

Review Article

Fibromyalgia Syndrome: An Overview of Pathophysiology, Diagnosis and Management

Firdous Jahan, Kashmira Nanji, Waris Qidwai, Rizwan Qasim

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Abstract

Fibromyalgia Syndrome (FMS) is a chronic condition causing pain, stiffness, and tenderness of the muscles, tendons, and joints. It is also characterized by restless sleep, tiredness, fatigue, anxiety, depression, and disturbances in bowel functions. The etiology of fibromyalgia remains unknown, but recent advances and discoveries have helped to unravel some of the mysteries of this disease. Research highlights some of the biochemical, metabolic, and immunoregulatory abnormalities associated with fibromyalgia. Management of FMS at the present time is very difficult as it has multiple etiological factors and psychological predispositions; however, a patient centered approach is essential to handle this problem.

Keywords: Fibromyalgia; Clinical features; Quality of life; Pathophysiology and management of fibromyalgia.

Introduction

Pain with its devastating and demoralizing effects remains a challenging problem for both patients and care givers.¹ Fibromyalgia is one of the most common diseases affecting the muscles manifested with pain, stiffness, and tenderness of the muscles, tendons, and joints. The painful tissues involved are not accompanied by tissue inflammation.²⁻³ Therefore, despite potentially disabling body pain; patients with fibromyalgia do not develop tissue damage or deformity.⁴⁻⁵ The pain of fibromyalgia is generally widespread, involving both sides of the body. Pain usually affects the neck, buttocks, shoulders, arms, the upper back, and the chest. "Tender points" are localized tender areas of the body that can bring on widespread pain and muscle spasm when touched.⁶⁻⁷

Firdous Jahn , Rizwan Qasim

Family Medicine Department, Oman Medical College, Sohar, Oman.
E-mail: Firdous@omc.edu.om

Waris Qidwai, Kashmira Nanji

Family vMedicine Dept. Stadium Road Aga Khan University Hospital, Karachi, Pakistan.

FMS typically presents in young or middle-aged females as persistent widespread pain, stiffness, fatigue, disrupted unrefreshing sleep, and cognitive difficulties, often accompanied by multiple other unexplained symptoms, anxiety and/or depression, and functional impairment of daily living activities.⁸⁻⁹ There is an overall 6% to 15% prevalence rate in the United States with a five times greater incidence among women than men. In rheumatology clinics, the rate of new diagnosis is approximately 10% to 20%, whereas in non-specialized settings, the rate is 2.1% to 5.7%.¹⁰⁻¹¹

Clinicians should be familiar with the signs and symptoms of fibromyalgia and diagnose the condition with minimum investigation.¹² Since the symptoms of fibromyalgia wax and wane related to stresses,¹³ treatment (as with that of other chronic diseases) is an ongoing process rather than management of a single episode.

In terms of conditions associated with fibromyalgia; there are certain conditions associated with fibromyalgia.¹⁷⁻¹⁹ (Table 1)

Pathophysiology

Although the etiology remains unclear, characteristic alterations in the pattern of sleep and changes in neuroendocrine transmitters such as serotonin, substance P, growth hormone and cortisol suggest that regulation of the autonomic and neuro-endocrine system appears to be the basis of the syndrome. Fibromyalgia is not a life-threatening, deforming, or progressive disease. Anxiety and depression are the most common association.¹⁴ Aberrant pain processing, which can result in chronic pain, may be the result of several interplaying mechanisms. Central sensitization, blunting of inhibitory pain pathways and alterations in neurotransmitters lead to aberrant neuro-chemical processing of sensory signals in the CNS, thus lowering the threshold of pain and amplification of normal sensory signals causing constant pain.¹⁵⁻¹⁶

The frequent co-morbidity of fibromyalgia with mood disorders suggests a major role for the stress response and for neuroendocrine abnormalities. The hypothalamic pituitary axis (HPA) is a critical component of the stress-adaptation response.¹⁷ In FMS, stress adaptation response is disturbed leading to stress induce symptoms. Psychiatric co-morbidity has been associated with FMS and needs to be identified during the consultation process, as this requires special consideration during treatment.¹⁸

Table 1: Conditions associated with fibromyalgia.

