

Opioids

Information for Health Professionals

Introduction

Opioid is the generic term for any substance that binds to the opioid receptors found in the central nervous system (CNS), peripheral nervous system (PNS), gastrointestinal tract, and other organs in the body. Opioids are classed as depressants because they act on the CNS to slow down breathing, heart rate, and brain activity. As an alternative to intravenous administration, opioids can be injected under the skin or into a muscle. They can also be smoked, chewed, snorted, or swallowed.

Opioids fall into four main categories:

- endogenous opioids (e.g., endorphins), which occur naturally in the body
- opium alkaloids (e.g., morphine and codeine), which are isolated from the opium poppy (*Papaver somniferum*)
- semi-synthetic opioids (e.g., heroin and oxycodone), which are modified forms of opium alkaloids
- fully synthetic opioids (e.g., methadone, fentanyl), which have similar properties and effects as the alkaloids and semi-synthetics, but are completely man-made

Endogenous opioids appear to function as neurotransmitters, relaying signals within the nervous system. They are the body's pain regulators and are the equivalent of opioid medications and drugs.

Opium alkaloids and semi-synthetic opioids are collectively known as opiates. Opium alkaloids originate in the seed pod of the opium poppy. The harvesting process involves cutting slashes into ripened seed pods, which then releases a white, milky, latex substance that dries to a sticky brown resin and can be scraped off the pods as raw opium. Further processing of the raw opium isolates morphine and codeine, which may be modified to produce semi-synthetic opioids such as heroin. Heroin is the opioid most commonly associated with misuse and abuse; however, in recent years prescription opioids, such as oxycodone, have become the most commonly used illicit opioid.

Opioids are particularly effective pain relievers, which has led to their widespread medical use. Prescription opioids come in various forms, such as tablets, capsules, liquids, injectables, suppositories, and skin patches. Opioids have also become well known as drugs of abuse because of their psychoactive properties and their ability to induce euphoria.

The misuse of prescription opioids entails the use of a prescription medication in a manner not intended by the prescribing physician. Prescription opioid misuse includes everything from borrowing or stealing medications from family and friends, to snorting or injecting crushed pills to get high. Prescription opioids may be acquired in a variety of ways. This includes legally acquiring a prescription from a single physician, or illegally obtaining prescription drugs by seeking out additional doctors ("double doctoring") prescription fraud, and street drug markets.

Oxycodone is one of the most commonly abused prescription opioids. In 2012, the branded version of oxycodone was delisted over concerns of abuse. It was replaced by a new formulation that is harder to abuse. Since its delisting, however, there has been a surge in counterfeit oxycodone appearing for sale

in Canadian communities. Some counterfeit drugs also contain illicit fentanyl (i.e., manufactured in illegal laboratories), which can be considerably more toxic than pharmaceutical-grade fentanyl.

Individuals using opioids, or other drugs, that are laced with fentanyl are at an increased risk of overdosing. Additionally, abuse of prescription fentanyl (which is approximately 100 times stronger than morphine), is becoming increasingly common and can also be lethal.

Medical use

Opioids, either by themselves (e.g., morphine) or compounded with non-opioid analgesics (e.g., codeine with acetaminophen), are used to treat moderate to severe pain that non-opioid analgesics alone cannot control. They also play an important role in the palliative care of people with terminal conditions or serious illnesses, such as cancer. In these cases, the need to provide adequate pain relief and to improve the person's quality of life outweighs most potential side effects or loss of mental alertness.

The use of opioids in the treatment of non-malignant chronic pain (sometimes referred to as chronic non-cancer pain or CNCP) has been a more complex and controversial issue. This is partly because of the concern that long-term use of opioids might lead to the development of an addiction. In addition, it has been argued that medication alone is not effective in addressing CNCP and that a multi-disciplinary team approach should be used to tackle psychological and social factors, such as physical inactivity, depression, and social isolation associated with chronic pain. Non-drug therapies including physiotherapy, stress management, exercise, and relaxation techniques are viewed as important adjuncts in the care of people with CNCP.

When prescribing opioids for CNCP, the goal is often to control pain to improve function, rather than to eliminate pain completely. Although a history of addiction would not rule out the use of opioid pain relievers, there needs to be a thorough assessment before they are prescribed and careful monitoring throughout treatment for any evidence of overuse or misuse of the medications.

Although they are best known for their pain relieving properties, opioids have other medical applications. Opioids, especially codeine, have long been used in cough medicines because they suppress the cough reflex. Through their depressant action on the CNS, opioids slow down the body's digestive process, leading to constipation. This property has been exploited as a way of treating chronic diarrhea. Diphenoxylate is an opioid with low addictive potential used in such cases.

