

FIBROMYALGIA:
AN EXAMINATION OF THE DISORDER AND ITS TREATMENTS

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Abstract

Fibromyalgia is a chronic pain condition that affects approximately 2–3 % of the world population, yet its origin remains unknown. The pain is often accompanied by anxiety, depression, and fatigue. Several risk factors may contribute to the development of fibromyalgia, including being female, being overweight or obese, and having traumatic past experiences. Many of the available treatments are used to address the symptoms and comorbidities or counter any risk factors present. There are three drugs approved by the FDA for treating fibromyalgia and several others that are efficacious or promising. Opioids, however, are not recommended for fibromyalgia. Diets such as the ketogenic diet and the Mediterranean diet may result in weight loss and decreased inflammation. Strength training, aerobic exercise, and stretching are each beneficial in decreasing pain and increasing overall quality of life, and they are even more effective when combined. Light therapy is not widely used or acknowledged, but the visual or cutaneous application of certain colors of light may elicit analgesic effects. Psychotherapy may aid in decreasing the severity of psychiatric symptoms and comorbidities and therefore may lead to reduced pain. A complete plan of care for individuals with fibromyalgia should consist of unique, patient-specific combinations of these treatments.

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What is fibromyalgia?

The prevalence of chronic pain is steadily increasing throughout the Western world. Pain that has existed for 3 months or more is classified as chronic, and it is a condition that approximately 21% of the U.S. population lives with.¹ There are several types of chronic pain including neuropathic, psychogenic, and musculoskeletal pain.¹ The prevalence and severity of chronic pain are higher in women than in men, which may contribute to the greater representation of women in pain clinics as they are more likely to seek treatment.² It is also far more prevalent in overweight and obese populations. With increasing BMI, patient reports of chronic pain of all types increase, with those classified as overweight having a 20% greater rate of chronic pain and those classified as morbidly obese having a 254% greater rate of chronic pain than those in the normal weight range.³ Chronic pain conditions are often accompanied by anxiety, depression, PTSD, and insomnia.²

Fibromyalgia is generally classified as chronic musculoskeletal pain and, like other pain disorders, is often accompanied by depression, anxiety, and/or insomnia, as well as headaches and rheumatic disorders.⁴ Approximately 2–3% of the world population has fibromyalgia, but this percentage varies depending on the diagnostic criteria used.⁵ Fibromyalgia is diagnosed by the presence of pain with palpation at several designated tender points.⁶ Generalized pain must exist bilaterally and persist for 3 months or longer to result in a diagnosis of fibromyalgia.⁶ There are three widely recognized sets of criteria for the diagnosis of fibromyalgia with different numbers of total and required tender points for diagnosis, but all are considered valid.⁷

The pathophysiology of fibromyalgia is not yet fully known or understood. It is thought that problems in processing pain in the brain cause hyperalgesia throughout the body, which is a common feature of fibromyalgia.⁶ This explanation, however, is still rather vague. Fibromyalgia

is difficult to treat because there are no solid data regarding its etiology. There are, however, risk factors associated with the presence of fibromyalgia that may aid in identifying proper treatment for individuals with this disorder.

Risk Factors for Fibromyalgia

First, females are at a much higher risk of developing fibromyalgia than males. There is no consensus on why this occurs, but most agree that it centers around the greater severity and frequency of the occurrence of stress as well as sex hormones. There have been mixed results on the effect of female-dominant sex hormones on pain, although in general, it appears that they exacerbate pain rather than reducing it.⁸ Martinez-Lavín attributes the greater prevalence of fibromyalgia in women to the changes prolactin, estrogen, and progesterone make to the physiology of the dorsal root ganglia.⁹ These alterations are thought to lead to an inappropriate relationship between the stress response and pain, and therefore hyperalgesia. It also appears that testosterone has protective properties against chronic pain in both males and females.⁸

