

# For fibromyalgia, which treatments are the most effective?

**Pouran Yousefi, MD**

Department of Family and Community Medicine, Baylor College of Medicine, Houston, Texas

**John Coffey, MLS**

Michigan State University, East Lansing

## EVIDENCE-BASED ANSWER

There is no single most effective modality for the treatment of fibromyalgia syndrome, and no objective comparison of the results from the different studies is available. Low-dose tricyclic antidepressants (TCAs) improve sleep quality and global well-being and have a moderate beneficial effect on tenderness and stiffness (strength of recommendation [SOR]: **A**, based on a systematic review of randomized controlled trials [RCTs]).

Selective serotonin reuptake inhibitors (SSRIs) may moderately improve fibromyalgia-related symptoms (SOR: **B**, based on a few RCTs). The serotonin and norepinephrine reuptake inhibitors (SNRIs) duloxetine (Cymbalta) and milnacipran

(Ixel, not currently available in the US) improve pain and other symptoms (SOR: **B**, based on single RCTs). Tramadol (Ultram) improves pain and other outcomes (SOR: **A**, based on a few RCTs). Cyclobenzaprine (Flexeril) improves both pain and sleep quality (SOR: **A**, based on a systematic review of RCTs).

Aerobic exercise improves overall functional capacity and sense of well-being for patients with fibromyalgia (SOR: **A**, based on a systematic review of RCT). Cognitive behavioral therapy improves patients' self-reported symptoms (SOR: **A**, based on RCTs).

## CLINICAL COMMENTARY

### Reassure patients that their condition is real and treatable

The care of patients with fibromyalgia can be very challenging. An important component of successful management of these patients' condition is helping them realize that we, as physicians, believe that their pain is real. It is important to

reassure them that even though fibromyalgia is not curable, it is treatable and is not a life-threatening condition. Based on expert opinion, combining 2 or more of treatments with the best supporting evidence for effectiveness seems to be the most successful approach to the management of fibromyalgia syndrome.

### ■ Evidence summary

Evidence supporting the effectiveness of TCAs is strong, especially amitriptyline, in fibromyalgia-related symptoms. A meta-analysis that included 10 trials of low-dose TCAs (eg, 25–50 mg of amitriptyline) showed moderate improvement in sleep, pain, fatigue, and overall well-being (number needed to treat [NNT] for improvement=4).<sup>1</sup> A meta-analysis of 5 RCTs on cyclobenzaprine, a muscle relaxant chemically related to TCAs, demonstrated its effect in improving pain and sleep disturbance (NNT=5).<sup>2</sup>

There is less evidence that other med-

ications are effective. Two of 3 RCTs of fluoxetine (Prozac) have shown that it was more effective than placebo, and 2 RCTs have shown that fluoxetine and sertraline (Zoloft) are comparable to amitriptyline.<sup>3</sup> Single RCTs conducted on duloxetine and milnacipran, new SNRIs, demonstrated them to be more effective than placebo in improving pain and scores on the Fibromyalgia Impact Questionnaire (FIQ).<sup>3</sup> Three RCTs have shown that tramadol (with or without acetaminophen) is more effective than placebo in improving pain, number of tender points and FIQ score.<sup>3</sup>

A single RCT has demonstrated that

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pregabalin (Lyrica), a new anticonvulsant, reduces pain more than placebo.<sup>3</sup>

Among nonpharmacological interventions, aerobic exercise and cognitive behavioral therapy have the strongest evidence of effectiveness. A systematic review assessing various exercise programs on symptoms of fibromyalgia showed that aerobic exercise produces short-term improvements in cardiovascular fitness, tender-point pressure pain threshold, and patient- and physician-rated global well-being. Three of these trials included long-term follow-up of the exercise group participants. Patients who continued exercising maintained their improved physical functioning.<sup>4</sup>

Cognitive behavioral therapy has been shown to reduce symptoms in 5 RCTs.<sup>3</sup> Combining cognitive behavioral therapy with education and exercise has also been effective in 5 additional RCTs.<sup>3</sup> Some evidence suggests that acupuncture, massage, warm baths, and biofeedback are effective, but this is limited because of methodological issues in the studies that have been conducted to date.<sup>3</sup>

### Recommendations from others

A recently published evidence-based guideline sponsored by the American Pain Society recommends low-dose TCAs, cyclobenzaprine, cardiovascular exercise, and cognitive behavioral therapy alone or with exercise as first-line therapy along with patient education and treatment of comorbid conditions. For patients that do not improve, it recommends a trial of an SSRI, an SNRI, tramadol, an anticonvulsant, combination medications, or referral.<sup>3</sup>

### REFERENCES

1. O'Malley PG, Balden E, Tomkins G, Santoro J, Kroenke K, Jackson JL. Treatment of fibromyalgia with antidepressants. *J Gen Intern Med* 2000; 15:659–666.
2. Tofferi JK, Jackson JL, O'Malley PG. Treatment of fibromyalgia with cyclobenzaprine: a meta-analysis. *Arthritis Rheum* 2004; 51:9–13.
3. Goldenberg DL, Burckhardt C, Crofford L. Management of fibromyalgia syndrome. *JAMA* 2004; 292:2388–2395.
4. Busch A, Schachter CL, Peloso PM, Bombardier C. Exercise for treating fibromyalgia syndrome. *Cochrane Database Syst Rev* 2002; 2:CD003786.

### CORRECTION

- A sentence was omitted from a Clinical Inquiry published in March (Scott S, Porter M, Quadri Y. How should we follow up a positive screen for anemia in a 1-year old? *J Fam Pract* 2005 Mar; 54(3): 272, 275–276). The first paragraph should have read (omitted sentence in boldface):

Healthy infants who test positive for anemia on routine screening at one year of age are most likely iron deficient and may be treated with an empiric trial of iron therapy (3–6 mg of elemental iron/kg/day); documentation of response to iron confirms the diagnosis of iron-deficiency (SOR: B; evidence from randomized controlled trials with some conflicting results; lack of evidence for long-term benefits/harms of screening strategies). **Further work-up for causes of anemia should be reserved for infants who do not respond to iron replacement.** In these cases, further testing with a complete blood count (CBC), mean corpuscular volume (MCV), red cell distribution width (RDW) and serum ferritin concentration may be effective in determining the cause of anemia (SOR: C; expert opinion).