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# TREATMENT OPTIONS FOR FIBROMYALGIA

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**Keywords:**

Fibromyalgia, chronic pain, diagnostic criteria, cognitive disturbance, neurotransmitter, tender points

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## ABSTRACT

Fibromyalgia is the most commonly encountered chronic widespread pain condition in rheumatology. Its aetiopathogenesis is still a matter of debate, but various pharmacological and non-pharmacological therapies are currently available for its treatments. This article describe the evidence based therapies that can be evaluate for the management of fibromyalgia.

**Introduction**

Fibromyalgia (FM) is a common rheumatological syndrome characterized by many chronic, diffuse musculoskeletal pain and tenderness with number of associate symptoms, among which sleep disturbance, fatigue and affective dysfunction are particularly frequent and that occur at once.[1] The painful tissue involve are not occur with tissue inflammation. The pain FM usually affects on the neck, buttocks, shoulders, arms, chest and the upper back. It affects between 2-10% of the general population, in all ages, ethnic groups and culture. FM's is up to seven times more common in females than males.[2]

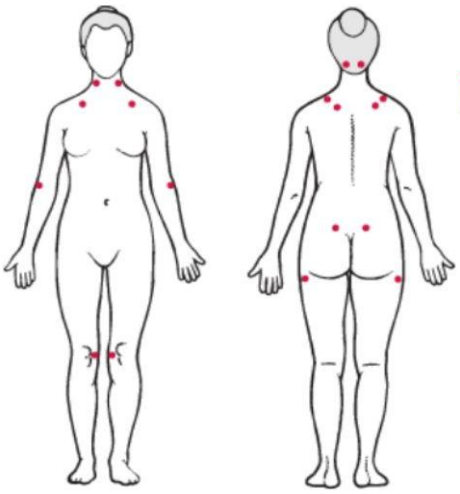
The specific causes of fibromyalgia are unknown. Many possible causes have been studied, including viral infections, hormonal disorders, muscle conditions and exposure to toxic substances in the environment. It is also causes to people who are genetically predisposed. When production of neurotransmitters is altered, the circuits that depend on these substances malfunction, which produces symptoms.

**Pathogenesis**

Individuals with FM have an abnormality in the pain processing and which produces the extreme sensitivity in tender points as well as visceral pain seen in IBS, noncardiac chest pain, headaches and bladder irritability.[3] It has some evidence that experience of pain and perception is dependant on a balance ofperipheral nociceptive inputs central descending facilitation and inhibition of nociceptive sensory processing, cortical processing and consequent emotional, physiological, autonomic hormonal and behavioural response.[4]Fatigue, sleep disturbance, tenderness, cognitive disturbance and mood disturbance are also common components of the syndrome.[2,5] The latest research has found that FM involves the changes in the body's neurotransmitters which are not only for the pain pathway, but also for proper operation of other circuits. The number of affected individual in the same family is often greater than expected, which suggest that genetics are also involves to develops fibromyalgia.[2]

**Diagnosis**

The American College of Rheumatology (ACR) 1990 diagnostic criteria required the presence of pain on both side of the body and above and below of the waist present for at least 3 months, with presence of at least 11 out of 18 tender points and not better explained by any other disorder. Using this criteria for diagnosis is problematic for more than 1 reasons. that's why, the ACR introduce the new provisional set of diagnostic criteria for FM in 2010 which represent a preferred way of diagnosis, or thinking about FM.[6]



# Fibromyalgia Pain Points

| **Part A**<br>**PAIN in last week** | | **Part B**<br>**SYMPTOMS in last week** |
|---|---|---|
| **Region** | | **Symptom** |
| **1. Left upper region**<br>☐ Left jaw<br>☐ Left shoulder girdle<br>☐ Left upper arm<br>☐ Left lower arm | **2. Right upper region**<br>☐ Right jaw<br>☐ Right shoulder girdle<br>☐ Right upper arm<br>☐ Right lower arm | **Grade the severity of the symptom***<br>Fatigue 0 ☐ 1 ☐ 2 ☐ 3 ☐<br>Waking unrefreshed 0 ☐ 1 ☐ 2 ☐ 3 ☐<br>Cognitive symptoms 0 ☐ 1 ☐ 2 ☐ 3 ☐ |
| **3. Left lower region**<br>☐ Left hip (buttock, trochanter)<br>☐ Left upper leg<br>☐ Left lower leg | **4. Right lower region**<br>☐ Right hip (buttock, trochanter)<br>☐ Right upper leg<br>☐ Right lower leg | **Have the following symptoms been bothersome in last months? (tick if yes)**<br>Headache 1 ☐<br>Abdominal pain 1 ☐<br>Depression 1 ☐ |
| **5. Axial region**<br>☐ Neck<br>☐ Upper back<br>☐ Lower back<br>☐ Chest<br>☐ Abdomen | **TOTAL POINTS:**<br>___ /19 = Widespread pain index | **TOTAL POINTS:**<br>___ /12 = Symptom Severity Score |

