

Reviews

Efficacy of acupuncture in the treatment of fibromyalgia

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Purpose of Review

Fibromyalgia is a highly prevalent chronic pain syndrome that affects up to 4% of the population and causes significant morbidity and disability, with an increasing associated cost. Though many approaches for treatment have been tested, therapy regimens are still elusive, and efficacy is limited. This review summarizes the background of fibromyalgia and acupuncture and reviews the latest and seminal literature discussing the application of acupuncture in fibromyalgia.

Recent Findings

Fibromyalgia is hard to treat, owing both to its chronicity and poorly understood pathophysiology and etiology. Current treatments target symptoms primarily, and few attempt to address the source. Efficacious treatment requires long-term treatment by a multidisciplinary team. Though several treatments exist, they still fall short with a substantial number of patients. Acupuncture, a form of integrative medicine, has been a part of traditional Chinese medication for generations. Evidence shows that it effectively treats different kinds of pain conditions, including migraines and chronic musculoskeletal pain. Recent studies showed evidence to support its use in fibromyalgia.

Clinical trials studying acupuncture in fibromyalgia have shown improvement in pain, quality of sleep, and quality of life, though the quality of evidence is mainly low to medium. Several studies were not able to provide evidence to support real over sham acupuncture. Weighing the overall evidence paints a picture of mixed results between equivocal results to positive. In analyzing these results, one must also consider publication bias supporting the dissemination of positive results.

Summary

An increasing number of studies support the utilization of acupuncture for the treatment of fibromyalgia. Though no head-to-head comparison was able to show the superiority of acupuncture to other therapies, mounting evidence supports its use as part of multimodal approaches to treatment with additive efficacy to traditional therapy. Further research will likely provide data on effective regimens and combination therapies.

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INTRODUCTION

Acupuncture is a form of integrative medicine and has been a significant constituent of traditional Chinese medicine (TCM) for hundreds of years. Acupuncture involves penetrating acupuncture points through the skin using and manipulating thin needles to improve the body's energy flow or *qi*, maintaining overall health and vitality.^{1,2} Its use for treating chronic pain in TCM has become of growing interest in the Western world, triggering many clinical trials and studies to determine the efficacy and creditability in treating chronic pain conditions, including chronic musculoskeletal pain, migraine, and osteoarthritis.^{2,3} The analgesic effects of acupuncture techniques associated with fibromyalgia, in particular, have become of growing interest due to the uncertainty behind its mechanism and effect in treating the disease.^{4,5}

Fibromyalgia is a musculoskeletal disorder that causes chronic, diffuse pain, fatigue, sleep difficulties, and cognitive impairment, along with numerous other comorbidities that can significantly affect the quality of life of those involved. Fibromyalgia is a common illness present in all populations worldwide, affecting anywhere from 2% to 4% of the general population.⁶ Fibromyalgia can occur in individuals of any gender and age; however, patients are predominantly middle-aged (40-60 years) and female.^{4,6} In addition, the prevalence of individuals with fibromyalgia seems to increase with age.⁶ The complexity of symptoms and uncertainty behind its pathophysiology causes the disease's diagnostic criteria to be much more difficult to distinguish. Many clinicians may use the diagnostic label of 'somatization disorder' or 'chronic widespread pain' for a patient with fibromyalgia-like symptoms.⁶ Thus, the number of people clinically diagnosed with fibromyalgia may be lower than the reported prevalence from epidemiological population studies.⁶ In other words, the actual prevalence of fibromyalgia may be higher in the community.⁷

Fibromyalgia is not only a complicated illness to diagnose and study, but it can also cause a heavy burden on a patient affected by the disease. This includes clinical, emotional, and financial burdens that overall disrupt a patient's daily life. Aside from the key symptoms of chronic, diffuse pain in the muscles and joints, comorbidities such as irritable bowel syndrome, psychiatric disorders, and rheumatic diseases have been noted in those with fibromyalgia.⁶ Chronic pain patients, including those with fibromyalgia, have been shown to have a greater likelihood of developing depression, anxiety, and other psychiatric disorders as a consequence of the presence of chronic pain.⁸ Thus, these factors cause the management of fibromyalgia to be difficult, ideally having to address aspects such as patient education, physical pain, emotional dysfunction, and other comorbid illnesses.^{4,8} However, despite being a primarily recognized central sensitization disorder, no effective treatments are presently available for fibromyalgia.⁴ In addition, fibromyalgia can cause a financial burden on a patient, having higher medical costs from healthcare utilization and pain-related pharmacotherapy than the general population.⁷

Studies on fibromyalgia continue to advance our understanding of its pathogenesis and pathophysiology, with

hopes of developing more effective therapy options and trying to reduce social and financial burdens.⁴ Our goal is to review the efficacy and safety of using acupuncture as an effective therapy option for patients with fibromyalgia, a chronic pain syndrome.

