Fibromyalgia, It's Treatment, and What the Pharmacist Should Know

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Program Overview:

To provide nurses and pharmacists with an understanding of a pharmacist’s role in the management of fibromyalgia.

OBJECTIVES:

After completing this program, participants will be able to:

- Describe at least 3 unique characteristics of fibromyalgia
- Describe at least 3 symptoms and 3 physical signs of fibromyalgia
- Describe the importance of patient education in the management of fibromyalgia
- Describe at least 3 classes of medications used to treat fibromyalgia
- Describe at least 2 investigational classes of treatments for fibromyalgia
- Describe at least 3 nonpharmacological treatments for fibromyalgia
- Describe the prognosis of patients with fibromyalgia
- Describe a stepwise approach to managing fibromyalgia
Fibromyalgia, Its Treatment, and What the Pharmacist Should Know

Fibromyalgia, the second most common illness encountered by rheumatologists, is a chronic pain disorder characterized by diffuse musculoskeletal pain, generalized fatigue, increased palpation tenderness, emotional and psychological changes, and sleep disturbances/non-restorative sleep.\textsuperscript{1,2,3} Currently the American College of Rheumatology defines fibromyalgia as widespread pain for at least 3 months and point tenderness in at least 11 of 18 designated areas.\textsuperscript{4} It is estimated that between two and four percent of the general population is afflicted with this illness - the majority being females over the age of 50.\textsuperscript{2,5} Fibromyalgia is now considered the most common cause of generalized pain in women between 20 and 55 years of age.\textsuperscript{6}

Although the etiology of fibromyalgia is uncertain, most agree that the pathogenesis is multifactorial and due to biological and psychosocial factors.\textsuperscript{7} More specifically, many experts attribute fibromyalgia to altered pain processing, stress-response abnormalities, dysregulation of serotonin and norepinephrine systems, and dysfunction of the autonomic nervous system.\textsuperscript{8} Particularly alarming is that many patients diagnosed with fibromyalgia suffer from severe disability and a significantly reduced quality of life. In addition, fibromyalgia is responsible for enormous direct and indirect healthcare costs.\textsuperscript{9}

**Signs and Symptoms**

Prior to diagnosing and treating fibromyalgia, it is important for all healthcare providers, including pharmacists, to familiarize themselves with fibromyalgia’s clinical presentation. Traditionally fibromyalgia is described as presenting with widespread pain, multiple points of
tenderness, and fatigue. Pain, the cardinal symptom of fibromyalgia, is often described by patients as waxing and waning in severity and commonly intensified by unaccustomed exertion, sleep deprivation, psychological stress, cold exposure, surgery, and soft-tissue injuries. The pain is mostly localized in the axial skeleton, although it can also affect the extremities. It is also described as having a diurnal variation in intensity, with 11AM – 3PM usually being the lowest in severity. Patients commonly make statements like, "I feel as if I hurt all over", or "it feels as if I always have the flu" and they typically describe pain throughout their muscles and joints, although synovitis never presents on examination.\(^\text{10}\) Fatigue, another universal symptom commonly reported by fibromyalgia patients, is caused by sleep disturbance and deprivation. Classically patients report feeling unrefreshed upon awakening despite sleeping 8-10 hours the night before.\(^\text{11}\)

As more is revealed about this disease, additional signs and symptoms are being described such as debilitating morning stiffness, Irritable Bowel Syndrome (IBS), headache, psychological distress, and self-reported cognitive decline.\(^\text{2}\) Bjorkegren showed in his 138 patient-study that fibromyalgia patients self-reported on average 17.7 symptoms, which was significantly more than those reported by control subjects. Of these reported symptoms, many have been rarely described in the literature such as eye problems (64% reported), sweating (52.6%), and dizziness (56.2%).\(^\text{2}\) Cognitive dysfunction, often an underappreciated symptom, was investigated in 2006 by Glass et al. It was shown that many fibromyalgia patients report difficulty with memory, information processing, and performing complex tasks at work. Although the causes are unknown, some have attributed cognitive decline in fibromyalgia to dysfunctional pain centers in the brain from abnormalities in cerebral blood flow. During painful
stimulation in patients with fibromyalgia, functional brain imaging shows augmented responses in specific pain centers. Furthermore, reduced p300 amplitudes on ERP studies have been described in these patients, suggesting a reduction in cognitive effort.\textsuperscript{12}

