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Naltrexone as a Therapeutic Agent

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Methadone, buprenorphine, and naltrexone are current drugs used in the treatment of the addiction to the opioid class of drugs. The main use of these medications is the effective treatment of heroin addiction. However, with the growing problem of addiction to opioid medications used in the treatment of chronic pain, Medication Assisted Treatment (MAT) programs have been broadened to include addiction to prescription medications as well as to illicit drugs. MAT programs, including Opioid Treatment Programs (OTPs), combine behavioral therapy and medications to treat substance use disorders. In previous issues of the Toxicology Times we have written about methadone and buprenorphine, and here we will show how naltrexone fits in with these medications.

Naltrexone was first synthesized in 1965 and has a very similar structure to naloxone and oxymorphone. As stated in a previous edition of Toxicology Times, naloxone is very quick acting and has a greater affinity at the binding sites than morphine. It is used in overdose situations to replace the opiate at the binding site and reverses the respiratory suppression. In these situations, naloxone will save the patient's life and restore normal breathing with minimal secondary effects. Oxymorphone is a powerful opiate that is used in pain treatment, is sought out by addicted prescription seekers, and sold on the street to those seeking relief from their addiction. The minor chemical structural differences between naltrexone, naloxone, and oxymorphone is a characteristic that allows the use of naltrexone as a treatment medication, naloxone as an emergency lifesaving treatment to restore breathing and oxymorphone as pain medication or as a drug of abuse.

Naltrexone works differently in the body compared to methadone and buprenorphine. There are three main opiate receptors in the human body which have different functions. Each receptor is either activated (agonist) or suppressed (antagonist) differently by each opiate. The receptors are noted by the Greek alphabetic symbol as either Mu, Kappa or Delta. Naltrexone works by completely blocking the three receptors and acts as an antagonist. Methadone is a full agonist at the Mu receptor and has negligible effect at the Kappa and Delta receptors. Buprenorphine is a partial agonist on the Mu receptor and an antagonist at the Kappa and Delta. These differences in the biochemical mechanism of action between naltrexone, buprenorphine, and methadone allow the medications to play different roles in the treatment of opioid use disorder. Methadone and buprenorphine are used during detoxification to manage withdrawal symptoms (because of their full and partial agonist activity) as well as opioid replacement during maintenance therapy. On the other hand, naltrexone binds and blocks the euphoric and sedative effects of heroin, morphine, and codeine, is proclaimed to reduce craving, and there is no abuse or diversion potential. Unlike methadone and buprenorphine, with naltrexone it is important that medically managed withdrawal (detoxification) from opioids be completed at least 7 to 10 days before naltrexone is initiated or resumed.

Extended-release injectable naltrexone is approved for treatment of people with opioid use disorder*. It can be prescribed by any healthcare provider who is licensed to prescribe medications and special training is not required. Research has shown that naltrexone decreases reactivity to drug-conditioned cues and decreases craving. Patients who have been treated with extended-release injectable naltrexone may have reduced tolerance to opioids and may be unaware of their potential sensitivity to the same, or lower, doses of opioids that they previously consumed. Extended-release naltrexone should be part of a comprehensive management program that includes psychosocial support.

Alcohol stimulates the release of endogenous opioids. When used as a treatment for alcohol dependency, naltrexone blocks the euphoric effects and feelings of intoxication. This allows people with alcohol addiction to reduce their drinking behaviors enough to remain motivated to stay in treatment and hopefully avoid relapse. Naltrexone is not addictive, nor does it react adversely with alcohol. Long-term naltrexone therapy extending beyond three months is considered most effective by researchers, and therapy may also be used indefinitely.

References:

*Treatment modalities from SAMHSA.