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Low-Dose Naltrexone Eases Pain and Fatigue of Fibromyalgia

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By [Crystal Phend](#), Staff Writer, MedPage Today
Reviewed by [Zalman S. Agus, MD](#); Emeritus Professor
University of Pennsylvania School of Medicine

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SAN FRANCISCO, April 17 -- Low doses of the anti-addiction drug naltrexone (Revia, Depade) may ease fibromyalgia symptoms, according to a small pilot study.

The drug reduced the severity of fibromyalgia symptoms by 30.2% compared with placebo, Jarred Younger, Ph.D., and Sean Mackey, M.D., Ph.D., both of Stanford University, found.

The benefits were most notable for fibromyalgia's hallmark symptoms of pain and fatigue, they reported online in *Pain Medicine*.

At the typical 50 mg dose that has been used for decades to treat alcohol and opioid drug dependence, naltrexone acts as a competitive antagonist of opioid receptors

AUDIO REPORT

Sean Mackey, M.D., Ph.D.
Associate Professor and
Chief of Pain Management
Stanford University
Stanford, Calif.

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Action Points

Explain to interested patients that fibromyalgia is a syndrome characterized by generalized pain and fatigue.

Caution patients that naltrexone is not

FDA approved for treatment of fibromyalgia.

Note that the small pilot study needs further validation.

But animal studies suggested that something very different happened when the dose was reduced 10-fold.

Rather than blocking the body's pain relief systems, naltrexone doses of around 4.5 mg modulated activity of glial cells to act as a neuroprotectant and suppressant of proinflammatory cytokines.

Dr. Mackey likened it to aspirin, which is an analgesic and anti-inflammatory agent at high doses but used as antiplatelet therapy for cardioprotection at low doses.

Anecdotal reports floating around the Internet suggested off-label low-dose naltrexone produced profound benefits for some fibromyalgia patients, he said.

But because low doses had never been formally studied for fibromyalgia or chronic pain conditions, Drs. Younger and Mackey conducted a placebo-controlled, single-blind, crossover design study in 10 patients with moderately-severe fibromyalgia who were not on opioid medications.

Every day during the two-week baseline, placebo, and washout periods and the eight weeks on 4.5-mg naltrexone, participants recorded their symptoms on a handheld Palm computer.

During naltrexone treatment, participants reported 32.5% lower daily, overall fibromyalgia symptom severity on the visual analog scale compared with baseline, whereas the reduction was only 2.3% during the placebo phase ($P<0.0005$ versus baseline and $P=0.003$ versus placebo).

These effects appeared to last beyond naltrexone dosing into the washout period ($P=0.891$ for symptom severity during dosing versus washout), although symptoms would likely return to baseline over a longer washout period, the researchers said.

Among the 10 patients, six had at least a 30% reduction in symptom severity on the drug compared with their reaction to placebo.

Dr. Mackey said this fits the mixed clinical results he's seen in intermittent off-label use.

"Some patients have had really profound improvements with it such that they're going back to work," he said. "I've had others that are getting no response at all to this."

The authors noted that "individual responder analyses showed that baseline levels of erythrocyte sedimentation rate was strongly correlated with drug response, and predicted over 80% of the variance in response to [low-dose naltrexone]." Individuals with higher sedimentation rates had the greatest reduction of symptoms.

"These results," they wrote, "which suggest the presence of inflammatory processes in some fibromyalgia patients, must be viewed with caution because of low sample size."

Among individual symptoms, low-dose naltrexone appeared to improve pain ($P=0.001$), fatigue ($P=0.008$), and stress ($P=0.003$).

A clear trend emerged for improvements in sleep quality ($P=0.022$) and mood ($P=0.386$ for sadness), Dr. Mackey noted, but "those findings didn't survive the rigorous statistics we applied."

The study used an adjusted $P=0.014$ threshold for significance.

Objective sensory testing in the laboratory suggested higher mechanical and thermal pain thresholds during naltrexone dosing, which "while small in absolute terms, represent significant improvements."

Patients actually reported greater tolerability with the drug than placebo, supporting the "long history of safe use" of the drug at the higher doses used to treat addictions, the researchers noted.

Nevertheless, long-term, chronic use remains a question, they cautioned.

"While we're enthusiastic about these initial results there's a lot of work that needs to be done before we would ever recommend [its use]," he said.

If validated, though, low-dose naltrexone could be a valuable add-on treatment with low costs (usually less than \$40 a month) and easy, once-a-day dosing, he added.

The study was supported by Jim and Connie Binns, the American Fibromyalgia Syndrome Association, and the Oxnard Foundation. Dr. Younger reported support from the Arthritis Foundation.

2 Comments

Primary source: Pain Medicine

Source reference: Younger J, Mackey S "Fibromyalgia symptoms are reduced by low-dose naltrexone: A pilot study" *Pain Med* 2009.

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