Musculoskeletal	Genitourinary	Gastro intestinal	Miscellaneous
<ul style="list-style-type: none"> • Nondermatomal paresthesia • Temporo mandibular joint syndrome • Hyper mobility syndrome • Restless legs syndrome • Rheumatoid arthritis • Systemic lupus erythematosus • Sjögren syndrome • Osteoarthritis • Chronic fatigue syndrome • Carpal tunnel syndrome • Myofascialpain syndrome 	<ul style="list-style-type: none"> • Dysmenorrhea • Interstitial cystitis • Vulvodynia • Female urethral syndrome • Vulvar vestibulitis • Premenstrual syndrome 	<ul style="list-style-type: none"> • Irritable bowel syndrome • Esophageal dysmotility 	<ul style="list-style-type: none"> • Tension/migraine headaches • Mitral valve prolapsed • Allergy • Vestibular disorders • Ocular disturbances • Anxiety disorders • Reynaud phenomenon • Thyroid dysfunction • Lyme disease • Hyperventilation • Cognitive dysfunction

Assessment of Fibromyalgia

Although fibromyalgia is the most common chronic widespread pain condition, it is often under diagnosed. The diagnosis of fibromyalgia has been shown to increase patient satisfaction and reduce healthcare utilization.

The assessment of Fibromyalgia is based on the criteria for the Classification of Fibromyalgia by the American College of Rheumatology, (ACR) 1990.¹⁹⁻²¹ The criterion involves:

- History of widespread pain has been present for at least three months.
- Pain in both sides of the body pain above and below the waist. Pain is considered widespread when all of the following are present:
 - Pain in 11 of 18 tender point sites on digital palpation (both side of the body): Occiput (2), Low cervical (2), Trapezius (2), Supraspinatus (2), Second rib (2), Lateral epicondyle (2), Gluteal (2), Greater trochanter (2), Knee (2).

A tender point hurts only at the area where pressure (enough to cause the examiner's nail bed to blanch, or about 4 kg) is applied, and there is no referred pain. An instrument known as a dolorimeter can be used to apply exactly 4 kg of pressure over the tender points during the examination.²²

New Diagnostic Criteria

Recently, ACR is proposing a new set of diagnostic criteria for fibromyalgia that includes common symptoms such as fatigue, sleep disturbances, and cognitive problems, as well as pain (Table 2). The tender point test is being replaced with a widespread pain index and a symptom severity (SS) score. The new criteria appear in a one-page symptom checklist format that will hopefully be more suitable for use in the primary-care setting.²³ A tender point evaluation is no longer required although a full physical exam is still recommended along with other diagnostic tests to identify causes for the patients' symptoms besides fibromyalgia. In place of the tender point count, patients (or their physician) may endorse 19 body regions in which pain has been experienced during the past week. One point is given for each area, so the score is between

0-19. This number is referred to as the Widespread Pain Index (WPI) and it is one of the two required scores needed for a doctor to make a diagnosis of fibromyalgia.

The second part of the score required to assess the diagnosis of fibromyalgia involves the evaluation of a person's symptoms. The patient ranks specific symptoms on a scale of 0-3. These symptoms include: Fatigue, Waking unrefreshed, Cognitive symptoms, Somatic (physical) symptoms in general (such as headache, weakness, bowel problems, nausea, dizziness, numbness/tingling, hair loss). The numbers assigned to each are added up, for a total of 0-12.

The diagnosis is based on both the WPI score and the SS score either:

- WPI of at least 7 and SS scale score of at least 5, **OR**
- WPI of 3-6 and SS scale score of at least 9.

Table 2: New ACR Diagnostic Criteria.

