁵ In my clinical experience as a rheumatologist who has treated FM patients for over 20 years, successful treatment of these other concurrent FM problems is essential to a good clinical outcome.

When a FM patient has a pain flare, it usually involves a CNS windup and central sensitization hyperalgesia. In my experience, it is essential to aggressively treat this type of pain before it causes a chronic escalation of the patient's pain symptoms. I encourage my patients to have adequate pain medication at home for the short-term treatment of this type of emergency, break-through pain. It is also important to note that specific pain generators are commonly present in FM patients that make their CNS pain worse. These pain generators can come from coexisting osteoarthritis, rheumatoid arthritis, systemic lupus, and other mechanical problems such as degenerative disc disease and spinal stenosis. Adequate control of these additional sources of pain, if present, is an important therapeutic challenge.

Pharmacology for Fibromyalgia

1. Antidepressants: These drugs block the biogenic amines that are abnormal in the CNS in FM.

a. Tricyclic antidepressant drugs (TCA):

Bedtime doses of low-dose amitriptyline, doxepin, or cyclobenzaprine (Flexeril, a muscle relaxant with TCA properties).

b. Selective serotonin reuptake inhibitors (SSRI):

Only 40-80 mg of fluoxetine (Prozac) have been shown to be effective in FM studies. The other SSRI's are effective in treating depression, but not pain and stiffness in most FM patients.

c. Serotonin-norepinephrine reuptake inhibitors (SNRI):

Duloxetine (Cymbalta) has the most promising studies for the treatment of FM pain at 60-120 mg.¹⁶ It is also effective in the treatment of neuropathic pain and depression. Venlafaxine (Effexor XR) has been shown to be effective in FM at 75 mg, and it is also effective in the treatment of depression and general anxiety disorder.

2. Anti-Epileptic Drugs: These drugs have been shown to be effective in the treatment of various neuropathic pain disorders and are widely used as analgesics.

a. Calcium channel inhibitors in the CNS:

Pregabalin (Lyrica) has been shown to block GABA uptake in the CNS and be effective in studies treating FM pain (up to 150 mg tid)¹⁷

as well as in patients with neuropathic pain and general anxiety disorders. Gabapentin (Neurontin) has been commonly used in FM and neuropathic pain.

3. Opioids

a. Tramadol (Ultram) and tramadol with acetaminophen (Ultracet):

are weak opioids working at the mu receptor as well as having TCA effects. They are effective in the treatment of acute and chronic pain and FM pain. Ultracet has been shown to be more effective than Ultram with fewer adverse effects in most studies. There is now a time-release form of Ultram available.

b. Long-acting opioids:

Fentanyl patch and time-release morphine have been shown to be effective for long-term use in chronic low back pain and osteoarthritis pain, but their use should be limited to only the most severe chronic pain patients due to concerns about addictive potential and adverse effects.

c. Short-acting opioids:

Hydrocodone and oxycodone, in combination with acetaminophen or ibuprofen, are excellent short-acting analgesics for acute peripheral and CNS pain. They should not be used for chronic pain except in rare instances due to concerns about addictive potential and adverse effects, including the potential for withdrawal-related symptoms of increased pain.

4. Muscle Relaxants

Muscle relaxants are commonly used both chronically for FM and for acute pain flares. Cyclobenzaprine (Flexeril) is the most effective due to its TCA properties.

5. Sedative Hypnotics

a. Non-benzodiazepines:

Zolpidem (Ambien) has been shown to improve FM sleep disturbances and fatigue.

b. Benzodiazepines:

Alprazolam (Xanax) has been shown to be effective in FM.

c. TCA's:

Amitriptyline and cyclobenzaprine (Flexeril) are most commonly used for sleep in FM.

Nonpharmacologic Treatment for Fibromyalgia

1. Education: When a FM diagnosis is made, and the condition is properly explained to the patient and family, the intensity of symptoms will often be reduced by one-third due to reductions in anxiety and abnormal pain processing. An essential goal of treatment is to empower the patient to understand his or her illness and learn how to best manage FM.

2. Physical therapy: Proper posture, balance, muscle tone, and exercise conditioning are important needs to correct in many FM patients. It is often necessary to prescribe physical therapy before the patient can successfully progress to an appropriate exercise program.

3. Exercise: Low impact, aerobic exercises are an important treatment for most FM patients to improve their pain, mood, and functional status. It is important to combine exercise with adequate stretching as well as energy conservation to prevent injury or FM flare. I find core exercises to be very important for many of my FM patients.

4. Cognitive behavioral therapy as well as psychological and behavioral therapies are being used in FM with increasing frequency and success. Energy conservation and reduced anxiety over chronic pain are important goals in the management of FM.

Conclusion

As my experience treating FM patients grows and the science regarding the illness and treatment options increases, I find myself becoming more and more optimistic about patient outcomes. The mainstay of treatment remains an excellent doctor-patient relationship where the patient is part of the medical team. This formula ensures a successful and positive relationship for both doctor and patient.

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