

Abstract:

The use of opiates and opioids by both adults and children is a growing problem in the United States. With the increased prevalence of prescription opioid misuse, efforts have been aimed to control the spread of this epidemic. Prescription opioids, however, only represent a portion of the opiate-like products available through prescription or illicit means. We describe the hazards and increased use of opioid-related products such as heroin, fentanyl, and buprenorphine as well as emerging products of abuse such as Kratom, loperamide, and carfentanil.

Keywords:

opiate; opioid; adolescent; heroin; emerging agents; naloxone; fentanyl; carfentanil; loperamide; buprenorphine; Kratom

Current Opiate and Opioid Hazards in Children and Adolescents

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The prevalence of opioid use in society has reached epidemic proportions. Seventeen million people worldwide engage in heroin and non-medicinal opioid use.¹ The United States constitutes 4.6% of the world's population, yet consumes 80% of the global opioid supply and 99% of the global hydrocodone supply. The US also consumes two-thirds of the world's illegal drugs.²

Deaths from unintentional overdose began to rise in the 1990's.³ By 2007, prescription opioid-related deaths exceeded the rate of death from cocaine and heroin combined.³ In 2014, poisoning deaths became the number one cause of accidental death.⁴ The drug overdose death rate increased significantly; from 12.3 per 100,000 in 2010 to 16.3 per 100,000 in 2015. This increase was driven largely by deaths from heroin and synthetic opioids.⁵ The Drug Enforcement Agency (DEA) has named prescription drugs, heroin, and fentanyl the biggest drug-related threats in the United States.⁵

There are two important exposure patterns to consider in the pediatric population. In the under age 6 group, most ingestions can be considered accidental or exploratory ingestions, and efforts to reduce the frequency should focus on poison prevention. When opioids are prescribed in the pediatric patient population, this must be done with great care. In September 2016, the

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American Academy of Pediatrics recommended discontinuing the use of codeine in young children because of documented respiratory depression and fatalities.⁶

In the adolescent age group, opioids and opiates can be used with the intention of getting high or experimentation. This is associated with risk for ongoing use and the potential for addiction.

Over the period of 2000 to 2015 there were 188,468 prescription opioid exposures in children under twenty according to the National Poison Data System (NPDS).⁴ The annual number and rate of exposure in children increased early in the study, but declined after 2009 with the exception of buprenorphine. Buprenorphine exposures increased from 2012 to 2015. Hydrocodone accounted for the highest proportion of exposures at 28.7%. In addition, teenagers had a 3-fold greater risk of serious outcome than children 0–5 years of age.⁴

It is becoming clearer that the risk of opioid dependence is related to the prescription length. A recent study looking at prescription length and risk of long-term opioid use found that of all patients given an opioid prescription, 2.6% will continue therapy for >1 year.⁷ The longer the initial prescription, the higher is the risk of subsequent opioid use. The highest probability of continued opioid use was for patients given an initial prescription for greater than 10 or 30 days of use.⁷ Educational efforts to promote safe opioid prescribing are needed in all specialties.

Pediatric Addiction Medicine specialists are scarce; only 1% of US Addiction Medicine diplomats are pediatricians.⁸ If available, an addiction specialist can be a valuable resource to pediatricians caring for dependent teens.⁸

In the remainder of the article we will discuss opioids of current importance. In general, comprehensive laboratory testing will not be available for many of these agents. It is essential for the clinician to be expert in toxidrome recognition. Specifically, patients poisoned with these agents exhibit the “opioid toxidrome.” The classic features of this toxidrome include altered mental status, miosis, and slow and shallow respirations. Track marks may be an additional sign of intravenous drug use.

HEROIN

Heroin (diacetyl morphine hydrochloride), an FDA schedule I drug, is among the most addictive illicit drugs and a cause of both short and long-term mortality. Originally derived from morphine and commercialized by Bayer Company in 1898, the addition of acetyl groups renders heroin more

lipophilic than morphine with a more efficient central nervous system (CNS) delivery.⁹ Progression from recreational heroin use to tolerance, dependence, and addiction is common and can be devastating to both patients and their families.¹⁰

Although prescription opioid deaths have plateaued in recent years, heroin-related deaths have more than tripled between the years 2010 and 2014.¹¹ In addition to efforts aimed at curtailing inappropriate opioid prescribing, the reported ease of availability and low purchase price of heroin are thought to be driving this transition.¹² Early prescription opioid use, especially in those aged 10 to 12, has been strongly correlated with future transition to heroin use.^{13,14}

The demographics of heroin use have also changed significantly in the past 50 years. While heroin was formerly thought to be largely a phenomenon of urban males, use has increased among women and those in non-urban areas.¹² Female heroin users are of particular interest because their progression to intravenous (IV) use is more rapid than their male counterparts.¹⁵

As the total number of heroin users has increased, the age of first use is decreasing. An earlier age of first use of heroin has been correlated with a higher lifetime prevalence of dependence, opioid use disorder, and progression to more dangerous routes of administration of heroin.¹³ The age-group with the highest rate of heroin use is young adults aged 18 to 25 years.¹⁴

Heroin is classified as a true opiate because, like morphine, it is derived from the natural alkaloid compounds contained in the resin of the opium poppy.¹⁶ Like all opiates and opioids, heroin acts on the mu, kappa, and delta opioid receptors. The target organ for heroin is the central nervous system (CNS), but opioid receptors also exist in the gastrointestinal tract, cardiac muscle, and the vascular system. Agonist activity at the mu-opioid receptor in the locus coeruleus of the CNS leads to downstream activation of dopamine receptors, a common reward pathway leading to addiction.^{10,17} Recurrent exposures to heroin can lead to receptor neuroadaptation and ultimately physiologic dependence in as little as 4 weeks in opioid-naïve individuals.¹⁸

Heroin can be used by multiple routes. It is typically insufflated, smoked, or injected intravenously or subcutaneously. As heroin purity and potency has increased in the past 3 decades, insufflation and smoking have become increasingly efficient routes of administration, often negating need for initial IV use.¹⁶ Once heroin use has been established, however, transition to injection is not uncommon.¹⁴

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