Second, past occurrences of physical and psychological trauma and diagnosis of post-traumatic stress disorder (PTSD) have been shown to increase the risk of fibromyalgia. The occurrence of childhood trauma may also affect the severity of symptoms in fibromyalgia.¹⁰ One possible explanation for this is the dysregulation of the hypothalamic-pituitary-adrenal (HPA) circuit. The HPA circuit is responsible for maintaining equilibrium in the body during stress by regulating cortisol release. However, in some cases, after periods of severe chronic stress, cortisol equilibrium is not brought back to the pre-stress/trauma baseline, resulting in a lasting state of hypocortisolism.¹¹ Hypocortisolism may result from decreased cortisol secretion, decreased cortisol sensitivity, or enhanced negative feedback of cortisol within the HPA axis.¹² Decreased cortisol signaling results in fewer anti-inflammatory signals, therefore increasing inflammation throughout the body.¹³

Third, there is a clear relationship between overweight/obesity and chronic pain.¹⁴ Approximately 14% of adults over 20 years-of-age worldwide are obese, whereas approximately

35% of those diagnosed with fibromyalgia are obese.^{15, 16} Not only do overweight and obesity often occur alongside fibromyalgia, but the data support that they are risk factors for chronic pain of all types including fibromyalgia.¹⁷

The occurrence of these risk factors is widely unavoidable, especially in the cases of female biology and traumatic events, but the risk can be significantly decreased with preemptive action. This preemptive action primarily consists of lifestyle habits to mitigate the risks. For example, men diagnosed with PTSD from combat who performed regular physical exercise were less likely to develop fibromyalgia than those who did not perform regular exercise.¹⁸ This shows the protective effects of regular exercise against the development of chronic pain after the occurrence of traumatic events. The use of coping mechanisms during periods of chronic stress may also decrease the risk of the dysregulation of the HPA axis and therefore the risk of fibromyalgia.¹³ It has also been shown that maintenance of a healthy weight or weight loss in those who are overweight decreases the risk of fibromyalgia.³ This is by no means an exhaustive list of actions that can be taken to mitigate these risk factors, but it appears that striving for being in good physical and mental health decreases the risk of fibromyalgia.

Interventions

Treatments for fibromyalgia are not curative but are mainly used to manage the unpleasant and often debilitating symptoms of fibromyalgia and the associated comorbidities. Since the underlying cause of fibromyalgia remains unknown, treatments cannot be based on addressing the root problem. Treatments for the comorbidities and those intended to reduce the severity of any present risk factors are often efficacious in decreasing pain and other symptoms of fibromyalgia, although the efficacy of treatments varies drastically from individual to individual. There is no doubt, however, that there are treatments that are commonly prescribed because of their significant efficacy in many individuals with fibromyalgia.

Pharmaceuticals

Pregabalin

Pregabalin is a drug approved by the FDA for the treatment of certain types of neuropathic pain, partial-onset seizures, and fibromyalgia.¹⁹ Although pregabalin is structurally similar to gamma-amino-butyric acid (GABA), it does not act on GABA receptors but on presynaptic calcium ion channels.²⁰ Pregabalin binds at the $\alpha 2\delta$ subunit of calcium ion channels in the CNS, decreasing the passage of calcium and therefore reducing the release of neurotransmitters noradrenaline and dopamine that contribute to convulsion in epilepsy and nociception in pain disorders.¹⁹

A dose of 300–450 mg pregabalin, divided in half for two daily doses, is recommended for the management of pain in individuals with fibromyalgia.¹⁹ Pregabalin has been shown to be efficacious in decreasing pain and improving sleep.²¹ At a daily dose of 450 mg, pregabalin is most efficacious in decreasing initial pain by 30% compared to other doses and other drugs.²² The most common side effects are not severe and usually dissipate with time or a tolerance is built to them.²³

Duloxetine

Duloxetine is a serotonin and norepinephrine reuptake inhibitor (SNRI) approved by the FDA for the treatment of depression, anxiety, neuropathic pain, and fibromyalgia.²⁴ Duloxetine inhibits the reuptake of serotonin and norepinephrine, increasing their presence in the synapse.²⁵ It has also been shown to increase dopamine in the prefrontal cortex, as norepinephrine transporters that are inhibited by duloxetine are the primary transporters responsible for the reuptake of dopamine in the prefrontal cortex.²⁴ It is hypothesized that serotonin and norepinephrine decrease the activity of dorsal horn neurons which is perceived by the brain as pain.²⁶

