Fibromyalgia -- A Physician's Guide

David A. Nye MD, 13Aug95

Fibromyalgia syndrome (FMS) is an underdiagnosed disorder of unknown etiology affecting over 5% of the patients in a general medical practice (Campbell 1983) and an estimated 2-4% of the general population (Wolfe 1993), women more often than men. Patients complain that they ache all over. A large number of other symptoms are often present, particularly fatigue, morning stiffness, sleep disturbance, paresthesias, and headaches (see table 2). On examination, areas of focal tenderness called tender points can be demonstrated in characteristic locations (table 3).

Etiology

There are many theories regarding the etiology of FMS, only a few of which I will discuss here. At this point there does not appear to be a majority of FMS researchers supporting any single theory. While it still must be said that the etiology is unknown, significant progress is being made in identifying an etiology, and much useful evidence has been collected.

FMS was first described as an inflammatory condition (Gowers 1904). When no evidence of inflammation could be found and an association was noted with depression and stress, the concept of "psychogenic rheumatism" was advanced (Boland 1947), but a number of studies have established that FMS is neither a psychosomatic nor somatiform disorder and that when present, anxiety and depression are more likely to be the result than the cause of FMS (Goldenberg 1989, Yunus 1994)

It has been suggested that the pain of FMS is related to microtrauma in deconditioned muscles and that exercise works by conditioning these muscles (Bennett 1989) However, muscle biopsy has tended to show only changes of disuse atrophy (Schroder 1993), and some tender points are not over muscles or tendons, such as the one over the medial fat pad of the knee (Smythe 1989). Furthermore, I've observed that exercise seems to work best if it mainly uses less-involved muscles.

Moldofsky has suggested that FMS may be due to non-restorative deep sleep (Moldofsky 1975, 1993). Amitriptyline (Elavil), the most commonly used medication for treating FMS, blocks serotonin reuptake and increases deep sleep (Baldessarini 1985). Serotonin is important in deep sleep and in central and peripheral pain mechanisms (Chase 1973). A number of other neurotransmitter, neuroendocrine, and immunologic

abnormalities have been identified in FMS patients, none with sufficient sensitivity and specificity to be diagnostically useful, but they have formed the basis for several other theories of the etiology of FMS. A cataloging of all of them is beyond the scope of this review Moldofsky points out that many of these changes can be induced simply through sleep deprivation (Moldofsky 1993).

Patients with FMS often report insomnia or light sleep as well as an increase in FMS symptoms after disturbed sleep (Campbell 1983). Hauri and Hawkins reported abnormal amounts of alpha activity on the electroencephalogram of FMS patients during deep sleep (Hauri 1973). Moldofsky et al. were able to induce FMS-like symptoms in normal volunteers by depriving them of deep sleep, except in subjects who exercised regularly (Moldofsky 1975). Subsequent trials have confirmed the value of aerobic exercise in the treatment of FMS (McCain 1988). Exercise increases time spent in deep sleep (Hobson 1968), perhaps the mechanism for its therapeutic efficacy. Deep sleep serves an important physical restorative function, probably modulated by growth hormone, which is released almost exclusively during stage 4 sleep in amounts that increase after exercise (Bennett 1989). Patients with FMS have been shown to have low levels of somatomedin C, a marker of growth hormone secretion (Bennett 1992).

The presence of considerable symptom overlap in FMS, chronic fatigue syndrome, and irritable bowel syndrome and the efficacy in all of low doses of amitriptyline has led to speculation that they may represent different facets of the same underlying, as yet unknown disease process (Goldenberg 1990a, Yunus 1989). Although no specific inheritance pattern has been identified, an increased incidence in relatives of affected patients has been noted (Pellegrino 1989). Development of the syndrome may require a predisposing factor, possibly inherited, as well as a precipitating factor, perhaps something disturbing sleep.

Diagnosis

Since FMS is a syndromic diagnosis, any patient who fits the diagnostic criteria of aching all over and the presence of at least 11 of 18 tender points (Table 3) has it by definition. It is not possible to accurately diagnose FMS without knowing how to do a tender point examination. It is not a diagnosis of exclusion. If a patient has typical symptoms of FMS (Table 2) but does not meet the tender point criterion, a diagnosis of "possible FMS" may be assigned and a therapeutic trial of standard treatment offered. Tender points should be looked for again on a return visit as they may be present some days and not others in some patients.

