Opioid Prescriptions Soar
Increase in Legitimate Use as Well as Abuse

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CAMPAIGNS TO MAKE PAIN CONTROL a priority have succeeded in raising patient and physician awareness of the need for analgesics, and now opioid pain medications are among the most prescribed drugs in the United States. However, this positive trend has been shadowed by growing abuse of these powerful medications.

This dichotomy is proving a persistent challenge for physicians, policy makers, and scientists trying to develop better strategies to thwart abuse while continuing to treat pain effectively.

“We have two public health crises going on at the same time: one is undertreated pain and the other is prescription drug abuse,” said Scott M. Fishman, MD, chief of the division of pain medicine at the University of California, Davis. “As we treat one of those problems and get doctors to treat more aggressively for pain, we’re simultaneously seeing numbers go up related to prescription drug abuse—and no one knows with any certainty if one is driving the other.”

AN UNDERTREATED PROBLEM

Pain is a serious, undertreated public health problem in the United States, with 19% of US adults reporting chronic pain and 34% reporting recurrent pain, according to a 2005 telephone survey of a random sample of 1,204 adults sponsored by news organizations and the Stanford University Medical Center, in California. Some 63% of patients with pain had spoken to their physician about their pain, but only 31% reported complete relief and 21% reported little or no relief.

The problem is expected to worsen as the population ages, with increasing rates of arthritis, cancer, back pain, and other conditions. Recognizing these needs, physicians have begun treating pain more aggressively, including using opioid pain medications. Between 1999 and 2002, oxycodone prescriptions increased 50% to 29 million in 2002, fentanyl prescriptions increased 150% to 4.6 million, and morphine prescriptions increased 150% to 4.6 million, and morphine prescriptions increased 60% to 3.8 million (Compton WM and Volkow ND. Drug and Alcohol Depend. 2006; 81:103-107). In addition to increased awareness of the importance of pain control, pain experts attribute the overall increases in prescription pain medication use to a variety of factors, including support and requirements for appropriate pain control from state medical boards and advances in the science of pain control. However, this increase in legitimate use of these medications has paralleled by a rise in abuse of these drugs, with a 91.2% increase in deaths due to opioid poisoning between 1999 and 2002 (Paulozzi LJ et al. Pharmacoepidemiol Drug Saf. 2006; 15:618-627).

By far the most commonly used prescription analgesic in the United States is hydrocodone/acetaminophen, which has been the most prescribed medication of any category for at least the past 5 years, based on data by a healthcare information company, Verispan (Yardley, Penn), published on RxList (http://www.rxlist.com). With more than 100 million prescriptions in 2005, this pain-killer now far exceeds the number of prescriptions for the second and third most prescribed medications—cholesterol-lowering atorvastatin, with about 63 million prescriptions, and the antibiotic amoxicillin, with about 52 million prescriptions. In 2004, the United States used 99% of the global supply of the opioid hydrocodone, according to the 2005 report from the International Narcotics Control Board. Between 2000 and 2004, medical use of hydrocodone increased 60% domestically.

Seddon Savage, MD, an American Pain Society board member and director of the Dartmouth Center on Addiction, Recovery, and Education in Hanover, NH, explained that physicians are likely to choose a short-acting opioid combination such as hydrocodone/acetaminophen for treating chronic intermittent pain, which provides patients with relief during acute episodes of pain. Also, it is easier for physicians to prescribe Schedule III drugs such as hydrocodone/acetaminophen because under current federal law they can provide...
patients with a prescription that may be refilled up to 5 times in 6 months. Refills are not currently permitted for Schedule II drugs, but the DEA has issued a proposed rule that would allow physicians to write serial prescriptions for up to a 90-day supply as long as each prescription specifies the earliest date that the prescription can be filled (http://www.deadiversion.usdoj.gov/fed_regs/rules/2006/fr0906.htm).

Despite lingering concerns surrounding prescription pain medications, many physicians have become more comfortable using these drugs as they have learned more about them, Savage said. “There has been an evolution in our understanding of opioid pharmacology and opioid actions, and an increase in our understanding of the physiologic responses to opioids,” she said. She explained that scientists have been able to distinguish physical dependence on a drug, which develops in appropriate circumstances while taking steps to avoid abuse and diversion, Gilson said. The Federation of State Medical Boards has crafted a model policy, adopted by many states, on regulating the use of controlled substances. The policy emphasizes adequate pain control and that physicians should periodically monitor patients to prevent abuse (http://www.fsmb.org/pdfs/2004_gropl_Controlled_Substances.pdf). It also outlines criteria for states to use when evaluating physicians’ treatment of pain (SEE BOX). In addition, there is also a greater array of state-sponsored continuing medical education courses for physicians that deal with pain management.

**ESCALATING ABUSE**

Despite such measures, there is a growing trend of abuse of prescription pain medications, with some indications that they are displacing street drugs. Leonard J. Paulozzi, MD, MPH, of the Centers for Disease Control and Prevention, and colleagues found that opioid analgesic poisoning was documented to cause 5528 deaths in 2002, more than either heroin or cocaine. While the National Institute on Drug Abuse has found a decline in use of illegal street drugs by youths, they have also documented alarming increases in the abuse of prescription pain medication by this group. In 2005, 9.5% of 12th graders surveyed reported nonmedical use of Vicodin (hydrocodone/acetaminophen) in the previous year and 5.5% reported using OxyContin (oxycodone), according to the 2005 Monitoring the Future survey.

