Introduction: Landscape of Opioid Dependence

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ABSTRACT

BACKGROUND: The use of opioids for chronic noncancer pain increased 222% from 1992 to 2002. Opioid dependence has also increased significantly, leading to a burden on patients, employers, insurers, society, and the entire health care system. It is imperative that opioid dependence is addressed and treated properly, in order to return patients to being productive participants in the workplace and society.

OBJECTIVE: To provide an overview of addiction, abuse, and dependence and identify risk factors for addiction.

SUMMARY: Studies have shown that intensive use of opioids is associated with increased utilization of costly health care services, prolonged disability, and continued use of opioids, leading to abuse and dependence in many patients. While identifying patients at risk for developing opioid dependence is difficult, there are many risk stratification tools now available to practitioners, including the Opioid Risk Tool (ORT) or Screener and Opioid Assessment for Patients with Pain (SOAPP). Understanding the differences between dependence, addiction, and tolerance is essential to managing patients on opioids.

CONCLUSION: It is imperative that patients be properly managed when being treated for pain. Physicians and employers have to be able to identify patients at risk for opioid abuse or exhibiting symptoms of opioid abuse and know how to address their needs.

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As part of the Food and Drug Administration Amendments Act (FDAAA) of 2007, the U.S. Food and Drug Administration (FDA) may require risk evaluation and mitigation strategies (REMS). The purpose of REMS is to assure the safe use of prescription drugs. In the future, the FDAAA may require providers of health care to obtain certification or special training to prescribe certain medications (such as opioids) and may also require pharmacies to be specially certified to dispense such medications. Additionally, they may require patients who use such medications to be enrolled in a registry or provide evidence of safe use conditions.

In response to such legislation and other legal concerns, many practitioners may shy away from prescribing opioid medications, resulting in undertreatment of pain. The proper management of pain may be affected by concerns over drug diversion, abuse, and addiction. Physicians should be utilizing current treatment guidelines and recommendations. Guidelines and recommendations for the treatment of chronic noncancer pain have been developed by the American Society of Interventional Pain Physicians, the American Chronic Pain Association, and joint guidelines by the American Pain Society and the American Academy of Pain Medicine that aim to best treat pain and reduce abuse and diversion. Guidelines have also been developed to manage patients with substance abuse disorders by the American Psychiatric Association and the Work Group on Substance Use Disorders. Current recommendations include having patients enter into pain management contracts, requiring routine random urine screenings and random pill counts, utilizing available tools to assess the risk of abuse, following proper prescribing practices, and re-evaluating therapy on an ongoing basis. If patients are carefully selected by their physician to receive opioids, nonopioid and nonpharmacological treatments are integrated into the care plan, and patients are assessed for their risk of abuse, proper pain management may be achievable while minimizing the risk of abuse and dependence.

In response to rising rates of opioid abuse and diversion, the FDA has issued black-box warnings on many opioids. Patients who are opioid naive should not be given medications such as extended-release oxycodone or fentanyl patches, lozenges, or buccal tablets. Misuse of products such as these may lead to increased rates of abuse and adverse events (including death). Many drug manufacturers are developing new formulations of opioids that have abuse deterrent properties such as controlled release mechanisms, agonist-antagonist combinations, and delivery devices with tamper resistant properties.

Addiction and abuse affects people of all ages and races. Addiction is similar to other chronic diseases such as diabetes and hypertension, though is rarely managed as such. Genetic studies over the last 10 years have provided evidence needed to define dependence as a chronic disease. Dependence is now beginning to be recognized as a brain disease with behavioral manifestations, as opposed to criminal behavior or a personality disorder. Continued abuse of drugs is not a voluntary behavior; drug abuse can take over a person’s ability to wield self-control. Brain imaging studies on drug-addicted patients have revealed changes in areas of the brain responsible for decision making, judgment, memory, learning, and behavior control; these changes may explain the destructive and compulsive actions seen in addiction.

The Harrison Narcotic Act of 1914 allowed physicians to treat opioid dependence. However, the U.S. Supreme Court overturned that act in 1919 and ended office-based opioid treatment. Not until 2002 did office-based opioid treatment return when the FDA approved sublingual buprenorphine for the in-office treatment of opioid dependence. While methadone clinics were established in the mid-1970s, methadone for opioid dependence is not approved for office-based treatment; as such, patients must report to a methadone clinic for treatment.