FIBROMYALGIA

Chronic pain is ongoing pain that usually lasts longer than six months, continuing after the precipitating injury or illness that caused it has healed. Some patients suffer chronic pain without any previous injury or apparent damage, with inflammatory pain signals remaining active for months to years. American Society of Regional Anesthesia (ASRA) describes that chronic pain may affect the entire nervous system, potentially in a permanent way, and change how one perceives nociceptive stimuli.

Fibromyalgia is a common cause of chronic widespread musculoskeletal pain, often accompanied by fatigue, cognitive disturbances, psychiatric symptoms, and a plethora of somatic symptoms.⁹ The American College of Rheumatology (ACR) set forth the 1990 Criteria for fibromyalgia as widespread pain in combination with tenderness at 11 or more specific sites. This was re-examined in 2010 by ACR to understand that fibromyalgia existed along a spectrum instead of the previous dichotomous evaluation. The updated 2010 diagnostic criteria include widespread pain for at least three months- without better explanation- and scoring of somatic symptoms.

EPIDEMIOLOGY

Fibromyalgia has a 2-3% prevalence or approximately four million adults per the CDC. Other studies have appreciated fibromyalgia on a spectrum of widespread chronic pain, with prevalence range from 2-6% dependent on the criterion used.¹⁰

RISK FACTORS

Fibromyalgia is most common in women between ages 20 and 55 years old, with Jones et al. finding fibromyalgia six times more common in women based upon modified 2010 criteria.¹¹ Stressful or traumatic events- such as PTSD- have been linked as risk factors for fibromyalgia.⁹ Additionally, a positive family history of fibromyalgia correlates with an increased risk of developing fibromyalgia. Musculoskeletal injuries are commonly reported, as well as irritable bowel syndrome, obesity, sleep disorders, and low education or socioeconomic status.¹² A plethora of other medical conditions are mentioned in correlation to fibromyalgia. However, conflicting data exist regarding their associated risk, suggesting multiple causal pathways and risk associations being different for subgroup demographics.¹²

PATHOPHYSIOLOGY

Fibromyalgia has an unknown etiology and unclear pathophysiology, however likely multifactorial.¹³ Fibromyalgia is often considered a spectrum disorder of pain regulation,

otherwise described as central sensitization with the potential peripheral component.¹³ Avenues of abnormal processing include a temporal summation of pain, impaired pain inhibitory control, upregulation of opioid receptors in the periphery while downregulated at the brain, and increased presence of Substance P neuropeptide in cerebrospinal fluid.^{14,15} Magnetic resonance imaging (MRI) analysis has shown a decline of grey matter volume in fibromyalgia patients- indicative of less concentrated GABA-A receptors, decreased neuronal plasticity, and diminished connectivity in the descending pain-modulating pathways.¹⁵

Genetic and stress-related factors likely interact to promote a state of chronic central and peripheral hyperirritability. Genetic predisposition seems to play a role, likely familial aggregation of lower pain thresholds.¹⁶ Genome-wide profiling identified a difference in expression of 421 genes in fibromyalgia, many important to pain processing.¹⁶ Many small studies suggest COMT (catechol-O-methyltransferase) polymorphisms are associated with fibromyalgia. However, more extensive controlled studies refute any direct correlation.¹⁷ Autonomic dysfunction and abnormalities in the hypothalamic-pituitary-adrenal axis are correlated with fibromyalgia. A marker for stress, serum cortisol levels, are higher in chronic pain patients and trended with neuropsychological impairment.¹⁸

CLINICAL PRESENTATION

Fibromyalgia is characterized by widespread musculoskeletal pain and is accompanied by other somatic symptoms. The core symptoms of fibromyalgia are generalized pain, fatigue, and sleep disturbances present for at least three months that is not explained by any other medical condition.¹⁹ The cardinal manifestation is widespread chronic pain, typically involving at least six sites, however common patient description includes “I hurt all over” for longer than three months.¹⁹ Although the tender sites may be described as muscular or joint pain, synovitis is not present on exam.^{9,19}

Persistent fatigue or sleep disturbances are also core features of fibromyalgia. Mimicking rheumatoid arthritis or polymyalgia rheumatica, patients will complain of morning stiffness or fatigue despite adequate sleep- with minor activities as well as prolonged inactivity aggravating symptoms.

Cognitive disturbances- deemed the “fibro fog”- present as attention deficits or struggling with rapid thought changes. However, subjective cognitive deficits are more common than objective measures and are attributed to levels of pain and depression.²⁰ Meta-analysis of eleven studies revealed concurrent major depression in one-fourth of patients and that over half of the fibromyalgia patients have a lifetime history of major depression.²¹ Headache is present in more than half of fibromyalgia patients, often including tension-type headaches and episodic migraines.^{19,21} Irritable bowel syndrome and gastroesophageal reflux disease are more familiar with fibromyalgia than in the general population.^{19,22}

Despite these symptoms, fibromyalgia does not cause any abnormality in routine laboratory testing, including complete blood counts, acute phase reactants, chemistries,

or imaging.

