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Confirmation: Low-Dose Naltrexone Eases Fibromyalgia Pain

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Authors and Disclosures

February 27, 2012 (Palm Springs, California) — A new study, reported here at the American Academy of Pain Medicine 28th Annual Meeting, shows that a low dose of the opioid antagonist naltrexone significantly reduces daily pain in patients with fibromyalgia.

The results suggest that a unique microglial target holds promise for treating this disorder, explained lead investigator Jarred Younger, PhD, from Stanford University School of Medicine in Palo Alto, California.

The findings from the study, which was rated among the top 6 of the meeting, strengthen those from a pilot study (*Pain Med*. 2009;10:663-672), also by Dr. Younger's group.

"We conclude now in 2 separate studies that low-dose naltrexone appears to be efficacious for fibromyalgia,...is easily tolerated, and we know it's cheap and easy to get hold of. We do need to do larger clinical trials and explore other dosages and medications," he said.

The placebo-controlled, double-blind, randomized, crossover study was completed by 27 women with fibromyalgia (mean age, 43 years) who were not taking any opioid analgesics and had no history of rheumatologic disorders.

Patients were asked to record daily pain and symptoms on a handheld computer during 2 weeks of baseline monitoring, 12 weeks of low-dose naltrexone 4.5 mg/day, 4 weeks of placebo, and 4 weeks of follow-up.

Naltrexone, which is normally dosed at 50 mg/day, is not commercially available in a 4.5 mg dose, so it had to be custom compounded, Dr. Younger explained.

Daily symptom monitoring offers valuable insight and was a strength of this study, said Dr. Younger. "It allows us to explore some really complex temporal dynamics of what happens when patients start taking [active] drug, how long it takes before they start feeling better, [and] what happens when they switch [to no active treatment]," he said.

"If you just bring someone in to find out how they're doing, you might bring them in on a bad day or a really good day; that will drastically change your results. If you take a lot of days and average across those, you'll get a more robust measurement because fibromyalgia symptoms vary considerably from day to day."

There was a significant reduction in pain from baseline in the naltrexone group, compared with the placebo group (48.5% vs 27.4%; *P* = .021). The difference between the groups was statistically significantly (*P* = .006).

Participants rated naltrexone to be as tolerable as placebo on a 100-point tolerability scale (89.2 vs 89.4). The only adverse effects reported more often for naltrexone were vivid dreams (37% vs 13%) and headache (16% vs 3%).

Dr. Younger said he believes that, at such a low dose, naltrexone is not having an opioid antagonistic effect, but is actually acting to suppress the function of microglia, which have been hypersensitized by some unknown trigger — whether an immune response, a physical trauma, or genetic predisposition.

"Something is sensitizing these microglia, and when they become activated, they release these proinflammatory cytokines and other agents.... When cytokines are released into the central nervous system, we know they cause sickness behaviors, and I think sickness behaviors induced by cytokines look a lot like the symptoms of fibromyalgia," he said.

"Others suggest that by temporarily blocking opioid receptors, you cause a subsequent increase in opioid levels later, but I don't think this is what is happening."

Asked about the high placebo response in the study (27.4%), Dr. Younger agreed it is curious.

"I've wondered if there's something about this disorder that makes [patients] particularly responsive to placebo," he said. But he added the publicity generated by the pilot study might have driven the second study's placebo response. "They came with such high expectations."

Asked to comment on the findings, session moderator James Watson, MD, from the Mayo Clinic in Rochester, Minnesota, said that "it is pretty novel as a treatment. I think the data were exciting, actually."

Next to comparable studies of other fibromyalgia treatments, such pregabalin, duloxetine, and milnacipran, "the data look quite good, and the side-effect profile [Dr. Younger] showed was outstanding, particularly relative to the side-effect profile of some of the medicines we commonly use in patients with fibromyalgia," Dr. Watson explained.

Dr. Watson believes that the biggest issue is that the low-dose formulation of naltrexone used in this study is not commercially available and has to be compounded specially for patients. "That's a big problem."

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NOTE: *Town & Country Compounding Pharmacy*, does Compound, Low Dose Naltrexone. Call us, contact info below.

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