Although there have been many abnormalities of laboratory and other tests reported in FMS, none is sufficiently sensitive or specific to be useful diagnostically. Therefore,

routine laboratory or other studies are not recommended. Because the list of possible symptoms is large in FMS, the differential diagnosis is also very large. Patients with FMS should have a comprehensive medical evaluation as part of the workup. In older patients a sedimentation rate may be useful to exclude polymyalgia rheumatica In patients with other symptoms of hypothyroidism, thyroid studies are indicated.

The current syndrome definition may not be the best one possible (Wolfe 1993) It has been argued that tender points have been over-emphasized, probably because historically rheumatologists have been more involved in the diagnosis and treatment of FMS than other specialists. In many patients who meet the criteria for diagnosis for chronic fatigue syndrome, the only difference between them and a typical FMS patient is the relative absence of pain. Some of these patients followed over time will subsequently develop tender points and then fit the criteria for diagnosis of FMS. Goldenberg's group found that 70% of patients with FMS met the CDC criteria for CFS (Buchwald 1987) and two thirds of patients with CFS met the ACR criteria for FMS (Goldenberg 1990b). It is unlikely that the majority of these patients have two separate disease processes. Perhaps dividing these two groups of patients on the basis of whether or not they have prominent pain is as artificial as division on the basis of prominence of any of the other twenty or so associated symptoms.

On the other hand, we are to some extent stuck with the current syndrome definition because it is these patients on whom all the important studies have been performed. If the syndrome definition is altered, we can't be certain that all of these results still apply to the new syndrome. This problem will disappear once we know the true etiology and can make an etiologic rather than syndromic diagnosis

Treatment

Most patients with FMS respond favorably to gentle aerobic exercise, maintenance of a regular schedule of adequate amounts of sleep, and low doses of amitriptyline or other medications known to improve deep sleep. In a retrospective chart review I performed, 30 of 36 patients (83%) had substantial improvement on this regimen. Several other medications have been shown in controlled studies to help, including cyclobenzaprine (Flexeril) (Quimby 1989) and alprazolam (Xanax) (Russell 1991). Diphenhydramine and trazodone seem to be useful as well, although I am not aware that they have been studied.

Imipramine, steroids, and non-steroidal anti-inflammatory drugs (NSAIDs) are among those which were found to be no more effective than placebo, although NSAIDs may be useful for simple analgesia (Goldenberg 1993). Benzodiazepines other than alprazolam are contraindicated as they block stage 4 sleep and may exacerbate FMS.

The serotonin-specific reuptake inhibitors such as fluoxetine (Prozac) have not been effective except to symptomatically treat any associated depression, consistent with the theory that the main mechanism of action of medications effective for FMS is to promote deep sleep (Wolfe, 1994).

There are many other unstudied "alternative" drug and herbal treatments, some of which may in the future be proven effective in controlled studies. I do not recommend these since they are as yet unproven scientifically and may have unrecognized toxicities, but I have given up trying to dissuade patients from trying them as long as it is not in place of conventional therapy.

Medications effective in the treatment of FMS appear to work mainly through an effect on deep sleep (Goldenberg 1986). They should be started at the lowest possible dose and increased every few days to a week to maximum relief of symptoms without unacceptable side effects. I allow patients to fine-tune the dose themselves. The starting doses and ranges of several medications useful in the treatment of FMS are listed in Table 1 in roughly the order I tend to try them.

Amitriptyline is an effective medication for FMS but it also has frequent side effects in doses sufficient to keep FMS symptoms well controlled. Particularly bothersome are weight gain, dry mouth, and daytime cognitive impairment. For this reason I usually start with other medications listed in Table 1. Diphenhydramine and trazodone are in common use because they seem effective and have less side effects, but have not to my knowledge been proven to work in controlled, blinded trials. It is often necessary to try several different medications in succession before finding one that works well with acceptable side effects. Some tolerance develops to the sedative effect of many of these medications, necessitating one or two dose increases after an initial good response to maintain it.

