

FIBROMYALGIA: A COMPLEX PAIN PROBLEM

Fahim Anwar¹, S. Fahim²

ABSTRACT

Fibromyalgia is derived from Greek words, “fibro” meaning fibrous tissue, “myo” meaning muscle and “algos” meaning pain. It is characterized by widespread constant musculoskeletal pain and allodynia (heightened painful response to pressure on various body parts). Other associated symptoms include extreme fatigue, sleep disturbances, joint stiffness, bladder and bowel problems, swallowing problems, sensory and cognitive abnormalities. The article gives a review of the latest literature in the management of fibromyalgia.

Key Words: Fibromyalgia, Pain, Management.

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¹ Consultant in Rehabilitation and Pain Management

Stobhill Hospital, Glasgow,

United Kingdom

Email: fanwar10@gmail.com

² Glasgow, United Kingdom

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INTRODUCTION

Fibromyalgia is derived from Greek words, “fibro” meaning fibrous tissue, “myo” meaning muscle and “algos” meaning pain. It is a disorder characterized by widespread pain and a heightened painful response to pressure on various body parts labeled as tender points.¹ Pain is not the only symptoms of fibromyalgia, as various studies have confirmed the presence of various other symptoms like extreme fatigue, sleep disturbances and joint stiffness.² Other minor associated symptoms are bladder and bowel problems³, swallowing problems⁴, sensory⁵, cognitive⁶ abnormalities and Systemic Lupus Erythematosus.⁷

The incidence of fibromyalgia has been reported to be 2 to 4% of the population⁷ and females are more likely to be diagnosed than males with ratio of approximately 9:1.⁸ It is most commonly diagnosed between the ages of 20 and 50, though onset can occur in childhood.⁸

Research Strategy:

A literature search of the Pubmed, Medline and ScienceDirect was carried out using the terms “Fibromyalgia”, “Chronic Pain” and “Management” between November 2011 and March 2012. The articles that included these terms were scanned initially and included in the study if they included management of chronic pain in fibromyalgia patients.

Diagnosis:

Fibromyalgia has been considered as a diagnosis of exclusion. There is no single test that can diagnose fibromyalgia and the essential diagnostics criteria are still a subject of debate and controversy. The Multicenter Criteria Committee of the American College of Rheumatology in 1990 developed the widely used and popular classification criteria currently used in clinical practice. It was initially developed for use in research but now accepted as a useful diagnostic clinical tool. According to this criterion, fibromyalgia is diagnosed in the presence of the following:

1. A history of widespread pain lasting more than three months—affecting all four quadrants of the body, i.e., both sides, and above and below the waist.
2. Tender points—there are 18 designated possible tender points (although a person with the disorder may feel pain in other areas as well). The patient must feel pain at 11 or more of these points for fibromyalgia to be considered.

Wolfe et al⁹ in 2010 published new diagnostic criteria, which replaced tender points with a widespread pain index and symptom severity scale. This criterion retains that the symptoms must have been present for at least three or more months and any alternate diagnosis has been ruled out by various investigations. The widespread pain index score is determined by counting the number of areas on the body where the patient has felt pain during the last week. There are 19 areas where the pain can be felt so, the score ranges from 0 to 19. The symptom severity score, on the other hand, is determined by rating the severity of three common symptoms: fatigue, waking unrefreshed and cognitive symptoms (on a scale of zero to three). An additional three points can be added to account for the extent of additional symptoms such as numbness, dizziness, nausea, irritable bowel syndrome or depression. The final score is between 0 and 12. To diagnosis fibromyalgia a patient should have a widespread pain index of 7 or more and a symptom severity score of 5 or more

alternatively a widespread pain index of 3 to 6 pain areas and a symptom severity score of 9 or more.

Despite the clear diagnostic criterion, controversy still exists about the true nature of the fibromyalgia as a disease.^{10,11}

Aetiology:

The aetiology of the fibromyalgia is still unclear. Several hypotheses have been proposed. Ngian et al¹² suggested that it is caused by neurological abnormalities causing pain, cognitive abnormalities and psychological symptoms. The evidence from literature also suggests that there is increased risk of fibromyalgia in families, suggesting the role of genetic factors in the development of the disease.¹³ The association of fibromyalgia and stress and stress-related disorders like chronic fatigue syndrome, post-traumatic stress and irritable bowel syndrome is well documented in the literature¹⁴. A systematic review conducted by Häuser et al¹⁵ in 2011 found significant association between fibromyalgia and physical and sexual abuse in both childhood and adult life. Wood¹⁶ in 2004 proposed that the symptoms of fibromyalgia are mainly due to dopamine deficiency within the central nervous system. Holman¹⁷ further investigated this in a randomized, double blind, placebo-controlled trial of pramipexole (dopamine agonist) in patients with fibromyalgia and showed significant improvement in symptoms. The evidence regarding association between the fibromyalgia and depression is overwhelming.¹⁸

