

Long-Term Opioids for Nonmalignant Pain

The dilemma: Undertreating patients with pain or overprescribing opioids?

Scrutiny of long-term use of narcotic analgesics for nonmalignant pain has sharpened because of increased frequency of use, higher awareness of adverse events, and more reports of deaths from unintentional overdose. According to the CDC, unintentional drug overdose is the second-leading cause of accidental death in the U.S., with about 40% of such deaths caused by prescription opioids.¹ A focus on perceived undertreatment of pain, coupled with aggressive marketing of opioids such as extended-release oxycodone (OxyContin), might have produced unintended negative consequences, particularly the long-term and potentially harmful use of opioids for nonspecific musculoskeletal pain. In several new studies, researchers addressed these issues.

In a study from two large western U.S. health plans with about 4 million enrollees, the prevalence of long-term opioid use for noncancer pain increased strikingly from 1997 to 2005 in all age groups. In older women (age, ≥ 65), the prevalence of chronic opioid use rose from 5% to nearly 9% during that 8-year period; in older men, the prevalence rose from 3% to 5%.

Among middle-aged people (age range, 45–64), the prevalence was also about 5% in 2005.²

In two studies, investigators evaluated a Medicare database from Pennsylvania and New Jersey that included beneficiaries who initiated analgesic therapy for nonmalignant pain from 1999 through 2005. In one study, researchers compared three cohorts, each with 4280 older arthritis patients whose demographic and clinical characteristics were matched except for the prescribed analgesic — nonselective nonsteroidal anti-inflammatory drug (nsNSAID), coxib, or opioid.

Compared with risk for adverse cardiovascular events in the nsNSAID group, relative risk was higher with coxibs and opioids by 28% and 77%, respectively. Relative risk for gastrointestinal bleeding was 40% lower with coxibs than with opioids or nsNSAIDs. Opioids were associated with a fourfold higher fracture risk, 70% higher risk for hospitalization, and doubling of all-cause mortality, compared with nsNSAIDs.³

In the other study, the researchers compared five cohorts, each with 6275 patients who used one of five different classes of opioids — codeine, hydrocodone, oxycodone, propoxyphene, or tramadol; otherwise the cohorts were similar demographically and clinically. Compared with hydrocodone, codeine was associated with 60% higher risk for adverse cardiovascular events; tramadol and propoxyphene were associated with lower relative risks for fracture (by 80% and 46%, respectively); and oxycodone and codeine were associated with doubled mortality.⁴

Editorialists commented on both of these studies and urged some caution with regard to their clinical implications, both because of methodologic weaknesses in cohort studies that involve administrative databases and because of the lack of biological plausibility for some of the results

(such as the cardiovascular risks of codeine). However, they emphasize that risk for falls and fractures and the associated excess all-cause mortality of long-term opioid use, particularly oxycodone and codeine, mandate greater caution in their use, greater focus on nonpharmacologic approaches to treating musculoskeletal pain, and additional controlled clinical trials.^{5,6}

Legislative and regulatory responses to opioid prescribing are on the horizon. The FDA has proposed a new Risk Evaluation and Management Strategy (REMS) for opioids, but the REMS has not been approved yet, because an FDA committee wants stronger requirements, including mandatory physician education programs. And, in Washington State, a new law that takes effect in mid-2011 will require documented evaluations (diagnosis, treatment plan, and objectives) before physicians initiate long-acting opioid therapy.¹ The law also will require written agreements signed by patients, periodic review of patients' progress, continuing education for physicians who prescribe long-acting opioids, and mandatory consultation with pain management specialists when physicians prescribe morphine equivalent doses exceeding 120 mg daily. Notably, the law does not apply to patients who have chronic pain caused by cancer, or acute pain caused by injury or surgery, or who are receiving hospice or end-of-life medical care.

Finally, in a provocative essay that captures the dilemma often experienced in primary care practice, a physician describes his struggle to simultaneously avoid undertreatment of pain and overprescribing of opioids. He concludes that an entirely new approach is needed, including more focus on mental health care, referral access to pain specialists, and guidelines that set clear limits on opioid dosage.⁷

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