How opioids work

When taken, opioids travel through the bloodstream and into the brain and throughout the body where they bind to opioid receptors in the brain, spinal cord, and digestive tract. Binding of opioids to the opioid receptors decreases neurotransmitters, like glutamate, that are responsible for transmitting pain signals while activating dopamine neurons and the dopamine reward system within the nucleus accumbens. This causes an intense euphoria that lasts briefly before producing a relaxed state for a few hours. Outside of the brain, opioids can relieve pain by blocking pain messages between neurons and interfering with their ability to signal a pain response to the brain. Additionally, opioids can act within the brain to alter a person's subjective experience of pain.

Opioids also act directly on the respiratory center in the brainstem in the CNS to slow its activity and decrease breathing rate. In high doses, opioids can completely shut down this system and stop breathing. When overdoses are apparent and fatalities do occur, they are normally caused by the respiratory depression arising from the effects of the opioids on the CNS. Taking more than one kind of CNS depressant at a time also has a cumulative effect on respiratory depression. Combining even

moderate doses of opioids with other substances such as alcohol or sleeping pills could result in a fatal overdose. Older adults have a higher risk of accidental misuse or abuse because they often have multiple prescriptions, increasing the likelihood of harmful drug interactions.

Short-term effects

Unlike alcohol, tobacco, and many other psychoactive substances, opioids are not directly harmful to the body if used appropriately. As with any psychoactive drug, the feelings experienced when using opioids depend on the specific drug, the amount used, how it is taken, drug tolerance, the setting or location, and the user's mental state. The most commonly reported side effects are drowsiness, warmth, a sense of well-being and contentment, and detachment from pain and anxiety. The euphoric effects are heightened when opioids are injected into a vein and produce an almost instantaneous, short-lived sensation often referred to as a "rush". These effects are exacerbated when opioids are used with other CNS depressants, such as benzodiazepines and alcohol.

If taken orally, the effects of opioids generally come on gradually within 10-20 minutes. If administered into the skin or a muscle, the effects come on faster, within 5-10 minutes. If the opioid is taken by injecting into a vein, the "rush" comes on within a few seconds and lasts a few minutes. An excessive single dose could potentially be fatal for someone who is not a regular opioid user, and has not developed a tolerance to their depressive action on the respiratory system. Even long-term opioid users are at risk if they accidentally or deliberately take a stronger dose than usual or resume their normal dosing after a period of abstinence.

Following the "rush", users may experience a period of sedation known as "nodding", which can last up to an hour. Breathing may slow, pupils constrict, and an overall feeling of well-being may occur. New users often experience nausea and vomiting. Opioids can also increase the risk of sleep apnea and mood changes, and decrease sexual interest and appetite.

Long-term effects

Long-term use of opioids can prompt users to increase their dosage to achieve desired effects. Additionally, withdrawal symptoms can be felt to a greater extent when dosages are lowered. Worsening pain, known as "opioid-induced hyperalgesia", as well as liver and kidney damage can occur when taking opioids. Other long-term effects that can develop as a result of opiate usage include collapsed veins (due to intravenous use), lung complications, mental disorders, sexual dysfunction, and menstrual irregularities.

For street drug users, it can be the lifestyle and patterns of behavior that accompany illicit opioid use that are of greatest risk, rather than the drugs themselves. Opioid drug users may have poor nutrition and living conditions, and may engage in high-risk activities in order to fund their dependency. Snorting or injecting opioids increases the chance of overdosing and permanent damage to veins and organs. Intravenous use is one of the main transmission routes for viruses including hepatitis C and HIV/AIDS. Infections from contaminated drugs or unsterile injecting equipment are common and can cause localized problems, such as abscesses or more serious conditions, such as endocarditis (an infection of the lining of the heart). Permanent damage to the lungs, liver, brain, and kidneys can also develop from the clogging of blood vessels due to additives like starch and sugar.

Opioids and pregnancy

Regular opioid use during pregnancy is associated with increased risk for miscarriage, premature delivery, and low birth weight. Using opioids during pregnancy is also associated with neonatal abstinence syndrome, a condition some newborns experience after exposure to certain addictive drugs

while in the mother's womb. When a pregnant woman takes opioids, there is a risk that the unborn fetus can become addicted along with the mother. Once born, the baby remains dependent on the drug and symptoms of withdrawal can occur because the baby is no longer exposed to the drug.

During pregnancy, the aim of treatment is to reduce withdrawal and prevent relapses through maintenance treatment with methadone, buprenorphine, or morphine. Management of newborns exhibiting signs of withdrawal includes pharmacologic treatment (e.g., methadone, buprenorphine, or morphine) and supportive care (e.g., swaddling, decreased stimulation, settling).

