Updated Treatment of Fibromyalgia Syndrome

Abstract

Fibromyalgia is a debilitating condition that is frequently misdiagnosed. It affects 2% of the population, with middle-aged women having the highest frequency. Fibromyalgia affects more women than men, and It becomes worse as you get older. Because medical treatment for fibromyalgia is typically only partial, health professionals must provide patients with ongoing assistance in order for them to become effective, active self-managers. There is no one-size-fits-all drug for fibromyalgia, but you do have a lot of options for treating your symptoms. However, Antidepressants in general such as “duloxetine” and Gabapentinoids drugs such as “pregabline” are the most used drugs. there is some evidence that NSAIDs may have a synergistic effect when combined with centrally active agents such as tricyclic antidepressants and anticonvulsants. Among non-pharmacological therapy, exercise and psychoeducational techniques have the most evidence of efficacy, but they must be personalized to the individual. In this review we will be looking at diagnosis and treatment of fibromyalgia.

Introduction:

Fibromyalgia (FM) is a musculoskeletal pain disorder characterised by continuous widespread pain. The disease is frequently accompanied by fatigue, cognitive disturbance, psychiatric, and numerous somatic symptoms. Fibromyalgia has an etiology that is unknown, as well as a pathophysiology that is unknown. Despite complaints of soft tissue discomfort, there is no evidence of tissue inflammation. According to current research, fibromyalgia is a pain control illness that is generally classified as a kind of central sensitization syndrome. [1]

There is no one-size-fits-all drug for fibromyalgia, but you do have a lot of options for treating your symptoms. Some medicines can help with aches and pains, while others can help you feel more energized or sleep better. To get relief from fibromyalgia, you may need to take more than one medication. The antidepressants duloxetine (Cymbalta) and milnacipran (Savella), as well as the epilepsy medicine pregabalin, have all been licensed by the FDA to treat fibromyalgia (Lyrica). [2]

Fibromyalgia can occur on its own, but it is more likely to be a stereotyped, maladaptive biological response of the body to the cumulative impacts of physical or psychological stress in genetically susceptible individuals. It's linked to

psychological and musculoskeletal problems, which can lead to poorer outcomes, although it can also happen after an infection. Furthermore, fibromyalgia may be more common in those with chronic medical conditions in general. [3]

FMS is not a recent condition. A cluster of FMS symptoms was collectively described as “Muskelschwiele” (muscle callus) and considered generalized body pain with rheumatism in the mid-ninth century in Germany, according to one of the first reports. Inflammation of the connective tissues was thought to be the underlying pathophysiology when the word "fibrositis" was used in the early 1900s to describe the disorder. The idea continued until systematic scientific research appeared in the literature in the 1970s, when an underlying inflammation was ruled out and fibromyalgia was recommended as a more neutral word. [4]

The ACR criteria have become a standard in FMS research since its inception in 1990. It have been utilized in the great majority of published FMS reports to date, bringing the literature together. The ACR standards, on the other hand, are not without flaws. The validity of the TP criterion is one of the primary concerns; especially, it is unclear what the number of positive TPs actually reflects. It's likely that the pain response to digital pressure on the TPs is a symptom of underlying nociceptive processing failure, resulting in generalised hyperalgesia. [4]

Etiology:

Fibromyalgia is a persistent pain condition with no recognized cause. This syndrome is not caused by a single incident; rather, it is triggered or aggravated by a combination of physical and/or emotional stressors, such as infections and emotional and physical trauma. Fibromyalgia is a pain regulation condition that is frequently characterized as central sensitization. There has been some evidence of a genetic susceptibility for fibromyalgia in several studies, but no clear candidate gene has been identified. Fibromyalgia causes changes in the central nervous system that affect pain and sensory processing.When compared to healthy controls, patients perceive noxious stimuli as painful at lower levels of physical stimulation. Fibromyalgia patients have higher than average increases in the perceived intensity of pain when they are exposed to rapidly repeated brief noxious stimuli. In people with fibromyalgia, there appears to be a weakness in the endogenous analgesic systems. By using functional neuroimaging techniques, variations in activation of pain-sensitive regions of the brain have been demonstrated. [1,5-10]

Epidemiology:

