ROLE OF MANUAL THERAPY AND MASSAGE IN THE TREATMENT OF FIBROMYALGIA: TESTING THE HYPOTHESIS

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Burhan Fatih Koçyiğit* http://orcid.org/0000-0002-6065-8002
Ahmet Akyol http://orcid.org/0000-0002-8953-5196
Serkan Usgu https://orcid.org/0000-0002-4820-9490
1Department of Physical Medicine and Rehabilitation, Faculty of Medicine, Kahramanmaraş Sütçü İmam University, Kahramanmaraş, Turkey
2Physiotherapy and Rehabilitation Application and Research Center, Hasan Kalyoncu University, Gaziantep, Turkey
3Physiotherapy and Rehabilitation Department, Faculty of Health Science, Hasan Kalyoncu University, Gaziantep, Turkey

*Corresponding author:
Burhan Fatih Koçyiğit, MD, Department of Physical Medicine and Rehabilitation, Faculty of Medicine, Kahramanmaraş Sütçü İmam University, Kahramanmaraş, Turkey;
Twitter handle: @BurhanFatihKoy1; E-mail: bfk2701@hotmail.com

Abstract
Fibromyalgia syndrome (FMS) is a chronic rheumatic disease in which pain is predominant and accompanied by fatigue, anxiety, depression, sleep disturbance and cognitive dysfunction. Although there are numerous pharmacological and non-pharmacological therapeutic alternatives, symptom control is frequently problematic. Manual therapy covers manipulating soft tissue and various joints using the hands. It is organized by mapping of soft tissue structures with rhythmically applied pressure to improve physical function, facilitate daily activities, promote rehabilitation procedures and decrease pain. Massage is generally accepted as an essential component of manual therapy. Stretching and mobilizations are also part of manual therapy. Although numerous beneficial effects of manual therapy and massage on the musculoskeletal system and pain have been proven, the data in FMS patients studies are inconclusive. We hypothesize that manual therapy and massage are beneficial therapeutic options for the control of symptoms of FMS patients. Furthermore, these strategies can be employed in conjunction with well-established and high-evidence therapeutic procedures. Future research should focus on establishing standardized protocols for manual therapy and massage, which is one of the major limitations. To ensure a high level of evidence, research studies with large sample sizes, long follow-up periods and methodologically complete are needed.

Keywords: Fibromyalgia, Manual therapy, Massage, Osteopathy

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INTRODUCTION
Chronic widespread musculoskeletal pain is central to the fibromyalgia syndrome (FMS), but is also characterized by a complicated clinical picture that includes fatigue, stiffness, sleep disturbances, cognitive dysfunction, and mood alterations [1]. Fibromyalgia is a musculoskeletal disorder that ranks third after low back pain and osteoarthritis in the list made considering the prevalence values [2]. As a result of the direct association of FMS with poor quality of life, patients
frequently seek medical support and healthcare costs increase. The annual number of consultations of FMS patients is almost twice that of healthy individuals [3]. Indirectly, the increase in work disability and absenteeism among FMS patients also has financial implications [4].

Various mechanisms contribute to the emergence of chronic pain in FMS [5]. FMS is classified as one of the central sensitization syndromes (chronic fatigue syndrome, irritable bowel syndrome, dysmenorrhea functional dyspepsia, migraine, temporomandibular joint dysfunction, myofascial pain syndrome, and restless leg syndrome etc.) [6]. Central sensitization describes a neural signal amplification process that causes a higher level of pain perception in the central nervous system [7]. A growing body of evidence suggests that pain processing mechanisms in the brain are altered in FMS, as evidenced by increased activation in pain-specific parts of the brain [8, 9]. Additionally, multiple studies have shown that there are differences in endogenous pain-inhibitory processes in FMS patients. This suggests that the balance between nociceptive and anti-nociceptive mechanisms cannot been achieved [10, 11]. High levels of substance P have been detected in the cerebrospinal fluid of FMS patients, which mediate to facilitate the perception of pain. Furthermore, FMS patients have a reduced presence of opioid receptors in brain areas that function in pain regulation [12]. It is difficult to determine the exact cause of the indicated nociplastic variations, but there is no doubt that the symptom complex in FMS is not due to a single mechanism. It has been reported that a genetic background, numerous genetic polymorphisms and peripheral mechanisms are also involved in the process [13, 14].

Painful stimuli provided by peripheral structures can trigger the nociplastic process or potentiate the existing condition in FMS patients. Considering the fact that joints can play a role as a source of peripheral pain, the high prevalence of FMS in rheumatic disorders can also be clarified [15]. Studies using microneurography in FMS patients have revealed that C-fibers show higher spontaneous activity and more sensitive to mechanical stimulation [16]. The hypothesis that peripheral factors can be responsible for pain in FMS is supported by the significant reduction of pain in areas outside the injection site, following local pain reduction after intramuscular injection of lidocaine [17].

