INTRODUCTION
Fibromyalgia syndrome (FMS) is a syndrome characterized by waxing and waning widespread musculoskeletal pain, muscle stiffness, fatigue and sleep disturbance, all of which result in functional impairment without an identifiable cause. The US prevalence is 2%, with a female predominance [18]. FMS incidence increases with age; it has been found to be as high as 7% between 60–79 years [16]. Its peak onset is between 30–50 years of age [14, 19]. Given the high prevalence of multiple morbidities in older adults, many of which share symptoms with FMS, diagnosis can be challenging. Co-morbidities (COPD, CHF, renal insufficiency, anemia, mood disorders, dementia, rheumatologic diseases, osteoporosis, malnutrition) often interact with, precipitate or exacerbate FMS. Therapeutic options are limited, not only due to medication side effects but also due to impaired patient function, which may prevent participation in non-pharmacologic interventions, such as aerobic exercise or cognitive behavioral therapy.

In elderly patients, FMS is usually diagnosed after multiple medical visits and costly diagnostic testing. The etiology is not known, but there are several theories concerning the cause of FMS, including abnormalities in pain processing and neurotransmitter release (low serotonin, elevated substance P) that provoke increased perception of pain, often with non-painful stimuli. Additional theories on its origin include muscle disease, stage 4 non-rapid eye movement sleep disorders and psychological factors [14]. The revision to the 1990 classification criteria by The American College of Rheumatology in 2010 incorporated a new case definition that includes widespread pain and symptoms of fatigue, waking up unrefreshed, cognitive complaints and somatic symptoms. These revisions were implemented to improve the clinical diagnosis of FMS, emphasizing that the old criterion of 11 out of 18 tender points is no longer necessary.

SS takes into consideration the degree of unrefreshed sleeping, fatigue and impaired cognition of the patient. Each of these three symptoms is scored from 0–3, depending on the severity over the past week. (0: no problem, 1: mild, 2: moderate 3: severe). The SS also factors in the extent (severity) of general somatic symptoms, e.g., muscle pain, irritable bowel syndrome, weakness, headache, cramps, blurred vision, dry eyes, hives. (0: no symptoms, 1: few symptoms, 2: moderate symptoms, 3: many symptoms).

SS is the sum of the severity of the three symptoms (fatigue, unrefreshed sleep and cognitive symptoms) plus the extent (severity) of somatic symptoms in general. The final score ranges from 0–12.

APPROACHES TO TREATMENT
IN THE ELDERLY PATIENT
To properly manage FMS, focus should be on predisposing and precipitating factors, prevalent symptoms and patient preferences. Research on the effectiveness of treatment of FMS is limited, and optimal treatment for elders remains unknown. Multiple review articles recommend a stepwise approach, combining pharmacological and non-pharmacological interventions. Since the etiology remains unclear, therapy is focused on the treatment of symptoms. Knowing precipitating factors and how to avoid them becomes all-important in the prevention of flares. Some known triggers include emotional stress, cold weather, illness and exertion.

Elderly patients may find it challenging to adhere to exercise or physical medicine and rehabilitation (PM&R). Additionally, for many it proves difficult to tolerate pharmacological intervention due to various side effects or a lack of efficacy. Because of these obstacles, a shared understanding of the goals of treatment by both patient and physician is crucial. Treatment targets include underlying causes, symptom management and activities of daily living (ADLs), knowing that not all symptoms can be eliminated. Patients also need to monitor symptoms and report them. Intact cognitive function is essential; when impaired, management becomes more challenging.

Currently 3 medications are FDA-approved for the treatment of FMS; duloxetine, pregabalin and milnacipran [9]. In
addition, multiple other medications and non-pharmacological interventions have been studied, the extent and rigor of evidence varies widely, and some should be avoided or used with caution in the treatment of elders.

**FDA-APPROVED MEDICATIONS**

A comparative analysis was done in 2010 of the three medications approved by the FDA for FMS; subjects were 30–50 years of age [9]. The author presented comparative data on the short-term [6-month] efficacy and harms of duloxetine, milnacipran, and pregabalin in FMS [9]. Among the 3 medications, there were no differences in pain control or dropout rate due to side effects. If depression was the predominant symptom, duloxetine showed the best response. If fatigue was predominant, milnacipran or pregabalin were better choices. In this analysis, milnacipran did not have any effect on sleep, duloxetine did not affect fatigue, and pregabalin did not affect depressive symptoms [9]. When choosing these medications for elderly patients, slow titration should be used to reach the minimum effective dose.

**PHARMACOLOGICAL INTERVENTION**

It is of great importance to take the minimum effective dose because of the wide profile of side effects that accompany many of the medications given to ameliorate the symptoms of FMS. The Beers Criteria for Potentially Inappropriate Medication in Older Adults is particularly useful, as the long-term results and applications of these medications for the elderly FMS patient remain unknown. In some cases, the side effects outweigh the therapeutic benefit, e.g.: NSAIDs.

