Dual Dependency on Cocaine and Alcohol in Opiate Addicts: Treatment Options

Tracie Gardner, Ph.D., and Thomas Kosten, M.D.

Dual-drug dependency is common and represents a complex management and treatment challenge. This month's column will briefly describe concurrent drug abuse with alcohol, cocaine, and heroin as well as describe current pharmacotherapies for multidrug dependence. In addition, we will briefly discuss the implications for combining behavioral therapies with medications to improve treatment efficacy.

Alcohol Abuse and Dependence

The management challenge of dual-drug dependency is complex and often can involve triple dependency on alcohol as well as opiates and stimulants. Detoxification of alcohol-dependent patients may be required.[1] Alcohol abuse relapse prevention after detoxification is a greater challenge and requires regular monitoring by breath alcohol levels and blood carbohydrate-deficient transferring, which can assess sustained abstinence when used as infrequently as every other week.[2]

In addition to monitoring for return to alcohol use, relapse prevention pharmacotherapy should be considered. Relapse prevention pharmacotherapies for alcohol include acamprosate, topiramate, and disulfiram (with monitored ingestion). The other important pharmacotherapy for alcoholism, opiate antagonists such as naltrexone (and nalmefene), are contraindicated since they may precipitate heroin withdrawal.

Acamprosate, when given at 666 mg t.i.d., has increased abstinence by 50% in over 3000 patients across a dozen clinical trials.[3,4] Side effects such as diarrhea are generally well tolerated. In an illustrative trial, 272 patients were enrolled and treated for 48 weeks.[5] Compared with patients taking placebo, acamprosate-treated alcohol dependent patients had twice the rate of sustained abstinence at 48 weeks (43% vs. 21%), and this difference from placebo was sustained at 96 weeks after starting the medication (37% vs. 17%). Thus, acamprosate appears to be a very effective approach to treating patients who are both heroin and alcohol dependent in order to maintain alcohol abstinence after detoxification.

Similar success has been described with topiramate versus placebo, but only in a single study thus far.[6] In this topiramate study, the patients had not been first detoxified from alcohol and were actively drinking when started on medication. The outcome again was remarkable, with an increase from no days abstinent at baseline to 44% of days abstinent by week 12, compared with 18% of days abstinent for the placebo group. Topiramate may therefore be started at a low dose in buprenorphine- or methadone-maintained alcohol abusing patients who do not need medical detoxification for alcohol. The treatment strategy would call for weekly increases of the topiramate dose for up to 8 weeks in order to attain a week of abstinence, followed by gradual discontinuation over several weeks once abstinence is attained. Simultaneously, patients may be started on acamprosate or disulfiram; the choice will depend on patient preference and need for either an anticraving medication (acamprosate) or an aversive agent (disulfiram).

Cocaine Abuse

Pharmacotherapy for cocaine abuse is a continuing challenge, but treatments such as buprenorphine, disulfiram, modafinil, and γ-aminobutyric acid (GABA) agonists are evolving,[7] as is the development of a cocaine vaccine.[8] Buprenorphine has dose dependently reduced cocaine abuse; less cocaine use is associated with higher doses of buprenorphine (e.g., 4 mg vs. 16 mg daily).[9,10] Thus, the first approach to a patient who is abusing cocaine and heroin might be to consider using buprenorphine and increasing the buprenorphine dose to at least 16 mg daily, if cocaine abuse persists at lower doses.

Disulfiram is a complex medication that appears to act on the catecholamine system to increase dopamine and decrease norepinephrine production. Disulfiram decreases cocaine craving and cocaine-induced priming, as shown in several human laboratory studies where cocaine has been administered with placebo and active disulfiram. At a cocaine dose of 2 mg/kg intranasally, disulfiram reduced peak cocaine-induced craving (or priming) by more than 50%.[11] Disulfiram also increased cocaine-free urine specimens in outpatient, placebo-controlled clinical trials, and in over 600 outpatients treated across 7 studies, the disulfiram group had a 35% higher rate of cocaine-free urine samples ($p < .01$ in meta-analysis).