For the treatment of fibromyalgia, a dose of 30 mg is administered once per day for a week before increasing the dose to 60 mg/day for continued use.²⁴ Doses of 120 mg/day have been shown to be efficacious, although the occurrence of side effects is more common at higher doses.²⁷ Duloxetine is efficacious in decreasing the pain associated with fibromyalgia, and compared to pregabalin, it is more efficacious in treating depression in individuals with fibromyalgia.²⁸ It is possible that the positive outcomes of duloxetine in individuals with fibromyalgia are primarily from its effect on the associated mental symptoms and comorbidities.²⁷

Milnacipran

Like duloxetine, milnacipran is an SNRI that inhibits the pre-synaptic reuptake of serotonin and norepinephrine; however, it does not inhibit the reuptake of dopamine in the prefrontal cortex. It is approved by the FDA specifically and solely for the treatment of fibromyalgia.²⁵ Although it shares a mechanism of action with other SNRIs, it is not used to treat depression or any other psychiatric disorders.²⁹

It is recommended to begin with a dose of 12.5 mg and double it gradually throughout the first week, maintaining a dose of 100 mg after day 7.²⁹ A dose of up to 200 mg may be appropriate

depending on the individual, but the total dose per day should be divided for administration of milnacipran two times each day.²⁹ Use of milnacipran is widely efficacious in managing pain in fibromyalgia in the long-term. Arnold and colleagues found that approximately 70% of participants found significant, consistent relief from pain with prolonged use of milnacipran.³⁰ However, they also found that side effects were common, with approximately 88% of the participants reporting at least 1 adverse event, the most common being nausea and headaches.³⁰

Opioids

Drugs in the opioid class are some of the most widely used drugs for treating chronic pain.³¹ The opioids include morphine and codeine, which are derived from the opium poppy, and synthetic drugs such as heroin and fentanyl.³² Opioids are agonists of the μ -opioid receptors, which are G-coupled protein receptors found in the CNS. The binding of opioids to these receptors causes a cascade of events including the closing of calcium ion channels which inhibits transmission of pain signals.³³ Their action also leads to the postsynaptic opening of potassium ion channels which inhibits pain signaling by hyperpolarization.³³

Prolonged, continuous use of opioids can, however, produce tolerance, meaning that the dose administered to produce analgesia would need to be increased repeatedly for an individual to continue experiencing analgesia.³⁴ Physical dependence on opioids is also common and can be observed by the presence of withdrawal symptoms when opioid use is abruptly discontinued.³⁵ Overdoses from opioid use are not uncommon, usually resulting from severe respiratory depression.³⁶ These physical realities of using opioids along with over-prescription and accessibility to illicit opioids have contributed to the opioid crisis in North America and parts of Europe.³⁶

Although opioids are still widely prescribed for most chronic pain conditions, they are not highly prescribed or recommended for pain management in fibromyalgia. One reason for this is that opioids are not as efficacious in managing pain in fibromyalgia as they are in other types of chronic pain. It has been shown that individuals with fibromyalgia have more endogenous opioids than those without fibromyalgia, which is thought to cause the μ -opioid receptor to be less sensitive to exogenous opioids.³⁷ Another reason for the low prescription of opioids for individuals with fibromyalgia is that the risk of dependence and abuse may be greater than the potential benefits they could provide.⁷

Others

Other groups of drugs are being examined for their efficacy in treating symptoms of fibromyalgia, although none are FDA approved or as widely prescribed for chronic pain as those previously mentioned. First, cannabinoids are beginning to be examined for their effects on symptoms of fibromyalgia. Thus far, the results have been positive, showing a decrease in pain and anxiety in individuals with fibromyalgia with the use of drugs in the cannabinoid group.³⁸ Psychedelics such as LSD and psilocybin are also being examined for their effects on chronic pain in fibromyalgia, although the results are currently inconclusive since the data are primarily from self-reported use rather than clinical trials.³⁹ There is, however, good reason for pursuing clinical trials for psychedelics in the chronic pain community because they are well tolerated and non-addictive compared to other solutions such as opioids.⁴⁰ There is a significant amount of data supporting the efficacy of amitriptyline, a tricyclic antidepressant, in treating fibromyalgia. In meta-analyses comparing the efficacy of amitriptyline to that of pregabalin, duloxetine, and milnacipran, it is just as efficacious or more efficacious in several regards such as improvement in sleep, fatigue, and reduction of pain by 50%.^{22, 41}