CURRENT TREATMENT OPTIONS (MOST POPULAR, FDA APPROVED)

Treatment of fibromyalgia can be challenging but generally requires an individualized multidisciplinary approach focused on reducing significant symptoms.^{9,19} Initial treatment approaches should focus on patient education, addressing comorbidities, and implementing exercise programs. Consistent low-impact aerobic exercise can improve pain and function and aid sleep, weight loss, and mood. Cognitive-based therapy can work well with drug monotherapy to also reduce somatic symptoms and pain.⁹

Initial drug monotherapy of low-dose tricyclic antidepressants (TCA)- such as amitriptyline- at night is highly effective and low-cost. Randomized control trials demonstrate up to 45% improvement in symptomology. However, the efficacy of TCAs may decrease over time.²³ Popular practice usually slowly builds to the recommended dose for three months before switching agent.⁹

Serotonin-norepinephrine reuptake inhibitors (SNRI) at breakfast may be reasonable alternatives in patients with severe fatigue or depression. Patients who experience intolerable TCA side effects may respond to an α_2 -ligand anticonvulsant- such as pregabalin. The US FDA approves duloxetine, pregabalin, and milnacipran for fibromyalgia treatment.⁹ A 2018 systematic review including 18 randomized trials suggests incremental benefit from SNRI over placebo. However, the benefit may be overshadowed by the adverse effects of duloxetine or milnacipran.²⁴ Another 2018 systematic review confirmed that pregabalin improved pain, sleep, and overall patient status with a wide range of efficacy.²⁵

There is no evidence that acetaminophen, nonsteroidal anti-inflammatory drugs, or opioid analgesics benefit fibromyalgia. Fibromyalgia patients on opioids have poorer outcomes. However, opioids often continue to be prescribed.²⁶ There is evidence that opioids interfere with the psychological benefits of multimodal plans, including worsened sleep disturbances and pain exacerbations.²⁷ Recent evidence concerning the use of cannabinoids in fibromyalgia is promising, though it is not without risk, and further research is required to define indications and treatment regimens better.²⁸

In treatment-resistant fibromyalgia, consultation with physiatry or pain management can appropriately be part of a multidisciplinary approach. Peripheral pain generators are thought to increase central centralization by increasing peripheral input. Dry needling of myofascial trigger points improved localized pain as well as spine mobility in a fibromyalgia cohort.²⁹ A 2019 analysis showed acupuncture was more effective than sham procedures at enhancing the quality of life in fibromyalgia. However was limited by study design and poor follow-up, leaving room for further investigation.³⁰

Current treatments mainly focus on symptomatic management. However, as new understandings of this disease process unfold, treatment focus should shift to resolving the underlying pain processing dysfunction and potential individualized gene therapy.

While many studies have evaluated monotherapy drugs, there is surprisingly little evidence evaluating combination drug therapy in patients unresponsive to monotherapy; however, small studies have shown promise.^{31,32}

Developments in transcranial neurostimulation are promising with direct current stimulation and transcranial magnetic stimulation for fibromyalgia patients. While studies show results with small, short-lived improvements in pain and depression compared to a sham procedure, trials are small, and the efficacy of routine, repetitive transcranial stimulation has been questioned, warranting further investigation.^{33–35}

ACUPUNCTURE

Acupuncture is the practice of inserting thin, solid needles into specific acupuncture points in the skin and, through various methods of manipulation, can provide therapeutic benefits.³⁶ Acupuncture has been an integral part of TCM for hundreds of years. It has gradually become more popular as a form of complementary and alternative medicine in the Western world, especially for chronic pain management.^{1,36,37} The practice of acupuncture was first formally recognized as far back as 200 BC in the medical text *The Yellow Emperor's Classic of Internal Medicine*, or *Huang Di Nei Jing*, one of the most influential texts in traditional Chinese medicine.^{1,36–38} Bian stones, or pointed stones, were the first form of needles to be utilized in acupuncture therapy.³⁷ With its fast-growing influence, the big stone was soon replaced by needles made with other types of material such as bamboo, bone, and metal.^{36,37}

Acupuncture comprises a range of different therapeutic methods depending on the way the needle is manipulated during the procedure. These methods can include traditional Chinese needle acupuncture, dry needling, heat acupuncture (i.e., moxibustion), electroacupuncture, mechanical acupressure, and laser acupuncture.^{1,5,39} Traditionally, acupuncture involves penetrating the skin's surface at certain acupuncture points with hair-thin, flexible needles.³⁶ These points can be targeted along the entire skin surface, soft tissues, or even defined points on a certain part of the body, including the head, ear, or hand (i.e., scalp, auricular, and hand acupuncture, respectively).⁵ After placement, these needles can be manipulated in various ways, such as manual needling, electrical stimulation, heat, or pressure.¹ These acupuncture points are thought to connect through pathways, or meridians, and their collaterals. By manipulating and stimulating the needles placed along the meridians, it is believed to realign and balance the body's energy flow, or *qi*.^{1,36} Thus, a balanced energy flow brings about optimal health by the belief of its connection to the body's homeostatic functions.⁴⁰

