

Naltrexone-Induced Nausea in Patients Treated for Alcohol Dependence: Clinical Predictors and Evidence for Opioid-Mediated Effects

O'Malley, Stephanie S. PhD; Krishnan-Sarin, Suchitra PhD; Farren, Conor MD; O'Connor, Patrick G. MD, MPH

Institution: Yale University School of Medicine, New Haven, Connecticut

Abstract:

Naltrexone, an opiate antagonist, is well tolerated by most alcoholic patients; however, a subset reports significant nausea that can limit the effectiveness of this therapy. The goal of this study was to identify risk factors for naltrexone-precipitated nausea to assist in the development of management strategies to maximize the overall effectiveness of naltrexone. On the basis of the hypothesis that alterations in the endogenous opioid system occur with repeated stimulation of endogenous opioids by alcohol, the authors predicted that the recency and intensity of alcohol use would be related to the risk of naltrexone-induced nausea. One hundred twenty alcohol-dependent subjects participated in an open-label trial of naltrexone. After 5 to 30 days of abstinence, subjects received an initial naltrexone dose of 25 mg followed by a dose of 50 mg daily thereafter for 10 weeks. New-onset adverse effects were rated mild, moderate, or severe after 1 week of naltrexone. Logistic regression analyses were used to predict moderate to severe nausea during the first week of therapy from pretreatment patient characteristics. Moderate to severe nausea was reported by 18 subjects (15%) and was linked to poorer medication compliance and heavier drinking during treatment. Risk of nausea was significantly predicted by age, gender, intensity of drinking, duration of abstinence, and the interaction of abstinence duration and intensity of drinking. At shorter durations of abstinence, lighter drinkers were more likely to experience nausea than heavier drinkers. However, the risk of nausea declined with longer periods of abstinence, particularly for lighter drinkers. Younger age and female gender were associated with higher rates of nausea. These results support the hypothesis that recency and intensity of alcohol use are related to opiate antagonist-precipitated nausea and suggest that long-term alcohol use may result in alterations in the endogenous opioid system. Potential strategies to minimize the risk of nausea in vulnerable individuals are discussed.