Definitions Related to the Use of Opioids for the Treatment of Pain

A consensus document from the **American Academy of Pain Medicine,** *the* **American Pain Society,** *and the* **American Society of Addiction Medicine.**

BACKGROUND

Clear terminology is necessary for effective communication regarding medical issues. Scientists, clinicians, regulators, and the lay public use disparate definitions of terms related to addiction. These disparities contribute to a misunderstanding of the nature of addiction and the risk of addiction, especially in situations in which opioids are used, or are being considered for use, to manage pain. Confusion regarding the treatment of pain results in unnecessary suffering, economic burdens to society, and inappropriate adverse actions against patients and professionals.

Many medications**,** including opioids, play important roles in the treatment of pain. Opioids, however, often have their utilization limited by concerns regarding misuse, addiction, and possible diversion for non-medical uses.

Many medications used in medical practice produce dependence, and some may lead to addiction in vulnerable individuals. The latter medications appear to stimulate brain reward mechanisms; these include opioids, sedatives, stimulants, anxiolytics, some muscle relaxants, and cannabinoids.

Physical dependence, tolerance, and addiction are discrete and different phenomena that are often confused. Since their clinical implications and management differ markedly, it is important that uniform definitions, based on current scientific and clinical understanding, be established in order to promote better care of patients with pain and other conditions where the use of dependence-producing drugs is appropriate, and to encourage appropriate regulatory policies and enforcement strategies.

RECOMMENDATIONS

The American Academy of Pain Medicine, the American Pain Society, and the American Society of Addiction Medicine recognize the following definitions and recommend their use.

I. Addiction

Addiction is a primary, chronic, neurobiologic disease, with genetic, psychosocial, and environmental factors influencing its development and manifestations. It is characterized by behaviors that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving.

II. Physical Dependence

Physical dependence is a state of adaptation that is manifested by a drug class specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, and/or administration of an antagonist.

III. Tolerance

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

DISCUSSION

Most specialists in pain medicine and addiction medicine agree that patients treated with prolonged opioid therapy usually do develop physical dependence and sometimes develop tolerance, but do not usually develop addictive disorders. However, the actual risk is not known and probably varies with genetic predisposition, among other factors. Addiction, unlike tolerance and physical dependence, is not a predictable drug effect, but represents an idiosyncratic adverse reaction in biologically and psychosocially vulnerable individuals. Most exposures to drugs that can stimulate the brain's reward center do not produce addiction. Addiction is a primary chronic disease and exposure to drugs is only one of the etiologic factors in its development.

Addiction in the course of opioid therapy of pain can best be assessed after the pain has been brought under adequate control, though this is not always possible. Addiction is recognized by the observation of one or more of its characteristic features: impaired control, craving and compulsive use, and continued use despite negative physical, mental, and/or social consequences. An individual's behaviors that may suggest addiction sometimes are simply a reflection of unrelieved pain or other problems unrelated to addiction. Therefore, good clinical judgment must be used in determining whether the pattern of behaviors signals the presence of addiction or reflects a different issue.

Behaviors suggestive of addiction may include: inability to take medications according to an agreed upon schedule, taking multiple doses together, frequent reports of lost or stolen prescriptions, doctor shopping, isolation from family and friends, and/or use of non-prescribed psychoactive drugs in addition to prescribed medications. Other behaviors which may raise concern are the use of analgesic medications for other than analgesic effects, such as sedation, an increase in energy, a decrease in anxiety, or intoxication; non-compliance with recommended non-opioid treatments or evaluations; insistence on rapid-onset formulations/routes of administration; or reports of no relief whatsoever by any non-opioid treatments.

Adverse consequences of addictive use of medications may include persistent sedation or intoxication due to overuse; increasing functional impairment and other medical complications; psychological manifestations such as irritability, apathy, anxiety, or depression; or adverse legal, economic or social consequences. Common and expected side effects of the medications, such as constipation or sedation due to use of prescribed doses, are not viewed as adverse consequences in this context. It should be emphasized that no single event is diagnostic of addictive disorder. Rather, the diagnosis is made in response to a pattern of behavior that usually becomes obvious over time.

Pseudoaddiction is a term which has been used to describe patient behaviors that may occur when pain is undertreated. Patients with unrelieved pain may become focused on obtaining medications, may "clock watch," and may otherwise seem inappropriately "drug seeking." Even such behaviors as illicit drug use and deception can occur in the patient's efforts to obtain relief. Pseudoaddiction can be distinguished from true addiction in that the behaviors resolve when pain is effectively treated

Physical dependence on and tolerance to prescribed drugs do not constitute sufficient evidence of psychoactive substance use disorder or addiction. They are normal responses that often occur with the persistent use of certain medications. Physical dependence may develop with chronic use of many classes of medications. These include beta blockers, alpha-2 adrenergic agents, corticosteroids, antidepressants, and other medications that are not associated with addictive disorders. When drugs that induce physical dependence are no longer needed, they should be carefully tapered while monitoring clinical symptoms to avoid withdrawal phenomena and such effects as rebound hyperalgesia. Such tapering, or withdrawal, of medication should not be termed detoxification. At times, anxiety and sweating can be seen in patients who are dependent on sedative drugs, such as alcohol or benzodiazepines, and who continue taking these drugs. This is usually an indication of development of tolerance, though the symptoms may be due to a return of the symptoms of an underlying anxiety disorder, due to the development of a new anxiety disorder related to drug use, or due to true withdrawal symptoms.

A patient who is physically dependent on opioids may sometimes continue to use these despite resolution of pain only to avoid withdrawal. Such use does not necessarily reflect addiction.

Tolerance may occur to both the desired and undesired effects of drugs, and may develop at different rates for different effects. For example, in the case of opioids, tolerance usually develops more slowly to analgesia than to respiratory depression, and tolerance to the constipating effects may not occur at all. Tolerance to the analgesic effects of opioids is variable in occurrence but is never absolute; thus, no upper limit to dosage of pure opioid agonists can be established.

Universal agreement on definitions of addiction, physical dependence, and tolerance is critical to the optimization of pain treatment and the management of addictive disorders. While the definitions offered here do not constitute formal diagnostic criteria, it is hoped that they may serve as a basis for the future development of more specific, universally accepted diagnostic guidelines. The definitions and concepts that are offered here have been developed through a consensus process of the American Academy of Pain Medicine, the American Pain Society, and the American Society of Addiction Medicine

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