Certain populations may benefit most from alcohol-dependence treatment naltrexone

15 March 2011

Naltrexone is one of the most effective pharmacological treatments for alcohol dependence. However, naltrexone does not work for everyone. A new study has found that naltrexone is effective for women, and individuals with the A118G polymorphism of the mu opioid receptor gene.

There are few pharmacological treatments for alcohol dependence (AD). An opioid receptor antagonist called naltrexone is one of the most effective, and yet it is not effective for everyone. This study investigated the influence of gender and the A118G polymorphism of the mu opioid receptor gene (OPRM1) on response to naltrexone, finding that naltrexone decreased alcohol-induced euphoria in women and those with the specific genotype.

Results will be published in the June 2011 issue of *Alcoholism: Clinical & Experimental Research* and are currently available at Early View.

"Naltrexone is one of the few medications approved for treating alcoholism," said Marco Leyton, William Dawson Chair in the Department of Psychiatry at McGill University and corresponding author for the study. "Naltrexone does not work for everyone, though."

"Naltrexone is a very specific drug that only acts on opioid receptors," added Charles P. O'Brien, Kenneth Appel Professor in the Department of Psychiatry at the University of Pennsylvania. "A significant percentage of alcoholics receive opioid stimulation when they drink alcohol and this produces good feelings such as euphoria. If they take naltrexone, they don't feel so much euphoria. While this doesn't cure their alcoholism, it makes them more responsive to treatment. They don't stop drinking right away, but they drink less. Thus, naltrexone goes well with 12-step programs and behavior therapy. For some people this is life saving; I have personally treated patients up to 20 years with naltrexone, but others only six to 12 months."

The effectiveness of a medication can depend on many different factors, said Leyton. "For naltrexone, there was already some preliminary evidence that gender and genetics were important, including a gene that is related to our body's natural morphine or 'endorphin' system," he noted.

Leyton and his colleagues administered either naltrexone or placebo to 40 social drinkers (20 men, 20 women), 18 to 50 years of age, for six days. On day 1 of the active treatment phase, subjects took 25 mg of naltrexone; if adverse side effects did not occur, subjects took 50 mg per day for the remaining five days. All of the participants but one were genotyped for the A118G polymorphism of the OPRM1 gene. At the end of each treatment period, participants received a single dose of their preferred alcoholic beverage, followed by an opportunity to work for additional alcohol servings.

"The study found that the medication decreased alcohol euphoria most clearly in two groups: women, and people with a gene related to the endorphin system," said Leyton. "These are exciting findings, but not entirely unexpected."

O'Brien agreed. "These results support previous research showing that naltrexone works best in a subgroup of alcoholics who have a certain genotype. We don't know about other subgroups who may respond, but in future we will genotype first and then select medication."

Both Leyton and O'Brien are optimistic that these findings can be used to "personalize" treatment options for AD individuals.

"Researchers and clinicians working together might make it possible to predict beforehand who will best benefit from one treatment versus another," said

Leyton. "To help create this envisaged 'personalized medicine' we need to identify more so-called 'biomarkers.'"

"We need to learn how to best identify this subgroup of alcoholics with a certain genotype when they enter treatment," said O'Brien. "If current studies are positive, the FDA may allow a change in the package insert specifying that the medication works best in those with G allele. We also know that it works well in those with a strong family history of alcoholism and those with high alcohol craving."

Provided by Alcoholism: Clinical & Experimental Research