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Is There a Magic Bullet? Pharmacologically Assisted Addiction Management: What Counselors Should Know

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Pharmacologically assisted addiction management (PAAM) has been an important adjunct to addiction treatment for years. PAAM is a natural outgrowth of the earliest attempts at palliative care (i.e., to relieve withdrawal symptoms). Once it was demonstrated that withdrawal symptoms could be relieved with other pharmacologic agents, the search was on to give clients an "edge" in the recovery process. It is important for the counselor to have a rudimentary knowledge of these agents for several reasons. The first is that with the advent of managed care, length of stays in the primary treatment center have significantly shortened and many of the clients are being referred to counselors in the community for follow-up care. Counselors will encounter many of these clients who have been placed on PAAM agents while in the treatment center and need to be maintained on these agents for a minimum of 6 months after discharge. Additionally, counselors can play a vital role in assisting with medication compliance, as well as client education.

PAAM agents work by different mechanisms of action (MOA) and are divided into four distinct categories: antidipsotrophic or metabolic (Antabuse), replacement (low dose nicotine replacement delivery devices), anticraving medications (Campral and Revia), or in the cases of opioids, manipulation of the opiate receptor through blockade (antagonist), substitution (agonist), or partial agonist, or partial agonist/antagonist combinations. Currently PAAM agents available on the U.S. market are indicated for use in alcohol dependent and opiate dependent clients.

The first attempt at PAAM for alcoholism occurred with the release of disulfuram (Antabuse) in 1948. A form of therapy, known as aversion therapy, was popular at that time and disulfuram was developed to interfere with the metabolism of alcohol. Alcohol is metabolized in a two step process by two enzymes. The first alcohol dehydrogenase, breaks alcohol down into acetylaldehyde. The second enzyme, acetylaldehyde dehydrogenase, breaks the acetylaldehyde into carbon dioxide (excreted by the lungs) and water (excreted by the kidneys). Antabuse works by interfering with the enzyme acetylaldehyde dehydrogenase so that an excess of acetylaldehyde is accumulated in the

body. Because of this accumulation of acetylaldehyde, the net result is a constellation of unpleasant symptoms that occur if the client consumes alcohol while taking Antabuse. These symptoms include facial flushing, headache, nausea, vomiting, profuse sweating, dizziness, weakness, and tachycardia. The theory is that the sensations are so unpleasant that the client will "avert" drinking while on Antabuse if they experience these symptoms. Antabuse has a long half life (4-5 days) so that if the client discontinues the medication and drinks within that window of time they will still develop symptoms. Unlike all of the other PAAM agents, the basis for action of Antabuse is on metabolism rather than brain activity. Antabuse, like all other PAAM agents should not be used alone, but rather as part of a comprehensive management strategy that includes psychosocial support.

The *sine qua non* of replacement PAAM is what is known as the "anti-priming action" of nicotine replacement therapy. The craving produced by cigarettes is caused by a drop in the nicotine level in the blood which triggers the symptoms of withdrawal: irritability, drowsiness, anxiety, lightheadedness, and most notably, craving. The development of low dose nicotine delivery systems (gum, patches, nasal sprays, and inhalers) has proven effective in reducing the cravings without reinforcing the need to increase the dosage. The purpose of these systems is to slowly reduce the blood plasma nicotine level to the point where cessation will no longer trigger craving. Once again, this therapy should be part of a comprehensive management strategy that includes psychosocial support.

Three alcohol anticraving drugs are available on the U.S. market: acamprosate (Campral), naltrexone (Revia), and most recently, a long acting depot injection of naltrexone marketed as Vivatrol. Campral has a chemical structure similar to that of the endogenous amino acid homotaurine. Homotaurine is a structural analog of the amino acid neurotransmitter GABA and the neuromodulator taurine. While the MOA of Campral in the maintenance of alcohol abstinence is not completely understood, it is postulated that chronic alcohol exposure alters the normal balance between neuronal excitation and inhibition by influencing GABA, and that Campral somehow restores this balance. In 1997, a pivotal European study demonstrated a 7-15% total abstinence rate at one year in patients treated with Campral vs. placebo (Geerlings, Ansoms, & van den Brink, 1997). In addition, it was found that these same patients spent an additional 64-178 days abstinent prior to relapse and that the cumulative days of abstinence, prior to relapse, was higher in the Campral group than in the placebo group. Once again PAAM with Campral should be part of a comprehensive management strategy that includes psychosocial support.