Manual therapy, in its simplest terms, involves the manipulation of soft tissue and various joints using the hands. Another definition is the organized mapping of soft tissue structures with rhythmically applied pressure to improve physical function, facilitate activities of daily living, support rehabilitation processes and reduce the level of pain [18]. Connective tissue massage is widely accepted as an important component of manual therapy. Additionally, manual therapy covers stretches and mobilizations [19] (Figures 1 and 2).

The efficacy of manual therapy in FMS patients has been evaluated in several systematic reviews [20-23]. Much of the studies in these systematic reviews involve spinal manipulation or massage, and there are conflicting results and inconclusive evidence regarding the efficacy of these therapies. However, in a meta-analysis of randomized controlled trials, massage therapy for at least 5 weeks has been reported to have immediate positive impacts on pain, depression and anxiety in FMS patients [24]. Failure to detect a high level of evidence in systematic reviews does not indicate that the method is ineffective. The difficulties in establishing the sham manual therapy and massage group for randomized controlled trials, and the lack of standardized treatment protocols, are barriers to high-quality studies. Small sample sizes and risk of bias are other important handicaps. Despite these limitations, we consider that it is difficult to conclude that manual therapy and massage are ineffective in FMS patients.

**HYPOTHESIS**

*Manual therapy and massage are effective treatment choices that can be used in symptom control in FMS patients. Additionally, these methods can be used along with well-established and high-evidence treatment methods.*

It has been reported that various massage maneuvers have different effects. For example, massage with moderate pressure was found to increase vagal tone and induce neurotransmitters serotonin and dopamine, which are associated with analgesic processes [25, 26].

A considerable and continuous focus on pain is required before the peripheral sensitization process can trigger central sensitization. Sources of pain that do not improve within a few months are linked to the progression to chronic widespread pain. As a result, resolving acute and subacute musculoskeletal disorders with correct and effective manual therapy-massage practices can prevent localized pain from becoming chronic widespread pain, increased sensitivity and the establishment of difficult-to-treat symptom complexes [27].
In FMS patients in whom the central pain pathways are hypersensitive, relatively minor sources of pain in one part of the body can potentiate the central sensitization processes. Manual therapy with the right techniques can reduce or completely resolve localized musculoskeletal pain. Thus, the process of inducing central sensitization of peripheral mechanisms is prevented [28].

It is well recognized that the muscles and fascia are generally in a hypertonic state in FMS patients, which induces the formation of trigger points-taut bands. Soft tissue mobilization and stretching are required to solve restrictions and increase local blood flow. In regions where myofascial trigger points occur, the environment is more acidic, the levels of substance P and other algogenic peptides rise, and oxidative stress increases. All these conditions increase pain sensitivity. Therefore, resolving trigger points and taut bands, increasing local blood flow and removing algogenic peptides with manual therapy and massage are beneficial in symptom control [29].

In FMS patients, massage has been found to reduce the levels of intramuscular inflammatory and algogenic cytokines, preventing local inflammation, and helping control widespread muscle pain [30]. In addition, it has been found that manual therapy and massage have positive effects on certain parts of the brain involved in stress and emotion regulation [31].

Manual therapy and massage exert a relaxing effect on the whole body, relieve muscle spasm, increase β-endorphin levels, and restore blood flow [32]. Manual therapy and massage have also been shown to regulate the sympathetic nervous system activity, hypothalamic-pituitary-adrenocortical axis and stress hormones, which have an important place in the etiopathogenesis of FMS patients [33].

Our hypothesis cannot be immediately tested due to several factors. First, there are no standardized protocols for manual therapy and massage. These applications contain many sub-techniques, and it is unclear which techniques are more effective. There is no consensus on application intervals. Practitioner experience and education can affect results. It is difficult to create a sham manual therapy and massage group for high-quality studies.

**AVAILABLE EVIDENCE**

Considering all the aforementioned mechanisms, manual therapy and massage can be regarded as part of the treatment regimen for FMS patients. One of the most important advantages of these treatments is the low potential for adverse effects. In particular, the practices of well-educated and experienced healthcare professionals can be relied on.

It has been suggested that moderate digital pressure-based manual therapy applied to the cervical region is effective in FMS patients [34]. In their randomized controlled trial, Nadal-Nicolas et al. [35] used this approach in FMS patients for 8 sessions over 4 weeks. The manual therapy group showed considerable improvement in pain assessments. A moderate level of pressure has been claimed to stimulate pressure receptors, thereby increasing vagal activity, which induces several positive effects detected in manual therapy.