Daily, gentle, low-impact aerobic exercise helps (McCain 1988), but too much or the wrong kind of exercise may exacerbate FMS symptoms. Patients who are deconditioned should start out with just 3-5 minutes of exercise every day and increase as tolerated. Most patients will need to get up to 20-30 minutes a day before they notice substantial benefit. The kind of exercise does not matter as long as it gets the heart rate into the aerobic range and does not aggravate the patient's pain If the pain is worst in the back and legs, for example, the patient should exercise just the arms. Some patients may need to try several different forms of exercise before they find one they can tolerate. Water exercise programs are particularly effective because they are non-weight-bearing. Walking is also popular. A small percentage of patients can never get up to an effective amount of exercise, but without it, few patients will notice much improvement in my experience. Exercise is most effective if done in the late afternoon or early evening, perhaps because of its known effect on deep sleep.

Getting adequate sleep is essential. FMS symptoms often appear during times of sleep disruption (Saskin 1986) such as may be brought on by an injury or other pain, stress, shift work, or having to get up to attend to young children. At times just re-establishing a regular sleep schedule may be enough to relieve symptoms. I have not been able to get any patient who works a night shift to improve substantially unless they can get onto a shift that allows them to sleep nights and keep a consistent bedtime.

Other coexisting sleep disorders such as obstructive sleep apnea (OSA) and periodic limb movements of sleep must be identified and treated. Not infrequently a spouse's snoring will greatly exacerbate the patient's symptoms, in which case treating the spouse's snoring or having the patient wear ear plugs will help 44% of men with FMS have been found to also have OSA (May 1993), a potentially life-threatening disorder which is important to treat in its own right. It is important to take a sleep history in all patients with FMS, including asking the spouse about snoring, apneas, and movements at night. In resistant FMS cases, referral to a sleep disorders center for polysomnography may be helpful. I have found that patients with another sleep disorder rarely respond to treatment for FMS until the coexisting sleep problem is corrected.

Patients must also be careful not to overdo physical activity. For example, once she is feeling better a FMS patient may try to catch up on all the cleaning she has been unable to do, but this may trigger a relapse that puts her in bed for several days. It is better to plan to spend a half an hour or an hour a day at these activities until they are completed. Patients must learn to sense when they have reached their limit and stop before they get into trouble.

Other treatment modalities which have been shown in controlled studies to be helpful include EMG biofeedback (Ferraccioli 1989), regional sympathetic blockade (Bengtsson 1988), and cognitive behavioral therapy (Goldenberg 1991). Many patients report that gentle massage as well as heat and rest help. Others find that, as with migraine, certain foods can precipitate their symptoms. Several patients have reported to me that their FMS symptoms improved significantly on a low-fat weight reduction diet started to lose the weight gained from taking amitriptyline. Most patients do better if they give up caffeine entirely. Alcohol tends not to be a problem as few patients with FMS seem to be able to tolerate it well, but it should be avoided because of its tendency to suppress deep sleep. Certain symptoms can be treated directly if treatment of the underlying disorder does not control them adequately, for example migraine headaches or depression.

FMS and myofascial pain syndrome (MPS), while probably separate entities, often coexist (Granges 1993). When they do each needs to be treated separately. MPS is associated with trigger points which should be distinguished from the tender points of

FMS. Trigger points are located over a band of taut muscle and cause pain that radiates away from the point of pressure. MPS is usually treated with avoidance of activities which worsen it, myofascial release physical therapy, and trigger point injections or dry needling.

Support and education are important. Patients need to be actively involved in their treatment and to have as clear an understanding of this complicated disorder as possible. Patients often elicit less sympathy and support from family, friends, and employers than they deserve because of the lack of physical stigmata of disease. By the time they get to see someone skilled in the management of FMS. many patients will have been told by at least one other physician that there is nothing wrong with them or that it is "all in your head" which can be quite demoralizing. An understanding approach by the physician and the patient's participation in a well-run support group may have considerable therapeutic benefit.

