

Pharmacological Therapy in fibromyalgia: A Literature Review.

Ágatha Oliveira Felice ^a, Guilherme Ribeiro Xavier ^b, Douglas Alves da Costa Canella ^c.

^a Faculty of Health Sciences, Federal University of Grande Dourados, Dourados, Brazil, agathaofelice@gmail.com

^b Faculty of Health Sciences, Federal University of Grande Dourados, Dourados, Brazil, guiribeiro31@hotmail.com

^c Faculty of Health Sciences, Federal University of Grande Dourados, Dourados, Brazil, douglas.canella@hotmail.com

Abstract. Introduction: Fibromyalgia is a chronic syndrome that impacts both the physical and cognitive aspects of patients, causing musculoskeletal pain, fatigue, sensitivity, and various other symptoms that significantly compromise their quality of life. Methodology: The research utilised Google Scholar, Scielo, and PubMed, considering articles in Portuguese and English from 2018 to 2023. Out of an initial 222 articles, 32 were selected after applying inclusion and exclusion criteria. Results and Discussion: Treatments for fibromyalgia involve multiple classes of medications, such as tricyclic antidepressants, non-opioid analgesics, NSAIDs, SSRIs, SNRIs, anticonvulsants, muscle relaxants, opioids, sleep-inducing drugs, and cannabinoids. Each class has a mechanism of action directed at different symptoms of fibromyalgia. The effectiveness varies among patients, emphasising the importance of an individualised treatment plan. Notably, studies on cannabinoids in the treatment of fibromyalgia are limited, but they indicate efficacy in treating chronic pain. Conclusion: Treating fibromyalgia requires a multifaceted and individualised approach, with various classes of medications available, each targeting different symptoms of the disease. More research on the use of cannabinoids is needed to solidify their effectiveness in treating fibromyalgia.

Keywords. Fibromyalgia/drug therapy, drug therapy

1. Introduction

Fibromyalgia is a complex and chronic medical condition characterised by a broad range of debilitating symptoms that challenge medical understanding and the quality of life of those who suffer from it. It is defined as a chronic pain syndrome that primarily manifests as generalised musculoskeletal pain, persistent fatigue, and extreme sensitivity in joints and muscles. The term "fibromyalgia" derives from the Latin "fibro" (fibrous tissue), "mio" (muscle), and "algia" (pain), thus reflecting the painful and debilitating nature of the condition. In addition to intense pain, individuals with fibromyalgia often report difficulties sleeping, cognitive problems, such as brain fog, and a range of additional symptoms, such as headaches, irritable bowel syndrome, and anxiety, suggesting that the disease goes beyond the mere

manifestation of physical symptoms. It involves a complex interaction between body and mind, resulting in a comprehensive impact on the quality of life of the affected individuals. Those with fibromyalgia face a constant battle against chronic pain, extreme fatigue, and cognitive dysfunction, often limiting their daily activities, social relationships, and even their professional potential. In this context, fibromyalgia medications aim not only to relieve physical symptoms but also to provide patients an opportunity to regain their independence and emotional well-being.

2. Methodology

In this literature review, three databases were used: Google Scholar, Scielo, and PubMed during the period from 2018 to 2023. The keywords used were "Fibromyalgia/drug therapy" and "drug therapy". A total of 222 articles were selected, and the research

was limited to articles in Portuguese and English conducted on humans. Inclusion criteria were studies that evaluated the clinical outcome after drug treatment in patients with fibromyalgia. Exclusion criteria were articles that discussed non-pharmacological therapy in patients with fibromyalgia, articles not related to the topic, and articles without scientific evidence. Titles were carefully analysed, and subsequently, 32 articles were selected.

3. Results and Discussion

The treatment of fibromyalgia typically involves the use of various medications to alleviate symptoms. The effectiveness of medications can vary from person to person, and what works best for one individual may not be the same for another, which is why treatment is individualised, usually after therapeutic testing. In this review, it was found that tricyclic antidepressants are the most common continuous therapeutic option for all patients. Non-opioid analgesics and non-steroidal anti-inflammatory drugs (NSAIDs) are also frequently used for momentary pain and inflammation relief, reserving opioids for more intense pains resistant to treatment. Serotonin reuptake inhibitors (SSRIs) and norepinephrine reuptake inhibitors (SNRIs) are prescribed when patients present with associated anxious and depressive symptoms. Anticonvulsants, at a specific dose, relieve neuropathic pain, and muscle relaxants reduce muscle tension and improve sleep quality. Finally, cannabinoids are recent medications that have shown effective analgesia for intense pains in patients with fibromyalgia, despite the scarcity of studies.