The theory of *de qi* is the central historical teaching for acupuncture. The flow of vital energy throughout the body remains connected by meridians, providing balance in the inner organs to the superficial skin.¹ This balance is known as the complementary, opposite forces of *yin* and *yang* in China.^{1,38,40,41} In the simplest terms, *yin* represents receptivity, quiescence, darkness, and tranquility, while *yang* represents strength, dominance, daylight, and arousal.^{1,41} Ultimately, the traditional Chinese belief is that by using the

acupuncture points as confluences to the meridians, the functional activities of the human body can be coordinated and harmonized by the balance of *yin-yang* forces and *qi* energy flow.^{1,40,41}

The traditional beliefs of acupuncture therapy focus on the human reflection of sensory perceptions to understand their overall state of being, including health and illness.^{1,41} This belief causes discordance with modern-day scientific perspectives due to the lack of true scientific evidence and plausible underlying mechanisms. Despite this, acupuncture is still widely recognized in the United States and western countries as a possible therapeutic option for chronic pain conditions, including general musculoskeletal pain, migraine, osteoarthritis, and fibromyalgia.^{5,42} In 2017, the Food and Drug Administration (FDA) recommended using non-pharmacological treatments, including acupuncture, as possible pain management therapies to be considered in response to the opioid epidemic in the United States.⁴² Although acupuncture therapy is not considered FDA approved for any specific illness, the instruments or tools used are FDA regulated as medical devices intended for the treatment and prevention of disease. These regulated devices include acupuncture needles and stimulating instruments used in electromagnetic acupuncture (EMA).⁴²

As studies on acupuncture therapy continue to advance, many research studies have proposed possible mechanisms of action that can explain acupuncture's analgesic effects. The mechanism of action for acupuncture analgesia involves pain-modulating pathways of the central nervous system and regulating various biochemical compounds.^{1,4,5,38,43} The theory suggests that the placement and manipulation of the acupuncture needles stimulate the nerve fibers in the skin and muscles (i.e., A-delta afferents, C fibers), conducting signals to the spinal cord.^{38,41,43} This further activates areas in the spinal cord, the periaqueductal gray area of the brain stem, and the hypothalamus arcuate nucleus, which are all endogenous pain-modulating systems in the body.^{1,5,38,41} Ultimately, endogenous opioid mechanisms are stimulated, causing the release of pain-modulating compounds such as beta-endorphins, enkephalins, serotonin, noradrenaline, and more into the plasma and cerebrospinal fluid, providing analgesic relief via inhibition of painful stimuli sensation and decreasing central pain perception.^{1,4,5,36,38,39,41,43}

The number of acupuncture studies and controlled clinical trials have increased over the years. It was determined effective for certain conditions such as postoperative dental pain, postoperative and chemotherapeutic nausea, and vomiting.^{1,38} For other conditions such as migraine, chronic musculoskeletal pain, osteoarthritis, and fibromyalgia, the evidence is either considered inconclusive or is considered promising with further research.^{1,2,5,36,38,44–46}

Acupuncture therapy, despite the lack of clinical data suggesting its efficacy in treating conditions like fibromyalgia, could still be recommended as a reasonable option for therapy for chronic pain conditions. Acupuncture is generally considered safe. Acupuncture needles are regulated to be thin, sterile, single-use needles, and the procedure should have little to no discomfort overall.³⁶ However, there could be some potential adverse events that can occur with

the procedure. Minor adverse events that have been reported are nausea, fainting, prolonged pain or bruising, psychological reaction, or aggravation of symptoms.^{36,47} Major adverse events such as organ puncture, the transmission of infection, and bleeding complications can also occur, though they are rare.^{36,47} This includes treatments causing hospitalization, permanent disability, or death.⁴⁷ Based on a prospective survey with 34,400 reported acupuncture treatments, a rate of serious adverse events was observed to be 0 to 1.1 per 10,000 treatments.⁴⁷ Overall, with little chance of adverse events, acupuncture has been determined to be safe as long as the practitioner is properly trained and remains attentive during the treatment.^{36,41,47}