Education, frequent follow-up visits, and reassurance help to get patients over the first few weeks of treatment. It may be difficult to convince patients to exercise when they experience fatigue and aching. It often takes two weeks or more before the beneficial effects of medication and exercise outweigh their side effects. Sometimes it takes several months of trying different medications in different combinations and adjusting doses before getting it right. The physician should check on the amount and type of exercise and sleep at return visits and reinforce their importance. Patients should be warned that despite optimum treatment and good initial results, brief relapses are common, often caused by temporary sleep disturbances. The patient will do best if she "gives in to it", takes hot baths, and tries to get extra rest during a relapse. A temporary increase in medication dose may also be necessary.

Conclusion

FMS is a common, chronic, and if untreated, often disabling disorder of unknown etiology associated with disordered deep sleep. Most patients can be helped with a combination of medication, exercise, and maintenance of a regular sleep schedule. Think of this condition in any patient with a complaint of aching and tiredness and look for associated symptoms and tender points to confirm the diagnosis. The common misconceptions that FMS is a psychosomatic or somatoforrn disorder, is untreatable, is a diagnosis of exclusion or a "wastebasket" diagnosis, and that most FMS patients are hypochondriacs or whiners are all completely unfounded.

Table 1: Some drugs useful in the treatment of FMS

Drug name	Starting dose (mgs)	Taken hrs before bed	Usual maximum Dose (mgs)
trazodone	50	0	600
diphenhydramine	50	1	300
cyclobenzaprine	10	1	60
alprazolam	0.5	1	6
carisoprodol	350	1	1400
5-hydroxytryptophan	100	1	600
amitriptyline	5	2	300

Table 2: Associated signs and symptoms (Wolfe 1990).

widespread pain	97.6% of patients
tenderness in > 11118 tender points	90.1
fatigue	81.4
morning stiffness	77.0
sleep disturbance	74.6
paresthesias	62.8
headache	52.8
anxiety	47.8
dysmenorrhea history	40.6
sicca symptoms	35.8
prior depression	31.5
irritable bowel syndrome	29.6
urinary urgency	26.3
Raynaud's phenomenon	16.7

Other commonly reported symptoms include dizziness, trouble with memory and concentration, rashes, and chronic itching (unpublished observations).

Table 3: Location of tender points (Wolfe 1990).

suboccipital muscle insertions at occiput
lower cervical paraspinals
trapezius at midpoint of the upper border
supraspinatus at its origin above medial scapular spine
2nd costochondral junction
2 cm distal to lateral epicondyle in forearm
upper outer quadrant of buttock
greater trochanter
knee just proximal to the medial joint line

To meet ACR 1990 diagnostic criteria for fibromyalgia, digital palpation with an approximate force of 4 kgs. must produce a report of pain in at least 11 of these 18 tender points. Other areas can be tender as well. The tenderness should be focal rather than diffuse. Tender points must be present on both sides of the body, above and below the waist and in the midline. Widespread pain must have been present for at least 3 months. Some accept a diagnosis of fibromyalgia with fewer than 11 tender points if several associated symptoms from table 2 are also present (Wolfe 1989).

References:

Baldessarini RJ. Drugs and treatment of psychiatric disorders In: LS Goodman and A Gilman eds, The pharmacologic basis of theraputics. 7th ed, New York MacMillan, p. 413, 198

Bengtsson A, Bengtsson M. Regional sympathetic blocade in primary fibromyalgia. Pain 33:161, 1988.

Bennett RM. Beyond fibromyalgia: ideas on etiology and treatment. J Rheumatol 16(suppl 19) 185, 1989

Bennett RM et al. Low levels of somatomedin C in patients with the fibromyalgia syndrome: a possible link between sleep and muscle pain. Arthritis Rheum 35:1113, 1992

Boland EW. Psychogenic rheumatism: the musculoskeletal expression of psychoneurosis. Ann Rheum Dis 6195, 1947.

Buchwald D et al. The chronic, active Epstein-Barr virus infection syndrome and primary fibromyalgia. Arthritis Rheum 30:1132, 1987.