3.1 Non-opioid analgesics

Non-opioid analgesics are often used in the treatment of fibromyalgia to help alleviate pain. Paracetamol (acetaminophen) is a centrally acting analgesic that has a mechanism of action not yet fully understood. It is believed to primarily act in the central nervous system by inhibiting the production of prostaglandins, chemical substances that trigger pain and fever. However, it lacks significant anti-inflammatory properties and, therefore, is not effective in reducing inflammation, which is a minor component in fibromyalgia.

3.2 Nonsteroidal anti-inflammatory drugs (NSAIDs)

NSAIDs are a class of medications often used to treat pain and inflammation in various medical conditions, including fibromyalgia. They work by inhibiting the enzyme cyclooxygenase (COX), which plays a role in the production of prostaglandins, chemical substances involved in the inflammatory response and pain perception. Inhibition of COX reduces the production of prostaglandins, resulting in less pain and inflammation. Since NSAIDs provide some temporary relief from pain in cases of fibromyalgia, their effectiveness is generally moderate, and they do not address the underlying cause of the condition. Additionally, their long-term use may be associated with side effects such as gastrointestinal problems (ulcers, bleeding) and cardiovascular issues, making their continuous use contraindicated.

3.3 Tricyclic antidepressants

Tricyclic antidepressants are used in the treatment of fibromyalgia with the aim of alleviating chronic pain symptoms, improving sleep quality, and helping regulate mood. Although these medications are primarily known for their use in depressive disorders, they are often prescribed to treat conditions in which chronic pain is a significant symptom, such as fibromyalgia. Their mechanism of action involves:

- Increasing neurotransmitters: elevating levels of neurotransmitters in the brain, such as serotonin and norepinephrine. This can help regulate pain perception and improve mood, which is important in managing fibromyalgia.
- Pain modulation: the ability to modulate pain perception at the central nervous system level, which can help reduce the intensity of pain experienced by patients with fibromyalgia.
- Sleep improvement: their sedative properties can enhance sleep quality, reducing the occurrence of sleep disturbances common in fibromyalgia. Improved sleep can contribute to an overall decrease in pain and a general sense of well-being.

3.4 Selective serotonin reuptake inhibitors (SSRIs)

SSRIs work specifically by inhibiting the reuptake of serotonin by neurons, resulting in higher levels of serotonin available in the brain. This can positively affect various aspects of fibromyalgia:

- Pain reduction: acting as a pain modulator, helping to decrease pain perception by the central nervous system.
- Sleep improvement: Adequate serotonin levels are essential for regulating the sleep-wake cycle. SSRIs can enhance sleep quality, which is often disrupted in fibromyalgia.
- Mood stabilisation: SSRIs can help alleviate the depressive and anxiety symptoms that often accompany fibromyalgia.

3.5 Serotonin-norepinephrine reuptake inhibitors (SNRIs)

SNRIs are used in the treatment of fibromyalgia to alleviate symptoms, especially chronic pain, in a manner similar to SSRIs. The mechanism of action of SNRIs involves increasing levels of norepinephrine, a neurotransmitter in the brain that plays a role in regulating the stress response, mood, and pain perception. This can positively affect various aspects of fibromyalgia:

- Pain reduction: Norepinephrine can act as a pain modulator, helping to decrease pain perception by the central nervous system.
- Sleep improvement: Adequate levels of norepinephrine can contribute to sleep regulation.
- Mood stabilisation: SNRIs can also have a positive effect on mood, alleviating symptoms of depression and anxiety.

3.6 Anticonvulsants

Anticonvulsants are used in the treatment of fibromyalgia to reduce chronic pain and symptoms such as fatigue and sleep disturbances. The mechanism of action of anticonvulsants in the treatment of fibromyalgia is not fully elucidated, but it appears to involve the modulation of neuronal excitability and the reduction of pain transmission in the central nervous system.

They affect ion channels in neurons, reducing excitability and pain signal transmission. This contributes to:

- Reduction of neuropathic pain: Anticonvulsants are effective in treating neuropathic pain, which can be a component of the pain experienced in fibromyalgia.
- Sleep improvement: Some of them have sedative properties that can enhance sleep quality.
- Reduction of neuronal excitability: By decreasing the excitability of neurons, these medications can help reduce pain perception and fatigue.

