

Review

# The Turkish Society of Physical Medicine and Rehabilitation (TSPMR) guideline recommendations for the management of fibromyalgia syndrome

Deniz Evcik<sup>1</sup>, Ayşegül Ketenci<sup>2</sup>, Dilşad Sindel<sup>2</sup>

<sup>1</sup>Department of Physical Medicine and Rehabilitation, Guven Hospital, Ankara, Turkey <sup>2</sup>Department of Physical Medicine and Rehabilitation, Istanbul University Istanbul Faculty of Medicine, Istanbul, Turkey

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### ABSTRACT

In the present study, we aimed to establish a national guideline including recommendations of the Turkish Society of Physical Medicine and Rehabilitation (TSPMR) for the management of Fibromyalgia (FM) syndrome. This guideline was built mainly in accordance with the 2017 revised European League Against Rheumatism (EULAR) guideline recommendations for the management of FM. A total of 46 physical medicine and rehabilitation specialists were included. A systematic literature search was carried out in PubMed, Scopus, Cochrane, and Turkish Medical Index between 2000 and 2018. Evidence levels of the publications were evaluated, and the levels of recommendation were graded on the basis of relevant levels of evidence, The Assessment of Level of Agreement with opinions by task force members was established using the electronic Delphi technique. Recommendations were assessed by two Delphi rounds and 7 of 10 points were deemed necessary for agreement. The treatment recommendations were classified as non-pharmacological therapies (6 main items), pharmacological treatments (10 items), and complementary therapies (5 items). These were recommended in the light of evidence, depending on the clinical and general condition of each patient. This is the first national TSPMR guideline recommendations for the management of FM in Turkey. We believe our effort would be helpful for the physicians who are interested in the treatment of FM.

Keywords: Fibromyalgia, guideline, management, recommendations.

Fibromyalgia (FM) is defined as chronic syndrome of unknown cause, resulting in widespread pain, fatigue, sleep disturbance, impaired cognitive function, and anxiety,<sup>[1]</sup> and possible causes are thought to be genetic, neurological, psychological, sleep-related and immunological.<sup>[2,3]</sup> In the literature, complaints or symptoms reported by more than 25% of patients with FM include widespread body pain, fatigue, morning stiffness, headache, paresthesia, sleep disturbance, subjective swelling, dry mouth, loss of libido, irritable bowel, dysmenorrhea, joint hypermobility, temporomandibular joint dysfunction, dermographism, Raynaud's phenomenon, and reticular color changes in skin.<sup>[4-7]</sup> The intensity of the symptoms fluctuates over time.<sup>[8]</sup>

It has been suggested that abnormal central and/or peripheral pain mechanisms play a role in

association with genetic factors in the development of common and chronic pain reported by patients with FM<sup>[9]</sup> and the condition develops due to individuals with genetic predisposition being exposed to physiological and psychological stresses related to the environment.<sup>[10,11]</sup>

Currently, there is no cure for FM. The main goals of treatment are to decrease symptoms and to maintain and improve the quality of life and function.<sup>[12]</sup> In clinical practice, pharmacological and non-pharmacological therapies such as physical therapy, exercise, and cognitive behavioral therapy (CBT) are co-administered. Treatment protocols which treat FM as a systemic disease rather than a regional or multifocal muscle disorder are preferred.<sup>[13-15]</sup> Methods using a single treatment modality cannot provide full efficacy in patients with FM, multidisciplinary

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Corresponding author: Deniz Evcik, MD. Güven Hastanesi, Fiziksel Tıp ve Rehabilitasyon Bölümü, 06540 Çankaya, Ankara, Turkey. e-mail: evcikd@yahoo.com

approach is considered the most effective method in clinical practice.<sup>[16,17]</sup>

Although there are several national and international guidelines in this field, there is no guide which contains studies and experiences in Turkey. Therefore, in the present study, we, for the first time, aimed to establish a national guideline including recommendations of the Turkish Society of Physical Medicine and Rehabilitation (TSPMR) for the management of FM in our country.

