Toxicity, Narcotics

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Introduction

Background

Pain is arguably the most common reason why patients seek treatment, especially in the ED. The modern physician wields many tools to relieve pain, the most potent of which are narcotics. The term narcotic specifically refers to any substance that induces sleep. In current practice, narcotic refers to any of the many opioids or opioid derivatives. In cultivation since approximately 300 BC, pure opium is a mixture of alkaloids extracted from the sap of unripened seedpods of *Papaver somniferum* (poppy). Opiates, such as heroin, codeine, or morphine, are natural derivatives of these alkaloids. The term opiate is often used (albeit slightly incorrectly) to refer to synthetic opiate derivatives, such as oxycodone, as well as true opiates.

Although opioids constitute a relatively small percentage of pure overdoses encountered in the ED, they merit particular attention because of the potential mortality they cause when untreated and the relative ease of reversing their effects. The notable prevalence of opioids in current prescribing patterns mandates that physicians maintain a high index of suspicion when treating the patient who is unconscious for unknown reasons.

Narcotic use and abuse have been reported as increasing in frequency in the past few years, a trend that has been blamed in increasing utilization of narcotics by medical personnel, as well as illicit drug abuse (Paulozzi, 2006). While increased availability certainly plays a role in narcotics abuse, the link between legitimate use and abuse is not well proven (Compton, 2006; Joranson, 2006).

Pathophysiology

Activation of opiate receptors results in inhibition of synaptic neurotransmission in the central nervous system (CNS) and peripheral nervous system (PNS). Opioids bind to and enhance neurotransmission at opiate receptors. The physiological effects of opioids are mediated principally through mu and kappa receptors in the CNS and periphery. Mu receptor effects include analgesia, euphoria, respiratory depression, and miosis. Kappa receptor effects include analgesia, miosis, respiratory depression, and sedation. Two other opiate receptors that mediate the effects of certain opiates include sigma and delta sites. Sigma receptors mediate dysphoria, hallucinations, and psychosis; delta receptor agonism results in euphoria, analgesia, and seizures. The opiate antagonists (eg, naloxone, nalmefene, naltrexone) antagonize the effects at all 4 opiate receptors.
Common classifications divide the opioids into agonist, partial agonist, or agonist-antagonist agents and natural, semisynthetic, or synthetic. Opioids decrease the perception of pain, rather than eliminate or reduce the painful stimulus. Inducing slight euphoria, opioid agonists reduce the sensitivity to exogenous stimuli. The GI tract and the respiratory mucosa provide easy absorption for most opioids.

Peak effects generally are reached in 10 minutes with the intravenous route, 10-15 minutes after nasal insufflation (eg, butorphanol, heroin), 30-45 minutes with the intramuscular route, 90 minutes with the oral route, and 2-4 hours after dermal application (ie, fentanyl). Following therapeutic doses, most absorption occurs in the small intestine. Toxic doses may have delayed absorption because of delayed gastric emptying and slowed gut motility.

Most opioids are metabolized by hepatic conjugation to inactive compounds that are excreted readily in the urine. Certain opiates (eg, propoxyphene, fentanyl, buprenorphine) are more lipid soluble and can be stored in the fatty tissues of the body. All opioids have a prolonged duration of action in patients with liver disease (eg, cirrhosis) because of impaired hepatic metabolism. This may lead to drug accumulation and opioid toxicity. Opiate metabolites are excreted in the urine, making urine toxicology useful. Renal failure also leads to toxic effects from accumulated drug or active metabolites (eg, normeperidine).

**Frequency**

**United States**

Opioids are prescribed widely, often in concert with other analgesics, including nonsteroidal anti-inflammatory drugs (NSAIDs) or muscle relaxants. Given all toxicologic presentations, pure opioid ingestions are generally a small proportion of ED overdose cases. The etiology of overdoses presenting to an ED often reflects local prescribing tendencies. Polypharmacy overdoses that include opioids can be a challenge for even the most experienced clinician. Fortunately, pharmacologic reversal of the opioid component can assist in the diagnosis of these potentially complex cases.

Data from the Drug Abuse Warning Network (DAWN) from 1990-1996 indicated that the abuse of opioid analgesics (as recorded from the number of hospital ED visits) is low; compared with the abuse of other drugs, the abuse of opioid analgesics accounts for 3.8-5.1% of ED presentations.

In 1998, a total of 36,848 opiate exposures (pure and mixed preparations) were reported to US poison control centers, of which 1227 (3.3%) resulted in major toxicity and 161 (0.4%) resulted in death.

**Mortality/Morbidity**

The predominant cause of morbidity and mortality from pure opioid overdoses is respiratory compromise. Less commonly, pulmonary edema, status epilepticus, and cardiotoxicity occur in the overdose setting.
Clinical

History

- Pertinent history may be obtained from bystanders, family, friends, or EMS providers. Pill bottles, drug paraphernalia, or eyewitness accounts may assist in the diagnosis.
- Occasionally, a trial of naloxone administered by EMS is helpful to establish the diagnosis in the prehospital setting.
- Ingestion time, quantity, and co-ingestants are important aspects of the history and should be ascertained.

Physical

- Opioid toxicity characteristically presents with a depressed level of consciousness. Opiate toxicity should be suspected when the clinical triad of CNS depression, respiratory depression, and pupillary miosis are present. Drowsiness, conjunctival injection, and euphoria are seen frequently. Needle tracks are observed occasionally, depending on the route of abuse. Street users commonly use heroin and morphine by subcutaneous ("skin popping") and intravenous ("mainlining") injection. Raw opium usually is eaten or smoked, and sometimes the powder is sniffed ("snorted"). Transdermal opioid patches, such as fentanyl, also may produce toxicity.
- Other important presenting signs are ventricular arrhythmias, acute mental status changes, and seizures. Reliance on pupillary miosis to diagnose opioid intoxication can be misleading. If sufficiently severe, hypertension and pupillary dilation may present because of CNS hypoxia. Morphine, meperidine, pentazocine, diphenoxylate/atropine (Lomotil), and propoxyphene sometimes are associated with mydriasis or midpoint pupils.
- The respiratory effort frequently is impaired opiate intoxication. Both bradypnea and hypopnea are observed. Rates as slow as 4-6 breaths per minute often are observed with moderate-to-severe intoxication. The body retains the hypoxic drive to breathe but may be overridden by the CNS sedative effects of a severe overdose.
- Mild peripheral vasodilation may occur and result in orthostatic hypotension. However, persistent or severe hypotension should raise the suspicion of co-ingestants and prompt reevaluation. Opioids prolong GI transit times, possibly causing delayed and prolonged absorption. Initial tendencies for nausea and emesis are transient. Pink frothy sputum, muscular rigidity, dyspnea, and bronchospasm strongly suggest pulmonary edema.
- Nightmares, anxiety, agitation, euphoria, dysphoria, depression, paranoia, and hallucinations are encountered infrequently, mainly with high doses. Pruritus, flushed skin, and urticaria may arise because of histamine release. Generalized seizures are infrequent; they occur most commonly in infants and children because of initial CNS excitation. In contrast, seizure activity in adults is suggestive of meperidine or propoxyphene ingestions. Hearing loss has been associated with heroin and alcohol but is generally considered recoverable.
References


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