

Buprenorphine and Buprenorphine/Naloxone: New Treatment for Opiate Dependence

Of the wide range of medical and non-medical treatments for addiction, some have proven successful while others have been — at times — barbaric and/or unsuccessful. The treatment of opiate dependence has been particularly unsuccessful over the years — it became clear that once dependence was established, opiate addicts were often intractable. Thus began the search for medications and strategies to assist the opiate addict in loosening the bonds of addiction. One solution has been the reorientation of drug treatment toward better management of the natural course of opiate addiction through the use of safer maintenance drugs. This approach views the goal of opiate treatment as both interrupting or reversing the pathological social processes that go along with heavy use of opiates and eliminating the damaging consequences of an endless cycle of withdrawal and drug craving.

Medically prescribed maintenance treatment — which attempts to replace more dangerous and often illegal drugs with safer legal ones — can interrupt the progressively worsening processes of opiate addiction by permitting the opiate-dependent person to end reliance on illicit drug markets. Furthermore, it can effectively neutralize the endless cycle of craving and avoidance of withdrawal. Maintenance can permit addicts to get on with their lives even though their addiction has not been “cured” (Drucker, n.d.a).

Opiate maintenance in practice

Evidence shows that opiate-dependent patients do not respond as well to traditional addiction treatment approaches.¹ Various medications (e.g., LAAM, naltrexone) have been tried with some success, though LAAM and naltrexone have not been universally successful. The pure agonist methadone has proven to have good merit for the treatment of the opiate abstinence syndrome and for the maintenance of the opiate addict. Patients receiving such therapy have been shown to remain in treatment programs at a rate 2.5 times greater than that of patients in traditional residential programs and 5 times greater than in drug-free outpatient programs (Reckitt Benckiser plc, n.d.).

Buprenorphine and buprenorphine/naloxone are the first narcotic drugs available for the treatment of opiate dependence that can be prescribed in an office setting under the Drug Addiction Treatment Act (DATA) of 2000. Methadone can be dispensed only in a limited number of narcotic treatment programs. Because of this, there have not been enough addiction treatment slots for patients desiring therapy. Under this new law, medications for the treatment of opiate dependence that are Schedule III, i.e., buprenorphine and buprenorphine/naloxone, can be prescribed in a doctor’s office by specially trained physicians.² This change is expected to provide patients greater access to needed treatment (FDA, 2002).

In the meantime, the pharmaceutical company Reckitt Benckiser has placed on the market two products containing buprenorphine. The first is Subutex®, a sublingual tablet that comes in a 2mg and 8mg doses. The second is a combination of buprenorphine and naloxone. This formulation is called Suboxone® and is also taken sublingually. Suboxone® comes in two strengths. One contains 2mg of buprenorphine combined with 0.5mg naloxone, and the other contains 8mg of buprenorphine with 2mg of naloxone.

Antagonists, agonists, and partial agonists

Many counselors ask, how is buprenorphine different from methadone? What are its advantages and disadvantages? A part of the answer lies in the fact that buprenorphine is a partial agonist. Naloxone is an opiate antagonist. This means that the medication effectively blocks the action of opiates at the receptor site. An opiate antagonist can be thought of as a “dummy key” that fits into

the lock of the opiate receptor. When the dummy key is in place, the knob will not turn and the opiate receptor cannot be activated. Moreover with the dummy key in the keyhole, no other key can be inserted, and no other opiate can activate the receptor.

Methadone (like morphine, heroin, and prescription opiates) is a full opiate agonist. This can be thought of as the key that opens the door completely. The more powerful the agonist and the higher the dose, the faster and the harder does the door open. When full opiate agonists are administered, the user experiences opiate effects depending on opiate type, dose, absorption, tolerance, and other variables. If an individual is exposed to enough full opiate agonist, overdose and death can be a result.

Buprenorphine is a partial opiate agonist. This can be thought of the key that opens the door, but this time the safety chain is in place. The door opens some, but not all the way. Increasing the dose of partial opiate agonists produces greater effects, but this effect is limited. No matter how fast or with how much force the door is opened, the safety chain remains in place. When administered sublingually as Suboxone® and Subutex® are, the maximum effect appears to occur in the 16-32mg range. Even if doses exceed this range, the drug effect plateaus. This is referred to as the ceiling effect. The authors know of no cases of overdose death from buprenorphine alone. However, cases of death have been reported where other substances, such as benzodiazepines, have been added to buprenorphine. Most reports come from France, where buprenorphine has been on the market since 1996 (New York Times, 2003). Buprenorphine has an advantage over methadone in that overdose is not a great concern. Buprenorphine can rarely create some subjective euphoria, but not to the degree of a full agonist (NIDA, 1992). It is abusable, especially in its injectable, form but not to the extent of other opiates. However, for purposes of maintenance, buprenorphine can only be as effective as approximately 60-80mg of methadone. There exists some percentage of opiate dependent individuals who require more than 80mg of methadone to become stable and feel well. For these addicts, buprenorphine may not be effective and methadone should remain the maintenance drug of choice.