# MATERIALS AND METHODS

This guideline was developed with the participation of 46 physical medicine and rehabilitation specialists who were the members of Soft Tissue Diseases and Myofascial Pain Working Group of the TSPMR.

# Literature search

A systematic literature search was carried out including articles in English published between 2000 and 2018 in PubMed, Scopus, and Cochrane. The publications were evaluated paying special attention with the following key words: "Fibromyalgia" and "Fibromyalgia Syndrome" in Turkish Medline.

This guideline was built mainly in accordance with the 2017 revised European League Against Rheumatism (EULAR) guideline recommendations for the management of FM. In addition, other guidelines, systematic reviews, meta-analyses, and clinical trials published until 2018 and Turkish publications from 2000 to 2018 were reviewed.

# Assessment of evidence

The evidence levels of the publications were evaluated are shown in Table 1. The levels of recommendations were graded on the basis of relevant levels of evidence, passing them through the common mental filter, to provide ease of use as weak, moderate, and strong. The Assessment of Level of Agreement with opinions by task force members was established using the electronic Delphi technique. Recommendations were assessed by two Delphi rounds and 7 of 10 points were deemed necessary for agreement.

## RESULTS

The treatment recommendations were classified as non-pharmacological therapies, pharmacological treatments, and complementary therapies.

Table 1. Evidence levels <sup>[1]</sup>
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	Level of evidence
Ia	Evidence from meta-analysis of randomized-controlled trials
Ib	Evidence from at least 1 randomized-controlled trial
IIa	Evidence from at least 1 well-designed, controlled, non-randomized study
IIb	Evidence from a well-designed, partially-experimental study of at least 1 other type
III	Evidence from well-designed, non-experimental, descriptive studies, such as comparative studies, correlation studies, and case-control studies
IV	Evidence from expert committee reports or ideas and/or from clinical experience of key authorities

### Non-Pharmacological Therapies

The efficacy of pharmacological therapies in FM is limited due to uncertain etiology. It is well-known that the majority of patients use non-pharmacological therapies.<sup>[8]</sup> The goal of non-pharmacological therapies of FM is to increase the physical functions and activity level and to improve the general health and emotional well-being of the patients.<sup>[15,18,19]</sup> Non-pharmacological therapies include patient education, exercise, physical therapy modalities, hydrotherapy/balneotherapy, massage, and CBT.<sup>[15]</sup>

# 1. Patient education

As a part of the treatment program in patients with FM, it is recommended to implement training programs to improve skills to cope with the disease (Evidence level Ia, Strong recommendation).

During the education process, the patient is informed about the syndrome and treatment options, the misbeliefs and misleading information about the disease are corrected, and it is clarified that the disease is not life-threatening.<sup>[15,20]</sup> Ensuring the implementation of self-management makes the patient to take responsibility for activities which would affect symptoms positively and to improve problem-solving abilities. Self-efficacy positively affects the patient's attitude and resistance to disease. It helps the patient to exhibit particular behaviors by controlling his/her emotions or to change his/her attitudes to reduce the severity of symptoms. In this way, the patient can benefit more from treatment.<sup>[15]</sup> However, several studies have shown that education alone is not enough in treatment, but should be a part of the treatment plan.[15,20-23]

# 2. Exercise

As a part of the treatment program in patients with FM, it is recommended that individual exercise programs should be implemented according to the patient's clinical status and general condition (Evidence level Ia, Strong recommendation).

The exercise program for FM patients should involve aerobic and strengthening exercises (Evidence level Ia, Strong recommendation).

There is no difference between the efficacy of land-based and aquatic exercises, and the choice should be made by the agreement of patient and the physician together, and an exercise setting enhancing compliance should be preferred (Evidence level Ia, Strong recommendation).