Management of Fibromyalgia:

Fibromyalgia presents a management challenge for treating pain management physicians, as there is no universally acceptable treatment/cure for this condition. The presentation of fibromyalgia is heterogeneous and the treatment approach is therefore tailored to the individual needs of the patient. Multidisciplinary team involvement is essential to achieve the goals of this individualized

rehabilitation programme. American Pain Society and European League Against Rheumatism¹⁹ (ELAR) have produced evidence-based guidelines for the treatment of fibromyalgia. The treatment options can be broadly divided into two approaches: pharmacological and non-pharmacological.

Pharmacological Approach:

Pregabalin (anticonvulsant) is the most evidence-based and widely used medication in fibromyalgia. Four published, randomized, placebo-controlled clinical trial showing the effectiveness of pregabalin.²⁰⁻²³ The results of these randomized controlled trials of pregabalin demonstrate that pregabalin reduces pain and improves other key symptom of fibromyalgia, such as sleep, and is associated with improvements in function, health-related quality of life, and global assessments. Crofford et al also found that number needed to treat for pregabalin is 6 when used in a dose of 450 mg/day for one patient to have a 50% reduction in pain.²¹

Gabapentin (anticonvulsant) has also been studied in a multicenter, randomized; placebo-controlled, 12-week mono-therapy trial.²⁴ The trial showed that mono-therapy with gabapentin 1,200 to 2,400 mg/day (3 times daily dosing), when taken for up to 12 weeks, significantly reduces pain and improves other important symptoms of fibromyalgia, including sleep, and is associated with improvements in functionality and global assessments. The decision to trial gabapentin or pregabalin first depends entirely on the individual patients keeping in view the low cost of gabapentin and the strong evidence of pregabalin for fibromyalgia.

Tricyclic antidepressants (TCAs) act by increasing serotonin and norepinephrine concentration by blocking their uptake. A meta-analysis published in Journal of American Medical Association in 2009 showed that TCAs significantly

improved pain, depression, fatigue and sleep in patients with fibromyalgia.²⁵ However, the TCAs side-effect profile is poor due to their interaction with adrenergic, cholinergic and histamine receptors. They should also be used with cautious in elderly and in the presence of ischemic heart disease.

Selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs), on the other hand, are tolerated generally well and have a low side-effect profile as compared to TCAs. SSRIs (fluoxetine, paroxetine and citalopram) have been studied in fibromyalgia but with very inconsistent results and therefore not recommended for use.²⁶ Venlafaxine (SNRI) although useful in management of neuropathic pain²⁷, was ineffective in the management of fibromyalgia in a randomized controlled trial.²⁸ Pooled results from two randomized, placebo-controlled trial showed duloxetine (SNRI) to be safe and efficacious for both the pain and functional impairment associated with fibromyalgia in female patients, while significantly improving quality of life.²⁹ Further clinical trial has shown duloxetine to be useful in other symptom domains of fibromyalgia³⁰. There is also sufficient evidence to recommend the use of milnacipran (SNRI) for fibromyalgia in treating both the pain and other symptoms associated with it.³¹

Opioids (except tramadol) use in fibromyalgia is a subject of debate and has proved to be controversial because of lack of efficacy data. The side-effects profile of opioids is very poor including abuse, dependence, addiction, constipation and opioid induced hyperalgesia. There is lack of randomized controlled trials for use of opioids in fibromyalgia. Intravenous administration of morphine in 9 patients with fibromyalgia did not reduce pain intensity in a small, double blind, and placebo-controlled study.³² A 4-year, nonrandomized study found that patients with fibromyalgia taking opioids did not report significant reduction in

pain at the 4-year follow-up, and experienced increased depression in the last 2 years of the study.³³ Opioids are therefore not recommended for use in fibromyalgia as their long-term use may worsen pain and have negative effect on mood and depression. Despite this, a survey of United States academic medical centers found that about 14% of patients with fibromyalgia were being treated with opioids.³⁴

Tramadol a centrally acting analgesic with atypical opioid and antidepressant-like activity is moderately effective in treating fibromyalgia pain, although the long-term efficacy is unknown.²⁸ A double blind crossover study compared tramadol with placebo in 12 patients with fibromyalgia.³⁵ Patients receiving tramadol reported 20.6% reduction in pain compared to placebo. A multicenter, double blind, randomized, placebo-controlled study examined the efficacy of a combination analgesic tablet containing tramadol (37.5 mg) and acetaminophen (325 mg) in 315 patients with fibromyalgia.³⁶ Patients taking tramadol and acetaminophen experienced an improvement in pain and physical function.