Fibromyalgia is an extremely complicated illness characterized by a wide array of signs and symptoms. Healthcare providers involved in the management of patients with fibromyalgia must be comfortable identifying the clinical presentation of fibromyalgia in order to optimize health outcomes.

**Classification and Diagnostic Criteria**

In an attempt to standardize fibromyalgia patients for clinical trials, certain classification criteria have been proposed. In 1990 The American College of Rheumatology (ACR) published their Classification for Fibromyalgia, which is currently the most widely used classification system in clinical trials. It is important for healthcare providers to realize that ACR’s system is rarely used in clinical practice, and is instead used, almost exclusively, for research purposes. Briefly, the criteria published by ACR include:

1) Symptoms of widespread pain for \( \geq 3 \) months, both above and below the waist, and affecting both the right and left sides of the body
2) Tenderness on palpation of at least 11 of 18 tender points on physical examination\textsuperscript{13}

As previously stated, the ACR criteria are rarely used in clinical practice. Instead, the diagnosis of fibromyalgia is mostly based on symptoms of widespread pain which often include chronic myalgias and arthralgias. Of particular importance is that on physical exam there is no evidence of inflammation or synovitis and laboratory testing is unremarkable. The physical exam will often reveal multiple discrete locations of tenderness. Provided that all other
diagnoses have been excluded, fibromyalgia can be diagnosed in patients without 11 points of tenderness as long as they present with symptomatology that is suggestive of fibromyalgia.\textsuperscript{10}

The diagnosis of fibromyalgia cannot be made based on laboratory, imaging, or any other diagnostic study, as all of these tests yield negative results in patients with fibromyalgia. In order to rule out other conditions, laboratory studies to reflect inflammation, such as CBC, ESR, CRP, are commonly ordered during an initial evaluation. If a patient’s history is suggestive of an autoimmune illness such as Rheumatoid Arthritis, then serologic tests like antinuclear antibody and rheumatoid factor can be ordered.\textsuperscript{10}

Before diagnosing a patient with fibromyalgia, all clinicians should ask their patients specific questions to rule out primary sleep and mood disorders which are commonly associated or confused with fibromyalgia. Patients should be asked about sleep apnea symptoms and repetitive limb movements, and if present should be referred to a sleep medicine specialist.\textsuperscript{14} At least 1/3 of patients diagnosed with fibromyalgia have comorbid depressive and anxiety disorders, and as such clinicians must inquire about symptoms that could reflect these illnesses. Specifically, patients should be asked about appetite changes, decreased enthusiasm and excitement from activities that used to bring joy, and suicidal thoughts, as these could suggest a treatable underlying anxiety or depressive disorder.\textsuperscript{10}

In summary, diagnosing fibromyalgia is not a simple or straightforward process. There are numerous nuances that healthcare providers must be aware of in order to arrive at an accurate diagnosis.