Fibromyalgia affects more women than men, with a prevalence of 2 to 3 percent in the United States and other nations. It becomes worse as you get older. Fibromyalgia is the most common cause of widespread musculoskeletal pain in women between the ages of 20 and 55. Many studies have revealed that the prevalence of adolescent depression is similar to that of adults. More than 40% of the patients sent to a tertiary care pain clinic satisfied the criteria for fibromyalgia. Patients who have rheumatic disease, are more likely to get fibromyalgia. [1]

Fibromyalgia is a debilitating condition that is frequently misdiagnosed. It affects 2% of the population, with middle-aged women having the highest frequency. Despite a lack of understanding of its pathophysiology, evidence for mechanism-based management approaches to this disease is growing. These are more likely to be helpful if introduced early, emphasising the importance of quick diagnosis in general practise. [2]

Irritable bowel syndrome, chronic fatigue syndrome, and temporomandibular joint dysfunction are all examples of functional somatic disorders that overlap with fibromyalgia. Despite the fact that functional somatic problems frequently co-occur with mood and anxiety disorders, research reveals that, while they are related to and may interact with psychological conditions, they are distinct. The syndrome is defined by broad somatic pain and deep tissue soreness, both of which are caused by neural pain pathways being sensitised. Fatigue, sleep disturbances, cognitive dysfunction, and psychological suffering can all occur in different combinations.Despite the absence of objective abnormalities on clinical examination, these symptoms persist. [3]

Diagnosis:

The initial effort at FM classification criteria dates from 1990 and is based on investigations conducted in 16 clinical and academic settings in the United States and Canada, bringing together both doubters and supporters. Several alternative diagnostic procedures have been presented since then. Of general, most researchers agree that various domains in FM should be assessed, including pain, sleep, mood, functional status, exhaustion, concentration/memory issues (i.e. dyscognition), and tenderness/stiffness. Pain intensity, physical functioning, emotional functioning, and overall improvement/well-being were the four primary areas that were initially measured.Sleep problems and weariness are reported by 70–80 percent of people with FM. FM diagnosis has also included depressive symptoms, anxiety, and mood states. Patients with FM who have a severely impaired function and quality of life

generally report impairment in various areas of function, particularly physical function. The development of novel disease-specific metrics for each of the important domains in FM has been a top goal since the late 1990s. In addition, studies supporting the validity of current instruments in the context of FM received a lot of attention. [11]

Preliminary fibromyalgia diagnosis criteria and symptom severity evaluation from the American College of Rheumatology: [1]

If all three of the following conditions are met, a patient is diagnosed with fibromyalgia:

1. Widespread pain index (WPI) is 7 and symptom severity (SS) score is 5, or the WPI is 3 to 6 and the SS scale score is 9.
2. For at least 3 months, symptomatology has been present at a similar level.
3. There is no other disorder in the patient's history that could explain the pain.

Ascertainment:

- WPI: Record the number of areas where the patient has had pain in the previous week, as well as the number of areas in which the patient has had discomfort. The score will range from 0 to 19. Shoulder girdle, left hip (buttock, trochanter), left jaw, left upper back shoulder girdle, right hip (buttock, trochanter), right jaw, right lower back upper arm, left upper leg, left chest neck upper arm, right upper leg, right abdomen lower arm, left lower leg, left lower arm, right lower arm, right lower leg, right lower leg, right lower leg, right lower leg, right lower leg, right lower leg, right lower leg, right lower leg,
- Fatigue, waking unrefreshed, and cognitive problems are all on the SS scale. Indicate the severity level of each of the three symptoms above over the last week using the following scale: 0 no issues; 1 minor or minor problems, which are usually minor or intermittent; 2 moderate, significant problems, which are frequently present and/or at a moderate degree; 3 severe: pervasive, continuous, life-disturbing problems. Indicate whether the patient has any of the following somatic symptoms: 0 indicates no symptoms, 1 indicates a few symptoms, 2 indicates a considerable number of symptoms, and 3 indicates a large number of symptoms.The severity of the three symptoms (fatigue, waking unrefreshed, and cognitive symptoms) is added to the severity of general somatic symptoms to calculate the SS scale score. The ultimate score ranges from 0 to 12. [1]

Non-Pharmacological Treatment:

