Acute pain is undertreated for many people in the United States. Although opioid analgesics are extremely important tools for the treatment of acute pain, their appropriate use is often poorly understood by both clinicians and patients. Among other issues, confusion about the risk of dependence, tolerance, and addiction with opioid therapy is a significant contributor to the undertreatment of pain. Dependence (the presence of a withdrawal symptom upon drug discontinuation) is a feature of opioid therapy, but is also common with many other types of commonly used medications. Tolerance to the effects of opioids is an expected response to ongoing treatment. Addiction is a primary neurobiological disease that occurs extremely infrequently when patients without preexisting substance use disorders receive opioid treatment for acute pain. However, inadequate pain relief can cause behaviors that resemble addiction, in some respects, a phenomenon that has been referred to as pseudoaddiction. Although the risk of addiction with acute opioid treatment is extremely low, rating scales to help identify patients who may benefit from closer monitoring for development of aberrant drug-related behaviors may be useful for some persons. Undertreatment of acute pain is a significant problem in the United States, which is at least partly attributable to the limited education about pain that most clinicians receive. Effective treatment of acute pain is essential to relieve patient suffering and improve quality of life, and it may also prevent the development of chronic pain.

Opioid analgesics are among the most common medications prescribed and dispensed by healthcare professionals, yet they are also among the most poorly understood. Among the many obstacles to effective pain management is the limited education that most clinicians receive about pain or opioid treatment. Patients, and many healthcare professionals, think that even a short course of treatment with an opioid analgesic can cause addiction. Largely as a result of this perceived risk of addiction, and the need to balance appropriate analgesia with care to keep these potent drugs out of the hands of people who do not need them, opioids are often prescribed cautiously by physicians and other healthcare providers, and are not used effectively by patients. However, there is considerable evidence that the risk of addiction is extremely low when opioids are used for short-term pain relief by patients who do not have substance use problems. Another limit to outstanding pain management occurs commonly when pharmacists in the community have incomplete information about the patient. Additionally, it is important for pharmacists to understand that the use of opioid pain relievers is not by itself a marker of current or future opioid addiction.
DEPENDENCE, TOLERANCE, AND ADDICTION

It is essential to understand the distinctions between dependence, tolerance, and addiction. Confusion about these concepts is a significant contributor to the undertreatment of pain in the United States.

According to a consensus statement by the American Academy of Pain Medicine, the American Pain Society, and the American Society of Addiction Medicine, dependence is defined by the presence of a withdrawal syndrome when a substance is suddenly removed, the dose is rapidly decreased, or the patient is treated with an antagonist that prevents the drug’s physiologic effect. Antagonists with the potential to produce a broad range of withdrawal symptoms, including central arousal (eg, insomnia, irritability, and agitation), autonomic symptoms (eg, diarrhea, rhinorrhea, and sweating), muscle spasms, and gastrointestinal cramping.

Dependence is a normal and expected consequence of chronic opioid treatment, and it is associated with a number of nonopioid drugs that should not be discontinued abruptly, including corticosteroids, anticonvulsants, antidepressants, and β blockers. For drugs that produce physical dependence, the risk of withdrawal symptoms may be reduced by gradually tapering and discontinuing the drug.

Tolerance occurs when the physiological response to a fixed drug dose diminishes over time, resulting in the need for increasing drug doses to produce the same effect. It should be noted that tolerance to different drug effects may develop at different rates. For example, tolerance often develops relatively quickly to the sedative and respiratory depressant effects of opioids, whereas tolerance to opioid-induced constipation develops gradually or not at all.

The term addiction is particularly misunderstood, even among healthcare professionals. According to the American Pain Society, the American Society of Addiction Medicine, and the American Academy of Pain Medicine, addiction is a primary neurobiological disease with genetic, psychosocial, and environmental components. This definition does not refer to any specific level of opioid dosing or length of time that the drug has been used. Addiction is characterized by a range of behaviors that may include diminished ability to control drug use, compulsive substance use, continued use of the substance despite harmful effects, and craving of the substance.

Although it is appropriate to be concerned about the potential for addiction and other adverse effects with opioid therapy, several studies have demonstrated very low rates of addiction among patients receiving opioids for acute pain. One chart review of nearly 12,000 hospitalized patients who received opioid medications identified only 4 patients with evidence of iatrogenic addiction (ie, addiction after treatment among patients who did not have a history of substance abuse before treatment). Perry and Heidrich conducted a survey of pain management strategies and outcomes associated with debridement at 93 burn units in the United States. Together, the physicians and nurses surveyed had treated more than 10,000 patients for debridement pain, and most of these patients had received opioids. Only 12% of the respondents reported that they knew of any patients who developed opioid addiction after hospital discharge. In every case but one, addicted patients had a history of previous substance abuse problems. The single reported case of iatrogenic addiction in a patient with no history of substance use was a 3-year-old child who was described as addicted to methadone upon hospital discharge. Sickle cell crisis is a hereditary condition that can produce severe pain of the bones, liver, lungs, and gut, which is often undertreated due to concerns about the risk of iatrogenic addiction. Surveys of patients who were treated with opioids for sickle cell crisis have suggested very low rates of iatrogenic addiction among these patients. For example, one survey of opioid-associated adverse events among 101 patients with sickle cell crisis identified 3 patients with opioid addiction. Other surveys have found rates of opioid addiction among patients treated for sickle cell crisis of fewer than 1 in 500 patients.