**Defining Dependence**

Substance abuse problems often fall into 1 of 2 categories: dependence and abuse. Individuals with opioid dependence may continue to use opioids even knowing there is some deleterious effect from the use of the substance. Addiction and physical dependence are not the same. Any patient on opioids has the potential of developing physical dependence and may suffer withdrawal symptoms upon the discontinuation of the opioid. Due to conflicting definitions of addiction and dependence, a consensus document from the American Academy of Pain Medicine, the American Pain Society, and the American Society of Addiction Medicine was developed in 2001. The panel defined the following terms:

**Addiction** is a primary, chronic, neurobiological disease with genetic, psychosocial, and environmental factors influencing its development and manifestations. It is characterized by behaviors that include 1 or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving. Addiction is comprised of 4 core elements (the 4 Cs): Compulsive use, inability to Control the quantity used, Craving the psychological drug effects, and Continued use of the drug despite its adverse effects. Some examples of compulsive use consist of preoccupation with taking the drug, stockpiling the drug, and utilizing multiple prescribers (“doctor shopping”) and/or pharmacies to obtain more of the drug. Inappropriate use also consists of selling the drugs to others or injecting/snorting drugs that were not designed to be consumed in that manner. Loss of control is when patients take their medication much more frequently or at higher doses than prescribed. Patients suffering from addiction may also experience a strong desire for the feeling...
they experience when taking the drug (feeling “high”), not for pain relief.4

Physical dependence is a state of adaptation that is manifested by a drug class-specific withdrawal syndrome that can be produced by abrupt cessation of a drug, a rapid dose reduction, a decreasing blood level of the drug, and/or administration of an antagonist.4,28 The Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) published by the American Psychiatric Association states that a definite diagnosis of “dependence” requires that 3 or more of the following 6 characteristic features be experienced or exhibited:28,30

1. A strong desire or sense of compulsion to take the drug;
2. Difficulties in controlling drug-taking behavior in terms of its onset, termination, or levels of use;
3. A physiological withdrawal state when drug use is stopped or reduced, as evidenced by the characteristic withdrawal syndrome for the substance or use of the same (or a closely related) substance with the intention of relieving or avoiding withdrawal symptoms;
4. Evidence of tolerance, such that increased doses of the drug are required in order to achieve effects originally produced by lower doses;
5. Progressive neglect of alternative pleasures or interests because of drug use, increased amount of time necessary to obtain or take the drug or to recover from its effects; and
6. Persisting with drug use despite clear evidence of overtly harmful consequences, such as harm to the liver, depressive mood states, or impairment of cognitive functioning.

Tolerance is a state of adaptation in which exposure to a drug induces changes that result in a diminution of 1 or more of the drug’s effects over time.28

Pseudoaddiction is another term that is used frequently. Pseudoaddiction refers to signs of addiction in patients whose addictive behaviors go away when their pain is brought under control.4 Examples of aberrant drug-related behaviors seen in pseudoaddiction include unauthorized dose escalation and hoarding of medications.6 Pseudoaddiction often occurs when a patient’s pain is poorly treated or undertreated. It is very hard to diagnose pseudoaddiction until the pain is brought under control, which is often hard to achieve.4 Certain patients may be misdiagnosed as addicts; to avoid this misdiagnosis, physicians should be educated about proper pain management strategies and be able to assess risk of addiction in their patients.25

Who Is At Risk for Developing Addiction?

Risk stratification should be performed when starting patients on opioids for chronic noncancer pain to mitigate risks and enhance benefits of opioid use.15 Practitioners need to learn how to assess the risk of addiction and aberrant drug-related behavior to protect patients at-risk for developing dependence and to better treat patients who may be at lower risk. In addition to risk stratification, risk management should include use of prescription-monitoring programs (if available), compliance monitoring, patient education, psychological screening and psychotherapy, and selection of abuse-deterrent formulations of narcotics when appropriate.32 As predisposition to addiction may be genetic, a family history and personal history of abuse of alcohol or illicit drugs should be obtained.24

There are several tools available to physicians to assess risk of addiction, including:5,33,34

- CAGE (Cutting down, Annoyance by criticism, Guilty feeling, Eye-openers)
- CAGE Aid (CAGE adapted to include drugs)
- ORT (Opioid Risk Tool)
- PADT (Pain Assessment and Documentation Tool)
- SOAPP (Screener and Opioid Assessment for Patients with Pain Version 1)
- SOAPP-R (Revised Screener and Opioid Assessment for Patients with Pain)

Prior to beginning opioid therapy for chronic noncancer pain, patients should also have a psychological assessment to determine their coping skills, social and familial stressors, and prior history of substance abuse.29,32 Risk factors for addiction are multi-factorial. There are environmental, social, biological, or genetic factors that may make an individual more susceptible to abuse and addiction of opioids.32 Genetics may account for between 40% and 60% risk of developing addiction.24 Patients with coexisting mental disorders also experience a higher rate of risk of developing dependence than the general population.24

Conclusion

Due to the increased utilization of costly health care services seen in opioid dependent patients, it is imperative that health care providers optimally manage their patients with chronic pain who require treatment with opioids.1,2,3,10 Inadequate or inappropriate treatment may lead to prolonged disability and continued use of opioids and may increase the risk of abuse, dependence, and diversion.1 While identifying patients at risk for developing opioid dependence is difficult, physicians should utilize risk stratification tools available to them to best manage their patients’ pain.6,11
REFERENCES