Albers et al. [20] created three groups in their research. The first is the individualized osteopathic treatment group, the second is the generalized osteopathic treatment group, and the third is the control group. Significant ameliorations in pain and fibromyalgia impact questionnaire scores were observed in the osteopathic therapy groups when compared to the control group.

Castro-Sánchez et al. [36] evaluated the short-term effects of manual therapy on FMS patients. FMS patients were randomly assigned to one of two groups: manual treatment or control. Patients in the experience group received manual therapy five days a week. The manual therapy program was found to be beneficial in terms of pain level, pressure-pain sensitivity, sleep quality, and depression symptoms.

Ceca et al. [37] assessed the efficacy of self-myofascial release therapy in their randomized controlled study and reported that the treatment program improved the quality of life in FMS patients. This improvement has been linked to myofascial tissue regeneration (i.e., tissue hydration, decreased fascial tension, or elimination of fascial constraints), which can lead to less fibroblast stimulation and therefore less proinflammatory cytokine segregation [38]. This can prevent continuous stimulation of peripheral nerve receptors and minimize the overreaction of the central nervous system [39].

Castro-Sánchez et al. [40] followed the participants for 6 months in their randomized controlled study. The experimental group received myofascial release and massage therapy. In the short term, significant improvements were detected in the experimental group in terms of pain, quality of life, sleep parameters, depression and anxiety compared with the control group.
At the sixth month follow-up, only sleep parameters were better.

Another mechanism that contributes to the efficacy of manual therapy and massage is as follows. The reduction of pain with manual therapy and massage applications is provided by stimulation of peripheral tactile sensory receptors. By stimulating the thick fibers, the effects of inhibitory interneurons in the substantia gelatinosa are enhanced. With the stimulation of thick fibers with manual therapy and massage, the nociceptive stimuli from the thin fibers (A delta and C) cannot pass to the spinal cord level and the pain is controlled as a result of the closure of the pathways [41].

COMBINATION TREATMENT
Marske et al. [42] created three groups in their study as follows: Gabapentin only (900 mg/day), osteopathic manipulative treatment and a combination of the two. In the follow-ups, pain scores decreased in the osteopathic manipulative treatment and combination group, but no similar effect was detected in the gabapentin only group. In a randomized controlled study evaluating the benefit of upper cervical manipulative treatment, the first group received multimodal therapy and the second group received multimodal therapy plus cervical manipulative therapy [43]. It has been found that incorporating upper cervical manipulative therapy within a multimodal program is beneficial in the treatment of FMS patients.

Panton et al. [44] evaluated the effectiveness of a combination of resistance training and chiropractic therapy in a randomized controlled trial. According to the results of this study, in FMS patients, resistance training improves strength, FMS impact, and strength subdomains of functionality. The addition of chiropractic treatment had positive influences on adherence and dropout rates to the resistance training and induced higher ameliorations in the subdomains of functionality.

Toprak Celenay et al. [45] formed two groups in a randomized controlled trial: combined exercise alone and combined exercise plus connective tissue massage groups. Although exercise alone was effective in this trial, it was shown that combining it with connective tissue massage provided additional improvements in pain, sleep, and fatigue.

ETHICAL AND CLINICAL IMPLICATIONS
Despite the growing number of studies showing that manual therapy and massage are effective treatment options in FMS patients, the level of evidence is still not high. One of the reasons for this situation is the lack of standardized treatment protocols. Manual therapy and massage contain numerous sub-techniques. Practitioners combine these sub-techniques based on their particular experience and education. Another issue is that the duration and number of sessions are unclear. Different application frequencies have been reported, once, twice or five times a week. Another point is the need to personalize these treatments. It would be correct to start with more superficial and soft applications in FMS patients with pronounced hyperalgesia and sensitivity. If such an approach is not pursued, the symptoms of FMS patients may worsen. High-quality studies with large sample sizes and long follow-up periods are required to overcome all of these difficulties. It is difficult to create a sham manual therapy and massage group in randomized controlled trials. Even if not applied with the right technique, compression, pressure applications, stretching and mobilization will have partial positive effects. Functional magnetic resonance imaging should be used to assess changes in the central nervous system activity in these studies to minimize the impact of this handicap. Additionally, algogenic peptides, cytokines, and other mediators whose levels alter after administration should also be identified. The focus should be on identifying the most effective manual therapy and massage sub-techniques. Thus, standardized treatment protocols can be provided.