Prior to discussing the next anti-craving drugs Revia and Vivatrol along with opiate receptor blockade, opiate receptor substitution, and partial opiate receptor blockade, a brief review of opiate receptor physiology is in order, as well as a discussion of the psychobiology of craving. There are a variety of opiate receptors in the brain, spinal cord, GI tract, respiratory tract, and other organs designated by the Greek letters *delta, gamma, kappa*, and *mu*. A drug that binds to the receptor and activates it is known as an *agonist,* whereas a drug that binds to a receptor but does not activate it is known as an *antagonist*. Some drugs function in a dose dependent manner, functioning as agonists

at lower doses and antagonists at higher doses and are known as *partial agonists.* The strength to which a drug binds to a receptor is known as *affinity* and the degree to which the drug activates that receptor is known as its *intrinsic activity. Dissociation* is the measure of disengagement from the receptor and is different from affinity. Dissociation, in part, accounts for the *half life* (T1/2) of the drug (a measure in which 50% of a fixed dose of the drug is metabolized and eliminated from the body, measured in hours).

With reference to alcohol addiction, the Dutch addiction scholar Roel Verheul has postulated three types of craving for alcohol: stress-reduction, disinhibition, and the reward-sensitivity (Verheul & Brink, 2005). The stress-reduction craving is a desire for the reduction of tension or arousal thought to be related to a dysregulation of GABA/GLU neurotransmitter systems, and thus would be amenable to Campral. The disinhibition form (loss of control) is similar to OCD. This lack can be either cognitive/attentional (obsessive) or behavioral, and is thought to be related to a deficiency in the baseline level of the neurotransmitter serotonin (5HT), thus may be amenable to SSRI's. The last form of craving is the reward sensitivity type, and is thought to be related to dysregulation of the endogenous opioid system the endorphins and enkephalins.

Naltrexone (Revia) is an oral anticraving agent approved for use in the U.S. in alcohol dependent patients. It is actually a full opiate receptor antagonist and its MOA is postulated to be blockade of the opiate receptors. When alcohol is initially consumed, it has been shown in some individuals that a massive release of endorphins occurs. These are the body's "natural opiates" and slot into the opiate receptors. They are full agonists and have high affinity and intrinsic activity but very fast dissociation and it is postulated that the dissociation from the receptor is in part responsible for the craving. Revia and its long acting counterpart, Vivitrol, are full opiate receptor antagonists, and so have high affinity, no intrinsic activity, and medium dissociation. In 1984, oral naltrexone was marketed as Trexan as a competition for the Methadone market; however, because of the lack of reinforcing effects (no intrinsic activity) it did not catch on in popularity. While a graduate student doing rat experiments at the University of Pennsylvania, Dr. Joseph Volpicelli noticed an effect on alcohol craving in rats and published one of the first clinical trials demonstrating the efficacy of oral naltrexone in treating alcohol dependent patients (Volpicelli, Alterman, Hayashida , & O'Brien, 1992). O'Malley et al. confirmed these studies that demonstrated patients on Revia (compared to placebo) had fewer alcohol cravings, stayed in treatment longer, had better treatment outcomes, and had fewer "slips" (1996). Of those that returned to drinking, those on Revia tended to have a shorter duration of alcohol consumption, drinking only a few drinks while those on placebo continued to drink until they were intoxicated (O'Malley et al., 1996). There was an unexpected experimental mortality, however, and most patients did not complete the 6 month protocol. This prompted a search for a long acting depot injection and in 2007, Vivatrol (long acting naltrexone) was released in the U.S. market. Results with Vivitrol are impressive, with an onset of anticraving action within 48 hours, a 90% reduction in drinking days per month, and 3 times as many patients abstinent at the 6 month mark—32% vs. 11% for placebo (O'Malley, Zweben, & Silverman, 2006). Once again Revia

and Vivitrol should be part of a comprehensive management strategy that includes psychosocial support.