These studies demonstrate that patients who use opioid medications for the short-term relief of even very severe acute pain are unlikely to develop opioid addiction. However, inadequately treated pain often results in pseudoaddiction, a pattern of behavior that superficially resembles some behaviors of an individual with addiction. These behaviors include using or requesting pain medication before the next scheduled dose, returning to the physician’s office to request other medications, or other behaviors that may resemble addiction but that are an understandable response to inadequate pain management.
Finally, it should be noted that pain is a complex, subjective phenomenon that is often difficult to precisely describe or categorize. Although pain is defined as an unpleasant sensory and emotional experience that is associated with tissue damage, there is often no clear relationship between the extent of tissue damage and the type or severity of pain experienced. Clinicians must therefore rely on the subjective self-reports of patients about their pain. In addition, pain is often categorized as either acute or chronic. Acute pain is generally defined as pain of recent onset and relatively limited duration (e.g., following surgery or an injury), whereas chronic pain is defined as pain that persists for longer than is required for the injury to heal, or that continues for an undefined, extended period of time. However, these distinctions are sometimes misleading, as different types of pain may occur simultaneously or sequentially in the same individual. For example, patients with cancer may experience ongoing chronic pain that is punctuated by episodes of acute pain, and patients with chronic painful conditions such as rheumatoid arthritis may experience injuries or require surgery.

IDENTIFYING HIGH-RISK PATIENTS

As noted previously in this article, the risk of iatrogenic addiction among patients without a history of substance abuse who are receiving opioids for acute pain is very low. Although it would be beneficial to identify the small subset of patients who are at greatest risk of developing addiction, it is difficult to accurately identify these individuals. Clinical rating scales have been developed to identify patients who have or are at risk of substance use problems with opioid therapy. The Revised Screener and Opioid Assessment for Patients with Pain (SOAPP)-R is a 24-question rating scale that was primarily designed to evaluate aberrant behaviors associated with long-term opioid therapy for patients with chronic pain. Questions on the SOAPP-R include:

- How often have you taken more pain medication than you were supposed to?
- How often do you have mood swings?
- How often have you felt a craving for medication?
- How often have others expressed concern over your use of medication?
- How often have you felt consumed by the need to get pain medication?

A second rating scale, the Opioid Risk Tool consists of only 5 items, which assess family and personal history of substance abuse (alcohol, illegal drugs, and prescription drugs). Although these rating scales may be useful under some circumstances, they will rarely be necessary for patients who are undergoing short-term opioid therapy because the risk of addiction for these patients is very low. In addition, acute pain generally diminishes with time, and the duration of exposure to opioid therapy is therefore typically brief for these patients.

THE IMPORTANCE OF EFFECTIVE MANAGEMENT OF ACUTE PAIN

The very low rate of addiction among patients using opioids for acute pain suggests that concerns about the risk of addiction should not hinder effective pain treatment for patients who need it. However, unfortunately, undertreatment of pain is common. Even in the postoperative setting, acute pain management is often less than ideal. In one recent study of 250 postsurgical patients, 82% reported experiencing some pain, 21% experienced severe pain, and 18% reported experiencing extreme pain. Despite significant advances in understanding the pathophysiology of pain and pain medications, the number of patients who experience moderate-to-severe postsurgical pain has not improved substantially over at least the past 2 decades. Even when opioids are prescribed for acute postoperative pain, many patients continue to experience moderate-to-severe pain. The undertreatment of surgical pain is often the result of inadequate education about pain and concern about the risk of opioid addiction.

Pain control is clearly an important goal to reduce patient discomfort and improve quality of life. In addition, inadequate pain relief is also associated with a number of other undesirable outcomes. Greater levels of pain and stress in surgical patients have been associated with suppression of endocrine and immune function, in addition to slower rates of healing and a more complicated postsurgical recovery. These endocrine-metabolic stress responses in surgical patients are reduced by a number of analsgesic techniques, including systemic or epidural opioid therapy. Strategies that produce more intensive analgesia in surgical patients have been shown to produce long-lasting reductions in postsurgical pain, and to significantly decrease the time between surgery and resumption of physical activity.
factors that were associated with unanticipated hospital admission or readmission among more than 20,000 patients who underwent same-day surgery over a 12-month period. Approximately 6% of patients were hospitalized immediately after surgery or within 30 days. Pain was described as the most common reason for unanticipated hospital admission or readmission, accounting for more than 33% of hospital admissions.

Considerable evidence also suggests that unrelied acute or postsurgical pain is associated with a significant risk of transition to chronic pain. A comprehensive review of risk factors for chronic postsurgical pain found that greater pain severity shortly after surgery was a significant predictor of chronic pain following thoracotomy and gallbladder surgery. Transient pain has been shown to stimulate long-term increased sensitivity to pain in a broad range of other settings, including neonatal heel lancing, infant circumcision, and acute herpes zoster.

Animal studies have demonstrated altered neuronal gene expression—an early marker of neuronal remodeling and long-term altered pain sensitivity—within only a few minutes of painful stimuli, with behavioral and histological alterations occurring within a few days. Thus, some experts have suggested that acute pain represents the initial step in a cascade of events that may, under the appropriate circumstances, culminate in widespread, long-lasting neurologic alterations and persistent pain.

CONCLUSIONS

Opioid analgesics are among the most important medications used in contemporary medical practice for patients in a number of settings, including surgery, dental procedures, musculoskeletal pain, and others. Although patients and clinicians are often concerned about iatrogenic addiction, several studies have demonstrated that the risk of addiction is low when opioids are used for the treatment of acute pain. In addition, a considerable body of evidence suggests that acute pain is often inadequately treated, and that untreated acute pain is a significant risk factor for progression to chronic pain. Concerns about the risk of iatrogenic addiction should not be an obstacle to effective pain relief for patients with acute pain in routine clinical practice.

REFERENCES