Cannabinoids are the subject of research in pain and have been studied in fibromyalgia. Skrabek et al³⁷ performed a double blind, randomized, placebo-controlled clinical trial to analyze the effects of nabilone on pain and quality of life in patients with fibromyalgia. After 4 weeks of treatment, patients who received nabilone ($n = 15$) experienced significant improvements in clinical pain, measured on a visual analog scale. Long-term data on efficacy and safety is not available.

There is weak evidence in literature regarding the use of dopamine D₃ receptor agonists³⁸ (pramipexole), centrally acting muscle relaxant³⁹ (tizanidine), and 5-HT receptor antagonist⁴⁰ (tropisetron) in fibromyalgia patients. There is currently no evidence that non-steroidal anti-inflammatory drugs⁴¹, steroids⁴² and NMDA receptor antagonists⁴³ are

effective in reducing pain and associated symptoms in fibromyalgia.

Non-Pharmacological Approaches:

The major non-pharmacological approaches for the management of fibromyalgia are cognitive behaviour therapy (CBT), physiotherapy and patient education. Cognitive behaviour therapy helps the patients improve the way they think about and cope with the diagnosis of fibromyalgia. The results of various clinical trials show that CBT is moderately effective.⁴⁴

The key to an exercise program in fibromyalgia is an individualized regimen that respects that patient's limitations. A patient who is in pain and poor condition may need to start at a very low level of exercise. Slow, steady progression is the key, as the micro tears in the muscle bundles take much longer to recover in fibromyalgia sufferers. There is strong evidence that exercise helps to improve fitness and sleep and may reduce pain and fatigue in patients with fibromyalgia.⁴⁵ Cardiovascular exercise is most beneficial in clinical studies for fibromyalgia symptoms.²⁸ Mannerkorpi et al⁴⁶ studies the aquatic based exercise programme for patients with fibromyalgia and found significant reduction in pain and fatigue. In a recent small single blinded randomized controlled trial, tai chi showed a relative benefit increase of 100% in fibromyalgia patients.⁴⁷

Education programmes explaining fibromyalgia and providing support are important therapeutic options. There is strong evidence that when patient education is combined with other management options, like exercise and self-management, it improves self-efficacy for coping with some symptoms of fibromyalgia.⁴⁸

The role of complementary therapy in the management of fibromyalgia had mixed results in literature. A systemic review of randomized clinical trials conducted by Mayhew in 2007 concluded

that acupuncture had the strongest evidence for efficacy and there was a moderate support for magnesium supplementation and massage therapy.⁴⁹ Another study evaluated the efficacy of mindfulness and Qigong movement therapy in 128 patients with fibromyalgia.⁵⁰ The authors found no significant difference between the groups in pain, tenderness, mood, walking or impact of fibromyalgia. The reason for mixed results for complementary therapy in literature is the lack of adequate controls in the clinical trials for these therapies.

CONCLUSION

Fibromyalgia is a disorder that present with various symptoms ranging from pain, fatigue, sleep disturbances, stiffness and mood disorders. Due to a lack of any specific underlying mechanism in fibromyalgia, the treatment is based on controlling the variety of symptoms. Multi-treatment approach, tailored to the individual needs of the patient, has the best chance of improving the symptoms and the functional outcome. The emotional disturbances, mood problems and sleep deprivation impact on perception and sensitivity and vulnerability to pain in fibromyalgia. A vicious circle exists between these and the pain and unless that vicious circle is broken, the outcome of managing pain does not improve in these patients.

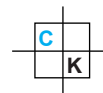
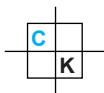
Clinical Message:

Fibromyalgia patients are the most difficult patients in chronic pain management clinics. Drug trials and intervention procedures often fails to resolve the symptoms. Self-management approach can help these patients to maintain quality of life. Multidisciplinary approach is usually required for proper management of fibromyalgia.

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CONFLICT OF INTEREST

Author declares no conflict of interest

GRANT SUPPORT AND FINANCIAL DISCLOSURE

NIL

KMJ web address: www.kmuj.kmu.edu.pkEmail address: kmuj@kmu.edu.pk