\textbf{Treatment – Education}
The importance of educating patients with chronic illnesses has long been appreciated by health care professionals. This is especially true for fibromyalgia since symptom management is the only treatment strategy currently available. Education should focus on a few critical areas. First, patients must be assured that fibromyalgia is a real disease, and not a fictitious condition that is just “in their head.” There is a large amount of evidence that simply carrying a diagnosis of fibromyalgia is therapeutic to the patient, the patient’s family, and society as a whole. For example, in a 2006 study Hughes, et al. showed that patients diagnosed with fibromyalgia receive less diagnostic studies and referrals than those patients without a diagnosis. Another study found that those with a diagnosis were prescribed fewer medications than their counterparts. Next, it is important to stress the benign nature of the disease. Patients need to be made aware that this is not a deforming condition that causes cosmetic problem, or one that is life threatening. Moreover, heightened pain responses from neurohormones, fatigue, sleep disturbances, and mood disruptions should be discussed, as this will allow patients to understand the rationale behind antidepressant treatments, should they be indicated. In order to entice patients to incorporate aerobic exercise and physical therapy regimens into their daily routine, healthcare providers should discuss the sluggish blood flow to muscles and the muscle spasms that are often involved in fibromyalgia. In addition, simple relaxation techniques and stress reduction programs can benefit these patients, and therefore patients should be educated about the importance of addressing depression, sleep disturbances, and symptoms of stress or anxiety. Furthermore, patients must understand the waxing and waning nature of fibromyalgia symptoms, although pain and fatigue oftentimes persist. Finally, clinicians should stress the high likelihood that patients will experience active and healthy lives despite having this chronic illness.
Education by itself has been proven to have a therapeutic effect for those with fibromyalgia. For example, a 2004 educational intervention study that utilized small group sessions, printed materials, lectures, and demonstrations to inform patients about fibromyalgia showed that those receiving the intervention had significantly more improvement than the controls, with beneficial effects lasting three to twelve months. Another study that investigated a 1.5 day multidisciplinary educational program showed that patients completing this program had significantly less pain and self-reported improvement in anxiety, stiffness, fatigue, and mood.

Patients with fibromyalgia are frequently misinformed about their illness. It is of utmost importance for healthcare professionals to educate their patients so that these misconceptions are alleviated and management is optimized.

**Treatment – Pharmacological**

The vast majority of treatments available to fibromyalgia patients involve medications. By far, the most consistently effective class of medications has been antidepressants such as Tricyclic antidepressants, SSRIs, and SNRIs.

Tricyclic antidepressants such as amitriptyline are most commonly used as an initial treatment in patients with fibromyalgia refractory to nonpharmacologic treatment. Many studies have shown that up to 45 percent of patients receiving these medications report improvement. For example, a 2008 meta-analysis showed that Amitriptyline 25-50 mg/day reduced pain, fatigue, and depressiveness, while improving sleep and quality of life, in patients with fibromyalgia. An additional meta-analysis showed amitriptyline to be superior to other
antidepressants in reduction of pain, sleep disturbances, and limitations in quality of life.\textsuperscript{20} The current recommendation is to use amitriptyline 25 – 50 mg at bedtime. Although these are smaller doses than those used to treat depression, adverse effects such as dry mouth, constipation, fluid retention, weight gain, groginess, and difficulty concentrating are commonly reported.\textsuperscript{9,20}

Cyclobenzaprine, a muscle relaxant that affects muscle tension, has been used in as many as 12\% of fibromyalgia patients.\textsuperscript{3} A 2004 meta-analysis investigated five randomized control trials and reported that those receiving cyclobenzaprine were three times as likely to self-report overall improvement. These patients also reported moderate reductions in pain, sleep, and other individual symptoms.\textsuperscript{3} Moldofsky, et al. showed in an eight-week, 36 patient randomized trial, that extremely low-dose cyclobenzaprine (1 – 4 mg at bedtime) significantly improved pain, fatigue, and depression more than control subjects who did not receive the medication. The authors were also able to show improved sleep patterns on electroencephalography, and postulated that improvements in sleep might be a surrogate marker for treatment efficacy.\textsuperscript{21}