Campbell SM et al. Clinical characteristics of fibrositis. I. A "blinded" controlled study of symptoms and tender points Arthritis Rheum 26:817, 1983.

Chase TN and DL Murphy. Serotonin and central nervous system function. Ann Rev Pharmacol 13:181, 1973.

Ferraccioli GF et al. EMG biofeedback in fibromyalgia syndrome. J Rheumatol 16:1013, 1989.

Gowers WR. Lumbago -- its lessons and analogues. Br Med J 1:117, 1904.

Goldenberg DL et al. A randomized controlled trial of amitriptyline and naproxen in the treatment of patients with fibromyalgia. Arthritis Rheum 29:1371, 1986.

Goldenberg DL Psychological symptoms and psychiatric diagnosis in patients with fibromyalgia. J Rheumatol 16(suppl 19): 127, 1989.

Goldenberg DL. Fibromyalgia and chronic fatigue syndrome: are they the same? J Musculoskel Med. 719, 1990.

Goldenberg DL et al. High frequency of fibromyalgia in patients with chronic fatigue seen in a primary care practice. Arthritis Rheum 33: 1132, 1990.

Goldenberg DL et al. The impact of cognitive-behavioral therapy on fibromyalgia. Arthritis Rheum 34(suppl 9):S190, 1991.

Goldenberg DL Fibromyalgia: treatment programs J Musculoskel Pain. 1(3/4):71, 1993.

Granges G, Littlejohn G. Prevalence of myofascial pain syndrome in fibromyalgia syndrome and regional pain syndrome: a comparative study. J Musculoskel Pain 1(2):19, 1993.

Hauri P, Hawkins DR Alpha-delta sleep. Electroenceph Clin Neurophysiol. 34:233, 1973.

Hobson JA Sleep after exercise. Science 162:1503, 1968.

May KP et al. Sleep apnea in male patients with the fibromyalgia syndrome. Am J Med 94 505, 1993

McCain GA et al. A controlled study of the effects of a supervised cardiovascular fitness

training program on manifestations of primary fibromyalgia. Arthritis Rheum 31:1135, 1988.

Moldofsky HD et al. Musculoskeletal symptoms and non-REM sleep disturbance in patients with "fibrositis syndrome" and healthy subjects. Psychosom Med. 37:341, 1975

Moldofsky HD A chronobiologic theory of fibromyalgia. J Musculoskel Pain 1(3/4):49, 1993 Pellegrino MJ et al. Familial occurrence of primary fibromyalgia Arch Phys Med Rehab 70:61, 1989.

Russell IJ et al. Treatment of primary fibrositis/fibromyalgia syndrome with ibuprofen and alprazolam -- a double-blind, placebo-controlled study. Arthritis Rheum 34:552, 1991

Saskin Pet al. Sleep and post-traumatic rheumatic pain modulation disorder (fibrositis syndrome). Psychosom Med 48:319, 1986

Schroder HD et al. Muscle biopsy in fibromyalgia. J Musculoskel Pain 1(3/4):165, 1993.

Smythe H. Fibrositis syndrome: a historical perspective. J Rheumatol 16(suppl 19) 2, 1989.

Wolfe F. Fibromyalgia: the clinical syndrome. Rheum Dis Clin North Am. 15:1, 1989.

Wolfe F et al. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia: report of the multicenter criteria committee. Arthritis Rheum. 33:160, 1990

Wolfe F. Fibromyalgia: on diagnosis and certainty. J Musculoskel Pain 1(3/4):17, 1993.

Wolfe F. The epidemiology of fibromyalgia. J Musculoskel Pain 1(3/4) 137, 1993.

Wolfe Fetal A double-blind placebo controlled trial of fluoxetine in fibromyalgia. Scand J Rheumatol 23(5): 255-9, 1994.

Yunus MB et al. A controlled study of primary fibromyalgia syndrome clinical features and association with other functional syndromes. J Rheumatol 16(suppl 19):62, 1989.

Yunus MB. Psychological factors in fibromyalgia syndrome: an overview J Musculoskeletal Pain 2(1):87-91 David Nye MD (nyeda@uwec.edu), Midelfort Clinic, Eau Claire, WI