**Fibromyalgia Severity Score = Widespread Pain Index + Symptom Severity (Score ___ /31)**

**Fibromyalgia diagnosis**

**a. Pain and symptom score thresholds**

**WPI ≥ 7 ☐ PLUS SSS ≥ 5 ☐**

**OR**

**WPI ≥ 4 ☐ PLUS SSS ≥ 9 ☐**

**and**

**b. Generalised pain present (pain in ≥ 4 regions, excluding jaw, chest, abdomen)**

* 0 =no problem; 1 = slight or mild problems, generally mild or intermittent; 2 = moderate, considerable problems, often present and/or at a moderate level; 3 = severe, pervasive, continuous, life disturbing problems

**Treatment of fibromyalgia**

Therapy and pathogenesis of FM still remain challenge for physicians due to the diversity of their symptoms. Although fibromyalgia is chronic syndrome and it is not curable symptomatic relief should goal of patient and physician. To treat FM combination of pharmacological and non-pharmacological treatments which including patient education, exercise and cognitive behavioural therapy.

**Non–pharmacological treatments:-**

**Patient education**

After diagnosis of fibromyalgia which includes primary care visits, diagnostic testing and drug prescriptions. The next step is patient education. Novel physiological support therapy results in FM includes virtual reality, Base Body Awareness Therapy (BBAT), Cognitive-Behaviour Therapy (CBT) and Group Music and Imagery (GrpMI) intervention. BBAT is a movement awareness training program that teaches patient how to correctly move in space and time, increasing awareness of body co-ordination.[7] Interventions with more supporting evidence, such as aerobic and/or resistance exercise, CBT, and tai chi were not listed by patient on the survey. Patient should be educated on the potential benefits of these treatment options and encouraged totry them. Patient should also be encouraged to identify stressors that worsen symptoms and to try approaches to lessen these stressors. Counselling on proper sleep hygiene can assist patient with improving sleep related symptoms.[5]setting expectations regarding illness prognosis and the role of the patient that Fibromyalgia is a chronic illnesses with good days ; treatment will improve symptoms but usually not eliminated them.[8] The National Fibromyalgia Association offers many free resource for patients, including online support forums, a digital magazine and information about local support groups.[5]

**Cognitive behaviour**

Some patient shows cognitive behaviour therapy and stress reduction techniques to be be effective.[8-10]CBT focuses on coping strategies, emotional control and cognitive physiology and shows successful results in counteracting mood disorders and disability of FM patients.[7,11]

**Exercise**

Exercise intensity should be increased very slowly avoid injury and flares of pain, which may cause to patient to abdomen and activity.[8]There is no clear evidence to to suggest that one specific exercise program is better than another. Instead most exercise seem to produce