It has been shown that strength and condition of muscles decrease in FM patients.<sup>[15,20,24,25]</sup> Loss of muscle strength causes the muscles sensible to microtraumas, causing pain and fatigue, thereby, creating a vicious cycle. The main goal of exercise is to break this vicious cycle.<sup>[20]</sup> Exercise may yield analgesic effect by increasing serum beta-endorphin levels. In patients with FM, it has been shown that decreased blood flow in the muscle tissue, and contractions in muscles, and changes in post-exercise pain modulation cause increased post-exercise pain. Recent three clinical trials with FM in the 2017 Cochrane review evaluated the role of physical activity and exercise in chronic pain management.<sup>[26]</sup> The review concluded that, although the level of evidence was low, physical activity and exercise were usually mild-to-moderately beneficial in terms of decreasing the severity of pain and improving physical functions. In addition, the incidence of adverse effects was low and the quality of life improved. Although patients are usually suggested aerobic exercises, in general, both the aerobic and strengthening exercises were found to be beneficial. Also, the aquatic and land-based exercises were found to have a similar efficacy.<sup>[8,27,28]</sup> In a study conducted with 57 patients in Turkey, the efficacy of balance exercises was investigated, and it was concluded that balance exercises were beneficial in terms of static balance and functional levels in FM patients.<sup>[29]</sup> An exercise program can be initiated with basic neck joint motion and posture exercises and continued with the whole body strengthening and aerobic exercises subsequently. It should be noted that, when pain severity and symptoms increase, the intensity of exercise should be reduced. Exercise should be increased by 10% after two weeks in the absence of any increase in complaints.<sup>[30]</sup>

## Aerobic exercises

In the 2017 Cochrane review evaluating aerobic exercises in patients with FM, 13 studies of a total of 839 participants were included.<sup>[31]</sup> Eight studies with 456 participants provided low evidence for pain intensity, fatigue, stiffness and physical functions, and moderate evidence for quality of life. In another review evaluating exercise therapies in FM, strengthening exercises provided improvement in general wellbeing and physical functions, although the combined exercise programs (aerobic and/or strengthening and/or stretching exercises) improved pain and physical functions further.<sup>[32]</sup>

# Strengthening exercises

The low-quality evidence obtained in a Cochrane review in 2013 including five studies showed that strengthening exercises on moderate and moderatesevere intensity provided a significant improvement in pain, tenderness, function, and muscle strength.<sup>[33]</sup> There was also low-quality evidence that FM patients could safely perform moderate-to-severe level exercises. In this review, aerobic exercise was reported to be more effective in pain relief than moderate strengthening exercises.

# Stretching exercises

Although there is insufficient evidence for the effectiveness of stretching exercises in FM, the results of the study comparing stretching and aerobic exercise in 76 sedentary FM patients showed an improvement in aerobic capacity, pain, and physical functions in both groups, whereas it was more evident in patients receiving aerobic exercise.<sup>[34]</sup> In a review of four studies, stretching exercises provided improvement in pain and pain-related quality of life and functions, although the authors concluded that further studies should be performed due to methodological drawbacks in most of the studies included.<sup>[35]</sup>

# • Aquatic exercises

Sixteen studies were included in a 2014 Cochrane review evaluating aquatic exercises in FM.<sup>[28]</sup> The aquatic exercise programs showed similar effectiveness to land-based exercises. In a study with 50 FM patients in Turkey, balneotherapy was compared with aquatic exercises and symptoms such as pain, fatigue, and morning stiffness were improved with both treatments.<sup>[36]</sup> In another study including 63 FM patients, aquatic exercises and home-based exercises were compared and, although similar efficacy was observed in both treatments, the duration of follow-up was longer in the group receiving aquatic therapy.<sup>[37]</sup> Recently, swimming or walking groups showed a similar improvement in a study including 75 FM patients.<sup>[38]</sup>

# 3. Physical therapy modalities

Evidence lacks to suggest performing electrotherapeutic modalities alone in FM patients (Evidence level Ia, Ib, IIa, Weak recommendation).

Electrotherapeutic modalities are recommended according to the patient's clinical status and general condition as a part of the therapy program in patients with FM (Evidence level Ia, Ib, IIa, Weak recommendation).