In Canada, the trend has become even more apparent. A study of nearly 600 drug users in 7 Canadian cities found that reported use of the illegal opioid heroin decreased across all of the cities by roughly 25% between 2001 and 2005 (Fischer B et al. CMAJ. 2006;175:1385), while use of prescription opioid drugs has become “the predominant form of illicit opioid use.” In 2005, about 30% of the study participants reporting abuse of heroin in the previous 30 days, whereas 37% reported illicit use of hydromorphone, 22% reported morphine use, and 22% reported oxycodone use. Most individuals abusing prescription opioids in the study reportedly obtained them directly from the medical system or indirectly through friends or partners.

Rémi Quirion, PhD, scientific director of the Institute of Neuroscience, Mental Health, and Addiction, in Montreal, which funded the study,
noted that greater access to prescription opioids on the illicit drug market, on the street, or perhaps even from health professionals may be one factor contributing to increased abuse. Another factor may be that unlike heroin use, which typically involves injections and related paraphernalia, prescription pain pills can be ingested more easily. In the case of extended-release formulations of oxycodone, abusers have learned they can circumvent this safety feature by chewing the pills, snorting crushed pills, or dissolving crushed pills and injecting the solution.

While it is important to ensure that patients who need pain relief continue to have access to prescription opioid drugs, Quirion said, physicians do need to “ask more questions to make sure when [patients] get this type of drug that they really need it for the treatment of their pain and after that that it’s not abused.”

In the United States, the abuse of prescription pain medications is widespread and is not concentrated in urban areas, as some may assume, according to an analysis of data from the National Survey on Drug Use and Health presented by Mario Moric, PhD, a clinical research statistician in the department of anesthesiology at Rush University, at the American Society of Anesthesiologists meeting in Chicago in October. Moric described a seemingly random distribution of prescription opioid abuse, with, for example, a very low rate of abuse in Illinois but a much higher rate in neighboring Indiana.

Moric said the cause of this distribution is unclear, but an early analysis found that prescription drug monitoring programs, which vary greatly between states, apparently are not influencing these trends. He also noted that many of the individuals surveyed reportedly did not get prescriptions for the drugs they were abusing from physicians; close to 60% reported they received the medications from friends and family. The Internet also appears to be playing less of a role than expected, Moric said.

Theft of pain medications from various points in the distribution chain such as pharmacies, hospitals, and delivery trucks may be an important source of drug diversion. Gilson and colleagues filed a Freedom of Information Act Request with the DEA to obtain a database of federally required reports of the quantities of drugs lost or stolen from DEA-registered businesses (Joranson DE and Gilson AM. J Pain Symptom Manage. 2005;30:299-301). Although reports from more than half the states were missing, a preliminary analysis found that in 2003 alone, 2 million doses of a half dozen Schedule II opioid analgesics—fentanyl, hydrocodone, meperidine, methadone, morphine, and oxycodone—were reported stolen from the supply chain, mostly from retail pharmacies. About 4 million doses of hydrocodone reportedly were stolen that year.

STEMMING ABUSE
In addition to pharmacy theft and stealing or sharing the prescription medications of friends and relatives, “doctor-shopping” (moving from physician to physician in an effort to obtain multiple prescriptions for pain medications) is another possible source of prescription painkillers for abuse. The relative contributions of these and other sources is not clear. “Identifying as many sources of diversion as possible will help us develop interventions,” Gilson said.

Currently, many tactics for reducing abuse of prescription analgesics focus on physicians through regulations or prescription monitoring. But until better information is available on the sources of diverted drugs, some fear such tactics will be ineffective and reduce legitimate prescribing of these drugs. “The longer the sole focus of intervention is on doctors, the more it will have a deleterious effect [on pain treatment],” Gilson said.

Physicians do, however, have an important role to play in minimizing abuse or diversion by patients legitimately prescribed these drugs. “Physicians do need to be aware of the abuse liability of these medications, and that there are mechanisms they can use to reduce the chance that the drugs [they prescribe] will be abused or diverted by the person they prescribe too,” Gilson said.

About 10% of the general population will develop an addictive disorder in their lifetime, often to alcohol which is widely available, Savage said. But it is difficult for physicians to precisely predict which patients might be vulnerable. Because of this uncertainty, she recommends that physicians thoroughly screen all patients for a personal or family history of substance abuse and monitor them carefully and regularly throughout treatment to provide opportunities to intervene if there are signs of a developing problem.

Currently, no national guidelines exist for the treatment of chronic noncancer pain, according to Gilson. But the American Pain Society and the American Academy of Pain Medicine have created an expert panel, including Gilson, to create such guidelines.

Fishman pointed out that such vigilant monitoring is simply the kind of risk management that is often used when beneficial but potentially harmful drugs are prescribed. For example, physicians who prescribe carbamazepine for patients with a seizure disorder order frequent laboratory tests to ensure that the drug is not inhibiting the production of blood cells. Similar vigilance is required with prescription opioids to monitor for signs of abuse or aberrant behavior, or even for signs that the drug is working and improving a patient’s level of function, he said. Fishman said he assesses each patient’s level of function at the start of treatment, establishes goals for the types of activities that pain treatment should allow them to participate in, and schedules follow-up visits to make sure function is improving. “The key doctors really need to understand is that when you treat pain and you treat it effectively, function should improve,” Fishman explained.

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