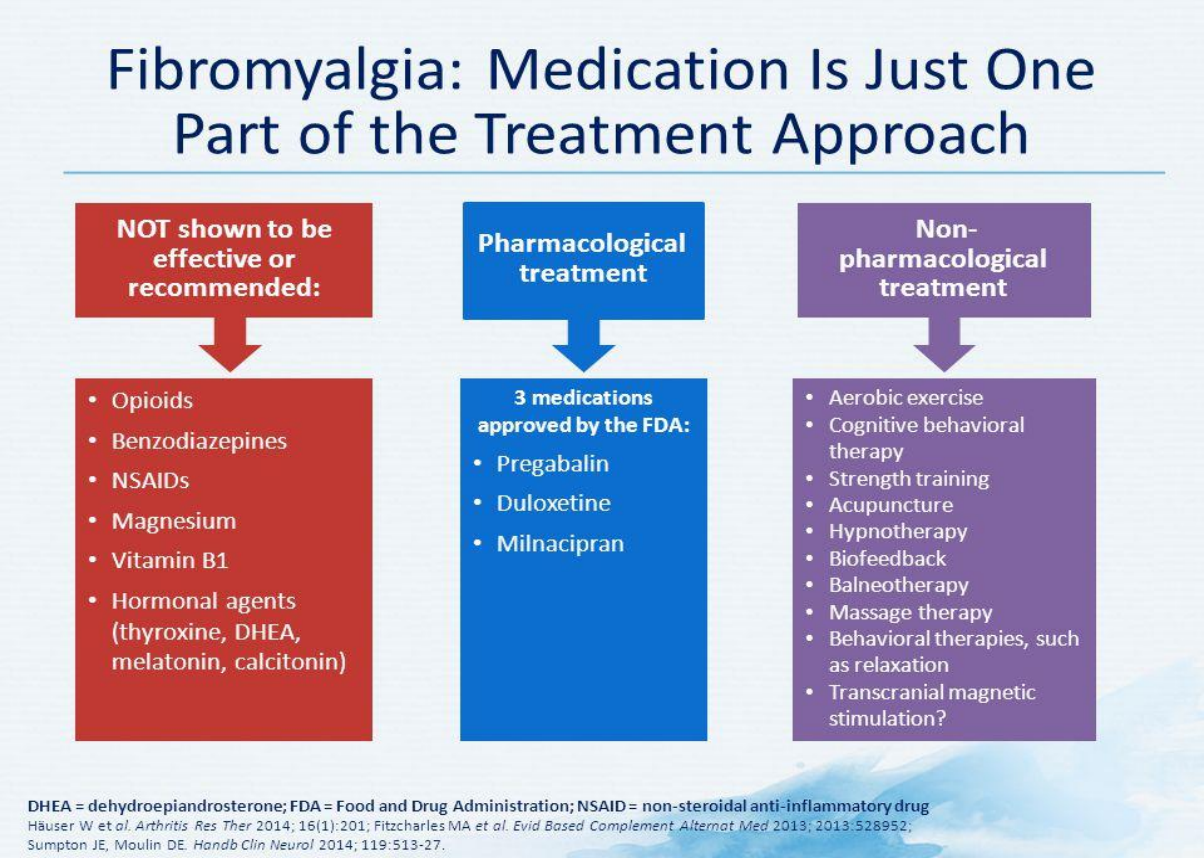
at least modest pain relief.[2]

The following exercise are shown to improve the symptoms of FM :

- Aerobic exercise, such as running, aerobic cases or swimming, according to a 2017 study.
- Tai chi, according to a 2018 study.
- Yoga, according to a 2017 study.

**Pharmacological treatments**

The U.S. food and drug administration (FDA) has approved three drugs specifically for treating FM. It includes : Pregabalin, Duloxetine, Milnacipran.




**Peragabaline**

Pregabalin was originally marked as an antiepileptic but is now commonly used for pain management.[12-13]Pregabalin is calm over active nerve and more rapidly absorbed (1 h) and has higher bio availability (99%).[14]It binds to the $\alpha_2$-δsubunit of presynaptic, voltage dependent calcium channel that widely distributed throughout the central and peripheral system which releases neurotransmitter such as glutamate, nornorepinphrine, and substance P many contributes to pain reduction in patient with FM.[5,12]Several studies have evaluated its effectiveness in around 10% of patients above that of placebo.[14]

Paragabalinfor FM patient talking paragabalin 300,450,600 mg daily but similarly with any other medications, patient with fibromyalgia are poorly tolerant of such doses. Comman side effect are associated with paragabalin include dizziness, somnolence and wait gain. Paragabline is best for the patient with prominent pain and sleep disturbance, and less effective for fatigue. Paragabalane is both recommended by the European League Against Rheumatism ( EULAR) and Canadian guideline.[12,15-16]

**Duloxetine**

Duloxetine is serotonin reuptake inhibitor (SNRI) originally marked for the treatment of depression, but several studies evaluate benefit in FM.It act on the serotonin and norepinephrine to dampen pain signals.The dose can range 30 to 120 mg daily, however many patient with fibromyalgia cannot tolerate dose above 60 mg. comman side effect include headache, palpitation, nausea and flushing.[12]

**Milnacipran**

Milnacipran is also SNRI recommended for the fibromyalgia. It report the pain in around 15% of patient above that placebo and improve the quality of life of patient.[17]The dose can range 25 to 50 mg daily. A 6 month trial shows that milnacipran was more likely to reduce pain and fatigue than placebo. It has similar side effect to deloxitine, but has stronger nor adrenaline quality than duloxetineand for this reason may be more stimulating.[18]