### Electrical stimulation (ES)

A 2017 review evaluating the role of ES in FM has included nine studies (6 transcutaneous electrical nerve stimulation [TENS], 3 electroacupuncture) with a total of 301 patients.<sup>[39]</sup> Although it was concluded that ES provided a significant reduction in pain, there was no significant difference in the quality of life and fatigue and the evidence level was defined as low. When only TENS was applied, no significant reduction in pain was observed, either.

# *Transcutaneous electrical nerve stimulation (TENS)*

Transcutaneous electrical nerve stimulation is successfully used in the treatment of acute and chronic pain conditions and seems to be effective on the mechanism of supraspinal and spinal pathways.<sup>[18]</sup> It is mostly applied between the frequency of 50 to 120 Hz and it provides pain relief by increasing the gamma aminobutyric acid (GABA), endorphin, enkephalin, and dynorphin levels in the spine.<sup>[40-42]</sup> In FM treatment, it is often used in localized pain.<sup>[15]</sup> A prospective controlled study in Turkey including 66 FM patients compared the effectiveness of exercise and TENS and reported that exercise combined with TENS provided better results in myalgic pain relief.<sup>[43]</sup>

# Pulsed electromagnetic fields

There are studies indicating pulsed electromagnetic fields and repetitive transcranial magnetic stimulation (rTMS) reduce pain and/or improve quality of life of patients with FM.<sup>[44-49]</sup> However, in a placebocontrolled study in Turkey, rTMS was applied to 25 patients and it did not provide significant long-term improvement.<sup>[44]</sup>

# Transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS)

A review evaluating the efficacy of non-invasive brain stimulation involving rTMS and tDCS in FM included 16 studies. The mean effect size for the improvement of pain, depression, sleep disturbance, tender points, and general health/functions was found to be 0.667, 0.322, 0.511, 0.682, 0.867, and 0.473, respectively. In addition, rTMS was evaluated as more effective than tDCS (effect size was 0.698 and 0.568; p<0.0001, respectively). Primary motor cortex (M1) stimulation was reported to be more effective than dorsolateral prefrontal cortical application and the authors concluded that both rTMS and tDCS methods could be used in FM patients.<sup>[50]</sup>

# Low-level laser therapy

Although low-level laser therapy has been suggested to reduce pain by creating photochemical reactions which alter neuronal activity, its use in FM is still controversial.<sup>[18,51,52]</sup> A study with 75 patients comparing placebo and amitriptyline and laser treatment showed that it was effective in pain reduction.<sup>[52]</sup>

# Ultrasound therapy

In a comparison study including 20 patients to evaluate the efficacy of ultrasound treatment and laser treatment in FM patients, reduction in the pain, stiffness and tender points was found with both treatments.<sup>[53]</sup> Another study including 20 patients showed improvement in pain, functions, and sleep.<sup>[54]</sup>

### Interferential current (IF)

In a study including 56 patients to evaluate the efficacy of IF current application for the treatment of FM, hot pack, vacuum electrodes with IF current and posture exercises with hot pack, vacuum treatment without IF and posture exercises were compared. The authors showed that no significant improvement in the analgesic effect was found in patients with FM.<sup>[55]</sup>

### 4. Hydrotherapy-balneotherapy

As a part of the treatment program in patients with FM, hydrotherapy/balneotherapy programs are recommended according to the patient's clinical status and general condition (Evidence level Ia, Moderate recommendation).

Four reviews investigating the efficacy of hydrotherapy and balneotherapy in FM included about 21 studies and 1,306 subjects.<sup>[56-59]</sup> In another review of 10 studies and 446 patients, an average of four-hour

hydrotherapy was compared with different methods and a significant reduction in pain was observed for 14 weeks.<sup>[58]</sup> In addition, in a review including 21 studies, there was a decrease in pain and an improvement in quality of life with hydrotherapy.<sup>[59]</sup> Balneotherapy also decreased pain and number of tender points and improved quality of life. Therefore, the authors found no strong evidence for the superiority of one method to another.