Another class of antidepressants that have been frequently used to treat fibromyalgia is dual reuptake inhibitors (SNRIs) like duloxetine, milnacipran, and venlafaxine. Since noradrenergic and serotonergic neurons are involved in pain inhibitory pathways that have been implicated in the pathogenesis of fibromyalgia, SNRIs are theoretically therapeutic. Duloxetine is a potent SNRI that has a similar affinity for both 5-HT and NE reuptake inhibition. A unique characteristic of duloxetine is that it lacks affinity for many other receptors such as muscarinic, histamine 1, 1-adrenergic, dopamine, 5-HT1A, 5-HT1B, 5-HT1D, 5-HT2A, 5-HT2C, and opioid receptors.\textsuperscript{22} In 2004 Arnold, et al. conducted an RCT that compared duloxetine to placebo
and showed that patients receiving duloxetine improved significantly more on the FIQ (Fibromyalgia Impact Questionnaire) than the subjects receiving placebo. In addition, the treatment group experienced significant reductions in Brief Pain Inventory average pain severity score, Brief Pain Inventory average interference from pain score, number of tender points, and FIQ stiffness score. They also had significantly greater improvement in mean tender point pain threshold, CGI-Severity, PGI-Improvement, and several quality-of-life measures.23 Another study investigating duloxetine sought to determine a longer term benefit than the one performed by Arnold, et al. In this six-month multicenter, randomized, double-blind placebo-controlled trial, 520 patients were randomized to daily duloxetine doses of 60mg, 120mg, or placebo. Those receiving duloxetine experienced a reduction in pain severity and mental fatigue within the first week of therapy along with improved global assessments at three and six months. The most common side effects were minor nausea, headache, and dry mouth, which usually presented within the first three months of initiation.24

Another SNRI that has been extensively studied is milnacipran. Milnacipran differs from duloxetine in that it has a three times greater affinity for norepinephrine than serotonin. Much like duloxetine, milnacipran has an extremely favorable safety profile because of its low affinity for muscarinic and histamine receptors. In a 12-week RCT of 125 patients, those receiving milnacipran had statistically significant pain relief and improvements in fatigue compared to those receiving placebo.25,26 In a larger RCT, 1196 patients receiving milnacipran 200mg/day showed statistically significant improvements in pain, fatigue, cognition, and multiple SF-36 domains. The only adverse effects reported from these studies were minor nausea, headache and constipation.27
Many researchers have sought to compare the efficacy of amitriptyline, duloxetine, and milnacipran in patients with fibromyalgia. A meta-analysis by Hauser, et al. sought to compare the efficacy of these three medications using symptom reduction (pain, fatigue, sleep disturbance and reduced health-related quality of life (HRQOL)) and acceptability as outcome measures. Their results showed amitriptyline to have a significant effect on pain, fatigue and sleep, but not on HRQOL. Duloxetine had a significant effect on pain, sleep, and HRQOL, but not on fatigue, while milnacipran had significant effects on pain, fatigue, and HRQOL, but not on sleep. When the medications were compared head-to-head, amitriptyline was superior to duloxetine and milnacipran in reduction of pain, sleep disturbances, fatigue and limitations of HRQOL. Duloxetine was superior to milnacipran in reducing pain, sleep disturbances and limitations of HRQOL. Milnacipran was superior to duloxetine in reducing fatigue. Amitriptyline was superior to duloxetine and milnacipran in 30% pain reduction. There were no significant differences in the drop-out rates (acceptability) between these three medications. The authors were able to conclude that their results support numerous guidelines that recommend amitriptyline to be the first pharmacological option for patients with fibromyalgia.²⁸

In addition to tricyclic antidepressants and SNRIs, SSRIs is another class of antidepressants that have been widely studied. Fluoxetine 80 mg/day was investigated in sixty female patients with fibromyalgia and was found to significantly improve patients’ pain score as evidenced by improvements in the Fibromyalgia Impact Questionnaire. These patients also showed improvements in fatigue and depression. The authors concluded that fluoxetine was effective at improving some symptoms in women with fibromyalgia.²⁹ In stark contrast to this
study, Wolfe, et al. showed that fibromyalgia patients receiving fluoxetine 20mg/day did not have any statistically significant improvements in their symptoms when compared to placebo.29