The administration of tramadol with acetaminophen, taken at average doses of 151 mg/d and 1238 mg/d respectively, has been shown to be effective in treatment for some of the pain associated with FMS [3]. Analgesics can be very beneficial initially, as we introduce other interventions to the management of symptoms; however, long-term use of pain medications is rarely a good solution, especially in an older population.

Tramadol may increase the risk of seizure when combined with other drugs for FMS, and may increase the risk of serotonin syndrome when administered with SSRIs or SNRIs [14]. SSRIs and SNRIs alone have been shown to be effective not only in treating the depressive symptoms of FMS, but also other symptoms as well.

Although no SSRI is FDA-approved for the treatment of FMS, citalopram, paroxetine, and fluoxetine have been shown to have therapeutic effects in non-depressed patients but the mean age of subjects in the following studies was only 50. Citalopram in doses of 20–40 mg/d improved well-being, without affecting other symptoms over a 4-month follow-up [1]. In elders, no more than 20 mg/d is recommended because of risk of QT prolongation per FDA Drug Safety Communication. Paroxetine, administered at a mean dose of 40 mg/d, was found useful in treating FMS symptoms in a randomized trial [12]. Fluoxetine has also been shown to be beneficial in the treatment of all aspects of FMS in multiple studies, with dosages ranging from 20–50 mg/d. Duloxetine and milnacipran are SNRIs that are FDA-approved for use in FMS. Duloxetine was approved on the basis of its ability to reduce

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**Table 1. Medications used in Fibromyalgia Syndrome**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Recommended dose</th>
<th>Comments</th>
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<tbody>
<tr>
<td>Anti-epileptics</td>
<td></td>
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</tr>
<tr>
<td>Gabapentin</td>
<td>100-600 mg daily</td>
<td>Target symptoms: Fatigue and pain. Titrate slowly. May cause sedation and dizziness. Dose should be adjusted for renal failure.</td>
</tr>
<tr>
<td></td>
<td>Max dose 1800 mg daily</td>
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</tr>
<tr>
<td>Pregabalin</td>
<td>150-300 mg daily</td>
<td>Target symptoms: Pain, fatigue and sleep. Sedation and confusion. Avoid in narrow angle glaucoma. Recommend baseline EKG and avoid if QT prolongation.</td>
</tr>
<tr>
<td></td>
<td>Max dose 450 mg daily</td>
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<tr>
<td>Tricyclic antidepressants (TCA)*</td>
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<tr>
<td>Nortriptyline</td>
<td>10-50 mg nightly</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Target symptoms: Pain, fatigue and sleep. Sedation and confusion. Avoid in narrow angle glaucoma. Recommend baseline EKG and avoid if QT prolongation.</td>
</tr>
<tr>
<td>Serotonin reuptake inhibitors (SSRIs)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>5-60 mg daily</td>
<td>Target symptoms: Depression. Better tolerability than TCA.</td>
</tr>
<tr>
<td>Citalopram</td>
<td>10-20 mg daily</td>
<td>Insomnia. Hyponatremia. Fluoxetine has long half life.</td>
</tr>
<tr>
<td>Serotonin norepinephrine reuptake inhibitors (SNRI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>25-100 mg daily</td>
<td>Target symptoms: Depression and pain. Avoid in those with uncontrolled hypertension, liver disease and open angle glaucoma.</td>
</tr>
<tr>
<td>Duloxetine</td>
<td>30-60 mg daily</td>
<td></td>
</tr>
<tr>
<td>Milnacipran</td>
<td>25-200 mg daily</td>
<td>Target symptoms: Fatigue and pain. Contraindicated with monoamine oxidase inhibitors and open angle glaucoma.</td>
</tr>
<tr>
<td>Analgesics</td>
<td></td>
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</tr>
<tr>
<td>Tramadol</td>
<td>25-50 mg every 6 hrs as needed</td>
<td>Target symptoms: Pain. May cause sedation and confusion. Avoid in patients with seizures. May cause serotonin syndrome in combination with SSRI or other antidepressants. Dose adjustment for renal failure.</td>
</tr>
<tr>
<td>Muscle relaxants*</td>
<td></td>
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</tr>
<tr>
<td>Cyclobenzaprine</td>
<td>5-10 mg nightly</td>
<td>Target symptoms: Pain, sleep and mood. Sedation. Similar side effects to TCA.</td>
</tr>
</tbody>
</table>

pain, fatigue, and depression. Recent studies have found that it is no more effective when administered at 120 mg/d compared to 60 mg/d [6]. It has a higher incidence of nausea and headache than the other two approved medications [9, 10]. Milnacipran, approved for its efficacy in improving pain, fatigue, and sleep quality, does not appear to have such limiting side effects. Twice-daily dosage is superior for pain control, and can be titrated up to a total of 200 mg/d. Two of three randomized, controlled trials showed improvement in cognition. Pain and fatigue improvements were seen within one week in responders to milnacipran. Milnacipran has no effect on depressive symptoms [2, 7, 14]. Nortriptyline, a tricyclic antidepressant (TCA), has been minimally studied but 10–30 mg/d before bedtime is a safer option for the elderly when compared to other TCAs; of note, nortriptyline is a prominent potentially inappropriate medication according to the Beers Criteria [5, 10].