Fatigue	Waking unrefreshed	Cognitive symptoms
0 = No problem	0 = No problem	0 = No problem
1 = Slight or mild problems; Generally mild or intermittent	1 = Slight or mild problems; Generally mild or intermittent	1 = Slight or mild problems; Generally mild or intermittent
2 = Moderate; considerable Problems; often present and/or at a moderate level	2 = Moderate; considerable Problems; often present and/or at a moderate level	2 = Moderate; considerable Problems; often present and/or at a moderate level
3 = severe: pervasive, continuous, Life disturbing problems	3 = severe: pervasive, continuous, Life disturbing problems	3 = severe: pervasive, continuous, Life disturbing problems

Laboratory Investigations

Laboratory testing, such as complete blood count, erythrocyte sedimentation rate, rheumatoid factor, antinuclear antibody, thyroid-stimulating hormone, T3, T4, creatinine phosphokinase, a serum muscle enzyme, vitamin D, ESR, CRP, renal function, and liver function tests are necessary to rule out other disorders. X-rays, blood tests, specialized scans such as nuclear medicine and CT scan muscle biopsy are normal in cases of fibromyalgia.

Management of Fibromyalgia

By the time many fibromyalgia patients reach the primary care setting or practice, they may have been seen by multiple healthcare providers. Patients are often frustrated or discouraged after receiving inadequate answers or diagnosis of their chronic ailments. Many are relieved to learn that there is an actual diagnosis and possible treatment options for their symptoms.²⁴⁻²⁵

Patients should participate in developing and initiating a care plan. Being a participant in their care will help the patient to assume control of their lives and focus on positive lifestyle changes rather than on chronic dysfunction. Patients must try to avoid exacerbating factors and limit anxiety and stress.²⁶⁻²⁷

A great majority of FMS patients can be managed well by Family Physicians in ambulatory care by managing stress, depression, pain and life style modification.²⁸ CNS agents, antidepressants, muscle relaxants, or anticonvulsants are the most successful pharmacotherapies.

Therapeutic Measures in FMS

Medications have a limited role in FMS treatment to limit symptoms, so patients can participate in non-pharmacologic modalities that provide long-term disease management such as exercise, behavioral and education. Non pharmacologic therapies should be used when possible.²⁹

Drugs

There are different pain medications which are useful in the management of FMS. Paracetamol, NSAIDs have been used but pain usually do not respond to them. Acetaminophen may ease the pain and stiffness caused by fibromyalgia. Besides analgesics, there are drugs used like antidepressant, anti convulsant, Dopamine agonist and Growth hormone.

Antidepressant Agents

Antidepressants have a long history in the treatment of chronic pain syndromes. The tricyclic antidepressants, selective serotonin reuptake inhibitors (SSRIs), or combinations of both, produce mild to moderate improvement in symptoms. Dosages should be gradually increased, not to exceed the recommended maximum for the drug. Even patients who are able to tolerate very small amounts of these medications may derive benefit from them. Antidepressants are most commonly used because of their effect on serotonin. Duloxetine, which is a Serotonin and Norepinephrine

reuptake inhibitor is used successfully. Dopamine agonists (e.g., pramipexole), Sodium Oxybate and growth hormone therapy have recently been introduced for FMS.³⁰⁻³¹

Life Style Modifications

Stress Management: Many patients with fibromyalgia have increased levels of stress and feelings of depression, anxiety, and frustration. Several treatment options are available such as cognitive behavioral therapy; including relaxation training, group therapy, and biofeedback, which are some of the useful options.³²

Exercise: Physical activity can be taken in many ways, including activities such as walking, jogging or sports.³³ Exercise is a way of responding to stress which allows the discharge of the energy the body is anticipating.³⁴

Alternative Therapies: Chinese herbal medications, Chinese herbal tea, acupuncture, Tai-chi are the different modalities available but more research is required in these fields.³⁵⁻³⁸ It has also been suggested that acupuncture triggers the release of endorphins into the blood stream and are body's natural pain relievers.³⁹

Conclusion

Fibromyalgia is a common rheumatologic syndrome characterized by heightened pain sensitivity, fatigue, sleep disturbance, and other symptoms as a result of dysregulation of neurophysiologic function. Many theories of etiology are under investigation. With the proper treatment coupled with a caring and well informed physician; patients with fibromyalgia should be able to improve function and reduce pain. A variety of neuro-modulatory agents are showing capability of beneficially affecting the symptom domains of patients with fibromyalgia. Treatment options currently exist to assist patients in relieving symptoms and preventing flare-ups. Prompt diagnosis and treatment of fibromyalgia patients may produce substantial improvement in quality of life.