Diet

Plans of care for patients with fibromyalgia often include dietary changes to aid in the management of symptoms. Because such a significant percentage of the population with fibromyalgia is overweight or obese, one of the goals of a dietary intervention is to achieve weight loss, and specifically, fat loss.³ Fat loss for overweight and obese populations is shown to decrease inflammation, which is thought to decrease the occurrence and severity of pain in chronic pain conditions such as fibromyalgia.⁴²

Ketogenic diet

The ketogenic diet was initially examined as a treatment for epilepsy in the early 1920s. During this time, it was found that after 2–3 days of fasting, the severity of seizures in epileptic patients decreased, and it was found that the fasting state, in which fats were metabolized to ketone bodies, could be mimicked with a high-fat, low-carb diet.⁴³ This is how the keto diet came to be used as a treatment for epilepsy, although it has also been used for weight loss and to treat Alzheimer's disease, certain types of cancer, type 2 diabetes mellitus, and chronic pain.⁴⁴⁻⁵⁰

The ketogenic diet has been shown to decrease biomarkers associated with inflammation and oxidative damage.⁵⁰ This diet can increase the production of GABA and it is suggested that ketone bodies may serve as antioxidants, decreasing oxidative stress in the body, although the data on this are conflicting.⁵¹ One of the ketone bodies produced in ketogenesis, β -hydroxybutyrate, has been shown to decrease inflammation.⁵²

It has been shown that chronic musculoskeletal pain can be reduced by the ketogenic diet. Field and colleagues found that after 12 weeks on a whole-food ketogenic diet, not only did the pain associated with fibromyalgia decrease significantly, but weight loss occurred and there was a decrease in depression and anxiety.⁵⁰ This result may be due to the increase of dopamine and

serotonin that have been shown to occur with the ketogenic diet.⁵³ It is also possible that the weight loss that occurs from following a ketogenic diet aids in the reduction of pain.

Mediterranean diet

Another diet that has been used to reduce inflammation is the Mediterranean diet. This diet mainly consists of seafood, vegetables, cheeses, nuts, and olive oil. Moderate intake of alcohol may be included in this diet as it has been shown to decrease the risk of heart failure.⁵⁴ The anti-inflammatory effects of the Mediterranean diet are thought to be brought about by the large amount of omega-3 fatty acids from fish, nuts, and olive oil.⁵⁵ These and other non-fat components of the diet are thought to reduce inflammation associated with chronic pain through their effects on the arachidonic acid pathway.⁵⁶ Inflammatory gene expression and immune cell activity may also be mediated by the Mediterranean diet.⁵⁶

In subjects with osteoarthritis, the Mediterranean diet has been shown to reduce the risk of the pain becoming worse over time and perhaps even prevent it.⁵⁷ However, the studies done on rheumatoid arthritis and the Mediterranean diet have been widely inconclusive regarding the reduction of pain and inflammation.⁵⁸ There have been very few studies done on the Mediterranean diet and its effects on the symptoms of fibromyalgia. However, in one study, it was shown that high adherence to this diet was associated with better bone health and increased emotional well-being in women with fibromyalgia.⁴²

Physical Activity

Certain types of exercise and physical activity have been shown to decrease pain and fatigue and improve mood and quality of life in patients with fibromyalgia.⁵⁹ Physical activity has long been seen as a safe, effective therapy for the management of symptoms. The types of physical activity examined for efficacy in the management of fibromyalgia symptoms include but are not limited to strength training, aerobic exercise, aquatic exercise, stretching, yoga, Pilates, and tai chi.⁵⁹

Serious adverse events from physical activity in participants with fibromyalgia have not been reported, although some high-intensity exercise regimens can be difficult to adhere to due to existing symptoms of pain and fatigue.⁵⁹ Another obstacle to managing symptoms of fibromyalgia with physical activity is the presence of kinesiophobia, or the fear of physical activity. Kinesiophobia can arise when one experiences chronic pain and wishes to avoid movement that he believes might cause more pain.⁶⁰ In addition, those with fibromyalgia are shown to have and report lower muscle strength, muscular and cardiovascular endurance, and flexibility than those without the disorder.⁶¹ Nonetheless, in clinical trials, participants have experienced significant improvements in symptoms of fibromyalgia through physical activity.