Living with fibromyalgia carries a greater strain than living with other rheumatic conditions and most other chronic illnesses. Because medical treatment for fibromyalgia is typically only partial, health professionals must provide patients with ongoing assistance in order for them to become effective, active self-managers. This is the most crucial of all the interventions for a successful life with this terrible multifaceted condition. This process, however, can be complicated by fibromyalgia-related cognitive dysfunction, which is frequently overlooked by medical practitioners. Among non-pharmacological therapy, exercise and psychoeducational techniques have the most evidence of efficacy, but they must be personalised to the individual. For all but the mildest cases, a pre-exercise biomechanical examination and subsequent exercise monitoring by a qualified physical therapist is recommended. The use of an actimeter can aid in the promotion of declining daily physical activity. All patients, especially those who are more psychologically distressed, should be referred to a psychologist. [3]

Although spa therapy does not affect the circadian pattern of these hormones, it does cause a number of endocrine reactions, including the release of adrenocorticotropic hormone (ACTH), cortisol, prolactin, and growth hormone (GH). In fibromyalgia patients, a dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis has been observed, which is characterised by mild hypocortisolemia and glucocorticoid feedback resistance. These findings may help to understand why spa therapy helps people with fibromyalgia. Based on four RCTs, systematic reviews of individuals with fibromyalgia determined that there is moderate evidence in support of balneotherapy use. [12]

Antidepressants:

Antidepressants and neuromodulating antiepileptics both improve fibromyalgia symptoms significantly. Serotonin and norepinephrine reuptake inhibitors have been reported to have the best efficacy and tolerability for fibromyalgia among antidepressants. Both duloxetine and milnacipran are antidepressants in the serotonin-norepinephrine reuptake inhibitor class that work by enhancing the activity of noradrenergic antinociceptive pathways. Both have been demonstrated to be effective in randomised, double-blind, placebo-controlled trials. [12]

Low-dose amitriptyline has long been the first-line treatment for fibromyalgia pain and sleep disturbances. The evidence for its usage, however, is of poor quality. Although the studies are limited and short-term, they suggest that 4.1 patients must

be treated in order for one to experience at least 50% pain alleviation. However, one patient out of every 3.3 will experience an adverse event. Amitriptyline's use is limited by the development of tolerance and weight gain, although it can be highly beneficial in the long run for a small group of people. [3]

The AWMF has given AMT a strong recommendation (10–50 mg/daily), however the EUALR guidelines suggest that just a low dose may be useful, despite a high degree of agreement. The Canadian recommendations adopt a more broad approach to AMT, recommending that all antidepressant classes, including SSRI and NSRI, be used to treat FMS, depending on the drug's individual efficacy, medical knowledge, patient characteristics, and cost. Nishishinya et al. also found that using AMT 25 mg/day for 6–8 weeks reduced pain, sleep, and fatigue, with no evidence for 50 mg/day. [13]

Tricyclic antidepressants (TCAs), particularly amitriptyline and the physiologically related cyclobenzaprine, are beneficial in the short term in the treatment of fibromyalgia. Tricyclic drugs increase norepinephrine and serotonin neurotransmission in the descending inhibitory pain pathways by decreasing serotonin and norepinephrine reuptake, resulting in pain relief. [12]

NSAID:

Ibuprofen and naproxen have been shown to be no better than placebo in terms of nonsteroidal anti-inflammatory drugs (NSAIDs), though there is some evidence that NSAIDs may have a synergistic effect when combined with centrally active agents such as tricyclic antidepressants and anticonvulsants. Furthermore, a poll of 1042 fibromyalgia patients indicated that 66.1 percent thought NSAIDs were more beneficial than acetaminophen. Despite the lack of clear data, it is reasonable to use basic analgesic medications and, in some groups, NSAIDS, in the care of fibromyalgia because of their tolerable side effect profile. [12]

Selective Serotonin Reuptake Inhibitors:

Although there is no unbiased evidence that SSRIs are superior to placebo in treating the major symptoms of fibromyalgia (pain, exhaustion, and sleep issues), they may be investigated for treating depression in this group of patients, according to a recent Cochrane review. In terms of SSRI recommendations, national and international guidelines are mixed. The EULAR guidelines are based on seven systematic reviews, whereas the AWMF meta-analysis is based on eight RCTs. The EULAR guidelines do not encourage their use, although the Canadian and