Affinity and dissociation

To understand some of the advantages that buprenorphine has over other opiate maintenance medications, the concept of affinity and dissociation are important. Affinity refers to the attraction that a molecule has for receptor sites. In this case, how strong is the affinity or how much does the mu opioid receptor like buprenorphine? The mu receptor will choose buprenorphine over other opiates and buprenorphine has such a high affinity that it will displace other opiates and preferentially occupy the binding site. This is a critical factor as buprenorphine occupies the receptor disallowing other opiates from having any effect. Not only does it occupy the site but also buprenorphine hangs around for a long time. There is a very slow dissolution as buprenorphine has a half-life of around 37.5 hours. In contrast, heroin is on and off the receptor in milliseconds (McNicholas, 2003).

At a buprenorphine dose of 16mg, there will be almost no binding of other opiates to the mu receptor sites. Why is this important? The following anecdote illustrates: Gina is a recovering heroin addict. She has been taking a maintenance dose of 16mg of buprenorphine. One night her boyfriend tells her that he does not want to see her anymore. Hurt and angry, Gina goes back into the neighborhood where she used to cop dope. She injects heroin into her venous system and gets no "high." This is because the buprenorphine with its high affinity and slow dissolution is occupying the mu receptor sites. The heroin has no place to bind and cannot deliver the highly euphoric impact of a full agonist.

Abuse potential

Buprenorphine can be abused, especially in its injectable form. However, it has a relatively low abuse potential when compared to full opiate agonists such as oxycodone, heroin, and morphine. The sublingual route has a much slower onset of effect and is less reinforcing. This suggests a much lower potential for abuse.

Repeated administration of buprenorphine can cause and maintain addiction. The degree of physical dependence is much less than that caused by a full agonist. Upon discontinuation, the resulting abstinence syndrome is less severe. The acute abstinence syndrome is about one-third as severe as coming off of morphine.

To reduce the potential for intravenous use, the manufacturer has added naloxone to buprenorphine (Suboxone®). This medication is taken sublingually. When placed under the tongue naloxone has poor bioavailability. In other words, very little is absorbed such that no withdrawal is precipitated in an opiate-dependent client. However, if Suboxone® is ground-up and injected, the naloxone becomes highly bioavailable and will precipitate an abstinence syndrome in those who are opiate dependent.

Sublingual buprenorphine has fair to good bioavailability. By using this route of administration, the maintenance patient will receive the buprenorphine and not the naloxone. This interesting formulation should decrease the abuse potential of the tablets. However, never underestimate the genius of the addict when it comes to learning how to abuse a substance.

Subutex® and Suboxone® have been studied in more than 2,000 patients and have been shown to be safe and effective treatments for opiate dependence. Common side effects of both drugs include cold or flu-like symptoms, headaches, sweating, sleeping difficulties, nausea, and mood swings. These effects can last a number of weeks. The risk of serious diminished breathing may be less with buprenorphine than other opiates when used in high doses or in overdose situations (FDA, 2002).

Drug interactions, cautions, and contraindication

Refer to the Subutex® and Suboxone® package inserts (http://www.fda.gov/cder/drug/infopage/subutex_suboxone/default.htm) for a complete listing of drug interactions, contraindications, warnings, and precautions.

Resources

American Academy of Addiction Psychiatry (AAAP)
7301 Mission Road, Suite 252
Prairie Village, KS 66208
Phone: 913-262-6161
Fax: 913-262-4311
Online Contact: www.aaap.org

American Association for the Treatment of Opioid Dependence (AATOD)
212 Broadway, Suite 301
New York, NY 10007
Phone: 212-566-5555
Fax: 212-349-2944

American Osteopathic Academy of Addiction Medicine (AOAAM)
5550 Friendship Blvd, Suite 300
Chevy Chase, MD
Phone: 301-968-4160
Fax: 301-968-4199
Online Contact: www.aoa-net.org

American Society of Addiction Medicine (ASAM)
4601 North Park Avenue, Arcade Suite 101
Chevy Chase, MD 20815
Phone: 301-656-3920
Fax: 301-656-3815
Online Contact: www.asam.org

Center for Substance Abuse Treatment (CSAT)
A Division of the Substance Abuse and Mental Health Services Administration
Room 12-105 Parklawn Building
5600 Fishers Lane
Rockville, MD 20857
Phone: 301-443-5700
Fax: 301-433-8751
Online contact: www.csat.samhsa.gov

National Institute on Drug Abuse (NIDA)
A Division of the National Institutes of Health
6001 Executive Boulevard, Room 5213
Bethesda, MD 20892
Phone: 301-443-1124
Online Contact: www.nida.nih.gov

Substance Abuse and Mental Health Services Administration (SAMSHA)
A Division of the United States Department of Health and Human Services
200 Independence Avenue, S. W.
Washington, D.C. 20201
Phone: 202-619-0257
Toll Free: 1-877-696-6775
Online contact: www.samsha.gov

Buprenorphine Physician Locator: buprenorphine.samsha.gov