Use of Buprenorphine in the Management of Opiate Addiction

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OPIATE ADDICTION – SCOPE OF THE PROBLEM

The United Nations Office on Drugs and Crime notes that opiates, particularly heroin, are the main problem drugs at a global level, with an estimated 15.6 million opioid abusers globally, including approximately 11.1 million heroin abusers. The World Health Organization estimates there are approximately 12.6 million injection drug users (IDUs) in the world, with injection drug use reported in over 150 countries and territories.[1] IDUs represent a major point of entry for HIV into a population; according to the Joint United Nations Program on HIV/AIDS, injection drug use accounts for up to 80% of HIV infections in Eastern Europe and Central Asia.[2]

In addition to the risk of becoming infected with HIV and transmitting it, use of injection drugs presents additional medical challenges. Unsafe injection practices have contributed to an international epidemic of Hepatitis C virus, with an estimated 120 million people infected worldwide.[3] Abscesses, endocarditis, and soft tissue infections are much more common in intravenous drug users than in the general population. Finally, regular use of opioids, regardless of the route of administration, results in lasting biological and physiological changes in the brain, including disruptions in inhibitions, motivation, and decision-making processes.[4]

OPIATE BRAIN PHYSIOLOGY

Most opiates are metabolized to some form of morphine, and these molecules bind to brain receptors labeled *mu* and *kappa* that are located in many parts of the brain, spinal cord and peripheral sensory nerves. These also serve as receptors for endogenous opiates. Exogenous opiates may be antagonists, partials agonists, or complete agonists.

BUPRENORPHINE PHARMACOLOGY

Buprenorphine is a relatively long-acting partial mu agonist and full kappa antagonist which is administered sublingually in opioid replacement therapy. It has high binding affinity at both receptors and competes with other agonists, such as methadone, heroin (diamorphine) and morphine, at the μ-opioid receptor. This high affinity blocks the effects of other opiates that might be used, and reduces or eliminates cravings in addicts on maintenance treatment. The elimination half-life of buprenorphine is 20–73 hours (mean 37). Because buprenorphine is mainly metabolized hepatically, there is no risk of accumulation in patients with renal impairment. The drug was originally designed to be administered on a Monday-Wednesday-Friday schedule (although few addicts tolerate such a schedule due to their psychological need for daily treatment).

Buprenorphine is commonly sold alone (Subutex®, others) or in a co-formulation with naloxone (Suboxone®) to prevent parenteral abuse. A complete antagonist, the naloxone portion of the formulation (which is ineffective sublingually but fully active parenterally) causes instantaneous withdrawal in abusers who try to inject Suboxone®. Addicts discover this promptly, and parenteral abuse is non-existent.

Due to extensive first-pass liver metabolism, oral dosing of buprenorphine is not feasible. Thus, buprenorphine is intended for sublingual administration, by which its bioavailability is relatively high (35–55%) while that of naloxone is low (10%). This contrast in properties allows the combination product of buprenorphine/naloxone (Suboxone®) to deliver the effects of the opioid without those of the antagonist.

Opioid agonist effects of buprenorphine are less than the maximal effects of full opioid agonists, such as morphine, and are limited by a 'ceiling' effect. Opiate-wise subjects have been given up to 70 times the recommended dose of buprenorphine without increased effect. As a consequence, addicts find that there is no advantage to overdosing as there is no commensurate increase in any opioid "high."

IN SUMMARY:

- Suboxone has little attraction as a drug of abuse because it cannot be injected (in its formulation with naloxone).

- Buprenorphine does not induce tolerance, so, unlike methadone, it does not require increasing doses to maintain effectiveness.
- Because of its high affinity for opiate receptors, buprenorphine will blunt or eliminate the effect of any other opiates taken to get high.
- Buprenorphine blocks opiate receptors and can reduce or eliminates opiate cravings in addicts.

CLINICAL USE OF BUPRENORPHINE

Numerous trials and reviews have established buprenorphine as safe and effective for use in stabilization and long-term maintenance of individuals with opioid dependence, as well as for acute detoxification. Because buprenorphine and buprenorphine/naloxone have such favorable safety profiles, the U.S. National Institute on Drug Abuse has identified the medications as *first line treatment* for opioid dependence.

Office-based treatment of opioid dependency with buprenorphine is effective and safe,[5] and it provides additional benefits, including minimization of contact with other drug users and of the stigma associated with drug dependence.[6]

Buprenorphine, alone or in combination with naloxone, may only be prescribed for opioid dependence by practitioners who have undergone a course in its use and been issued a supplementary DEA number. Initially, such qualified practitioners may have only 30 addicted patients each, but later they may petition to increase that number to 150.

In a randomized controlled trial, Johnson and colleagues found that buprenorphine was effective in maintaining patients in treatment and reducing the consumption of illicit opioids.[7] So-called maintenance therapy should ideally be continued for at least a year at which time attempts to taper and stop treatment may be undertaken in patients who wish to stop treatment.

For acutely detoxifying opiate addicts, buprenorphine is started when the addict is in full-blown withdrawal and may be maintained for 3 to 7 days. Because of its long half-life, the drug may be stopped abruptly, but nonetheless it is often tapered over a few days.

Finally, buprenorphine may be used in chronic pain patients, especially in those with a history of addiction. In patients with chronic osteoarthritis, transdermal buprenorphine demonstrated good efficacy and tolerability.[8] In a randomized controlled trial of patients with chronic low back pain, it was effective at managing pain in patients who had previously received opioids.[9] It is well-tolerated and may be administered daily sublingually or with weekly transdermal patches. Because of its reduced analgesic properties compared with morphine, buprenorphine treatment for chronic pain may need to be augmented with NSAID's or acetaminophen.

DIVERSION AND ABUSE

The risk of abuse of buprenorphine is low because of its pharmacology. However, both Subutex® and Suboxone® have significant street value and these drugs are often diverted. Their value comes from use by addicts who want to try to de-tox on the street, or for use in attempting to cut down on their tolerance for illicit opioids, since doing so would reduce the cost of their drug habits. Both Subutex® and Suboxone® are often sold or traded on the street in attempts by addicts to obtain another drug of their choice in exchange.

BUPRENORPHINE AT LGH

The Recovery Care Medicine Clinic at the Lancaster General Hospital has been open for the past 2 years and is operating at 100% capacity (about 50 opiate addicts) on an outpatient basis at 554 North Duke Street. Patients must be referred from within the LGH/LGMG community and are initially seen weekly. If they demonstrate compliance, visits can be stretched out to as far apart as eight weeks. Each patient is urine drug tested at every visit, and any patient testing negative for buprenorphine is dismissed instantly from the program. Any patient who tests positive for cocaine, opiates, THC, or other drug of abuse more than once is similarly discharged. Every patient must also demonstrate that he/she is participating actively in a counseling program on an ongoing basis. After a year of treatment, attempts are begun to reduce and stop Subutex®.

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