ACUPUNCTURE IN FIBROMYALGIA

EFFICACY

The efficacy of acupuncture in the treatment of fibromyalgia was measured and reported by various scales depending on the study in question. This includes, but is not limited to, the visual analog scale (VAS), the Fibromyalgia Impact Questionnaire Score-Revised (FIQ-R), Fibromyalgia Severity Scale (FSS), and custom surveys.^{48,49} Acupuncture for women with fibromyalgia randomized control trial (RCT) compared group acupuncture to group education and reported no statistically significant changes in the education group, but statistically significant changes in symptoms, pain, and fatigue acupuncture group at four weeks follow-up; data measured via FIQ-R.⁵⁰ Sham acupuncture is often used as placebo/control in acupuncture trials involving needle insertion into skin away from true/real acupuncture points. Karatay et al. reported beneficial results in regard to the quality of life, tender point count, pain, fatigue, and depression after one month in both the real and sham acupuncture therapy groups as measured by physical exam, VAS, FIQ, Beck Depression Inventory (BDI), and Nottingham Health Profile (NHP); this effect did not extend to seven months. After true acupuncture, serum serotonin levels increased, and substance P levels decreased from baseline. Serum serotonin also increased with sham acupuncture. Simulated acupuncture therapy, the other control used in this study, showed similar results except for no improvements in FIQ and increased substance P levels.⁵¹ A meta-analysis of acupuncture therapy for fibromyalgia RCTs reported moderate-quality evidence in decreasing pain short term and low-quality evidence long term. Additionally, low-quality evidence supporting a statistically significant increase in quality of life in the real acupuncture group compared to sham. The systemic review included two RCTs that measured no statistically significant difference in pain between real and sham acupuncture, although this evidence was rated low quality. Quality of evidence was determined by the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) tool accounting for the risk of bias, inconsistency, etc..⁴ A German meta-analysis of three RCTs reported statistically significant improvements in sleep quality with real acupuncture compared to sham acupuncture. An additional RCT included did not report any statistically significant changes, except sleep quality

which rapidly improved. Fatigue improved in three individual RCTs, but no statistically significant difference between real and sham acupuncture therapy was observed when analyzed together.⁵² There was a statistically significant decrease in pain intensity at one- and two-months intervals in a real vs. sham acupuncture RCT. The study included older depression and pain assessment modalities such as the BD1 and short-form health survey (SF-36) not typically used in other studies. Scores were reportedly better with real acupuncture compared to sham.⁵³⁻⁵⁵ In a 100 double-blind study of the effects of real vs. sham acupuncture in treating fibromyalgia, no statistically significant difference was found between the two groups.⁵⁶ An overview of systematic reviews of complementary and alternative interventions, including acupuncture, aromatherapy, chiropractic, herbal medicine, homeopathy, hypnotherapy, osteopathy, and reflexology, reported acupuncture to have the best effectiveness. Its effects were debatably greater than sham acupuncture.⁵⁷ Results of an improvement in fibromyalgia symptoms with real acupuncture RCT reported statistically significant differences in FIQ-R after one month with fatigue and anxiety improving the most with real acupuncture compared to simulated acupuncture. There was no difference in physical functionality between real and simulated acupuncture.⁵⁸ Yüksel et al. reported no statistically significant difference in fatigue, FIQ scores, or VAS pain scores between transcutaneous electrical nerve stimulation (TENS) and acupuncture. TENS and real acupuncture decreased pain and increased EEG inhibitor activity as measured from baseline.⁵⁹ A pilot study comparing physical therapy modalities such as hot packs and electrical nerve stimulation found improvements in FIQ and short-form McGill pain questionnaire for both groups. No statistically significant difference in scores between these groups, however.⁶⁰ Literature supports the efficacy of alpha-lipoic acid, coenzyme Q10, magnesium, tryptophan, and vitamin D in FMS treatment. The nutraceutical product Migratens® contains these ingredients. In acupuncture vs. Migratens® RCT, acupuncture treatment statistically significantly decreased pain and increased quality of life at one-month, three-month, and six-month intervals compared to the Migratens® control.⁶¹ A pragmatic study on acupuncture for fibromyalgia reported 85.4% of patients improved in FIQ-R with 40.6% showing clinically significant improvement at eight weeks when acupuncture as an adjunct to a patient's currently unresponsive to traditional pharmacologic therapy. In addition, there was a statistically significant reduction in neuropathic pain and tender points as measured by PDQ and physical examination, respectively. Traditional pharmacologic treatment was defined as patients stable on duloxetine 60 mg/day and pregabalin 300 mg/day and other patients stable on another pharmacologic for at least three months. Paracetamol and tramadol were given as needed throughout acupuncture therapy to a max of 3 grams/day and 150 mg/day, respectively.⁶² A meta-analysis comparing the efficacy of acupuncture and pharmacological treatment in fibromyalgia reported two trials with statistically significant decreases in pain with acupuncture and moxibustion (a traditional Chinese medicine therapy) compared with the drug amitriptyline in four weeks. A third trial included measured the efficacy of acupuncture and moxibustion vs. flu-