# 5. Massage

# There is poor evidence that the massage therapy is effective in FM patients.

In a review and meta-analysis of nine studies, massage was compared with TENS, standard care, relaxation, and acupuncture.<sup>[60]</sup> However, there was methodological problems in all these studies. Although there was no significant effect of massage on pain, in a subgroup analysis, five weeks or longer massage was associated with a positive effect.

## 6. Cognitive-behavioral therapy (CBT)

# Cognitive behavioral therapy is recommended as a part of the treatment program in patients with FM (Evidence level Ia, Weak recommendation).

There are six reviews involving 2,031 patients on CBT.<sup>[27,61-66]</sup> Twenty-three studies were included in the Cochrane review in 2013; however, these studies were reported to have a poor quality.<sup>[65]</sup> Mostly, CBT studies were performed as a single method, and no positive effect was detected and contradictory results were obtained in multi-method CBT programs. Improvements in pain and function were found in studies in which CBT and exercise programs were administered together.<sup>[62]</sup> In addition, it was reported that CBT provided a mild reduction in pain and disability and its effects sustain for a long time.<sup>[65]</sup>

# **Pharmacological Treatments**

Drugs shown to be effective in FM are tricyclic antidepressants (TSA), cyclobenzaprine, tramadol, serotonin-noradrenaline reuptake inhibitors (SNRIs), and certain antiepileptics.<sup>[27]</sup> The choice of pharmacological treatment in patients with FM should be based on the patient's clinical features, adverse effects, and response to treatment.<sup>[1,67]</sup> Treatment is recommended to be titrated gradually starting with low doses.<sup>[1,12,15,68]</sup> Studies with drug combinations are limited and it is generally recommended to start treatment with monotherapy.<sup>[15,69]</sup> In conclusion, the aim of drug treatment, administered concurrently with patient education and non-pharmacological therapies, is to bring the patients to a level for their coping with the symptoms.<sup>[70]</sup>

# 1. Antiepileptics

Pregabalin can be used at a dose of 300 to 450 mg/day in patients with FM, when pain is the dominant symptom with concomitant sleep disturbance and fatigue (Evidence level Ia, Moderate recommendation).

Data on the use of gabapentin in FM patients are insufficient, and a benefit-risk calculation should be made (Evidence level Ib, Moderate recommendation).

In a Cochrane review including five studies with 2,758 patients reported that pregabalin provided a mild improvement in pain reduction and sleep disorders, whereas the efficacy in fatigue was less beneficial.<sup>[71]</sup> A recent prospective, randomized study involved 209 FM patients showed that pregabalin had positive effects on sleep problems.<sup>[72]</sup> In a safety review including eight studies, pregabalin treatment was found to be associated with somnolence, dizziness, weight gain, and peripheral edema. Most of the patients reported side effects of pregabalin therapy which were usually mild-to-moderate and well-tolerated in the long-term.<sup>[73]</sup>

In a *post-hoc* analysis of a crossover, randomized, placebo-controlled study including 209 FM patients using pregabalin treatment was found to improve sleep parameters.<sup>[72]</sup>

A Cochrane review of 2017 on the efficacy of gabapentin for FM pain included only one trial of 150 patients and the evidence was considered insufficient to support or refute the suggestion that gabapentin could reduce pain in FM.<sup>[74]</sup>

## 2. Monoamine oxidase inhibitors (MAOIs)

# The use of MAOIs in FM patients is not recommended (Evidence level Ia, Strong recommendation).

The efficacy and safety of MAOIs in FM have been investigated in four reviews including 241 patients.<sup>[27,75-77]</sup> Due to lower comparative efficacy to TSAs and the intensity of adverse effects, their use is not recommended.<sup>[1,27,76,78]</sup> In a prospective study carried out in Turkey investigating the efficacy and tolerability of moclobemide therapy in 21 FM patients, there was no significant improvement in symptoms other than pain and it was concluded that moclobemide could be used in patients with FM who had severe depression.<sup>[79]</sup>

# 3. Nonsteroidal anti-inflammatory drugs (NSAIDs)

# The use of NSAIDs in FM patients is not recommended (Evidence level Ia, Weak recommendation).

A review of two small-scale studies and a Cochrane review of 2017 showed that there was a limited efficacy of NSAIDs in FM.<sup>[27,75,80]</sup>

# 4. Selective serotonin reuptake inhibitors (SSRIs)

The use of SSRIs in FM patients is not recommended; however, they can be used in the treatment of depression and anxiety disorders in patients with FM (Evidence level Ia, Weak recommendation).

