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ADVANCEMENT IN NON PHARMACOLOGICAL TREATMENT STRATEGIES FOR THE MANAGEMENT OF FIBROMYALGIA SYNDROME

Health Science

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ABSTRACT

Fibromyalgia is a chronic idiopathic progressive musculoskeletal pain syndrome, which affects a large proportion of the population; around 2-4 % worldwide. The prevalence of fibromyalgia across the globe is much higher in women than in men and the ratio is approximately 9:1. Besides musculoskeletal pain, which is the major symptom of the disease, patients manifest cognitive impairment, sleep disturbances, memory loss, anxiety and depression. There is no permanent cure for the disease. Devastating pain and related syndromes of the fibromyalgia and the lack of proper treatment strategy make the patient hopeless and reduce their quality of life Therefore, they have to completely rely on the medications which can temporarily attenuate the pain and other related symptoms such as psychological disorders, fatigue, morning stiffness, sleep problems and various other health issues, but fail to improve the quality of life and lead to drug dependence and tolerance in most clinical cases. Nowadays, various lifestyle interventions such as e yoga, exercise regimens , tai-chi, hydropathy, physiotherapy and others have emerged to improve the quality of life of fibromyalgia patients. Most of them are non invasive and cost-effective however, these methods are under trials and available to patients, subject to their participation in different trial-based studies. In addition to these, some advanced non-invasive therapeutic interventions such as rTMS, Biofeedback techniques and TENS are also replicated by the researchers in their investigations. Most of the interventions are certainly low-cost practices, which can be easily adopted in day-to-day life at home; but their effectiveness and reliability are not so good. The two most common hurdles which increase the treatment burden for a clinician are the large variability in FM symptoms from severe pain to psychological distress and sleep disturbances and the long-term sustainability of the benefits of interventions to avoid recapitulation of symptoms after leaving the treatment regime. And furthermore, this reduces the quality of life and overall well-being of the patients. Considering the huge impact of fibromyalgia on quality of life of the patient , It is pertinent at this stage to focus more on the non-invasive management strategies for this disorder.

KEYWORDS

Fibromyalgia Syndrome, Pain Management, Lifestyle Intervention, Therapeutic Intervention

INTRODUCTION:

Fibromyalgia is a common neurologic chronic health problem that causes widespread pain and tenderness (sensitivity to touch); the pain and tenderness tend to come and go, and move about the body. Most often, people with this chronic illness are fatigued and have sleep problems (ACR Definition). It is diagnosed by a history of chronic widespread pain for at least 3 months and demonstration of significant pain in at least 11 out of the 19 tender points [1]. Musculoskeletal pain is the most common symptom of the disease; it is distributed to specific tender points, most of which are paired and present on the dorsal surfaces of the neck, shoulder, and back of the patients, it shows mild to severe pain for at least 3 months; which worsen with age [1]. Fibromyalgia can be diagnosed and treated on the basis of widespread pain Index (WPI) and Symptom Severity Score (SSS) of the patient (ACR, 2010). Besides persistent musculoskeletal pain, other high rated symptoms of fibromyalgia includes morning stiffness, fatigue, poor quality of sleep, anxiety, depression, cognitive impairment and memory loss [2] (see Figure 1). However, the musculoskeletal and neurological examinations are normal in most of the fibromyalgia patients [3]. There are various pathophysiology of the disease like oxidative burden, inflammation, sensitization due to chronic pain and tenderness. Amongst them, most are contraindicatory and thus the disease is still idiopathic in nature. Few genes are also found to be involved in the pathophysiology of the disease, like SLC64A4, TRPV2, etc; most of which are transporters and ion channels [4]. Incidence of FM has been reported over 2% in the general population [5]. This disorder predominantly affects women between 30-60 years aged in a ratio of 9:1 compared to men [6]. It is interesting to note that men have less fatigue, morning stiffness, and irritable bowel syndrome when compared to women [7]. Interestingly symptoms of FM have also been reported in juveniles and clinical presentation is quite similar to adult patients [8].