Paroxetine is another commonly used SSRI that has been studied extensively in fibromyalgia patients. In a very large study of 116 patients, an increasing dose of a continuous release formulation of paroxetine (12.5 mg/day to 62.5 mg/day) was compared with placebo. Those patients receiving paroxetine were more likely to achieve a ≥25 percent improvement in FIQ score (57 versus 33 percent) when compared to those receiving placebo, and this difference was statistically significant. The authors were not able to, however, show a statistically significant difference in secondary outcome measures such as pain, tender points, and disability.8

Another class of medications that have been investigated in fibromyalgia patients is NSAIDs. Since fibromyalgia is not a disease associated with inflammation, it is not surprising that the majority of the literature has failed to find any therapeutic benefits in fibromyalgia patients treated with NSAIDs. For example, patients treated with naproxen, ibuprofen, and prednisone did not show statistically significant improvement in any of their symptoms compared to those that received placebo. There are a few studies suggesting NSAIDs may have some benefit when used synergistically with certain antidepressants and anticonvulsants, but this evidence remains inconclusive.10

Certain analgesic medications have been shown to show some benefit in fibromyalgia, with tramadol being the analgesic most widely studied. Tramadol is unique in its mechanism of action, which includes mu-opioid activity and inhibition of serotonin/norepinephrine reuptake. In a 91-day, 315-subject study, those patients that received a tramadol/acetaminophen
combination (75mg tramadol/650mg acetaminophen, 4 times per day) had significantly less pain, along with improvements in physical functioning and health transition indexes. The study group was significantly more likely to have an improvement in pain of at least 50% than the control group (35% versus 18% placebo). Furthermore, there was no significant difference in discontinuation due to adverse effects between those receiving the tramadol/acetaminophen combination and those receiving placebo.³⁰

Anticonvulsants such as pregabalin and gabapentin have been shown to have analgesic effects by affecting specific calcium channels and the release of certain neurotransmitters. A recent meta-analysis of 2,918 patients that investigated these medications showed pregabalin and gabapentin to significantly reduce pain, improve sleep, and quality of life. In a randomized trial that investigated pregabalin, it was shown that 450mg/day significantly reduced pain while also improving sleep, fatigue, and quality of life.³¹ Another trial showed significant benefits in pain, fatigue, and quality of life for those receiving pregabalin 450mg/day and 600mg/day, although there was no difference in benefit between these two doses. The authors did show increased dizziness and nausea in the higher dose group.³² Currently, the recommendation is to begin pregabalin with a small nighttime dose of (25-30mg) that is then titrated to 300 or 450 mg/day.³⁴ Gabapentin’s safety and efficacy in fibromyalgia has been studied in a 12-week, 150 patient randomized trial where gabapentin (1200-2400mg/day) was shown to significantly reduce pain when compared to those that received placebo. Gabapentin was well-tolerated and only minor adverse effects such as nausea, lightheadedness, weight gain, and dizziness were seen.³³ Currently, the recommendation is to begin gabapentin with a small nighttime dose of 100mg that is then titrated to 1200-2400 mg/day.³⁴
In addition to the medications previously mentioned, many investigational pharmacological treatments have been studied. Pramipexole, a dopamine agonist, was shown to significantly improve pain when compared to placebo. Nabilone, a synthetic cannabinoid, and sodium oxybate, a synthetic preparation of gamma hydroxybutyrate (GHB), have shown some benefit for pain and sleep, although no firm conclusion can be drawn from the studies to date.

Fibromyalgia is a chronic illness characterized by debilitating physical, mental, and emotional symptoms. Fortunately, numerous medications exist that have proven benefit in managing these symptoms. The exact medication regimen that is used must be individualized to each patient’s history, physical exam, and symptomatology.

**Treatment – Nonpharmacological**

Although numerous pharmacological treatments have shown efficacy in managing fibromyalgia symptoms, most evidence suggests that nonpharmacological interventions may be just as effective. It is important for healthcare providers to familiarize themselves with these therapies as they often negate the need for medications.

