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Opioid Analgesics—Risky Drugs, Not Risky Patients

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From 1999 to 2010 the number of people in the United States dying annually from opioid analgesic–related overdoses quadrupled, from 4030 to 16 651.[1] Patients' predisposition to overdose could not have changed substantially in that time; what has changed substantially is their exposure to opioids. During this same time, the amount of opioids prescribed also quadrupled.[1] The increase in prescribing occurred in the context of a greater emphasis on treating pain following efforts by the American Pain Society, the Veterans Health Administration, The Joint Commission, and others to increase recognition and management of pain, as well as advocacy by pain societies urging physicians to use opioids more readily for patients with chronic noncancer pain.

Even though it is well known that prescription opioid use can lead to addiction or overdose, some opioid manufacturers and pain specialists suggest that few patients are susceptible to these risks.[2,3] To distinguish low-risk from high-risk patients, use of screening tools, including the Screener and Opioid Assessment for Patients with Pain, has been advocated.[4] Medication guides include statements such as "the chance [of abuse or addiction] is higher if you are, or have been, addicted to or abused other medicines, street drugs, or alcohol, or if you have a history of mental problems."[5] While there is likely to be a gradient of risk across patients, this statement may reassure clinicians that people with opioid addiction are different from most patients for whom they provide care.

However, opioid dependence is much more common than previously believed and has been estimated to affect more than one-third of patients with chronic pain.[6] No screening tool has sufficiently high sensitivity to rule out problems with opioids. Reported sensitivities of these tests for observed "aberrant drug-related behavior" (eg, dose escalation outside the treatment plan or forging prescriptions)[4] among patients with chronic pain are generally within a range between 70% and 90%,[4] which means that they miss 10% to 30% of patients at high risk of misuse or addiction.

In addition, some industry-sponsored educational brochures suggest that physicians should ignore signs of opioid dependence in low-risk patients.[7] For instance, some patients might not be considered at high risk of misuse even though they may use more opioids than prescribed (one definition of misuse). Some authors have stated that behaviors such as taking more opioids than prescribed may represent pseudoaddiction,[7] a concept introduced in a case report in 1989[8] as "abnormal behavior developing as a direct consequence of inadequate pain management."[8] However, this concept remains untested, without scientific studies validating diagnostic criteria or describing long-term clinical outcomes. Nonetheless, some pain societies have promoted this concept[9] and suggest that some patients demonstrating behaviors typical of opioid addiction may actually require higher doses.[9]

Rather than representing iatrogenic undertreatment of pain, however, behaviors described as pseudoaddiction may represent predictable responses to opioid exposure. Long-term opioid use typically results in tolerance. A standard clinical solution is to increase opioid dose. However, contrary to the view that there is no maximum safe dose if opioids are increased gradually over time, death from opioid overdose becomes more likely at higher doses.

The most important risk factor for opioid analgesic–associated dependence or overdose is not a feature of any individual patient but instead simply involves receiving a prescription for opioids. For example, newly prescribed opioids after short-stay surgery are associated with a 44% increase in risk of becoming a long-term opioid user within 1 year.[10]

Another potential complication of screening for risk of opioid abuse is that identifying patients who should not receive opioids can stigmatize them, leading to consequences that do not help them. Patients who are questioned about substance use and then excluded from an expected treatment may feel embarrassed or abandoned. The decision to address a patient's pain should not depend on

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substance use history. Screening should be used primarily to identify and offer treatment to patients with opioid addiction.

Before prescribing opioids, a more useful and important question than a patient's likelihood of dependence is whether benefits of opioids in relieving pain are likely to outweigh the risks of the drugs. For pain control at the end of life, the answer to this question is often yes. If the indication for opioids is chronic noncancer pain, the answer to this question will be no much more often than many physicians may realize. Despite widely held views about the efficacy of opioids for pain control, systematic reviews have not found sufficient evidence that long-term opioid use controls noncancer pain more effectively than other treatments.

Physicians have a professional and ethical responsibility to understand the expected benefits and risks of medications and to balance these appropriately. When benefits of opioids are likely to outweigh risks, such as in severe acute pain unlikely to respond to other therapies, it is appropriate to use opioids, prescribing the lowest effective dose and with a duration limited to the likely duration of the acute pain. However, when risks outweigh benefits, as will often be the case for chronic pain, opioid use should be avoided in favor of other treatments.

Some physicians may think that only a small fraction of their patients are put at risk by taking high doses of opioids. However, the risk of opioids stems primarily from these drugs, not from patients. Low-risk patients given large enough doses will have a high risk of overdose. Patients given moderate doses for prolonged periods will have a high risk of opioid dependence. While a patient's estimated individual risk should be considered, physicians should pay close attention to the drug dose and duration. All patients exposed to opioids would benefit from judicious prescribing and close follow-up.

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