Eight reviews evaluating the use of SSRIs in FM were assessed; most of these reviews addressed to the use of antidepressants in FM in a general aspect.<sup>[75,76,81-86]</sup> In some of the studies evaluating the use of antidepressants in FM, SSRIs was reported to have a less effect than TSAs.<sup>[79,83]</sup> In a 2015 Cochrane review of seven placebo-controlled studies (two with citalopram, three with fluoxetine, and two with paroxetine) yielding a total of 383 patients, SSRIs were shown to be more effective than placebo on pain, fatigue, and sleep problems which are the main symptoms of FM.<sup>[86]</sup> The authors concluded that they could be used in the treatment of depression in patients with FM.

# 5. Serotonin-noradrenaline reuptake inhibitors (SNRIs)

Serotonin-noradrenaline reuptake inhibitors (i.e., duloxetine, milnacipran) can be used in the treatment of FM (duloxetine 60 mg/day, milnacipram 100 to 200 mg/day) (Evidence level Ia, Moderate recommendation).

Serotonin-noradrenaline reuptake inhibitors are thought to act in FM via inhibition of serotonin and noradrenaline, which are effective on descending pain inhibition pathways.<sup>[1]</sup> In a Cochrane review, a total of 6,038 patients were evaluated in five duloxetine and five milnacipran studies, and pain improved slightly better than placebo with both drugs.<sup>[87]</sup> However, other symptoms did not show a significant difference between placebo or between the two drugs.

# 6. Cyclobenzaprine

Cyclobenzaprine is not recommended for use in FM patients due to the lack of sufficient data to demonstrate its efficacy and high risk of side effects (Evidence level Ia, Weak recommendation). Cyclobenzaprine is a centrally acting muscle relaxant structurally similar to TSAs.<sup>[1]</sup> In a single systematic review of 312 patients, 85% of the patients experienced adverse effects and only 71% were able to complete the study.<sup>[1,27,88]</sup> Preparations of cyclobenzaprine are not available in Turkey.

## 7. Tramadol

Tramadol can be used in patients with FM for a short period of time and with a dose up to 150 mg/day (Evidence level Ia, Weak recommendation).

Tramadol, a weak opioid, has mild SNRI effect <sup>[1,27]</sup> In two reviews of 313 and 422 patients, one study evaluating the efficacy of tramadol in FM was performed.<sup>[75,89]</sup> In these studies, among monotherapy and combination treatment with paracetamol, tramadol was found to decrease FM-related pain.<sup>[75,89]</sup>

# 8. Tricyclic antidepressants

Amitriptyline can be used at a dose of 10 to 25 mg/day in patients with FM below 60 years of age, who do not have any cardiac problems and who do not use other antidepressant drugs (Evidence level Ia, Weak recommendation).

As the analgesic effect has been shown to decrease with higher doses, dose titration is not recommended in patients who does not respond to 25 mg/day.

# Amitriptyline is not indicated in the treatment of FM in Turkey.

Amitriptyline, a TSA, has been suggested to offer multiple benefits in patients with FM, by blocking adrenoceptors and 5-Hydroxytryptamine (5-HT) receptors and, possibly, histamine and muscarinic receptors, stimulating peripheral adenosine A1 receptors, binding to opioid and N-Methyl-D-Aspartate (NMDA) receptors, and interacting with sodium, potassium, and calcium channels.<sup>[90]</sup> According to the pooled analysis of five reviews including 13 studies involving 919 patients, amitriptyline administered at a dose of 25 to 50 mg/day showed a moderate effect on pain and sleep disorder and could possibly lead to a reduction in fatigue.<sup>[1,27,81,82,91-93]</sup>

## 9. Capsaicin

# As a part of the treatment program in patients with FM, capsaicin can be used for regional pain (Evidence level Ib, Weak recommendation).

