MedicalXpress

Clinical trial indicates gabapentin is safe and effective for treating alcohol dependence

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The generic drug gabapentin, which is already widely prescribed for epilepsy and some kinds of pain, appears to be safe and effective in the treatment of alcohol dependence. The finding comes from a 150-patient randomized, placebo-controlled, double blind clinical trial conducted by scientists at The Scripps Research Institute (TSRI).

"Gabapentin's effect on drinking outcomes is at least as large or greater than those of existing FDA-approved treatments," said Barbara J. Mason, Pearson Family Professor and co-director of the Pearson Center for Alcoholism and Addiction Research at TSRI, who led the new research. "Plus it's the only medication shown to improve sleep and mood in people who are quitting or reducing their drinking, and it's already widely used in primary care—that's an appealing combination."

The new research was published by the journal *JAMA Internal Medicine* on November 4, 2013.

Reducing Cravings, Depression, Sleeplessness

As a relatively safe, effective and well-tolerated drug, gabapentin has the potential to fill a large gap in the treatment of alcohol dependence. About eight and a half-million Americans are thought to have the condition, yet each year only a tiny fraction of them are prescribed one of the FDA-approved medications for alcohol dependence, due in part to the limitations of the existing drugs used for treatment.

The lack of treatment is striking in light of alcoholism's enormous adverse impact on society. In addition to its other effects on the lives of individuals and their families, alcoholism promotes cancer, liver disease, strokes and heart attacks, as well as various other disabilities. Worldwide, about one out of 25 deaths is attributable to alcohol misuse.

In the new study, Mason and her colleagues randomly assigned each of 150 recently abstinent people with alcohol dependence to be treated with 900 mg or 1,800 mg of gabapentin or with a look-alike placebo. Over 12 weeks of treatment, the high-dose group ended up refraining from heavy drinking twice as often as the placebo group (45% vs. 23%) and entirely abstained four times as often (17% vs. 4%). The drug also significantly reduced the number of drinks consumed, as well as patient reports of cravings, depression and sleeplessness. None of the treated patients reported serious side effects.

Patients who received the lower, 900-mg dose of gabapentin showed intermediate benefits compared to the high-dose group, likely reflecting what clinicians call a "dose-response effect"—a good indication that the treatment really is working.

"I think that we can now have confidence in the pharmacological effect of this drug," Mason said.

Filling a Gap

Two FDA-approved therapies for alcohol dependence have been around for decades. The first, disulfiram (Antabuse®), interferes with the body's normal enzymatic breakdown of alcohol, making drinking an unpleasant experience. The second, naltrexone (ReVia®, Vivitrol®), blocks the opioid brain-cell receptors that help mediate the sense of reward during drinking.

Both treatments aim to blunt the pleasure-seeking motivation that helps initiate alcohol dependence. But they are relatively ineffective against the anxiety, depression, sleeplessness and other protracted withdrawal symptoms that help maintain alcoholism once it has been established. They are also, by design, somewhat unpleasant—which often discourages patients from using them.

A newer drug, acamprosate (Campral®), the only other medication approved by FDA for alcoholism treatment, does aim to normalize dysregulation in brain stress systems following acute withdrawal, similar to gabapentin. But it has shown only modest benefits on the whole in clinical trials, with no efficacy noted for mood or sleep.

Gabapentin has a favorable safety profile and appears to work by normalizing levels of the neurotransmitter GABA in an emotion-mediating part of the brain called the amygdala, thereby reducing anxiety and other stress-related withdrawal symptoms. A previous, proof-of-concept study of gabapentin by Mason's group also found effects like those reported in this study in patients with cannabis dependence.

Gabapentin's quieting effect on overactive brain areas has led to its approval by the FDA for treating epilepsy and neuropathic pain. It is also now widely prescribed "off-label" for other pain-related conditions, including migraines.

"I'm excited about the possibility that now more people will get treatment," said Mason. "We really need to do more about treating alcohol dependence."

More information: "Gabapentin Treatment for Alcohol Dependence: A Randomized Controlled Trial," *JAMA Internal Medicine*, 2013.