



Reprinted from BrainWork, Vol. 13 No. 6 November-December 2003

New Vistas in Addiction Treatment: Easier Access, Greater Choice of Medications

Addiction to alcohol and other drugs is undoubtedly one of the biggest health problems worldwide. In the United States alone, almost 12 million people are addicted to or “dependent on” various substances (excluding tobacco), according to recent government statistics. Even though most of those affected by substance abuse or dependence are aware of the harmful consequences of their behavior, very few receive medical treatment for their condition. This is partly because most people—including many physicians—view addiction not as a medical disorder but as a character flaw or a sign of moral weakness.

But another important reason for most addicts’ failure to get treatment is the lack of availability of effective medications. A survey of almost 1,400 substance abuse specialists has found, for example, that they very rarely prescribe either of the two drugs currently available in the United States for treating alcoholism. This is mainly because the doctors don’t think these drugs are very effective—an opinion that is backed up by a large number of studies, according to the authors of the survey.

However, this situation is about to change, some experts say, as more and more medications are found to be effective for treating substance use disorders. In addition, there is a trend for moving the diagnosis and treatment of addictive disorders from specialized treatment centers to the doctor’s office, where patients could receive these services in much greater numbers.

New Weapons in “Battle Against the Bottle”

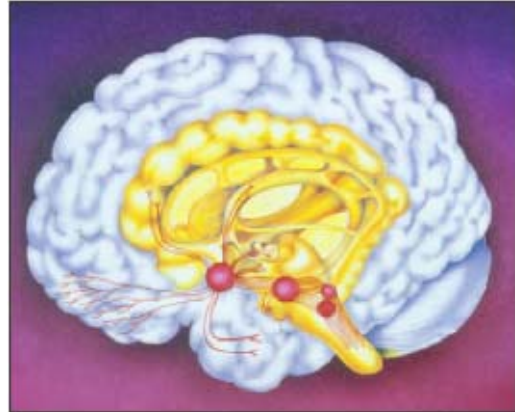
The most effective medication that is currently available in the United States for the treatment of alcohol dependence is a drug called naltrexone, according to Charles O’Brien, an addiction expert at the University of Pennsylvania. Naltrexone reduces the craving for alcohol by blocking the activity of opioid receptors, which in turn inhibits the release of dopamine inside the brain’s “reward system,” O’Brien explains.

Although naltrexone can help some alcoholics, it does not work for everyone, and even when it does, it is only moderately effective. Some studies indicate that its effectiveness might be boosted by combining it with some other medications, such as acamprosate, which

has already been approved for treating alcoholism in Europe, Latin America, and Australia.

“Because acamprosate acts on a different neurochemical target than naltrexone, its corresponding effect on craving is thought to be distinct,” O’Brien notes. “Rather than blocking the opioid receptors that help confer the neurochemical ‘reward’ associated with alcohol consumption,” acamprosate modulates receptor activity of another neurotransmitter, glutamate-NMDA, and it appears to reduce the intensity of craving after drinking cessation. “Since the two medications work on completely different receptor systems, there is reason to believe that their results might be additive,” O’Brien contends.

The anti-nausea medication ondansetron also appears to be useful for treating alcohol dependence in so-called “early-onset” alcoholics, who become dependent on alcohol before age 25 and are thought to have a strong biological predisposition to become alcoholics. In a clinical trial that involved 321 subjects and was published in the journal *Psychopharmacology* last year, Bankole Johnson of the University of Texas at San Antonio and colleagues found that early-onset alcoholics who had been treated with ondansetron plus behavioral counseling for a period of 12 weeks experienced significantly reduced craving and drank considerably less alcohol during that time than those who had received behavioral treatment and placebo. Ondansetron exerts its anticraving effect “by ameliorating some serotonergic abnormality” in early-onset alcoholics, the authors suggest.



This diagram shows in red the binding sites and pathways of opiate drugs such as buprenorphine.