Other promising agents have very different pharmacologic actions. Modafinil has significantly increased cocaine-free urine samples, with rates of 45% for modafinil compared with 20% for placebo.[12] Several GABA-enhancing agents such as tiagabine, gabapentin, and vigabatrin also are being examined. While gabapentin has not shown efficacy, both tiagabine and vigabatrin appear to be promising. In a recent clinical trial, tiagabine increased cocaine-free urine specimens by 80% from baseline, while placebo increased them by only 20% from baseline.[13] Thus, several medications from different classes of pharmacologic actions are showing promise for treatment of cocaine abuse.

Contingency management (CM) treatments can enhance the efficacy of pharmacotherapy. Contingency management conditions can be used to reinforce attendance at treatment sessions, compliance with medications, and reduction in cocaine abuse. For reducing cocaine use, patients are given payment for drug-free urinary toxicology (UTOX). For consecutive cocaine-free urines there is an escalating reinforcement schedule. For example, an initial payment of $3 per clean UTOX will be increased by $1 for each consecutive clean UTOX to a maximum of $15 per result. Positive or missed UTOX is penalized by resetting the amount earned for a clean UTOX back to $3.

In a study of bupropion plus CM,[14] the proportion of cocaine urine specimens by week steadily decreased for the patients who received CM plus bupropion, while those who received bupropion alone, CM alone, or neither bupropion nor CM showed no significant reduction in cocaine urine results during this 24-week clinical trial. The effect of bupropion on decreasing cocaine urine samples was easily seen in the patients who also got CM. For both CM groups, the proportion of cocaine-positive urine samples started at 70% at week 1, then dropped to 35% from weeks 12 to 24 for the bupropion plus CM group, while for the placebo plus CM group, the cocaine urine specimens remained between 55% and 60% throughout the 24 weeks. Thus, CM plus bupropion reduced cocaine-positive UTOX within the first 13 weeks and maintained these reductions across the 6-month study.

Finally, an anticocaine vaccine is under development. This vaccine produces antibodies that bind to injected cocaine and decreased cocaine self-administration in rodents.[15] The vaccine produces substantial amounts of antibodies within 6 to 8 weeks of initial vaccination in humans and acts to keep cocaine out of the brain.[8,16] Cocaine antibody levels rise as dosing is

repeated, even more than antibody levels increase with increasing vaccine dose. For example, peak antibody levels increased more with 5 vaccinations at 82 μg (410 μg cumulative dose) than with 4 vaccinations at 82 μg (328 μg cumulative dose) (320 vs. 200 antibody units). Furthermore, antibody levels with 4 doses at 82 μg (328 μg cumulative dose) increased to twice the levels attained with 3 vaccinations at an almost 10 times higher dose of 709 μg (2127 μg cumulative dose) (100 vs. 200 antibody units). These higher vaccine doses and more repeated dosing are associated not only with higher antibody levels but also with less relapse to cocaine use. The percentage of patients relapsing in a high versus low dosage group was 30% vs. 75% for any cocaine use and no relapse vs. 30% relapse for heavy cocaine use.

In summary, heroin addicts are commonly dually dependent on cocaine and alcohol. Pharmacotherapies for alcohol dependence include acamprosate, topiramate, and disulfiram. The promising stimulant pharmacotherapies include disulfiram, modafinil, and tiagabine or similar GABA-enhancing agents. Combining contingency management with medications is highly effective for enhancing the efficacy of cocaine therapy. Sustained treatments such as the cocaine vaccine offer great promise to prevent relapse.

Drs. Gardner and Kosten are with the Menninger Department of Psychiatry and Behavioral Sciences, Baylor College of Medicine, and the Michael E. DeBakey VA Medical Center, Houston, Tex.

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Corresponding author and reprints: Tracie Gardner, Ph.D., Michael E. DeBakey VA Medical Center, Research 151 – BLDG 110, Room 225, 2002 Holcombe Boulevard, Houston, TX 77030 (e-mail: tgardner@bcm.edu).

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