

Opioids for Chronic Pain: First Do No Harm

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Among the remedies which it has pleased Almighty God to give to man to relieve his sufferings, none is so universal and so efficacious as opium.

Attributed to Thomas Sydenham, circa 1680¹

Overdose deaths from prescription painkillers have skyrocketed in the past decade. Every year, nearly 15,000 people die from overdoses involving these drugs—more than those who die from heroin and cocaine combined.

National Center for Injury Prevention and Control²

Opioids are a large family of biologically active peptides that bind to and activate receptors in humans and can reduce pain and induce euphoria. Humans have a voracious appetite for opioids to the extent that our own brains produce them (eg, endorphins), and many people avidly consume those that are produced by plants or synthesized by factories in our environment. Opioids have shaped the course of human history and are arguably one of the most powerful, ubiquitous, useful, and deadly substances in our medical armamentarium.

Our society is agonizingly ambivalent about what role opioids should play in our lives. There is no question that opioids are effective analgesics in the treatment of pain caused by acute injury or surgery, and they are invaluable in the palliative care of patients with cancer and other lethal diseases. But we have criminalized the nonmedical use of opioids and deploy vast armies of combatants in the (largely ineffective)

war on such drugs as heroin and opium. The greatest medical and recreational use of opioids in the United States falls between these two extremes and is fostered by the prescription of opioid medications for chronic noncancer pain.^{3,4}

What should be our policy that determines how and when to use opioids for our patients with chronic noncancer pain? The 2 articles in this issue of the *Annals* discussing opioid use and misuse illustrate the complexity of this question. In Grattan et al's study of patients on long-term opioid therapy for chronic pain at 2 of the largest health plans in the country, patients with no history of a substance use disorder were much more likely to "misuse" opioids if they were depressed.⁵ The misuse that patients admitted to during a telephone interview was using their prescribed opioids to treat stress or insomnia rather than pain itself or using more opioids than had been prescribed. Perhaps most interesting is that misuse was common even in patients without depression, occurring in more than one-third of patients.

Patients with severe depression as measured on the 9-item Patient Health Questionnaire were even more likely to misuse opioids than were patients with no or moderate depression. Although this self-report of opioid misuse is already surprisingly high, it may well be even more common than reported in this study. Given that patients are more likely to deny overuse when questioned, and that those patients who didn't respond to the interview may represent a group who are less compliant with instructions, it is reasonable to surmise that opioid misuse probably occurs very frequently in any population using them for prolonged periods of time.

Zweifel⁶ focuses his discussion on the most difficult issue that clinicians wrestle with as they try to help patients with chronic noncancer pain: pain is impossible to measure. Pain is a normal (and protective) physiological response to the physical and emotional vicissitudes of life itself, and anyone who lives long enough will have chronic pain as an obli-

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gate consequence of aging. Zweifler cuts this clinical Gordian knot by recommending a strict standard for initiating opioid therapy for chronic disease: "objective evidence of severe disease." Although this dictum has the virtue of brevity, it fails the test of clinical utility. Chronic pain is predominantly a condition that is experienced in the central nervous system, and the event that first triggered the pain may no longer exist or may be impossible to determine.⁷ A guideline that requires definitive objective confirmation of severe disease—especially in an era where magnetic resonance screening can show clinically irrelevant anomalies in a large proportion of patients⁸—is likely to lead to as many false-negative and false-positive diagnoses as the much-maligned visual analog pain scale that is currently in widespread use.

So what is the clinician to do? This is what we know about the use of opioids for chronic noncancer pain:

1. The volume of prescribed opioids has increased 600% from 1997 to 2007.⁸
2. During roughly the same period, the number of unintentional lethal overdoses involving prescription opioids increased more than 350%, from approximately 4,000 in 1999 to more than 14,000 in 2007.⁹
3. Risk of overdose or death increases with higher doses of opioids, especially in patients who concurrently use other respiratory depressants such as benzodiazepines.¹⁰
4. There are treatments for chronic pain that are much safer than opioids, including, but not limited to, physical therapy, cognitive behavioral therapy, low-dose tricyclic medications, and treatment of co-occurring psychiatric illnesses.^{11,12}
5. High doses of opioids do not reliably decrease patients' report of the magnitude of chronic pain, nor do they improve patients' overall health and function.¹³

Thus it is reasonable to conclude that opioids for chronic noncancer pain are not appropriate therapy for most patients in primary care settings. When other interventions fail or are inadequate, cautious evidence-based consideration of low-dose opioids as an adjunct to other therapies may be considered. Entering into chronic opioid therapy requires a long-term commitment by clinician and patient alike to use this powerful, precious, and dangerous medication with care and diligence. As clinicians and as patients, we need to develop a generous measure of respect for the power of opioids to do harm as well as provide relief from pain.

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