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References

1. Blyth FM. Chronic pain—is it a public health problem? *Pain* 2008 Jul;137(3):465-466. PubMed doi:10.1016/j.pain.2008.04.013.
2. Mease PJ, Clauw DJ, Arnold LM, Goldenberg DL, Witter J, Williams DA, et al. Fibromyalgia syndrome. *J Rheumatol* 2005 Nov;32(11):2270-2277.
3. Shleyfer E, Jotkowitz A, Karmon A, Nevzorov R, Cohen H, Buskila D. Accuracy of the diagnosis of fibromyalgia by family physicians: is the pendulum shifting? *J Rheumatol* 2009 Jan;36(1):170-173.
4. Mease P, Arnold LM, Bennett R, Boonen A, Buskila D, Carville S, et al. Fibromyalgia syndrome. *J Rheumatol* 2007 Jun;34(6):1415-1425.
5. Schmidt-Wilcke T, Clauw DJ. Fibromyalgia: from pathophysiology to therapy. *Nat Rev Rheumatol* 2011 Sep;7(9):518-527.

6. Perrot S. Fibromyalgia syndrome: a relevant recent construction of an ancient condition? *Curr Opin Support Palliat Care* 2008 Jun;2(2):122-127.
7. Culpepper L. Evaluating the patient with fibromyalgia. *J Clin Psychiatry* 2010 Sep;71(9):e25.
8. Gerdle B, Björk J, Cöster L, Henriksson KG, Henriksson C, Bengtsson A. Prevalence of widespread pain and associations with work status: a population study. *BMC Musculoskelet Disord* 2008;9:102.
9. Wolfe F, Ross K, Anderson J, Russell IJ, Hebert L. The prevalence and characteristics of fibromyalgia in the general population. *Arthritis Rheum* 1995 Jan;38(1):19-28.
10. Hite KP, Harth M. Classification, epidemiology, and natural history of fibromyalgia. *Curr Pain Headache Rep* 2001 Aug;5(4):320-329.
11. Assumpção A, Cavalcante AB, Capela CE, Sauer JF, Chalot SD, Pereira CA, et al. Prevalence of fibromyalgia in a low socioeconomic status population. *BMC Musculoskelet Disord* 2009;10:64.
12. Bartels EM, Dreyer L, Jacobsen S, Jespersen A, Bliddal H, Danneskiold-Samsøe B. Fibromyalgia, diagnosis and prevalence. Are gender differences explainable? *Ugeskr Laeger* 2009 Nov;171(49):3588-3592.
13. Winfield JB. Psychological determinants of fibromyalgia and related syndromes. *Curr Rev Pain* 2000;4(4):276-286.
14. Arnold LM, Hudson JL, Keck PE, Auchenbach MB, Javaras KN, Hess EV. Comorbidity of fibromyalgia and psychiatric disorders. *J Clin Psychiatry* 2006 Aug;67(8):1219-1225.
15. Staud R. Is it all central sensitization? Role of peripheral tissue nociception in chronic musculoskeletal pain. *Curr Rheumatol Rep* 2010 Dec;12(6):448-454.
16. Yunus MB. Role of central sensitization in symptoms beyond muscle pain, and the evaluation of a patient with widespread pain. *Best Pract Res Clin Rheumatol* 2007 Jun;21(3):481-497.
17. Tanriverdi F, Karaca Z, Unluhizarci K, Kelestimur F. The hypothalamo-pituitary-adrenal axis in chronic fatigue syndrome and fibromyalgia syndrome. *Stress* 2007 Mar;10(1):13-25.
18. Bradley LA. Psychiatric comorbidity in fibromyalgia. *Curr Pain Headache Rep* 2005 Apr;9(2):79-86.
19. Woolf AD. The bone and joint decade 2000-2010. *Ann Rheum Dis* 2000 Feb;59(2):81-82.
20. Katz RS, Wolfe F, Michaud K. Fibromyalgia diagnosis: a comparison of clinical, survey, and American College of Rheumatology criteria. *Arthritis Rheum* 2006 Jan;54(1):169-176.