Strength training

The goal of strength training is to increase muscle strength by gradually increasing the amount of resistance applied to the muscles.⁶² Strength training has been shown to have numerous benefits on physical and mental health. First, strength training is effective in the reversal of muscle loss due to a sedentary lifestyle, aging, poor diet, and other causes.⁶² Second, it has been shown to increase bone mineral density.⁶³ To these results, strength training may be able to help prevent the occurrence of falls and bone breakages in elderly populations. This method of physical activity

has also been shown to decrease body fat, possibly by the increase in resting metabolic rate seen during consistent strength training.⁶⁴ Finally, strength training is useful in reducing depression and anxiety.^{63, 65}

In participants with fibromyalgia, the effects of strength training on the different symptoms of fibromyalgia seem to vary from study to study. In a meta-analysis of exercise interventions for managing fibromyalgia symptoms, Sosa-Reina and colleagues found that strength/resistance training was significantly effective in decreasing pain and moderately effective in increasing the overall quality of life in participants with fibromyalgia.⁶⁶ They found that strength training was only mildly effective in treating depression. However, the results of a clinical trial in which approximately 1/3 of the participants (N=16) were assigned to do 2 sessions of strength training for 12 weeks showed that strength training significantly decreased depressive symptoms but was not as efficacious in decreasing pain as stretching.⁶⁷ Yet another meta-analysis conducted by Busch and colleagues showed that resistance training is effective in reducing pain associated with fibromyalgia and increasing overall well-being, although it is not the most effective form of physical activity to bring about these outcomes.⁶⁸

Some of these discrepancies and lack of conclusion regarding the efficacy of strength training compared to other types of physical activity may result from the small cohort sizes of several of these studies. However, disregarding comparison to other types of activity, it can be concluded that strength training is effective in decreasing pain and improving the overall quality of life in patients with fibromyalgia. To maximize the efficacy of strength training in managing fibromyalgia symptoms, the variable aspects of strength training, such as intensity, number of sets and repetitions, frequency, and duration of strength training must be examined. Da Silva and colleagues examined these factors and found that, for maximal efficacy in managing symptoms of

fibromyalgia, strength training should be done twice per week for 8–12 weeks.⁶⁹ Exercises should be performed in 1–2 sets of 4–12 repetitions and each repetition should be performed at an intensity of 40–80%.⁶⁹ Based on the literature, strength training performed within these boundaries allows for the maximal effect of strength training on symptom management in fibromyalgia.

Aerobic exercise

Aerobic exercise is physical movement that causes the body to use oxygen to produce energy, often called cardiovascular exercise or just cardio. Due to the energy use in this type of exercise, it may be effective in bringing about weight loss in overweight and obese populations, especially when paired with restricted calorie intake.⁷⁰ The secondary effects of weight loss from aerobic training include lowered risk of cardiovascular disease, decreased prevalence or severity of diabetes, and decreased inflammation.⁷¹ It has also been shown to increase cognitive function and mental performance.⁷² Possibly through weight loss and/or its positive impact on cognitive function, regular aerobic exercise has also been shown to increase the human life span.⁷³

Aerobic exercise may also be useful in the management of symptoms of fibromyalgia. Sosa-Reina and colleagues found that aerobic exercise significantly decreases pain severity in those with fibromyalgia, being the most effective type of physical activity for managing this symptom.⁶⁶ Bidonde and colleagues performed a meta-analysis of studies in which aerobic exercise was examined as a treatment for fibromyalgia and found that it may improve health-related quality of life (HRQL), but it seemed to have minimal positive effects on pain and physical functioning.⁷⁴ Certain types of aerobic exercise, such as Zumba dancing, may improve memory and physical functioning as well as symptoms of depression and pain associated with fibromyalgia.^{75, 76}

There are some inconsistencies in the data due to the unreliability of individual clinical trials. However, the most consistent results include that exercise increases HRQL and may, minimally to moderately, decrease pain severity in patients with fibromyalgia. The intensity of aerobic exercise for individuals can be measured by the percentage of maximum heart rate (MHR) achieved during a session. Approximately 30–60 minutes of exercise 2–3 times per week in which 50–80% MHR is achieved is sufficient for bringing about positive effects of aerobic exercise in individuals with fibromyalgia.⁶⁶ It is recommended to begin at a lower intensity in the range of 45 – 60% MHR and progressively increase the intensity of exercise sessions until 80% MHR is achieved.⁷⁷