**Off- label Drug Therapies**

**Antidepressant Agents**

Antidepressant have long history in the treatment of chronic pain syndrome. The tricyclic antidepressants, selective serotonin reuptake inhibitors (SSRIs), or combinations of both, produce mild to moderate improvement in symptoms. Dosage should be gradually increased, not to exceed the recommended maximum for the drug. Amitriptyline is recommended by all treatment guideline. Duloxetine which id serotonin and norepinephrine reuptake inhibitor is used successfully. Dopamine agonist (e.g., pramipexole), sodium Oxybate and growth hormone therapy have recently been introduced for fibromyalgia syndrome.[19-21]

**Cyclobenzaprine**

Cyclobenzaprine is a medication with similar tricyclic structure to amitriptyline, but but it not known to have antidepressant effects.[22] Five trials were included in a meta-analysis comparing cyclobenzaprine, at dosages of 10-30 mg daily, with placebo. Sleep and pain symptoms improved for three times the number of patient taking cyclobenzaprine versus placebo. Cyclobenzaprine shows adverse effect in 85% patients as similar to amitriptyline.[23]

**Gabapentin**

Gabapentin is antiepileptic medication that is some time used to treat FM. It has similar mechanism of action as pregabalin, and exerts its effects via modulating neuronal voltage gated calcium channels.[12] Compared with placebo gabapentin titrated to a dosage of 1200-2400 mg/day significantly improved the pain severity score.[24] Other scale of symptom severity, including an assessment of sleep, showed benefits with gabapentin compared with placebo. Dizziness, weight gain, and sedation were note.[5]

**Venlafaxine**

Two small open- label studies with venlafaxine have been conducted, one using immediate release venlafaxine 37.5-375mg daily in 15 patients and one using venlafaxine 75 mg daily in 20 patients. In both trials, pain improved from baseline using a visual scale and pain questionnaire.[25-26]More data are needed to recommend venlafaxe as an alternative to duloxetine or milnacipran for fibromyalgia.[5]

**Selective Serotonin Reuptake Inhibitors**

Fluoxetine, paroxetine, and citalopram have been studied for the treatment of fibromyalgia. In general, they are better tolerated than tricyclic antidepressants, especially for those experiencing anticholinergic adverse effects, but these drugs have less efficacy for fibromyalgia symptoms.[27]

**Dopamine Agonists**

Dopamine agonists may decrease adrenergic arousal that may contribute to disordered sleep in patients with fibromyalgia. Pramipexole and ropinirole have been studied for the treatment of fibromyalgia. In a small 14-week trial of 60 patients with pramipexole, 42% of patients had a 50% or more reduction in their pain score using a visual analog scale, compared with 14% of patients taking placebo. A trial of ropinirole found on benefit; however, the discontinuation rate was high (63%) for both intolerance and lack of efficacy.[28]

**Pain Medications**

Although pain is a characteristic feature of fibromyalgia, analgesics often of limited clinical value.

**Tramadol**

For those patients who can tolerate its adverse effects, tramadol may be beneficial in reducing the severity of pain associated with fibromyalgia. A trial of tramadol in the treatment of fibromyalgia pain found that 69% of the 100 patients were able to tolerate the drug in an open-label run-in phase.[29]Of those 69 patients, 35 were randomised to tramadol in the double-blind placebo-controlled phase. Compared with placebo, the patient receiving tramadol showed statistically

significant improvements in pain intensity, pain relief, and myalgic scores. A careful consideration of adverse effects and the abuse potential should be considered before tramadol is used for fibromyalgia pain relief.

**Opioids**

Opioids are not recommended for fibromyalgia because this drug may actually worsen symptoms such as fatigue and cognitive impairment. A 1-year observational study evaluated the use of opioids in 1700 adults with fibromyalgia and found that patient taking nonopioid pain relievers demonstrated greater improvement in assessments such as the BPI and FIQ.[30]

**Other Pain Medications**

Non steroidal anti-inflammatory drugs and acetaminophen act peripherally and are therefore less likely to be of benefit for the centrally mediated pain mechanism that are associated with fibromyalgia.

**Conclusion**

It is difficult to draw definite conclusion concerning the most appropriate approach to managing FMS because of the methadological limitatiions of the available studies and the fact that the heterogeneity and nonstandardized nature of their therapeutic program make them difficult to compare. Multidisciplinary pharmacologic, rehabilitative, and cognitive-behavioral approach currently seems to be the most effective.

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