

Opioid Antagonist: Issue of “Over-The-Counter” Naloxone

An Interview with Darryl S. Inaba, PharmD, CADC V, CADC III

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receptor to block other opioids or endorphins from activating that site. Opioids can fit into some of the different receptors and not others, resulting in partial effects. As a result, small doses of an opioid can fit into an endorphin receptor as an agonist but larger doses cause the receptor to hyperpolarize or “freeze up” like a lock that has been jammed. It then becomes an antagonist. This type of receptor site activity is known as an inverse agonist. (Inaba and Cohen, 2014; Brunton, L. L., et al., 2011; Lowenson, J. H., 2011)

NAADAC: How do naltrexone, naloxone and buprenorphine differ?

DR. INABA: Both naltrexone and naloxone are opioid antagonists and are often referred to as “pure antagonists” as they only block the opioid receptors without having any partial agonist activity. The chemical properties of naloxone make it poorly absorbed if taken orally or sublingually but it is absorbed effectively when snorted into the nasal passages and lungs. Naloxone is also very short-acting in the brain (45 minute to 1 hour) and, as a result, can be used as an antidote for opioid overdose. Naltrexone can be absorbed by oral and sublingual routes of administration, is much longer acting (24 hours or longer), has some toxicity to the liver, and may block some opioid receptors that naloxone fails to block. Naltrexone is used as a prophylactic to block opioid addiction relapse by preventing the effects of the drug if an individual slips during recovery. It has also been shown to decrease craving and is approved for both alcohol and opiate addiction treatment. Naltrexone has also been used to decrease cravings in pathological gambling, stimulant, and nicotine use disorders. Even behavioral disorders like trichotillomania and kleptomania have responded to naltrexone therapy. (Aboujaoude, E., Salame, W. O., 2016; Lahti, T., et al., 2010)

Buprenorphine is an opioid inverse agonist. This means that it has both opioid-like properties and can also be a blocker of opioids, whereas naloxone and naltrexone only block opioid effects. At low doses, it is a powerful opiate agonist (even more powerful than morphine or heroin), but as its dosage is increased, it deactivates and blocks the opioid receptors in the brain to act as an opioid antagonist. This action makes it safer to use both for the treatments of pain and opioid use disorder. By 2012, the Wall Street Journal reported on IMS (Inventory Management System) Health National Disease and Therapeutic Index that U.S. prescriptions for buprenorphine in the treatment of pain greatly outnumbered methadone prescriptions. (WSJ, 2012)

NAADAC: Why is there a move to have opioid antagonists be allowed to be sold as “over the counter” medication?

DR. INABA: Our nation is in the midst of a major opioid addiction and overdose death epidemic. The very grim evidence of such is incontrovertible:

- U.S. has 4.6% of the world’s population and consumes 80% of the world’s opioids, yet there is no or little evidence for their efficacy in the long-term treatment of chronic pain.

This column’s questions on the recovery and relapse were submitted by *Advances in Addiction & Recovery* readers. Some questions were edited for length and clarity. Submit your questions for Dr. Inaba to jgleason@naadac.org.

NAADAC: What is the best way for me to explain to my clients the difference among opioid agonists, antagonists, and partial agonist?

DR. INABA: Opioids like oxycodone and heroin affect the brain by attaching to specific sites on neurons known as receptors. These receptors activate, modify or stop actions that the brain processes through a process known as a synapse. This is how brain cells communicate to each other and to the rest of the body. Opioids bind to endorphin receptors that are present in the brain. The brain has different types of receptors for different types of endorphin molecules and when these receptors are activated, the result is decreased pain, altered mood, mitigated stress, suppressed cough, and other effects. You can think of this like different padlocks on brain cells that are opened, partially opened, closed or plugged up when an opioid slips into a specific lock and is mistaken for one of the brain’s natural endorphin molecules.

An opioid agonist is a drug that binds to a receptor site and acts like or mimics the effect usually achieved by the brain’s natural endorphin molecule. An antagonist binds to the endorphin receptor site, does not activate it, and sits in the receptor to block it from the action of opioids or endorphins. The antagonist is like a condom that covers the receptor site to prevent it from being activated. A partial agonist/antagonist only activates a portion of the receptor site resulting in partial effects and sits in the



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- Prescriptions for opioids have more than tripled in the past 20 years.
- By 2010, prescription overdose deaths, primarily from the consumption of opioids, were greater than auto accident deaths in the U.S.
- The 2016 United Nations reports that the U.S. has the highest drug overdose death rate in the world with a growing incidence of illicit fentanyl analogs laced heroin overdoses.

(Reuben, D. B., et al., 2015; UNODC 2016)

The tragedy of this is that an effective, easy to administer antidote with few side effects exists to counteract the lethal effects of opioid overdose. Particularly in its newer nasal administration form, naloxone serves as a powerful antidote. When sprayed into the nostrils, it will bring an opioid overdosed victim back into consciousness in a matter of seconds. When an accidental overdose occurs, it often takes several minutes to get the victim to an emergency room or for medical professionals to arrive with naloxone to treat the overdose. Many cities now provide their police officers and other first responders with naloxone kits since they are more likely to arrive on the scene of an overdose before other medical help can arrive and this change has resulted in many deaths being averted. In my small city of Medford, Oregon, police officers were provided with these kits last year and have been credited with saving several dozen lives in the first few months of the new program being implemented. The detox unit of the Addictions Recovery Center where I work has begun to train and provide clients coming through our unit with these kits, and in the two weeks since this training began, two lives have been saved. Needless opioid deaths continue to increase throughout the nation and making naloxone kits available to everyone “over the counter” (non-prescription) so that anyone can purchase them and have one on hand when they come upon an opioid

overdose will work to save lives. California (AB 1535 signed into law 2014) and other states have legislated availability of “over the counter” naloxone to combat the rash of opioid overdose death.

I believe that allowing naloxone to be sold over the counter is good common sense, though there are some caveats to keep in mind. First and foremost, one should always make the 911 call to get emergency medical help intervention when using naloxone. Its duration of action is much shorter than that of most opioids, so the overdosed victim may only temporarily come out of their coma only to go back into one when the naloxone wears off since the longer acting opioid will still be in their system. The victim may also have other medical problems or complication that can be addressed by getting formal medical assistance. Some of the illicit fentanyl analogs that are used to lace heroin are so powerful that naloxone may not effectively reverse their toxic effects. This also occurs when the user combines opiates with other drugs, particularly with benzodiazepines and heavy consumption of alcohol. Another thing to consider is the potential of precipitating opioid withdrawal symptoms when naloxone is used in a person who has developed physical addiction to opioids. Finally, even when used in someone not physically addicted, one should expect and be prepared for an angry and somewhat belligerent victim when he or she comes back to consciousness after the reversal of opioid effects. (Inaba and Cohen, 2014; Brunton, L. L., et al., 2011; Lowenson, J. H., 2011)

Those who struggle with substance related and addictive disorders do not fully engage in recovery until they come to desire recovery more than just about anything else. Naloxone has made it possible for thousands of individuals to have a second chance to come to that understanding. Sobriety is a change that can be accomplished before a person with addictive disorder experiences the ultimate consequence (death) from this powerful medical disorder. In many instances, naloxone has even hastened this understanding by bringing those with an opioid use disorder back from the very edge of that consequence to provide them with a new sense of meaning and value for their future potential contributions to their families and communities.

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