3.7 Muscle relaxants

Muscle relaxants are used in the treatment of fibromyalgia with the goal of reducing excessive muscle tension, muscle spasms, and pain associated with chronic muscle tension. These medications can help improve the mobility of these patients. They predominantly act on the central nervous system to induce muscle relaxation. The mechanism of action may vary from one medication to another, but generally involves reducing the excitability of neurons or interfering with the transmission of nerve signals in the muscles.

- GABAergic Agonism: Some muscle relaxants work by increasing the activity of gamma-aminobutyric acid (GABA), an inhibitory neurotransmitter in the central nervous system. GABA reduces neuronal activity and, thus, helps relax the muscles.
- Ion Channel Blockade: Other muscle relaxants may affect specific ion channels in nerve cells, decreasing the transmission of signals that cause muscle contraction.

3.8 Opioids

Opioids are often prescribed as potent analgesics to alleviate intense pain in various medical conditions. In fibromyalgia, they may be considered in exceptional cases when other treatments have been ineffective, and the pain is extremely debilitating. The function of opioids in the treatment of fibromyalgia is to provide temporary relief from chronic pain. They act on opioid receptors in the central nervous system, including mu, delta, and kappa

receptors. These medications have the ability to block pain transmission and alter pain perception in the brain. The mechanism of action involves reducing the nervous system's response to pain, resulting in pain relief.

3.9 Sleep-inducing medications

Sleep inducers, also known as hypnotics or sedatives, are designed to help patients fall asleep more easily and maintain a more continuous and restorative sleep. Sleep inducers may have different mechanisms of action depending on the specific medication. Some common mechanisms include:

- Enhancement of the inhibitory effect of the neurotransmitter GABA: Many sleep inducers, such as zolpidem and eszopiclone, enhance the effect of the neurotransmitter gamma-aminobutyric acid (GABA) in the brain. GABA is an inhibitory neurotransmitter that helps reduce brain activity, promoting drowsiness and facilitating sleep.
- Activation of specific receptors: Some sleep inducers, like ramelteon, work by activating melatonin receptors in the brain, which helps regulate the sleep-wake cycle and promote sleep.
- Interference with the activity of excitatory neurotransmitters: Some medications, such as trazodone, can affect the activity of excitatory neurotransmitters like serotonin and norepinephrine to induce sleep."

3.10 Cannabinoids

The mechanism of action of cannabinoids, including cannabidiol (CBD), for the relief of chronic pain involves interaction with the body's endocannabinoid system. The endocannabinoid system is a signalling system that plays a significant role in regulating various physiological functions, including pain perception, inflammation control, and modulation of the immune system. Cannabinoids, both endogenous and exogenous, interact with receptors of the endocannabinoid system to affect these functions. They influence the relief of chronic pain through:

- Activation of Cannabinoid Receptors: CBD interacts with receptors of the

endocannabinoid system, including CB1 and CB2 receptors. CB1 receptors are predominantly located in the brain and central nervous system, while CB2 receptors are mainly found in immune cells and peripheral tissues. Activation of these receptors by CBD and other cannabinoids can modulate pain perception.

- Reduction of Inflammation: They have anti-inflammatory properties and can reduce the body's inflammatory response.
- Pain Transmission Modulation: They can decrease the activity of neurons that transmit pain signals and increase the activity of neurons that inhibit pain, helping to reduce the perceived intensity of pain.
- Influence on Central Sensitization: They can modulate central sensitization, making the nervous system less responsive to chronic pain.
- Mood and Stress Regulation: CBD, in particular, has anxiolytic and antidepressant effects that can improve emotional well-being and indirectly aid in the relief of chronic pain.

4. Conclusion

Fibromyalgia is a chronic condition characterised by musculoskeletal pain, fatigue, and sensitivity in muscles and joints, along with various other symptoms that affect both the physical and cognitive aspects of patients, significantly impacting their quality of life. Some medications used include tricyclic antidepressants, non-opioid analgesics, NSAIDs, SSRIs, SNRIs, anticonvulsants, muscle relaxants, opioids, sleep inducers, and cannabinoids. Each class of medication has a specific mechanism of action, targeting different symptoms of fibromyalgia, from pain modulation to sleep improvement and mood regulation. The effectiveness of treatments varies among individuals, making it crucial to individualise the treatment plan to optimise the patient's well-being. Studies supporting the use of cannabinoids in the treatment of fibromyalgia are still limited, with more significant scientific evidence for chronic pain management.

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