Musculoskeletal Symptoms	Non-musculoskeletal Symptoms	Other Complications
• Pain in muscle and joints • Fatigue • Morning stiffness • Jaw and neck pain • Restless leg syndrome • Movement and posture problems	• Headache • Memory loss • Anxiety • Depression • Cognitive impairment • Sleep disturbances	• Problem with vision • Skin problems • Dizziness • Nausea • Gastrointestinal problems • Dysmenorrhea

Figure 1: Fibromyalgia as a syndrome

There is no permanent cure of the disease; treatment strategies for FM are general in nature and include the use of both pharmacological and non-pharmacological symptoms management strategies; former comprises of common medications like: acetaminophen, ibuprofen, naproxen, cyclobenzaprine, amitriptyline, and aspirin [2]. Some of the FDA approved antidepressants and analgesics drugs are pregabalin, duloxetine and milnacipran which help to control symptoms of fibromyalgia syndrome. Amitriptyline are also used to control symptoms; but pure opioids should be avoided [9]. Following lifestyle and therapeutic interventions are extensively being studied by the researchers across the globe:

- Physical Activity and Exercise: Stretching, aerobic and resistance exercises (EULAR Recommendation, 2019)
- Massage Therapy
- Hydrotherapy
- Yoga and Meditation
- Repetitive Transcranial Magnetic Stimulation (rTMS)
- Transcutaneous Electric Nerve Stimulation (TENS)
- Vibrator therapy

In the present article, we are going to review all the newer advancements in the treatment strategies for the management of pain and related symptoms of fibromyalgia syndrome in the past 3 decades. Fibromyalgia is among one of the newest diseases which was discovered in the late 20th century. Lack of proper treatment strategy and the pin-point cure of the disease, make patients more worried and hopeless which ultimately degrades the quality of life of the fibromyalgia patients. Management of fibromyalgia becomes more cumbersome as it comprises of diverse symptoms from sleeplessness and fatigue to psychological distress. Timeline of some of the relevant interventions according to its implementation in the clinical trials and optimistic approach are given in Figure 2.

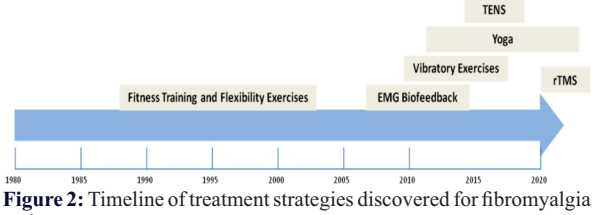

Figure 2: Timeline of treatment strategies discovered for fibromyalgia patients:

Classical Treatment Strategies For Fibromyalgia Patients:
Fibromyalgia as a syndrome was recognized in the late 20th century; earlier it was thought to be a musculoskeletal problem linked with either chronic low back pain or chronic fatigue syndrome [6].

Physical Activity And Exercises
Since, musculoskeletal pain is the primary symptom of fibromyalgia; so, researchers started working toward rehabilitation techniques like physical, aerobic, resistance and cardiovascular exercises for management of the disease. Within few years of discovery of the disease; scientists across globe started to prove physical exercises as a novel intervention for the management of fibromyalgia and related symptoms. In 1988, McCain and colleagues recruited 38 fibromyalgia patients in a study to validate the effect of 20 weeks of cardiovascular fitness training and simple flexibility exercises (3 sessions/week) and found significant improvement in musculoskeletal pain and psychological distress [10]. Aerobic fitness training and stretching exercise are also beneficial for fibromyalgia patients [11]. Moreover, Physical Activity, comprising at least twice a week can reduce fatigue, depression and other FM related symptoms [12]. Exercise is widely used as a treatment option to minimise micro-muscle trauma and central sensitization and emphasise low-intensity exercise, individualise exercise, and maximise self-efficacy [13-14]. Benefits of exercise therapy, jogging, cycling and swimming are well documented from various RCTs in the fibromyalgia patients [15-16]. Vibration therapy program is also useful and feasible for improving dynamic balance in women with FM [17]. EULAR recommended physical activity as one of the treatment strategies of fibromyalgia.

Massage Therapy
Massage therapy could be considered as one of the alternative and complementary treatments for the management of fibromyalgia syndrome [18]. Massage therapy with duration ≥5 weeks had beneficial immediate effects on improving pain, anxiety, and depression in patients with fibromyalgia [19]. While, another pilot study suggest modest benefits to FM patients at four weeks which is not significant at later time-points [20]. So, there are fewer and contraindicatory findings about the beneficial effect of massage therapy in fibromyalgia.

Water Therapy
Aquatic Physical Training (APT) contributes to increase variable oxygen uptake and improve clinical symptoms of fibromyalgia, but no association has been established yet [21]. A 16 week hydrotherapy program (45 minutes, twice a week) was found effective to improve quality of life, pain intensity and fibromyalgia impact in women with fibromyalgia syndrome despite of any changes in scapular kinematics due to adaptive movement pattern due to chronic painful condition [22-23]. In-pool exercise education programme (n=134) showed a small but significant improvement in health status of fibromyalgia patients as compared with that of education only and patients with milder symptoms improved most with this treatment strategy [24]. Water therapy including deep water running and in-pool aquatic training, may be recommended as a non-pharmacological complementary approach for the management of FMS in improving pain, postural control, fatigue, and quality of life - these therapeutic effects are achieved by the physiological changes caused by in-water exercising [23, 25-26]. Nowadays, warm-water exercising and water-based Ai Chi program are also recommended to improve mental and physical health and the quality of life in women with fibromyalgia [27-29].