Stretching

Stretching is the intentional lengthening of muscles, usually with the goal of increasing range of motion. Stretching, especially when paired with a warm-up routine, has been shown to prevent injuries in certain types of athletes when performed before physical activity.⁷⁸ Increased flexibility of the joints through stretching in elderly populations has also been shown to decrease the severity of injury and aid in recovery when injury does occur.⁷⁹ Stretching has also been examined for its effect on fibromyalgia and the related symptoms and comorbidities.

It is broadly agreed upon that stretching increases HRQL, although some studies have shown that stretching is effective in decreasing the severity of pain while others have shown that stretching only has a minimal effect on pain in fibromyalgia.^{66, 67, 80} Similar to the other forms of physical activity previously discussed, there seems to be no consensus on the extent of the efficacy of stretching for mediating the symptoms of fibromyalgia. There is also no consensus regarding whether stretching is the best form of physical activity for treating any of the symptoms. This is, in part, probably due to poor study design and a lack of consistency in stretching protocols.⁸⁰

However, based on the data, there is no harm in stretching, and it will likely result in a minimal to large improvement in pain and HRQL. Recommendations for stretching to decrease pain and manage other symptoms of fibromyalgia are rather scarce and inconsistent in the literature. If stretching is recommended, it is recommended as an addition to other types of physical activity.

Exercises in combination

Combinations of various forms of physical activity are most efficacious in mediating the symptoms of fibromyalgia. Sosa-Reina and colleagues recommend a combination of strength exercise, aerobic exercise, and stretching to decrease depression.⁶⁶ There is a clear benefit from combining strength training and aerobic exercise, although there is not yet a clearly defined protocol for how to combine these in order to bring about maximum positive results.⁷⁷ It can be concluded that performing strength exercises, aerobic exercises, and stretches will bring about greater strength, aerobic capacity, and flexibility, respectively, and increases in overall health and well-being will certainly accompany these physical improvements.

Light Therapy

The use of light has been shown to improve or exacerbate pain and symptoms associated with fibromyalgia. The effect of light depends on its wavelength (color) and the method of light administration. The light used for such therapies includes several wavelengths in the visual spectrum, ultraviolet⁵⁷, and infrared (IR) light. One method of administration is visual: the viewing of certain wavelengths of light. Another method is the direct cutaneous application of light to a certain region of the body using LEDs or laser therapy. Regarding fibromyalgia, light therapy may be used to treat pain, migraines, insomnia, and depression.⁸¹⁻⁸⁴

Pain moderation through the viewing of light is attributable to both visual and psychological pathways. Rods and cones in the retina of the eye respond to incoming light, and cones respond differently to various wavelengths of light.⁸⁵ Intrinsically photosensitive retinal ganglion cells (ipRGCs) are responsive to ambient light and are responsible for sending signals to the pineal gland as a key process in regulating circadian rhythms.⁸⁶ There is also evidence that the viewing of certain colors of light induces a psychological response that changes the way pain is perceived.⁸⁷ All of these pathways may play a role in the exacerbation or moderation of pain in response to viewing light.

The absorption of light by the skin may also elicit analgesia. Hemoglobin and melanin absorb light in the dermis and epidermis, respectively, hemoglobin absorbing blue light and melanin absorbing UV light best.⁸⁸ However, shorter wavelengths such as these do not penetrate the skin as deeply as longer wavelengths do. For example, UV light may only be able to penetrate the epidermis, but red light can penetrate the epidermis and the dermis.⁸⁹ Red and IR light are primarily absorbed by cytochrome c oxygenase (CCO), which is the fourth enzyme involved in the mitochondrial electron transport chain.⁹⁰ The depth to which light is also thought to be

dependent on beam width, with maximum depth achieved at a beam width of 10 mm.⁸⁹ The absorption of light by these routes, as well as other routes unique to certain ranges of wavelengths that will be discussed below, causes downstream effects that may lead to decreased pain in the patient with fibromyalgia.