AWMF guidelines approve. In comorbid depressive/anxiety disorders, fluoxetine 20–40 mg/day or paroxetine 20–40 mg/day can be explored for a limited time. In a tiny RCT of 40 patients, citalopram was found to be ineffective in the treatment of FMS. [13]

Cyclobenzaprine:

Cyclobenzaprine is a 5-HT2 receptor blocker that relaxes muscles by acting on a subfamily of serotonin receptors. It has a structure similar to amitriptyline and is widely prescribed to FMS patients. According to a comprehensive evaluation of the literature, it provides a substantial advantage in decreasing sleep disruptions but only a minor benefit in pain relief. Moldofsky et al. previously demonstrated that bedtime very low doses of cyclobenzaprine improved pain and sleep in patients with an unique sleep architecture.The use of a sublingual formulation of low-dose cyclobenzaprine (TNX-102SL, 2.8 mg) to improve nonrestorative sleep in FMS patients has been reported; however, this formulation has now failed to meet key pain-related endpoints, and its development has been halted. [14-17]

Gabapentinoids:

Pregabalin and gabapentin, the two main members of this class of medicines, work by binding to the alpha2delta subunit of voltage-gated calcium channels in the CNS. They were originally employed as anticonvulsants, but are now mostly used to alleviate chronic pain. The FDA has approved pregabalin for the treatment of FMS, and it is suggested in guidelines. Pregabalin improved pain and sleep disruptions in a number of placebo-controlled clinical trials.However, it was not found to significantly reduce tiredness complaints in some trials when compared to placebo, and none of the trials suggested any improvement in depression symptoms. In addition to their lack of effect on depressive symptoms and very insignificant effect on anxiety, a meta-analysis of randomised controlled trials on both pregabalin and gabapentin emphasised their effect in relieving pain, exhaustion, sleep, and overall quality of life. [14,18-24]

Cannabinoids:

Tetrahydrocannabinol (THC) and cannabidiol (CBD) are the two main active ingredients in cannabinoids (CBD). The former is the psychoactive component, which operates through CB1 and CB2 receptors to alter pain (as well as emotions). The latter possesses analgesic and anti-inflammatory properties. As a result, the THC:CBD ratio impacts the overall effect of the product. CB1 cannabinoid

receptors are mostly located in the central nervous system and peripheral nervous system. Their agonists operate as pain modulators along sensory pathways. In terms of the endocannabinoid system's complicated role in pain modulation, FMS is thought to be caused, among other things, by a lack of endocannabinoid activity. [14]

Opioids:

The use of powerful opioids in the treatment of FMS has been discouraged. With greater levels of endogenous opioids in the CSF and decreased central -opioid receptor availability, patients with FMS have a deficit in opioid-mediated descending anti-nociceptive activity, which may explain why exogenous opioids are ineffective in this group of patients. Tramadol is a mild opioid that acts as a combination agonist and inhibitor of 5-HT and norepinephrine reuptake. It is possible that this latter action is the key to its efficacy in FMS when compared to other opioids. [13]

In fibromyalgia sufferers, tramadol has been demonstrated to be effective. It's an unusual pain reliever with a distinct effect on the central nervous system (serotonin and norepinephrine reuptake) than conventional opioids. It is typically administered at a dose of 200–300 mg/day to treat fibromyalgia-related pain, either alone or in conjunction with acetaminophen. Improvements in sleep adequacy and sleep duration were significantly different between the tramadol/acetaminophen and placebo groups, but not for the other sleep parameters.Although only a few cases of seizures and serotoninergic syndrome have been reported when it is combined with selective serotonin reuptake inhibitors (SSRIs), serotonin-noradrenalin reuptake inhibitors (SNRIs), monoamine oxidase inhibitors (MAOIs), and triptans, there is a theoretical risk of seizures and serotoninergic syndrome when it is combined with these drugs. [12,25-30]

Conclusion:

There is no one-size-fits-all drug for fibromyalgia, but you do have a lot of options for treating your symptoms. Low-dose amitriptyline has long been the first-line treatment for fibromyalgia pain and sleep disturbances. Antidepressants in general such as “duloxetine” and Gabapentinoids drugs such as “pregabline” seems to be the most effective drugs that can be used and also the most often used ones, with NSAIDs not much of a big use. Non pharmacological approaches also can be used such as psychological treatments for depressive patients and other techniques such as spa.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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