oxetine and amitriptyline with a similar result: a statistically significant decrease in pain in the acupuncture and moxibustion group. Two included trials measured the tender point count after acupuncture treatment or traditional pharmacological treatments. The acupuncture group displayed a statistically significant decrease in tender points when compared to either amitriptyline or fluoxetine. An increase in pain threshold was determined to occur with acupuncture adjunct to pharmacologic therapy and exercise compared to pharmacologic and exercise alone at three- and six- months intervals but not twelve months onwards.⁶³ A similar review of RCTs demonstrating the efficacy of acupuncture vs. eight weeks of fluoxetine treatment reported five studies with statistically significant improvements in pain as measured with VAS. Two additional studies reported statistically significant improvements in VAS scores that extended up to three months.⁶⁴ Karatay et al. reported neuropeptide Y (NYP) levels to be higher in patients receiving acupuncture. This was associated with a statistically significant decrease in pain and tender point count, supporting a role NYP could play in pain control and a possible mechanism of this control acupuncture exerts for its therapeutic effects.⁶⁵ A systematic review on non-pharmacological treatments for chronic pain found that acupuncture was associated with improved function at six- and twelve-month following treatment. A published survey on patient satisfaction with pharmacologic and non-pharmacologic treatment of fibromyalgia also found that acupuncture had the highest satisfaction compared to physiotherapy, psychotherapy, diet, exercise, and pharmacologic treatment.⁶⁶

SAFETY, ADVERSE EVENTS

Most studies reported no adverse events for acupuncture in fibromyalgia. However, the evidence must be judged carefully considering that many studies are of relatively small sample sizes and underreport benign symptoms, as seen in a systemic review reporting low-risk side effects unspecified or not reported at all.⁶⁴ When studying the effects of real acupuncture versus sham acupuncture, researchers found no subject in either experimental or control groups to report any side effects.⁵³ Similarly, in a systemic review investigating noninvasive, non-pharmacological interventions in the treatment of chronic pain, there was no evidence to suggest acupuncture was associated with any form of harm,⁶⁷ a patient survey on treatment satisfaction and perceived tolerability of various forms of pharmacological and non-pharmacological treatments for fibromyalgia, reported the highest satisfaction with acupuncture therapy attributable to the tolerability of the treatment.⁶⁶ An RCT investigating symptomatic improvement in fibromyalgia with acupuncture further supported the tolerability of acupuncture therapy, reporting minimal adverse effects though unspecified.⁵⁸ There has been speculation on the association of acupuncture with vasovagal symptomatology. Vasovagal symptoms have been reported to occur in up to 1% of patients receiving acupuncture therapy.⁶⁸ A meta-analysis of five RCTs comparing Verum and sham acupuncture in the treatment of fibromyalgia reported vasovagal symptoms to occur.⁵² However, a RCT comparing real acupuncture to

sham acupuncture and placebo-controlled groups reported no vasovagal symptoms.⁵¹ The resolution of vasovagal symptoms appears to be due to the patient's positioning, with no vasovagal events reported in the supine position. The more common symptoms reported included bruising, small hematomas, and discomfort at the puncture site.^{4,51,52,56,57,61,68,69} Rarely, patients with fibromyalgia reported an exacerbation of preexisting symptoms after acupuncture therapy.^{4,57} There have been more rare and severe conditions that have occurred in some studies. A case of pulmonary embolism was reported in a control group receiving sham acupuncture, although a direct association between pulmonary embolism and sham acupuncture therapy was rejected.⁵² There have been reports on more severe conditions associated with puncture wounds after acupuncture treatment. A German study conducted in 2001 concluded the lungs to be the most affected with 23 reported cases of pneumothorax and two of those cases ending lethally. The same study commented on the effects of infected needles and subsequent sepsis and endocarditis.⁶⁸

CONTRAINDICATIONS

There are no specific contraindications for acupuncture in the treatment of fibromyalgia, though patient selection could affect outcomes and satisfaction with therapy. One study reported a loss to follow-up for a couple of study subjects due to poor tolerance to needles.⁶² Another publication, more specifically targeting the complications related to acupuncture treatment, reported patients with valvular disease and immunodeficiency to need to be treated on a case-by-case basis. Infected needles resulting in sepsis and endocarditis are rare but have been reported, as well as unintended exaggerated vagal response. There are currently no clear guidelines on therapy or patient selection, and patients should be triaged on an individual basis considering their risk profile and chances of success.⁶⁸

CONCLUSION

Fibromyalgia is a common syndrome of widespread chronic pain that affects about 2-4% of the general population, though its prevalence is likely underestimated. It is accompanied by chronic pain, fatigue, sleep disorders, cognitive impairment, and psychiatric derangements. It is difficult to diagnose and more difficult to treat; it causes significant morbidity and disability, is a source of chronic pain, and takes a significant emotional and financial toll on patients.

Unfortunately, the etiology and pathophysiology of fibromyalgia are still not completely clear, which hinders the ability to develop targeted therapies. This results in many suggested therapies, though efficacy is variable, and many patients continue to suffer symptoms despite therapy. Level 1 evidence exists so far only in support of physical exercise. Effective therapy requires a tailored, multidisciplinary treatment plan with a long-term commitment from both the patient and therapists. Many treatments are suggested addressing chronic pain and associated complaints, including exercise, pharmacotherapy, non-traditional pharmacotherapy such as CBD, and recently evidence emerging to support complementary medicine approaches and

acupuncture.