More recently, the same team of researchers reported in *The Lancet* that 12 weeks of treatment with the anticonvulsant drug topiramate reduced heavy drinking and increased days of abstinence in a group of 150 alcoholics by about 25 percent. “At the end of the 12 weeks, patients on topiramate reduced their drinking, their craving, and their quality of life improved significantly, when compared to [those treated with] placebo,” said Nassima Ait-Daoud, one of the researchers involved in the study.

The scientists hypothesize that topiramate may combat craving by inhibiting alcohol-induced release of dopamine in the midbrain. According to Bankole Johnson, the study’s lead investigator, “topiramate’s properties could make it an attractive candidate for co-treatment with other specific medications for treating either early-onset or late-onset alcoholism.” George Koob, director of the psychopharmacology division at the Scripps Research Institute, also thinks that successful treatment approaches will probably involve a combination of several medications (or one medication

with a number of different ingredients) that “hit several molecular targets.”

Topiramate may also be effective for cocaine addiction, according to a study presented in Florida earlier this year at the annual meeting of the College on Problems of Drug Dependence. Researchers from the University of Pennsylvania School of Medicine and Philadelphia Veterans Affairs Medical Center, Philadelphia, enrolled 40 cocaine-dependent individuals in the double-blind, placebo-controlled trial, which lasted 14 weeks. Half were given increasing doses of topiramate (up to a maximum of 200 mg/day), while the other half received placebo.

An analysis of urine samples showed that, after a one-week period of abstinence, most subjects in the placebo group gradually resumed their cocaine use over the course of the study. However, most patients treated with topiramate remained largely drug-free throughout the 14 weeks. The investigators therefore concluded that topiramate “may hold promise for relapse prevention in cocaine-dependent patients.”

Office-based Treatment

The number of prescription drugs that can be used to combat substance dependence continues to grow for other drugs of abuse as well. For example, in a recent study published in *The New England Journal of Medicine*, Paul J. Fudala of the University of Pennsylvania School of Medicine and colleagues found that the pain medication buprenorphine (alone or in combination with naloxone), administered in a doctor’s office, was safe and effective in the treatment of heroin addiction.

In the past, heroin addiction could only be treated at specialized addiction treatment facilities, primarily using methadone, a synthetic form of heroin. However, access to such facilities is rather limited, and typically only a small minority of addicts get appropriate treatment, according to H. Westley Clark, director of the Center for Substance Abuse Treatment, Substance Abuse and Mental Health Services Administration, Department of Health and Human Services. “There are only about 1,200 regulated opioid-treatment programs nationwide, and six states have no such programs,” he writes in a related editorial.

Buprenorphine is an opiate-receptor agonist (i.e., it enhances the effects of opiates), and it is used in many countries for the treatment of moderate to severe pain. Because it is a partial agonist, buprenorphine is not as dangerous as methadone, says Markus Heilig, a professor of psychiatry at Sweden’s Karolinska Institute who has studied the effects of both medications. “Methadone is a full agonist, so if a person takes an overdose, they will get respiratory depression and they will die. The toxicity of buprenorphine is much lower, so if you increase the dose, you will reach a plateau, and no respiratory depression will occur,” he explains.

Although it is much safer than methadone, buprenorphine can still be abused, Heilig notes, “if addicts chase the euphoria and inject it, instead of taking it by mouth.” Therefore, another drug, naloxone, is sometimes added to the preparation to counteract the effects of buprenorphine and “to prevent addicts from getting a kick out of it,” should they try to inject the medication, he says.

“Naloxone is not absorbed if you take it orally, so as long as people take their combination the way they’re supposed to, then naloxone is just irrelevant.”

Buprenorphine may also be effective for alcohol dependence, Heilig says: “It looks very promising in animal experiments, but the data are just not in yet from human studies.” What is important, however, is that the idea of treating addictions with pharmacological

agents has now become widely accepted, Heilig contends. “I don’t think we’re going to cure addiction from one day to another,” he says. “What’s going to happen is we’re going to find some drugs that will fit some patients and other drugs that will fit others. That’s the way most fields in medicine have developed, and this development has now started in the field of addictive disorders.”

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