Perhaps the most significant breakthroughs in PAAM have occurred in the area of opiate dependency utilizing known opiate receptor physiology. Many options exist from full antagonist therapy to substitution therapy with an agonist that has a longer T1/2, to the latest drug to receive FDA approval the partial agonist, buprenophine (Subutex). Beginning in the mid 1960s, Vincent Dole and Marie Nyswander pioneered the use of methadone to treat heroin addiction in New York City. The 1974 Narcotic Addict Treatment Act created a closed distribution system limiting the use of methadone to government regulated opiate treatment programs (OTPs) also known as methadone clinics. Methadone, a full opiate agonist, then lends itself to the theory behind opiate substitution therapy, (i.e., substituting a drug with a much longer half life [methadone T1/2=24 hours] for a drug with a shorter T1/2 [heroin=8 hours]). After the client develops pharmacodynamic tolerance, it is the empty receptor site that produces the withdrawal symptoms including significant drug craving. Substitution therapy eliminates the peaks and troughs, thus breaking the craving cycle and, due to the longer T1/2, produces much less euphoria; therefore the addict becomes "more functional" due to less impairment. Freed from the cycle of symptoms of acute withdrawal and significant drug craving, the addict can develop normal interests and pursue a more healthy and productive lifestyle. Regardless of your opinion of substitution therapy, the data indicate that well run OTPs have been shown to decrease heroin consumption, decrease related criminal behavior, increase employment, improve mental and physical health, and decrease the incidence of needle sharing as well as HIV transmission (McLellan et al., 1993; Metzger et al., 1993). Methadone is a full receptor agonist, however, and as such, will produce physical dependence so that acute withdrawal symptoms do occur after the discontinuation of methadone.

The greatest advance in PAAM for opiate dependency, in this author's opinion, has been with the release of buprenorphine in 2000. The Drug Addiction Treatment Act of 2000 provides a waiver from the special provisions of the 1974 Narcotic Addict Treatment Act, thus allowing physicians with 10 hours of training and a special DEA number to administer and prescribe bupenorhine outside of the OTP setting. This has been a boon to literally millions of opiate dependent patients, removing the stigma of methadone maintenance.

Buprenorhine is a partial opiate receptor agonist which has high affinity, medium intrinsic activity, and low dissociation. There are several advantages to utilizing buprenophine over other agents for both detoxification and ongoing maintenance. Because of its high affinity and low intrinsic activity, buprenorphine binds to the opiate receptor tighter than other agents, thus alleviating withdrawal symptoms while at the same time because of its low intrinsic activity producing less "opiate euphoria." Its partial agonist effects imbue buprenorhine with several other clinically desirable pharmacologic properties: since there is lower "opiate euphoria," there is less abuse potential, a lower level of physical dependence (i.e., less withdrawal discomfort) if the drug is abruptly stopped, and a greater therapeutic window (i.e., less overdose potential compared with full opiate agonists). Because buprenorphine has a low dissociation constant, it

dissociates from the receptor very slowly, thus having a longer half life, leading to once daily dosing. One of the drawbacks of buprenorphine is the "precipitated withdrawal" syndrome. Because of its high affinity but low intrinsic activity, if given too soon after the discontinuation of a full opioid agonist it will displace the remaining agonists from the receptor; but because of the low intrinsic activity, the net effect is a decrease in agonist effect, thus a "precipitated withdrawal syndrome." Another obstacle of using buprenorphine as a detoxification agent is retention in the treatment setting—many patients are reluctant to wait until full blown withdrawal is established prior to receiving treatment with buprenorphine.

Subutex (sublingual buprenorphine) has been approved as a detoxification agent for acute opioid withdrawal. A number of clinical trials have proven its efficacy in the management of heroin or other opioid withdrawal (Bickel, Amass, Crean, & Badger, 1999; Parran, Adelman, & Jasinksi, 1994) and have shown efficacy in removing patients from methadone maintenance (Johnson, Strain, & Amass, 2003; Amass, Kamien, & Mikulich, 2001).

Once the patient has been detoxified from opiates with Subutex, they can be maintained with Suboxone. Suboxone is a combination drug which combines the bupenorphine molecule with the antagonist naltrexone. This prevents the clients from getting the reinforcing effect of opiates if they use while on Suboxone, as all of the opiate receptors are blocked by the naltrexone. Several clinical trials have demonstrated efficacy of buprenorphine vs. placebo (Fudala et al., 2003) and buprenorphine vs. methadone (Petitjean et al., 2001). Using outcome measures of illicit opioid use, retention in treatment, and assessment for adverse effects, studies have shown that buprenorphine treatment reduces opioid use, retains patients in treatment, has few side effects, and is acceptable to most patients (O'Connor & Fiellin, 2000).

What is the role of the professional counselor (PC) in PAAM? The answer is: a critical one! Since most prescribing physicians work on a 15 minute billing cycle, they often have little time for patient education. In addition, research has shown that psychological interventions aimed at pharmacotherapy adherence improve addiction treatment outcomes (Reid et al., 2005). Enter PCs who differ from prescribing physicians in that they have both more contact with their clients and more in depth knowledge on how to form a strong therapeutic alliance. The PC is in a much better position to address the knowledge and attitudinal barriers to patient-treatment adherence. How can the PC influence this and promote medication compliance? They certainly should ask for—and listen to—the client's beliefs and attitudes about prescribed medication. They should work to understand the client's perspective rather than trying to correct or contradict his/her perspective. PCs should ground any discussion of compliance concerns within the client's point of view. PCs should also withhold from responding until the client has discussed all major views for and against medication. Lastly, PCs should firmly understand that it is the client's subjective beliefs rather than objective medical evidence that ultimately influences client's medication compliance.