Acupuncture, the practice of introducing solid needles into specific points in the body, targeting the flow of qi, has been practicing in TCM for hundreds of years. Evidence supports its use in several syndromes of chronic pain. More recently, the practice of acupuncture has expanded to include not only traditional Chinese acupuncture but also dry needling, heat acupuncture, electroacupuncture, and acupressure by both mechanical means and laser. The mechanism by which acupuncture provides pain relief is unclear. However, studies suggest neuromodulation stemming from skin stimulation leads to neurotransmitters' release into the plasma and CSF that promote pain alleviation.

Several clinical trials were carried out and were able to show alleviation in pain and improvement in accompanying symptoms and quality of life with acupuncture; however, most studies could offer short-term success without durable response, indicating the acupuncture is more likely to be a facet in chronic therapy. In addition, several studies showed a decrease in pain modulators, such as substance P and NYP, due to acupuncture.

Overall, the findings from various acupuncture studies are limited due to methodological reasons, small sample size, or lack of robust evidence.^{1,5,44,45} Further acupuncture research must be done to examine the true efficacy of using acupuncture therapy to treat chronic pain conditions such as fibromyalgia.¹ Most notably, several studies have been unable to prove the superiority of acupuncture over sham treatments, raising the concern of the degree of the placebo effect. However, given the positive evidence in most studies examining the use of acupuncture as an adjunct to exercise, physical therapy, or pharmacological treatment, and in light of the safety and availability of the treatment, there seems to be increasing evidence supporting the incorporation of acupuncture as part of multi-modality treatment plans for fibromyalgia. Further studies will likely aid in determining effective regimens and proper patient selection.

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CONFLICT OF INTEREST

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Table 1. Clinical Efficacy and Safety

Author (Year)	Groups Studied and Intervention	Results and Findings	Conclusions
Mist et al. (2018) ⁵⁰	Thirty women with confirmed, symptomatic fibromyalgia treated with twenty treatments of either group acupuncture or group education over 10 weeks.	Statistically significant improvements in FIQ-R and Global Fatigue Index for group acupuncture at the end of treatment and four weeks following, neither of which seen in group education.	Group acupuncture improved symptoms, pain, and fatigue. It is safe and tolerable.
Karatay et al. (2018) ⁵¹	75 women with fibromyalgia randomized into real acupuncture, sham acupuncture, or simulated acupuncture therapy; treated biweekly for four weeks.	Serum serotonin levels increased with sham and real acupuncture. Substance P levels decreased in real but increased in simulated acupuncture. Real and sham acupuncture improved NTP, VAS, FIQ and BDI after treatment. These effects continued for three months. Simulated acupuncture improved NTP, VAS and BDI.	Real acupuncture therapy may be an effective therapy for fibromyalgia long-term. Substance P and serum serotonin levels offer an explanation for acupuncture's mechanism of action.
Zhang et al. (2019) ⁴	Meta-analysis of twelve RCTs of real vs sham acupuncture for fibromyalgia found over several research databases, including PubMed. Quality of evidence determined via GRADE tool.	Significantly better improvement in pain and quality of life with real acupuncture over sham graded low-to-moderate quality. Real acupuncture long-term effects were also greater than sham.	Acupuncture can be safely and effectively used in patients with fibromyalgia.
Kim et al. (2019) ⁵²	Meta-analysis of ten RCTs of real vs sham acupuncture in the treatment of fibromyalgia.	Real acupuncture resulted in greater improvements in pain, sleep quality, and general status than sham acupuncture. Improvements in fatigue were not seen.	Real acupuncture is greater than sham acupuncture in treating fibromyalgia symptoms, although evidence for improved fatigue was not found.
Uğurlu et al. (2017) ⁵³	50 women randomized into real or sham acupuncture groups and treated for 12 sessions over eight weeks.	Real and sham acupuncture improved VAS, VDI, FIQ at one- and two-month intervals after the first treatment. Real acupuncture improved scores greater than sham.	Acupuncture improves pain and symptoms of fibromyalgia, although the sham effect was important as well.
Assefi et al. (2005) ⁵⁶	100 patients with fibromyalgia randomized into fibromyalgia-specific acupuncture, acupuncture for another condition, nonacupoint needle insertion, or simulated acupuncture and treated bi-weekly for 12 weeks.	VAS scores did not differ in real acupuncture from either of the sham acupuncture groups.	Acupuncture is not better at pain reduction than sham acupuncture in fibromyalgia treatment. No adverse effects were reported.
Martin et al. (2006) ⁵⁸	50 patients with fibromyalgia randomized into real acupuncture or simulated.	Significant improvements in FIQ with real acupuncture compared to simulated with the largest discrepancy at a one-month follow-up. Fatigue and anxiety were most improved, and activity and physical function were unchanged.	Acupuncture improves fibromyalgia symptomatology with the greatest improvements in fatigue and anxiety.
Yüksel et al. (2019) ⁵⁹	42 fibromyalgia patients and 21 healthy volunteers were randomized into acupuncture or TENS application groups. EEG recordings were obtained before and after treatment.	Decreased pain and increased inhibitor activity found on EEG posttreatment reported for both acupuncture and TENS.	TENS and acupuncture are beneficial in fibromyalgia treatment.
Di Carlo et al. (2020) ⁶²	8 weeks of weekly acupuncture treatment in 96 fibromyalgia patients unresponsive to optimal drug therapy as determined by baseline FIQ-R, PDQ, and PHQ15 scores	85.4% of patients improved in FIQ-R, with 40.6% showing clinically significant improvement. 14.6 decreased in FIQ-R. Neuropathic-like features and somatic symptoms were significantly improved as measured by PDQ and PHQ15, respectively.	Acupuncture is an effective treatment in high-severity fibromyalgia unresponsive to other forms of therapy.