Two studies and 157 patients were included in a review evaluating the use of capsaicin and favorable effects on pain were reported with topical use.<sup>[27,94]</sup>

# 10. Drug combinations

Drug combinations may be administered in FM patients, who do not respond to monotherapy, under careful observation and with consideration of the adverse effects (Evidence level Ib, Weak recommendation).

### **Complementary Therapies**

### 1. Acupuncture

Acupuncture can be used as a part of the treatment program in patients with FM according to the patient's clinical status and general condition (Evidence level Ia, Weak recommendation).

Using acupuncture therapy, the aim is to obtain therapeutic effect by stimulating specific regions of the body with heat, pressure, laser and fine needles.<sup>[8]</sup> Eight reviews evaluating acupuncture use in FM comprised up to 16 studies and up to 1,081 patients.<sup>[95-102]</sup> Nine trials (n=395) were included in a 2014 Cochrane analysis examining the benefits and safety of acupuncture treatment for FM.<sup>[95]</sup> Moderate-quality evidence showed that adjunct acupuncture therapy reduced pain by 30%, compared to standard therapy alone. In a randomized-controlled trial of 93 FM patients, acupuncture with escitalopram treatment was compared with escitalopram monotherapy. The addition of acupuncture to escitalopram showed no significant difference in FM-related symptoms, except a higher decline in the number of tender points.<sup>[103]</sup> In a prospective, multi-center, controlled trial including 153 patients which was published in 2016, acupuncture and sham acupuncture were compared and acupuncture was found to be effective by 14% with a higher decrease in pain severity.<sup>[104]</sup> This effect sustained at one year, and side effects were considered mild and infrequent.

# 2. Mind-body treatments

Mindfulness and meditative movements (Tai chi, Yoga, Qi gong) can be used as a part of the treatment program in patients with FM according to the patient's clinical status and general condition (Evidence level Ia, Weak recommendation).

According to a review of six trials including 674 patients, mindfulness-based stress reduction was found to decrease pain, although the level of evidence was low.<sup>[105]</sup> In another review published in 2017, although the evidence was controversial, it was concluded that mindfulness techniques could provide an effective complementary treatment approach for FM patients, particularly when combined with other reliable techniques, such as exercise and CBT.<sup>[106]</sup> In a systematic review and meta-analysis including seven trials and 362 patients comparing Tai chi, Yoga, Qi gong, and mindfulness with aerobic exercise, education and stretching, moderate beneficial effects on sleep and fatigue were reported.<sup>[107]</sup> According to an overview of systematic review articles and updated guidelines published in 2017, meditative movement therapies were strongly recommended, being effective in FM patients.<sup>[108]</sup> In a randomized trial including 44 FM patients in 2016, Tai chi was compared with education alone and a significant improvement was reported in pain, sleep, and quality of life.<sup>[109]</sup>

# 3. New treatment approaches

The new treatment approaches that have not yet had sufficient evidence are not recommended in FM patients (Evidence level Ib, IIa, Strong recommendation).

Recent studies in the field of FM include different methods such as typing, laser, hyperbaric oxygen therapy, optic nerve stimulation, lidocaine infusion, and neurostimulation; however, clinical evidence of these methods is still insufficient.<sup>[110-118]</sup>

# 4. Nutritional supplements and complementary medicine products (Homeopathy, Phytotherapy)

Apart from the nutritional recommendations which support a healthy diet and achieving the target weight, no special nutrition, supplements, and complementary medicine products are recommended in FM patients (Evidence Level Ia, Strong recommendation).