The most widely studied nonpharmacological intervention with proven efficacy is a regimented aerobic exercise routine. Many patients with fibromyalgia have been shown to have cardio-pulmonary levels far below average due to a sedentary lifestyle. These patients are often debilitated by pain and depression that prevents them from having an active lifestyle. A 2008 meta-analysis investigated the efficacy of many exercise interventions. The meta-analysis of 2,276 patients showed that aerobic-only exercise had significant effects in global well-being,
physical function, pain, and tender points. In addition, strength training, although insufficiently evaluated, showed trends toward significant benefits in fibromyalgia symptoms.\textsuperscript{37}

As previously stated, fibromyalgia patients are oftentimes compromised in their ability to exercise as a result of their disabling symptoms. Therefore, it is imperative that healthcare providers recommend a gradual adoption of exercise that includes low impact activities such as brisk walking, biking, swimming, and water aerobics, for which exercise physiologists and physical therapist can provide invaluable direction.\textsuperscript{38}

Psychological therapies, in addition to exercise, are effective nonpharmacological treatments in patients with fibromyalgia. Of the wide variety of therapies, Cognitive Behavioral Therapy (CBT) has been the most widely studied with the most proven benefit. Patients with fibromyalgia can be plagued with abnormal thinking patterns such as pain-catastrophization and depressive thinking. The goal of CBT is to change these disordered thinking patterns by modifying one’s behavior. A meta-analysis by Glombiewski, et al. that studied 1396 patients showed CBT to be superior to other psychological therapies for short-term fibromyalgia pain intensity reduction. Additionally, CBT was more effective than other psychological treatments in reducing sleep problems. Finally, CBT was shown to have proven efficacy in treating depression in fibromyalgia patients.\textsuperscript{39}

Other nonpharmacological interventions that have received attention are tai-chi, acupuncture, and stress-reduction programs. Tai chi is a mind–body practice that originated as a martial art that combines meditation with gentle and graceful motions along with deep breathing and relaxation. Tai chi’s goal is to move vital energy throughout the body. Tai Chi is an
intervention that combines physical, psychosocial, emotional, spiritual, and behavioral elements. Since fibromyalgia has, both mind and body attributes, tai chi could theoretically benefit patients with fibromyalgia. For example, in a 66-patient randomized control trial patients engaging in tai-chi (one-hour sessions twice weekly) had significant improvement in FIQ scores when compared to a control group (wellness education and stretching) after 12 weeks of the intervention. These patients maintained their improved scores at 24 weeks, and no adverse effects were reported. The authors concluded that the results are promising, but merit longer term follow-up investigations.40

Another suggested nonpharmacological intervention for fibromyalgia is mindfulness-based stress reduction (MBSR) programs, which are 8-week group programs that use mindfulness meditation techniques and yoga exercises. MBSR’s goal is to have participants develop nonjudgmental awareness of experiences in the moment within a context of openness, kindness, tolerance, and acceptance of perceptible sensory, mental, and emotional phenomena. Although in theory MBSR programs would be effective, the evidence does not suggest this. For example, a 3-armed randomized trial studied MBSR in 177 female patients with fibromyalgia with the major outcome being Health Related Quality of Life (HRQoL). Those that were engaged in an MBSR program had a statistically significant short-term improvement in HRQoL, but this benefit vanished after two months. The authors concluded that MBSR may have some short-term benefit in patients with fibromyalgia, but more research is needed to elucidate any long-term benefit.41

Acupuncture is another nonpharmacological intervention that has been the focus of study. Martin, et al. was able to show a large improvement in pain for those patients receiving
acupuncture when compared to control subjects. However, this improvement did not reach statistical significance likely due to a small sample size.\textsuperscript{42} In 2010 Langhorst, et al. conducted a systematic review and meta-analysis of 385 patients receiving acupuncture in 7 randomized control trials. The authors did discover some improvement in pain, but this improvement did not reach statistical significance and disappeared at the latest follow-up. There was also no reported improvement in fatigue or sleep disturbance.\textsuperscript{43}

Numerous nonpharmacological interventions can improve symptoms in fibromyalgia patients. Of these, aerobic exercise and CBT show the strongest evidence for benefit. The evidence for acupuncture, tai-chi, and stress-reduction programs are currently only suggestive.