Yoga And Meditation
Yoga is culturally believed as a strategy to direct attention and attitude toward wellness of mind and body. To restore sensorimotor dysfunction and alleviation of pain, yoga therapy is formally being investigated in fibromyalgia patients. Robust evidence already exists that documents the role of yogic lifestyle intervention and relaxation techniques in the management of fibromyalgia [30]. Yoga improves quality of life and act as analgesia through physiological mechanisms - hypothalamic-pituitary-adrenal (HPA) axis and parasympathetic nervous system tuning [31]. Yoga negotiates the increased morning cortisol levels in chronic pain patients [32-33]. An eight week yoga awareness program, comprising 2 hours of yoga once a week, was found to significantly reduce pain and other fibromyalgia related symptoms subjectively (n=53) than the patients on standard care [34]. On contrary, Curtis and colleagues subjectively studied the effect of an eight-week Mindfulness Based Stress Reduction (MBSR) in 173 fibromyalgia patients; authors claim no improvement in pain and psychological symptoms like sleep problems, quality of life and cognition after intervening patients with 2.5 hours MBSR session (once a week) and 45 minutes home practice (5 sessions/week) [35]. Reductions in pain catastrophizing behaviour and pain inventory along with sleeplessness were noticed after six weeks of weekly 210 minutes yoga session (5 days home video practice) by another group too [36]. Twice a week gentle *Hatha* yoga was also found to reduce FM related symptoms [37]. Since, yoga can improve pain experience, it would be logical to assume that yoga might be acting, at least in part, to favourably modulate the perceptual control over pain.

Modern Treatment Strategies For Fibromyalgia Patients:
Transcutaneous Electrical Nerve Stimulation
Transcutaneous Electrical Nerve Stimulation (TENS) is an emerging technique to treat patients with various musculoskeletal problems. Four weeks of active TENS use showed a significant improvement in movement-evoked pain and other clinical outcomes of fibromyalgia syndrome as compared to sham analog [38]. Most vital advantage of TENS is its simultaneous application at different tender points for fatigue and pain relief with no side effects [18, 39]. Pain relief and inhibitory activity was also reported on quantitative electroencephalography after TENS for 20 minutes [40]. Another study demonstrated modest treatment effects of reduced disease impact, pain and functional impairment from wearable TENS in individuals with fibromyalgia. Patients with higher pain sensitivity exhibited larger treatment effects. Wearable TENS may be a safe treatment option for fibromyalgia patients [41]. TENS restores central inhibition in primary fibromyalgia and consequently reduces pain, fatigue, and hyperalgesia in the patients [42]. High-frequency TENS could be a potential adjuvant therapy for fibromyalgia patients for relieving pain, anxiety, fatigue, stiffness and in improving ability to work [43].

Biofeedback Techniques
Electromyography is a diagnostic tool to assess muscle activity but its application as restorative therapeutic intervention in fibromyalgia is recently reported by few authors [44]. EMG Biofeedback (BFB) is an established intervention in the rehabilitation of headache and other pain disorders but it showed no health status improvement fibromyalgia patients [45]. While other literature suggests that EMG biofeedback therapy could be a useful treatment modality to reduce pain of FM patients, along with improvements in quality of life, movement and number of tender points [46]. Although, there are paucity of literatures for EMG biofeedback but it is an emerging therapy to manage fibromyalgia syndrome; more clinical trials are required to recommend it for therapeutic use. Heart rate variability biofeedback may also be a useful treatment strategy for fibromyalgia, perhaps mediated by autonomic changes [47]. Hence, newer techniques such as heart rate variability biofeedback techniques also seem to be promising.

Vibration Therapy
Whole body vibration therapy is an emerging intervention for fibromyalgia; it has been shown to improve functional disability and pain sensitivity of fibromyalgia patients immediately after the therapy program; which was not maintained in the follow-ups [48]. Greater benefits were suggested with the use of rotational rather than vertical whole body vibration. The use of the rotational modality is recommended in the standard therapy program for patients with fibromyalgia [49]. Sonic wave vibration therapy can also lead to acute and chronic pain reduction and improves quality of life in patients with fibromyalgia [50]. Other non-nociceptive somatosensory stimulation like vibrotactile stimulation also has potential role in the symptomatic treatment of fibromyalgia patients [51].