<p>Lannuccelli et al. (2017)⁶⁵</p>	<p>30 fibromyalgia patients and 20 healthy subjects received acupuncture therapy with before and after levels of serum neuropeptide Y.</p>	<p>Baseline neuropeptide Y was higher in controls than fibromyalgia patients. NYP levels were significantly reduced after treatment, along with a reduction in pain and tender point count.</p>	<p>Acupuncture contains analgesic properties, and NYP plays a role in this pain control.</p>
<p>Rico-Villademoros et al. (2020)⁶⁶</p>	<p>Spanish cross-sectional study spanning two years measured treatment satisfaction with pharmacological and non-pharmacological treatments of fibromyalgia. Measured via 10-point numerical rating scale (NRS).</p>	<p>The most commonly reported non-pharmacologic treatments were physical exercise and diet. The most common drugs prescribed were tramadol and benzodiazepines. The highest satisfaction reported with acupuncture and poor satisfaction reported with pharmacologic treatments.</p>	<p>Several therapies lack adequate study, including acupuncture, thus insufficient evidence to support the superiority of acupuncture over other treatment modalities.</p>

Table 2. Comparative Studies

Author (Year)	Groups Studied and Intervention	Results and Findings	Conclusions
Perry et al. (2017) ⁵⁷	Overview of 15 reviews of alternative therapies for fibromyalgia using AMSTAR and ROBIS to evaluate quality.	Low-quality evidence supporting acupuncture improvements in pain compared to standard or no treatment. "Good" evidence supporting no difference between real vs. sham.	Limited effectiveness of real acupuncture for fibromyalgia. High-quality RCTs are needed to further assess efficacy and side effects.
Ozen et al. (2019) ⁶⁰	44 female patients with newly diagnosed fibromyalgia and randomized to either 10 sessions of acupuncture or 15 sessions of PT modalities (hot packs, TENS, and ultrasound to tender points)	Improvements in SF-MPQ and FIQ scores for both treatment groups. There was no difference in scores between groups.	PT modalities and acupuncture are effective in treating fibromyalgia, though one is not superior to another.
Vittorio et al. (2020) ⁶¹	60 female patients were randomized to either receive Migratens® or acupuncture for three months.	Acupuncture reduced pain at one-, two-, and three-month intervals post-initiation of therapy. Migratens® improved pain at one month with improvement at three-month.	Migratens® and acupuncture seem effective options in the treatment of fibromyalgia.
Bai et al. (2014) ⁶³	Meta-analysis of 9 trials which included comparing a) real vs. sham acupuncture, b) acupuncture vs. drugs, and c) acupuncture + drugs + exercise vs. drugs + exercise.	a) Statistically significant difference in VAS, FIQ, and multidisciplinary pain inventory in real vs. sham acupuncture 4 weeks posttreatment, but not 7 weeks posttreatment. b) Statistically significant difference in VAS and tender point count after acupuncture + moxibustion when compared to either amitriptyline or fluoxetine at 4 weeks posttreatment c) Statistically significant difference in pressure pain threshold with acupuncture + drugs + exercise when compared to exercise + drugs alone at three- and six-month intervals. This did not extend to 12 and 24 months.	Insufficient evidence to support the superiority of real acupuncture over sham in fibromyalgia treatment. Evidence supporting acupuncture effectiveness over pharmacologic treatments, though the evidence was considered low quality or high-risk bias. Acupuncture combined with drugs and exercise could increase pain thresholds, but further study is needed.
Chen et al. (2019) ⁶⁴	Review of RCTs of acupuncture vs. control or vs. pharmacologic therapy in treating chronic pain.	Three trials reported improved pain outcomes in fibromyalgia after acupuncture when compared to nonpenetrating needles at acupoints and remained at one- and three-month follow-up. Five trials reported improved pain outcomes in fibromyalgia patients after acupuncture therapy when compared to eight weeks of fluoxetine.	Evidence supporting acupuncture over no treatment in chronic pain management with reasonable evidence supporting acupuncture superiority over drugs. Effectiveness was rated low-quality due to inadequate study.

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