Patients should be informed that manual therapy and massage treatments may not have the same effect in every case and that the level of benefit may vary between patients. Detailed information should be given about the applications and the final decision should be made by the patient.

CONCLUSION
Although manual therapy and massage do not have a high level of evidence for treating FMS, they can be used alone or along with other treatment methods in appropriate patients. The frequency of adverse effects is low in applications performed by trained and experienced health professionals. The hypersensitivity level of patients should be evaluated prior to the application and the treatment program should be tailored accordingly.

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CONFLICTS OF INTERESTS

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DISCLAIMER

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Fig. 1. Manual Therapy Demonstration

Fig. 2. Manual Therapy Demonstration
ФИБРОМИАЛГИЯНЫ ЕМДЕУЕ КӨЛМЕН ЕМДЕУЕ МЕН МАССАЖДЫН РЕЛІ: ГИПОТЕЗАНЫ ТЕСТИЛЕУ

Түйіндеме
Фибромиалгия - бұл шаршау, мазасыздық, депрессия, ыққының бүзілуы және когнитивтік дисфункциямен бірге жүретін созылым ревматикалық ауру. Фибромиалгияны емдеудің қип теген фармакологиялық және фармакологиялық емес терапевтик әдістері бар, бірақ симптоматикалық емдеу өз бінеше проблемалы болып табылады. Қолмен емдеу жұмысақ тіндер мен бұйындарға іс-қыімдыдалар жұрғізу әдісін, физикалық функцияларды жақсарту, қунделікті арекеттерді қесіп тұру, өңіздеуші өзінділігін арттыру және ауырсынуды азайту үшін ырғақты қоңырғылықты қысықтық емдеу құндылығын қысқырлыққа жұмысқа тіндердің құрылысының кесінін сүгіну көрсетеді. Массаж қолмен емдеудің әжырамас болған өз болып табылады. Созылу да қолмен емдеудің бір болған өз болып табылады.

Қолмен емдеу мен массаждың тірек-қызыл жүйесіне оң әсері дәлелденгеніне қарамастан, фибромиалгиямен ауыртылып, науқарадың қоңырғылығына қарай, бар емдеулер дерекетін сенімді емес. Қолмен емдеу және массаж фибромиалгиямен ауыратын науқарады сымптомдарды жақсарту үшін тәуелді тәуелді емдік деп санаймыз. Қолмен емдеудің өздерін қаныға ауақұр, массаж емдеудің өздерінің таныған әсірін, жақсы жұмысқа жатқу құндылығын шықтырып, аны қорықтырып, ғылымдарды арқылы жақсарту үшін ақыр қонырғылықты қысықтық емдеу құндылығын қысқырлыққа жұмысқа тіндердің құрылысының кесінін сүгіну көрсетеді. Массаж қолмен емдеудің ажырамас болған өз болып табылады.

Түйін сөзі: фибромиалгия, қолмен емдеу, массаж, остеопатия
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РОЛЬ МАНУАЛЬНОЙ ТЕРАПИИ И МАССАЖА В ЛЕЧЕНИИ ФИБРОМИАЛГИИ: ТЕСТИРОВАНИЕ ГИПОТЕЗЫ

Резюме
Фибромиалгия – хроническое ревматическое заболевание, сопровождающееся утомляемостью, тревогой, депрессией, нарушениями сна и когнитивной дисфункцией. Существует множество фармакологических и нефармакологических средств и методов лечения фибромиалгии, однако симптоматическое лечение зачастую оказывается проблематичным. Мануальная терапия включает в себя манипуляции с мягкими тканями и суставами и заключается в картировании структур мягких тканей ритмично прикладываемым давлением для улучшения физических функций, облегчения повседневной деятельности, повышения эффективности реабилитационных процедур и уменьшения боли. Массаж считается неотъемлемой частью мануальной терапии. Растяжка также является частью мануальной терапии. Несмотря на то, что уже доказано положительное воздействие мануальной терапии и массажа на опорно-двигательный аппарат, данные имеющихся исследований пациентов с фибромиалгией неубедительны. Мы предполагаем, что мануальная терапия и массаж являются эффективным вариантом терапии для снятия симптомов у пациентов, страдающих фибромиалгией. Мануальную терапию можно использовать в сочетании с другими хорошо зарекомендовавшими себя терапевтическими процедурами с высокой степенью доказательности. Дальнейшие исследования должны быть сосредоточены на разработке стандартизированных протоколов мануальной терапии и массажа. Чтобы гарантировать высокий уровень доказательности, необходимы методологически полные исследования с большими размерами выборки и длительными периодами наблюдения.

Ключевые слова: фибромиалгия, мануальная терапия, массаж, остеопатия
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