Opioid Antagonist Decreases Relapse in Parolees and Probationers

Extended-release naltrexone, a full-mu opioid antagonist, significantly reduces the relapse rate in criminal justice offenders.

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April 12, 2016 – A new phase 2 clinical trial shows that extended-release naltrexone decreased relapse rates in opioid dependent criminal justice offenders when compared to the standard treatment of counseling and community treatment programs.

The new study, conducted by Dr. Joshua D. Lee and colleagues at the New York University Langone Medical Center, was published in *The New England Journal of Medicine* on March 31, 2016.

Extended-release naltrexone, a full-mu opioid antagonist, was recently approved by the FDA in 2010 for the treatment of opioid dependence. Extended-release naltrexone offers several benefits over traditional agonist therapeutics such as buprenorphine or methadone, since the drug is not addictive and can be administered on a monthly schedule.

A small pilot study found that administration of extended-release naltrexone is a feasible treatment option for opioid dependent criminal justice offenders. In the present randomized, multisite study, researchers tested the efficacy of extended-release naltrexone as compared to the usual treatment for opioid dependence over 6 months.

Extended-release naltrexone significantly reduced the relapse rate among criminal justice offenders (43% vs. 64% for naltrexone vs. usual treatment, $P<0.001$). Furthermore, patients assigned to the extended-release naltrexone group had a significantly longer median time to relapse when compared to the usual treatment group (10.5 weeks vs. 5 weeks, $P<0.001$). In the treatment group, 74% of patients submitted opioid-negative urine samples as compared to 56% of the control group over the 6-month treatment period ($P<0.001$).

While discontinuation of an opioid antagonist can lead to overdose events, extended-release naltrexone did not increase the risk of overdose in this study. Moreover, no participants in the extended-release naltrexone group overdosed during the study period as compared to 7 participants in the usual treatment group ($P = 0.02$).

Extended-release naltrexone had no significant effect on secondary outcome measures, including cocaine use ($P = 0.71$), intravenous drug use ($P = 0.43$), heavy drinking ($P = 0.77$), unsafe sex ($P = 0.71$), and reincarceration ($P = 0.38$). Additionally, opioid use among participants was not significantly different 54 weeks post-treatment ($P = 0.91$), indicating that the intervention lost efficacy after discontinuation of treatment.

Adverse effects included headache (19% vs 8.4% for extended-release naltrexone vs. usual treatment) and gastrointestinal upset (18.3% vs. 1.9%). Patients in the usual treatment group were significantly more likely to experience serious adverse events, including depression, suicidality, COPD, overdose, and death ($P = 0.006$).

“Future research would be needed to determine whether long-term or continuous treatment with extended-release naltrexone – similar to buprenorphine or methadone maintenance therapy –

could help maintain the short-term benefits observed in this trial and improve longer-term outcomes," Dr. Lee wrote in *The New England Journal of Medicine.* "As is the case with any chronic illness, symptoms of opioid-use disorder are more likely to recur with the discontinuation of effective pharmacotherapy," he added.

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