NOTE: A 2012 systematic review and meta-analysis of the role of antidepressants in the treatment of FMS noted that although a small number of patients experienced substantial symptom relief, the majority of patients experienced intolerable adverse effects and only modest relief of symptoms. The conclusion was that physicians and patients should be realistic about the potential benefits of antidepressants in FMS [10].

Anticonvulsants are another class of drugs that have some utility in the improvement of symptoms of FMS in the elderly, although little research has been done in an older population [8]. Gabapentin was shown in a 2007 randomized, double-blind, placebo-controlled trial to be useful in the treatment of pain and improved sleep and quality of life. Higher doses produced excess adverse effects, especially in older adults [8, 16]. Pregabalin, unlike gabapentin, is FDA-approved for FMS and has more data supporting its use. A recent meta-analysis that included 5 RCTs showed that doses ranging from 150–600 mg/d were effective in improving pain, sleep, and quality of life. Like gabapentin, higher doses result in more adverse effects in older adults – accordingly, the dose should be titrated slowly to the minimum effective dose [8, 16].

For patients struggling with side effects and contraindications, a low dose [1–4 mg/d] of cyclobenzaprine, although not FDA-approved, has been shown in clinical trials to cause significant improvements in pain, and depressive symptoms, without limiting side effects [5, 17]. In older adults, a low starting dose of 1–5 mg/d is recommended. In general however, muscle relaxants should be used as a last resort for the management of FMS symptoms in elderly patients, in accordance with the Beers Criteria. A 2004 meta-analysis showed that there were no improvements in fatigue or tenderness in studies that used doses of 10–30 mg/d; however, tenderness has been shown to improve with administration of 1–4 mg/d [5, 17]. Lower dosages have been shown to be beneficial, and have fewer side effects. Along with these improvements comes increased nights of restorative sleep [17].

NON-PHARMACOLOGICAL APPROACHES TO TREATMENT

Patient Education

Patient education is paramount in the control of FMS symptoms, beginning by acknowledging the disease and learning about its complexity. Clinicians need to work closely with patients to establish goals of treatment, and to encourage patients to report changes in symptoms [4, 14].

Exercise

Multiple studies and systematic reviews demonstrate that supervised, paced aerobic exercises have positive effects on global well-being and physical function, and possibly on pain and tender points. Gradual increase in exercise intensity prevents exacerbation of the pain that ultimately could lead to patient non-adherence to the program or acute worsening of symptoms [16, 17]. Water-based exercise programs have also been shown to be helpful in improving tender points and sleep quality [4, 11].

Cognitive Behavioral Therapy (CBT)

In most studies, CBT improved pain-related behavior, self-efficacy, coping strategies and overall physical function, and are most effective when combined with comprehensive programs. There was no evidence in subjects above 50 years of age [7, 13, 15].

Multi-component intervention and Multidisciplinary Approach

A 2009 meta-analysis of 9 randomized controlled clinical trials that met the inclusion criterion of utilizing at least two non-pharmacological therapies [educational or psychological interventions and at least one exercise program], showed that multi-component therapy could effectively reduce pain, fatigue and depressed mood. It also showed that efficacy declines over time; long-term effects are inconclusive [7]. This major analysis, like every study noted above, may not be relevant to older adults as subject age was 30–50 years. Unfortunately, a non-pharmacological approach, including multi-component interventions, seems to lack conclusive results. Further research will be of utmost importance in targeting appropriate treatment [16].

CONCLUSION

Fibromyalgia-related physical disability and discomfort affects older adults profoundly. It is important to acknowledge that the complexity of symptoms and the lack of specific treatment make FMS challenging to manage. The evidence base in the FMS literature is limited to patients <50 years. The limited response to drug treatment in elderly patients, and their increased susceptibility to adverse effects, as well as baseline restriction in mobility make treatment even more challenging. Both the short-term and long-term effects of any treatment remain unknown. Accordingly,
individualized treatment programs are recommended. Recognizing treatment limitations, educating patients and implementing multimodal therapy is currently recommended to limit disease burden and disability.

References