Repetitive Transcranial Magnetic Stimulation
Fibromyalgia is a psychosomatic problem rather than a peripheral syndrome. So, non invasive brain stimulation could be a potential tool to restore sensory and motor aberrations using direct stimulation of the brain areas responsible for cortical plasticity in fibromyalgia. There is an increased cortical excitability of the fibromyalgia patients due to chronic pain condition [52-53]. Low frequency brain stimulation is a non invasive tool to treat patients with chronic pain conditions with minimal adverse effect. rTMS is also recommended by FDA for its use in treating patients with depression. Repetitive Transcranial Magnetic Stimulation (rTMS) for four weeks at dorsolateral prefrontal cortex was proved to improve pain and related symptoms of fibromyalgia when targeted [54-55]. Transcranial Direct Current Stimulation

(tDCS) can also result in significant pain relief in FM patients and may be an effective complementary treatment strategy [56]. High frequency rTMS can also have the similar effect like physical exercise in ameliorating pain, emotional status and related impact of women with fibromyalgia [57]. Hence, neuromodulation techniques are quiet safe and can be suggested for immediate relief in pain and related impact of fibromyalgia patients.

All the major treatment strategies along with details are systematically summarized in the Table 1.

Table 1: Evolution of treatment strategies for patients with fibromyalgia syndrome

Authors	Sample Size	Intervention	Duration	Inferences
McCain et al. 1988	FM = 38	Cardiovascular fitness training or Simple Flexibility exercises	20 Week (3 sessions/week)	Improvement in FM associated symptoms and psychological distress
Valim et al. 2003	FM = 76	Aerobic fitness training or Stretching exercises	20 Weeks	Exercises are beneficial to patients with FM
Babu et al. 2007	FM = 30	EMG Biofeedback	6 Days, 45 minutes	Biofeedback reduces pain in along with improvements in quality of life, movement and number of tender points in FM patients.
Etnier et al. 2009	FM = 16	Physical Activity program	18 Weeks (2 sessions/week)	Significant reduction in fatigue, depression and FM symptoms
Gusi et al. 2009	FM = 21	Tilt vibratory exercise	12 Weeks, 30 minutes daily (3 sessions/week)	Useful and feasible for improving dynamic balance in FM patients
Carson et al. 2011	FM = 53	Yoga program & Waitlist	8 Weeks (2 hours/week)	Significant reduction in FM symptoms
Rudrud et al. 2011	FM = 10	Gentle Hatha Yoga	8 Weeks (Twice/week)	Hatha yoga reduced FM related symptoms
Dailey et al. 2013	FM = 103	Transcutaneous Electrical Nerve Stimulation	4 Weeks (2 hours daily)	Active TENS use can significantly improve movement-evoked pain and other clinical outcomes of FM.
Avila et al. 2017	FM = 20	Hydrotherapy program	16 Weeks, 45 minutes (Twice/week)	Hydrotherapy was effective to improve quality of life, pain intensity and fibromyalgia impact
Lazaridou et al. 2019	FM = 36	Yoga Program	6 Weeks (weekly) Daily home video practice (5 days/week)	Improved pain and impact, Sleep Quality Improved
Pujol et al. 2019	FM = 77	Gentle vibrotactile stimulation	3Weeks (3hours at night)	Support a potential role for vibrotactile stimulation in the symptomatic treatment of fibromyalgia
Tanwar et al. 2020	FM = 90	Repetitive Transcranial Magnetic Stimulation at DLPFC	4 Weeks	Right DLPFC rTMS can significantly reduce pain and associated symptoms of FM
Mingorance et al. 2021	FM = 20	Rotational whole body vibration	12 weeks	Improvements in functional disability, static equilibrium and vibration sensitivity and a reduction of pain sensitivity.

FM – Fibromyalgia, EMG – Electromyography, DLPFC – Dorsolateral prefrontal cortex

Conclusion and Future Directions:

Although few FDA approved drugs are available to get symptomatic relief from fibromyalgia symptoms but there is no permanent cure of the disease. In past two decades some of the non invasive treatment strategies like lifestyle interventions such as medical yoga therapy, vibration therapy, and repetitive Transcranial Magnetic Stimulations are emerging and could have potential role in management of fibromyalgia syndrome to a certain extent. Clinical trials on non pharmacological treatment modalities are mainly focussed on assessing symptoms using subjective outcomes; there is also a need to incorporate objective assessment tools for better visualization of the effect of these interventions.

Conflict of Interest: There is no conflict of interest till date.

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