

Opioid Analgesics

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Abstract

Chronic pain is an international health issue of immense importance that is influenced by both physical and psychological factors. Opioids are useful in treating chronic pain but have accompanying complications. It is important for clinicians to understand the basics of opioid pharmacology, the benefits and adverse effects of opioids, and related problematic issues of tolerance, dependence, and opioid-induced hyperalgesia. In this article, the role of psychiatric comorbidity and the use of validated assessment tools to identify individuals who are at the greatest risk for opioid misuse are discussed. Additionally, interventional treatment strategies for patients with chronic pain who are at risk for opioid misuse are presented. Specific behavioral interventions designed to improve adherence with prescription opioids among persons treated for chronic pain, such as frequent monitoring, periodic urine screens, opioid therapy agreements, opioid checklists, and motivational counseling, are also reviewed. Use of state-sponsored prescription drug monitoring programs is also encouraged. Areas requiring additional investigation are identified, and the future role of abuse-deterrent opioids and innovative technology in addressing issues of opioid therapy and pain are presented.

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Chronic pain is a serious international problem of immense proportion that can negatively impact every facet of daily living.^{1,2} It has been estimated that annually more than 100 million Americans have chronic pain.³ Chronic pain affects more individuals than diabetes, cancer, and heart disease

combined and is the major reason people visit their primary care physicians. Chronic pain can interfere with sleep, employment, social life, daily activities, and overall quality of life. Chronic pain can also have a negative effect on mood, appetite, energy level, and sexual activities and can contribute to recurrent worried

thoughts about finances, family interactions, and future disability.^{4,6}

The usefulness of opioids in the treatment of acute and cancer-related pain has been confirmed by several studies.⁷ An estimated 5 to 8 million Americans use opioids for chronic pain.⁸ Yet, many physicians and other health care professionals are reluctant to support the use of opioid medication for patients with chronic noncancer pain because of concerns regarding adverse effects, tolerance, and addiction.^{9,10} Addiction, in particular, is of prime concern given its intensely negative consequences and its relatively broad prevalence. Over the past decade, there has been a steady increase in use of prescription opioids in the United States, which has been the main contributing factor to the skyrocketing incidence of opioid abuse. The number of opioid prescriptions written for pain increased from 76 million in 1991 to an estimated 219 million in 2011.¹¹ This increase has paralleled the increase in opioid-related overdoses and hospitalizations.¹² Because of increased availability, prescription opioids have become the most abused class of drug in the United States, with more deaths related to opioid abuse than to cocaine and heroin combined.¹² Many drug abusers prefer prescription opioids not only for their easier availability compared with street drugs but also for their greater purity due to their regulated manufacture.^{12,13} In fact, patients in the United States consume 80% of all opioid prescriptions worldwide, and prescription drug abuse is perceived to be the fastest growing drug problem in America.¹² Unfortunately, most clinicians are not adequately prepared to properly diagnose, treat, and closely monitor patients with chronic pain who are prescribed opioids, even though studies have shown that those patients who are at greater risk for misuse of opioids are most likely to be prescribed opioids.¹³

In this article, we present a current review of the pharmacology of opioids and its uses and discuss misuse and abuse issues that are often present when treating patients prescribed opioids for chronic pain. We will also provide an overview of assessment and treatment strategies designed to improve adherence to opioid prescriptions and briefly explore unresolved clinical questions and future considerations.

OVERVIEW OF OPIOIDS FOR PAIN

Opioid Clinical Pharmacology

The term *opioid analgesics* refers to a broad class of drugs including (1) alkaloids extracted from poppy seeds (morphine, codeine) and their semisynthetic derivatives (oxycodone, hydromorphone, oxymorphone) and (2) synthetic phenylpiperidines (meperidine, fentanyl) and synthetic pseudopiperidines such as methadone.¹⁴ Opioid analgesics act on 3 major classes of receptors: μ , δ , and κ receptors. Each of these classes of receptors has its representative endogenous ligand (eg, endorphin for the μ receptor and dynorphin for the κ receptor). These classes of opioid receptors are widely distributed throughout the central and peripheral nervous system as well as other systems such as the gastrointestinal tract. On the basis of their pharmacodynamic profiles, opioid analgesics can also be classified as a full agonist at opioid receptors (eg, morphine, fentanyl) or an agonist-antagonist such as buprenorphine.¹⁵

Benefits and Adverse Effects of Opioids

Activation of opioid receptors produces profound analgesia mediated through a combined presynaptic and postsynaptic effect. Presynaptically, opioid analgesics act on primary nociceptive afferents (inhibition of calcium channels), resulting in the reduced release of neurotransmitters such as substance P and glutamate implicated in nociceptive transmission. Postsynaptically, opioid analgesics directly inhibit postsynaptic neuronal activity by hyperpolarizing cell membranes via opening potassium channels. Other effects of opioids (eg, antitussive, reducing gastrointestinal tract motility) also have practical therapeutic use.¹⁶

Because of a widespread distribution of opioid receptors both within and outside the nervous system, opioid analgesics also produce a broad spectrum of adverse effects including euphoria, dysphoria, sedation, respiratory depression, constipation, suppression of endocrine systems, cardiovascular disorders (eg, bradycardia), convulsion, nausea, vomiting, pruritus, and miosis.¹⁷ Although the extent of these adverse effects may differ among individual opioids depending on dose regimen, these effects substantially narrow

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