Is there a Magic Bullet? The resounding answer is no. Addiction is considered a bio-psych-social phenomenon and PAAM only addresses one component of addiction—the biological component. PAAM is rarely sufficient treatment for drug addiction and

treatment outcomes usually demonstrate a dose-response effect based on the level or amount of psychosocial support provided. For most patients, drug abuse counseling, individual or group, along with participation in self-help groups are considered necessary. PAAM is one tool available to the clinician to add to their therapeutic armamentarium; however, it should not be used alone, but rather should always be combined with other therapeutic techniques, most notably psychosocial support and participation in self-help groups.

References

Amass, L., Kamien. J. B., & Mikulich,S. K. (2001). Thrice-weekly supervised dosing with the combination buprenorphine-naloxone tablet is preferred to daily supervised dosing by opioid dependent humans. *Drug and Alcohol Dependence 61*(2), 173-181.

Bickel, W.K., Amass, L., Crean, J.P., & Badger, G.J. (1999). Buprenorphine dosing every 1, 2, or 3 days in opioid dependent patients. *Psychopharmacology* 146(2), 1999.

Fudala, P. J., Bridge, T. P., Herbert, S., Williford, W. O., Chiang, C. N., et al. (2003). Buprenorphine/Naloxone Collaborative Study Group. Office-based treatment of opiate addiction with a sublingual-tablet formulation of buprenorphine and naloxone. *New England Journal of Medicine, 349*(10), 949-958.

Geerlings, P., Ansoms, C., & van den Brink, W. (1997). Acamprosate and prevention of Relapse in alcoholics. *European Addiction Research, 3*, 129-137.

Johnson, R. E., Strain, E. C., & Amass, L. (2003) Buprenorphine: How to use it right. *Drug and Alcohol Dependence, 79*, S59-S77.

McClellan, A. T., Arndt, I. O., Metzger, D. S., Woody, G. E., & O'Brier, C. P. (1993). The effects of psychosocial services in substance abuse treatment. *Journal of the American Medical Association, 269*(15), 1953-1959.

Metzger, D. S., Woody, G. E., McClellan, A. T., O'Brien, C. P., Druley, P., et al. (1993). Human immunodeficiency virus seroconversion among intravenous drug users in-and-out of treatment: An 18 month prospective follow-up. *Journal of Acquired Immune Deficiency Syndrome, 6*(9), 1049-1056.

O'Connor, P. G., & Fiellin, D. A., (2000). Pharmacologic treatment of heroin-dependent patients. *Annals of Internal Medicine, 133*(1), 40-54.

O'Malley, S. S., Jaffe, A. J., Chang, G., Schottenfeld, R. S., Meyer, R. E. (1996). Six-month follow-up of naltrexone and psychotherapy for alcohol dependence. *Archives of General Psychiatry, 53,* 217-224.

O'Malley ,S. S., Zweben, A., & Silverman, B. (2006) Abstinence and self-help participation outcomes with extended-release naltrexone (XR-NTX) for alcohol dependence. Abstract presented at the 37th American Society of Addiction Medicine (ASAM) Annual Medical Scientific Conference, May 4-7th 2006.

Parran, T. V., Adelman, C. L., & Jasinski, D. R. (1994). A buprenorphine stabilization and rapid-taper protocol for the detoxification of opioid-dependent patients. *American Journal on Addictions, 3*(4):306-313.

Petitjean, S., Stohler, R., Deglon, J. J., Livoti, S., Waldvogel, D., et al. (2001). Double-blind randomized trial of buprenorphine and methadone in Opiate dependence. *Drug and Alcohol Dependence, 62*(1), 97-104.

Reid, S., Teeson, M., Sannibale, C., Matsuda, M., & Haber, P. S. (2005). The efficacy of compliance therapy in pharmacotherapy for alcohol dependence: A randomized controlled trial. *Journal of Studies on Alcohol, 66*, 833-841.

Verhuel, R., & Brink, W. V. D. (2005). Causal pathways between substance use disorders and personality pathology. *Australian Psychologist, 40,* 127-136.

Volpicelli, J. R., Alterman, A. I., Hayashida, M., & O'Brien, C. P. (1992). Naltrexone in the treatment of alcohol dependence. *Archives of General Psychiatry 49*, 876-880.