**Prognosis**

The prognosis for most patients with fibromyalgia is unfortunately suboptimal, with the majority of patients continuing to experience chronic pain and fatigue indefinitely. In a 538 patient-study pain, fatigue, sleep disturbances, and depression were essentially unchanged after eight years of follow-up.\textsuperscript{44}

Specific psychological factors have been shown to have prognostic significance in fibromyalgia patients and these include:

- An increased sense of control over pain
- A belief that one is not disabled
- That pain is not a sign of damage

The behaviors with a favorable prognostic effect are:
• Seeking help from others
• Decreased guarding during examination
• Exercising more
• Pacing activities

Patients exhibiting these factors and behaviors had statistically significant improvements in numerous fibromyalgia outcome measures. The patients that had poor outcomes were more likely to “catastrophize” their pain than those with better outcomes.\textsuperscript{45}

Although no studies to date have shown an increased mortality rate in those with fibromyalgia, some have attributed fibromyalgia to serious health conditions. For example, patients with fibromyalgia were shown to have increased risk of cerebrovascular disease, liver cirrhosis, and biliary tract disease.\textsuperscript{46} Fibromyalgia has even been associated with higher suicide risks.\textsuperscript{47,48}

Fibromyalgia is a chronic relentless disease that carries a poor prognosis when untreated. It is crucial for patients to receive the appropriate treatments to improve their chances for a normal and healthy life.

\textbf{Current Guidelines, Recommendations, and a Stepwise Approach}

It is important to emphasize that fibromyalgia is a complicated pain disorder that is difficult to treat. Since there are numerous treatment options available to fibromyalgia patients, it is important to lay out a simple and understandable approach to management. A recommended stepwise approach should begin by confirming the diagnosis (diagnosis of exclusion) and offering an explanation that emphasizes the chronic but nonprogressive nature of fibromyalgia. If concomitant disorders exist such as depression, restless legs syndrome, sleep apnea, bursitis and
tendonitis, these should be managed appropriately. Next, if pharmacological treatments are indicated they should be chosen based on the strength of evidence-based guidelines. Patients may be started on either a low dose of amitriptyline (or another tricyclic antidepressant) or cyclobenzaprine at nighttime while using simple analgesics as needed during the day. Pregabalin, duloxetine, and milnacipran are also available but these should be prescribed on an individualized basis, and usually after other therapies have failed. Over-the-counter NSAIDs are not recommended unless combined with certain drugs with CNS activity. Tramadol can be added in select cases for pain relief, although potential abuse and addiction issues must be appreciated.\textsuperscript{10,49}

In addition to medications, certain nonpharmacological interventions should be recommended. Low-impact aerobic activities such as walking, biking, swimming, or water aerobic exercises should be individualized and initiated once a diagnosis of fibromyalgia has been made. Combined with an ongoing exercise program, a referral for cognitive behavioral therapist is appropriate and is an invaluable treatment option when combined with aerobic exercise.\textsuperscript{34}

For those fibromyalgia patients unresponsive to the above interventions, referral to a rheumatologist or other specialist is warranted to confirm the diagnosis and provide additional treatment advice. It is likely that multidisciplinary therapy is most useful in this select patient population.\textsuperscript{34}

**Conclusion**

Fibromyalgia is a chronic disease characterized by widespread pain, fatigue, sleep disturbances, and depression. Patients unfortunate enough to carry this diagnosis are more likely
to experience disability and a diminished quality of life. Fortunately, numerous treatment options exist for these patients that include education, medications, psychological treatments, exercise programs, and other investigational approaches. Each treatment has its own advantages and disadvantages, and should be individually tailored to each patient. By doing so, patients can have an excellent chance to live normal and healthy lives.
References