IR and red light

IR and red light are administered by laser or LED to the surface of the skin, not by the eye, to manage pain. The viewing of red light has been shown to exacerbate pain in studies done on participants with migraines.⁹¹ The administration of red and IR light to the skin is called low-level laser therapy (LLLT) or, to include the use of red and IR LEDs, photobiomodulation (PBM).⁹² The absorption of photons by CCO is what causes desired changes when using PBM.⁹³ It is theorized that the reduction of oxygen to water by CCO is sometimes inhibited by nitric oxide, but nitric oxide is displaced when CCO absorbs a photon, allowing for the reduction of oxygen and therefore the synthesis of more ATP.⁹⁴ In inflamed, oxidatively stressed cells, the downstream effect of red and IR light on CCO is the decrease in inflammation and reactive oxygen species.⁹³

Photobiomodulation has been shown to improve symptoms of fibromyalgia significantly. In a meta-analysis of 9 randomized-controlled trials carried out by Shu-Wei Yeh and colleagues, it was found that monowavelength LLLT improved pain scores, fatigue, depression, and anxiety, and reduction of the number of tender points in participants with fibromyalgia in comparison to the use of a placebo laser. In one trial, LLLT was used alongside LEDs, and this combination seemed to result in a more significant reduction of pain and the number of tender points compared to LLLT alone. Similarly, LLLT and LED therapy together with exercise significantly improved symptoms compared to exercise alone, but LLLT and exercise did not significantly improve symptoms compared to exercise alone. The cutaneous application of red and IR light is a treatment

option for patients with fibromyalgia that could significantly improve their quality of life and decrease their pain scores.

Green light

Green light has been shown to reduce migraine pain significantly through the cone pathway in the eyes in comparison to other wavelengths of light.⁹¹ There are many pathways in which green light modulation of pain may occur. Ibrahim and colleagues showed that green light acts as an analgesic through opioid receptors in rats.⁹⁵ They also found that tolerance to the antinociceptive properties of green light did not occur with prolonged use, compared to the use of morphine, with which tolerance occurs within three days in rats. They also found that green light therapy decreased calcium influx through the N-type calcium channel, which may have contributed to anti-allodynia and anti-hyperalgesia.

Martin and colleagues conducted a study on the effect of observing green LED light in people diagnosed with fibromyalgia.⁸² Participants were told to sit at a distance of 1–2m from green (525 nm) LEDs for 1–2 hours per day for 10 weeks in an otherwise dark room. They were told not to look at the light and not to fall asleep, but they could read, write, or perform any other activities if they were done by the green light alone. They found that after 10 weeks, the initial mean pain score of 8.4 out of 10 had decreased to a mean of 4.9 out of 10. Participants who had green light exposure for ≥ 1.5 hours/day experienced a greater reduction in pain than those who had < 1.5 hours/day of green light exposure.

Visual exposure to green light may be an efficacious therapy or co-therapy for reducing pain in patients with fibromyalgia. However, compliance might prove to be an issue since most people do not have 1–2 hours per day to set aside for sitting in a dark room with only green light. One solution to this could be the use of contacts that only allow green light to enter the eyes. In

Ibrahim's study on rats, exposure to ambient indoor lights with green contacts was shown to be just as efficacious in reducing pain as exposure to green light without contacts.⁹⁵ If the contacts are made to be well-tolerated and non-irritating, the use of green contacts for 1–2 hours per day in patients with fibromyalgia might be a reasonable therapeutic approach for reducing pain.

Blue light

There is less data on the effects of blue light on pain and the symptoms of fibromyalgia than there are on other wavelengths. Blue light may not be as efficacious in reducing pain by cutaneous application due to its inability to fully penetrate the dermis, although it certainly has applications in conditions of the epidermis and dermis, such as acne, psoriasis, and wound healing.⁸⁹ The effects of blue light on pain were investigated in a study conducted by Reuss and colleagues, in which pain was induced in the dominant forearm of participants (n=30) by high-density transcutaneous electrical stimulation.⁹⁶ After pain was induced, a blue light LED collar, previously placed on the forearm, was turned on. Blue light was shown to decrease the severity of pain experienced by the participants. This, however, is the only known study in which blue light is examined for its effect on pain, and there are no studies to be found on the efficacy of cutaneous blue light on chronic pain or fibromyalgia.