21. Wolfe F, Smythe HA, Yunus MB, Bennett RM, Bombardier C, Goldenberg DL, et al; Report of the Multicenter Criteria Committee. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia. Report of the multicenter criteria committee. *Arthritis Rheum* 1990 Feb;33(2):160-172.
22. Harden RN, Revivo G, Song S, Nampiaparampil D, Golden G, Kirincic M, et al. A critical analysis of the tender points in fibromyalgia. *Pain Med* 2007 Mar;8(2):147-156.
23. Wolfe F. The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptoms severity. *Arthritis Care Res* 2010 May;62(5):600.
24. Goldenberg DL. Multidisciplinary modalities in the treatment of fibromyalgia. *J Clin Psychiatry* 2008;69(Suppl 2):30-34.
25. Burckhardt CS. Multidisciplinary approaches for management of fibromyalgia. *Curr Pharm Des* 2006;12(1):59-66.
26. Staud R. Treatment of fibromyalgia and its symptoms. *Expert Opin Pharmacother* 2007 Aug;8(11):1629-1642.
27. Sarzi-Puttini P, Buskila D, Carrabba M, Doria A, Atzeni F. Treatment strategy in fibromyalgia syndrome: where are we now? *Semin Arthritis Rheum* 2008 Jun;37(6):353-365.
28. Nijs J, Mannerkorpi K, Descheemaeker F, Van Houdenhove B. Primary Care Physical Therapy in People With Fibromyalgia: Opportunities and Boundaries Within a Monodisciplinary Setting. *Phys Ther* 2010 Dec;90(12):1815-22. Epub 2010 Sep 16.
29. Clauw DJ. Pharmacotherapy for patients with fibromyalgia. *J Clin Psychiatry* 2008;69(Suppl 2):25-29.
30. Häuser W, Thieme K, Turk DC. Guidelines on the management of fibromyalgia syndrome - a systematic review. *Eur J Pain* 2010 Jan;14(1):5-10.
31. Rooks DS. Fibromyalgia treatment update. *Curr Opin Rheumatol* 2007 Mar;19(2):111-117.
32. Culpepper L. Nonpharmacologic care of patients with fibromyalgia. *J Clin Psychiatry* 2010 Aug;71(8):e20.
33. Jones KD, Adams D, Winters-Stone K, Burckhardt CS. A comprehensive review of 46 exercise treatment studies in fibromyalgia (1988-2005). *Health Qual Life Outcomes* 2006;4:67.
34. Busch AJ, Schachter CL, Overend TJ, Peloso PM, Barber KA. Exercise for fibromyalgia: a systematic review. *J Rheumatol* 2008 Jun;35(6):1130-1144.
35. Wang C, Schmid CH, Rones R, Kalish R, Yin J, Goldenberg DL, et al. A randomized trial of tai chi for fibromyalgia. *N Engl J Med* 2010 Aug;363(8):743-754.
36. Cao H, Liu J, Lewith GT. Traditional Chinese Medicine for treatment of fibromyalgia: a systematic review of randomized controlled trials. *J Altern Complement Med* 2010 Apr;16(4):397-409.
37. Callahan LF, Freburger JK, Mielenz TJ, Wiley-Exley EK. Medical skepticism and the use of complementary and alternative health care providers by patients followed by rheumatologists. *J Clin Rheumatol* 2008 Jun; 14(3):143-147.
38. Porter NS, Jason LA, Boulton A, Bothne N, Coleman B. Alternative medical interventions used in the treatment and management of myalgic encephalomyelitis/chronic fatigue syndrome and fibromyalgia. *J Altern Complement Med* 2010 Mar;16(3):235-249.
39. Itoh K, Kitakoji H. Effects of acupuncture to treat fibromyalgia: a preliminary randomised controlled trial. *Chin Med* 2010;5:11.