In a systematic review of six randomized-controlled trials comparing traditional Chinese medicine (TCM) with pharmacological treatments, TCM appeared to be effective for FM pain.<sup>[119]</sup> In another review, there was insufficient evidence on complementary and alternative medicines, either taken orally or applied topically.<sup>[120]</sup> In two reviews on homeopathy, the evidence was regarded as unsatisfactory.<sup>[121,122]</sup>

# 5. Other complementary therapies

The number of studies including manipulation, chiropractic methods, biofeedback, hypnosis, sensory art treatments, and magnetotherapy is limited and there is insufficient scientific evidence in patients with FM.

# Multidisciplinary and Interdisciplinary Treatments

As a part of the treatment program in patients with FM, the application of multidisciplinary or

# interdisciplinary treatments are recommended according to the patient's clinical status and general condition (Evidence level Ia, Strong recommendation).

Multidisciplinary approaches require а combination non-pharmacological of and pharmacological therapy modalities. The benefits and risks of these modalities should be taken into consideration and should be planned after the evaluation of pain intensity, function, associated features such as depression, fatigue, sleep disturbance, and patient preferences and comorbidities.<sup>[27,123]</sup> In a randomized-controlled trial, long- and short-term interdisciplinary treatment approaches including CBT, education, and exercise training for reducing pain intensity, controlling disease activity and improving physical functions were found to be effective.<sup>[124]</sup> In another study, moderate to relatively high correlations were found between the patient's perception of improvement and pre-post changes on pain, fatigue, and functional disability with tailored multidisciplinary treatment.<sup>[125]</sup> Multidisciplinary approach was found to be more effective than the standard approach,

Table 2. Summary of the treatment recommendations

Non-Pharmacological Therapy	Recommendations		
Patient education	Strong recommendation		
Exercise	Strong recommendation		
Physical therapy modalities			
Electro-therapeutic applications	Weak recommendation (As a part of the treatment program)		
Massage	Insufficient scientific evidence		
Cognitive behavioral treatment	Weak recommendation (As a part of the treatment program)		
Pharmacotherapy	Moderate recommendation (Pregabalin)		
Antiepileptics	Moderate recommendation (Gabapentin - Benefit-risk calculation should be made)		
Monoamine oxidase inhibitors (MAOIs)	Strong recommendation (Not recommended)		
Nonsteroidal anti-inflammatory drugs (NSAIDs)	Weak recommendation (Not recommended)		
Selective serotonin reuptake inhibitors (SSRIs)	Weak recommendation (Can be used in the treatment of depression and anxiety disorders in patients with FM)		
Serotonin-noradrenaline reuptake inhibitors (SNRIs)	Moderate recommendation (Duloxetin, milnacipram)		
Cyclobenzaprine	Weak recommendation (Not recommended)		
Tramadol	Weak recommendation (Can be used for a short period and with a dose up to 150 mg/day)		
Tricyclic antidepressants	Weak recommendation (Amitriptyline can be used at a dose of 10-25 mg/day in patients with fibromyalgia (FM) below 60 years of age, who do not have any cardiac problems and who do not use other antidepressant drugs)		
Capsaicin	Weak recommendation (As a part of the treatment program)		
Drug combinations	Weak recommendation (Can be used in FM patients, who do not respond to monotherapy under careful observation)		
Complementary Therapies			
Acupuncture	Weak recommendation (As a part of the treatment program)		
Mind-body treatments			
• Mindfulness	Weak recommendation (As a part of the treatment program)		
Meditative movements	Weak recommendation (As a part of the treatment program)		
New treatment approaches	Strong recommendation (Not recommended)		
Nutritional supplements and complementary medicine products	Strong recommendation (Not recommended)		
Other complementary treatments	Strong recommendation (Not recommended)		
Multidisciplinary and Interdisciplinary Treatments	Strong recommendation		

and internet-based home telemedical surveillance system increased treatment compliance in a web/ internet-based telemonitoring of a randomizedcontrolled trial.<sup>[126]</sup>

In conclusion, this is the first national TSPMR guideline recommendations for the management of FM in Turkey. We believe our effort would be helpful for the physicians who are interested in the treatment of FM and provide further contribution to the management of FM patients. The summary was given in Table 2.

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