Tolerance and Dependence

Continued use of most opioids leads to the development of tolerance, meaning that increased amounts of the drug or medication are required to maintain constant levels of pain relief or euphoria. When opioids are being used for their psychoactive properties, tolerance often reaches the point where feelings of euphoria are no longer attainable and users report having to continue taking their medication or drug just to function and feel normal. When tolerance takes place, it can be challenging for physicians to discern whether a person is developing a drug problem, or has a medical need for increased dosage to control their symptoms. As a result, physicians should be aware and observant of the symptoms and behaviors of their patients to treat them appropriately.

Psychological dependence or addiction to opioids is marked by cravings and a compulsive need to continue taking the medication or drug despite any harmful or negative consequences arising from its use. Psychological dependence is typically associated with a loss of control. For example, a person may start with appropriate use of an opioid medication for pain control, but then progress to misuse or abuse because they become addicted to its psychoactive effects. They may use their medication more rapidly than it was prescribed and could even escalate double doctoring or buying medication on the street to ensure a continued supply.

Withdrawal and treatment

Prolonged opioid use is also characterized by physiological changes in the body's pain control and other mechanisms, leading to physical dependency. Once this is established, abrupt cessation of use will produce withdrawal symptoms. Even when opioids are being appropriately prescribed and consumed, physical dependency can occur over time if an appropriate tapering plan is not developed. In such cases, once the opioid medication is no longer required, the dose should be slowly reduced to avoid placing the person into withdrawal.

Withdrawal from opioids, unlike that from alcohol, is not life-threatening but can produce high levels of discomfort and symptoms similar to a severe case of gastroenteritis. Commonly, these will start to occur between 8 and 24 hours after the last dose, depending on the type of opioid used. Usual symptoms include aches (especially in the joints and back), sweats and chills, restlessness, stomach cramps, vomiting, diarrhea and insomnia. Most of these effects will peak between 36 and 72 hours after the last dose and will generally last for seven to 10 days; however, some symptoms, such as insomnia, might take several weeks to fully subside. Withdrawal symptoms can be minimized through medical management and slow taper protocols.

Opioid agonist treatment, combined with psychosocial interventions, is effective in treating opioid dependency. It reduces illicit opioid use, criminal activity, HIV risk behaviors and transmission, and deaths from overdose. Buprenorphine and methadone are often used in opioid agonist treatment. Research has shown that buprenorphine and methadone maintenance is more effective when used in conjunction with cognitive and behavioral approaches. Alberta Health Services' Opioid Dependency

Program (ODP) provides opioid agonist treatment and counseling services to individuals who are addicted to opioids and unable to achieve abstinence without additional support. Needle exchange programs and supervised consumption sites are both available for Albertans to access as well.

Naloxone is a medication that can completely reverse an opioid overdose. It is typically included as a part of emergency overdose response kits, and is commonly used by medical personnel in emergency departments and ambulances. Naloxone kits are also available to the public in many Alberta pharmacies, emergency departments, and community walk-in clinics. People treated with naloxone still require medical care as it simply provides a window of time in which the effects of the opioid are blocked and the patient can regain their full breathing function. Additionally, other substances besides opioids may have been ingested and may require different medical treatment.

Who uses opioids?

It is difficult to obtain an accurate picture of illicit opioid use in Canada and Alberta for a number of reasons. Most studies do not differentiate medical use from street use; those that do often concentrate only on heroin. Prevalence of heroin use is often too low to report in general population surveys and tends to be grouped together with unrelated substances, such as steroids and solvents. In 2015, opioid pain relievers were used by 13% of Canadians aged 15 years and older. Among those using opioid pain relievers, 2% reported abusing them.

Emergency room visits and overdose deaths from opioids have increased markedly in Canada. On average in 2017, there were 16 hospitalizations a day due to opioid poisoning in Canada. In Alberta, youth aged 15 to 24 have the highest and fastest-growing rates of emergency room visits due to opioid poisonings. Between 2016 and 2017, the number of apparent opioid-related deaths in Canada increased by 34%, with over 92% of these deaths classified as unintentional. In this same period, the number of opioid-related deaths involving fentanyl or fentanyl analogues increased 81%.

Opioids and the law

Under Canada's *Controlled Drugs and Substances Act*, both illicit substances, such as heroin, and prescription opioids, such as oxycodone, are classified as Schedule I drugs. For charges tried by summary conviction, the maximum penalty for first-time possession of opioids is a \$1000 fine and/or six months in prison. For subsequent offences, the maximum penalty is a \$2000 fine and/or 12 months in prison. For charges tried by indictment, possession can result in seven years in prison, while trafficking, exporting, importing, or producing opioids can result in life imprisonment.

On May 4, 2017, the *Good Samaritan Drug Overdose Act* became law. This law provides exemption from charges of simple possession of a controlled substance, and charges concerning pre-trial release, probation order, conditional sentence or parole violations, for people who call 911 for themselves or another person suffering from an overdose. This law also includes exemption for anyone who is at the scene when emergency help arrives.

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