

Substance Abuse Overview

Substance abuse remains a significant global problem. As part of the National Institute on Drug Abuse (NIDA) educational track at this year's APA meeting, a symposium chaired by Herbert Kleber, MD, Columbia University, provided attendees with an overview of the traditional and new treatments available for the treatment of drug abuse and dependence.



In the first address, Adam Bisaga, MD, New York Psychiatric Institute, highlighted the current trends in the treatment of cocaine abuse. Bisaga notes, "There are 14 million cocaine users, two-thirds of which reside in the Americas." Twenty percent of cocaine users are expected to become dependent on the drug, 5% of which will become dependent in the 1st year.

Traditional psychosocial methods in the treatment of cocaine abuse have focused on two stages. The first stage is to help the user achieve initial abstinence. The second stage is to help the user achieve lasting abstinence. Pharmacological interventions may aid in reaching these two goals.

Because the rewarding effects of cocaine are largely mediated by the dopamine system, ie, cocaine primarily acts as a dopamine reuptake inhibitor (though it also has effects on serotonergic and noradrenergic systems), traditional pharmacological management of a cocaine disorder has focused on blocking this primary action. Unfortunately, there have been no major breakthroughs in treating cocaine addiction by focusing on this mechanism of action (for example, with dopamine antagonists). Rather, treatment now focuses on the brain adaptations that occur via chronic cocaine use. Chronic cocaine use has been shown to remodel the neural circuits mediating reward.

The ideal medication for cocaine abuse would achieve a number of goals: a) decrease cocaine use, b) induce abstinence, c) prevent relapse, d) be safe in combination with cocaine, e) have a low abuse potential and facilitate treatment compliance (Gorelick DA et al. *Drugs* 2004;64:1547-73).

One approach for treating cocaine addiction is the agonist approach. Dopamine agonists may counteract the decreases in functional dopamine hypoactivity that occur when an individual becomes abstinent. These drugs may also block (or inhibit) the effects of cocaine itself. Drugs currently under investigation include modafinil (a dopamine transporter inhibitor), cabergoline (a dopamine receptor agonist) and d-amphetamine (a dopamine enhancer). All show some efficacy, though concerns remain over abuse potential [Leiderman DB et al. *Addiction* 2005;100 (Suppl 1): 1-11].

A second approach involves drugs that antagonize cocaine's neurobiological actions. Although drugs like reserpine, olanzapine, topiramate, tagabine and gabapentin continue to be assessed within this context, there is generally poor

compliance with monoamine antagonists by cocaine addicts.

A cocaine vaccine is another potential treatment for cocaine abuse and dependence (Prete A. *Addict Biol* 2007;12:133-51). The premise of the cocaine vaccine is to develop a drug that increases the immune response to the cocaine molecule. The benefits of such a vaccine are that the effects would be continuous and extended. The negative aspect of a cocaine vaccine is that it would take multiple injections to induce immunity, there would be individual variability in the response to the vaccine, and the vaccine most likely only be used by highly motivated patients.

Antidepressants may also be effective in treating individuals with cocaine addiction. Both bupropion and desipramine have shown some efficacy in reducing cocaine use by individuals with a significant cocaine addiction (Rounsaville BJ. *Biol Psychiatry* 2007;56:803-9).

Addressing opiate addiction, Dr. Kleber began by noting, "There are between 800,000 and one million heroin addicts. Prescription opiate abusers are two- to three-times the number of heroin addicts. Most are not in treatment". Adolescents are now commonly abusing prescription opiates rather than injecting heroin.

The only cure in the context of opiate addiction is cure for withdrawal or cure for overdose. If a patient is in withdrawal, administering buprenorphine, methadone or clonidine relieves the withdrawal symptoms. If an individual presents to the emergency room in the throws of an opiate overdose, administering an injection of naloxone will immediately reverse the effects of the drug.

Often patients with an opiate addiction, however, request help from clinicians in order to reduce or manage their drug habit. Outpatient treatment usually employs pharmaceuticals as an adjunct to psychosocial interventions. In other words, the goals of medications are not to cure, but rather to give a window of opportunity for patients to comply with the psychosocial intervention. Pharmacological agents have been shown to reduce instances of drug craving, or to manage the opiate addiction in a short- or long-term maintenance program.

There are a host of medication options which include agonists (eg, methadone), partial agonists (eg, buprenorphine), antagonists (eg, naltrexone and its depot form) and anti-withdrawal medications [eg, clonidine and refexine (which is not yet available in the US)]. Dr. Kleber adds, "When the phone rings and the patient looking for an appointment and says his problem is opiates, you should breathe a sigh of relief. Unlike [other drugs], this is a condition where we do have very effective medications." The issue is finding the best medication for the particular patient.

Psychosocial interventions are a commonly used to help patients with a primary diagnosis of addiction. Edward Nunes Jr, PhD, Columbia University, suggested that Motivational Interviewing may increase adherence with medications. Motivational Interviewing is essentially a "way to talk", states Nunes. It is used as a precursor to other treatments and encourages internally driven change.

Once in treatment, therapists should mix and match their approaches based on the patients need. Tailoring programs will increase treatment adherence, abstinence and decrease relapse.

Frances Levin, MD, Columbia University, notes that you must also address co-morbid diagnosis when dealing with a substance abusing population. If you have a psychiatric disorder other than substance abuse, there is an increased risk of developing a drug problem, the reverse being true as well.

For patients with depressive disorders, antidepressants had modest effect sizes in the decrease of substance abuse. In fact, data has shown that treating depression decreases the risk of relapse (McDowell D et al. *Drug Alcohol Depend* 2005;80:209-21). Drugs being considered for these duly diagnosed patients include sertraline, venlafaxine and mirtazapine. Anxiety disorders are also commonly reported to be co-morbid with substance abuse, in which case buspirone, paroxetine and sertraline may be beneficial.

One major point Dr. Levin stresses is that treating the psychiatric problem alone does not treat the substance abuse problem. There is a need for combined treatment of both the psychiatric and substance problems.