As for the visual pathway, it is common to restrict the visual intake of blue light due to its effects on sleep. Blue light has been shown to decrease melatonin secretion in humans, therefore possibly affecting the ability to and quality of sleep.⁹⁷ While no studies have been published on blue light and sleep specifically in participants with fibromyalgia, the studies that have been done may still apply to those who experience sleep disturbances as a symptom of fibromyalgia. There seems to be inconsistency in the data regarding blocking the visual intake of blue light before bed. Some studies have found that restriction of blue light via blue-blocking glasses 2–3 hours before

bed has hastened the onset of sleep and decreased the number of times participants wake up throughout the night, however, a few studies show no significant difference between groups using blue-blocking glasses and clear placebo glasses.⁹⁸ The data generally point toward improved quality of sleep with blue-blocking glasses before bedtime due to increased melatonin production in the absence of blue light, although this method does not always seem to be efficacious.⁹⁸

Psychotherapy

Psychotherapy is another treatment option for those suffering from fibromyalgia. Trauma and severe stress increase the risk of developing fibromyalgia and psychiatric comorbidities are highly prevalent in individuals with fibromyalgia.⁴ The use of psychotherapy to address these issues, especially in combination with other treatments, has shown to be effective in improving psychiatric symptoms, pain, and overall quality of life.⁹⁹

CBT

The most common type of psychotherapy for treating fibromyalgia is, by far, cognitive-behavioral therapy (CBT). CBT was designed to help patients identify and correct their dysfunctional cognitive patterns, such as distorted initial thoughts in reaction to an event, logical errors, and unfounded beliefs about themselves.¹⁰⁰ For individuals with fibromyalgia, the goal of CBT is to replace catastrophizing and other stress-related thoughts with positive, but realistic, cognitions about symptoms and life events.¹⁰¹ It may also be used to address PTSD in individuals with fibromyalgia.¹⁰² In general, CBT has been shown to elicit minimal to moderate relief from the symptoms of fibromyalgia and is usually paired with another type of treatment, such as pharmacotherapy.¹⁰¹

Others

Other types of psychotherapy commonly used for fibromyalgia focus on the connection between mind and body. Mindfulness, or intentional awareness and acceptance of one's thoughts, emotions, and physical state, has been shown to be beneficial in improving pain, or perhaps pain perception, in individuals with fibromyalgia.⁵ Electromyographic (EMG) biofeedback involves the application of electrodes to the skin over skeletal muscles that hold tension during a stress response such as the frontalis or upper trapezius and provides visual or auditory feedback to the participant

based on muscular tension.¹⁰³ EMG biofeedback is shown to be effective in bringing awareness to stress, helping with the process of relaxation, and decreasing pain in fibromyalgia.¹⁰⁴ These techniques can be used individually or in combination with CBT and other types of treatments for fibromyalgia.

Conclusion

Although the etiology of fibromyalgia remains widely unknown and not all risk factors are present throughout the population of individuals with fibromyalgia, there are promising results from various types of treatments for managing the symptoms and comorbidities of the disorder. Most of the treatments discussed are not generally used as stand-alone treatments but are paired with other types of therapies for a more well-rounded and efficacious approach to managing symptoms. The most efficacious treatment combinations for fibromyalgia include both pharmacological and non-pharmacological treatments.¹⁰⁵ Combinations of treatments should be highly individualized and unique to each patient depending on their symptoms, comorbidities, any present risk factors, and their willingness to implement the treatments.

After a diagnosis of fibromyalgia is made, the severity of pain and the presence of anxiety, depression, insomnia, fatigue, and any other comorbidities should be considered. Risk factors should also be accounted for, as their presence may influence the components included in a plan of care. The desires of the patient regarding his treatment are also important to take into account. For example, one patient may want to begin with treatments other than pharmacotherapy while another might not have the time to implement treatments such as exercise and CBT each week. Without thorough knowledge of the disease and the unique needs of the patient, forming an effective plan of care would be nearly impossible. Therefore, physician awareness of the symptoms, risk factors, available treatments for fibromyalgia, and patient preferences is critical in allowing for the creation of an appropriate and effective plan of care for each patient with fibromyalgia. Similarly, being well-equipped with knowledge of the disorder and available treatments would empower individuals with fibromyalgia to better collaborate with their physicians to come up with a plan of care that best addresses their needs.

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