Medical News & Perspectives p1621
Hospitalizations Surge Among Seniors Prescribed Opioids
CDC to Clinicians: Be Alert for Children With Poliolike Illness

Clinical Trials Update...................p1624
Telephone Counseling and Safer Sex
Rivaroxaban Effective for Cardioversion
Mepolizumab May Reduce Asthma Exacerbations
Cognitive Therapy, Medication for Depression

Health Agencies Update p1625
NIH Funds Creation of Database of Cellular Signatures
Report Predicts Fewer Uninsured but More Growth in Health Spending
Tweaking Proposed Food Safety Rules
Teens' Use of Drugs, Alcohol, and Tobacco Declines

News From the CDC.....................p1626
Vaccine-Related Diseases Affect Young Immigrants
Can Coupons Help Curb Obesity?

Medical News & Perspectives

Analysis Reveals Large Increase in Hospitalizations in Recent Years Among Older Patients Prescribed Opioids

Rita Rubin, MA

A government "statistical brief" on opioid-related hospitalizations didn't get much press coverage when it was posted in August, but at least a few findings merit a closer look.

The report, from the Agency for Healthcare Research and Quality (AHRQ), focused on trends in hospitalization of adults related to use of prescription opioid painkillers (not illicit drugs) during 1993 to 2012 (http://1.usa.gov/1oR7djl). It found that the biggest jump in the rate of such hospitalizations during that period was in people 85 years or older, followed close behind by 65- to 84-year-olds and 45- to 64-year-olds.

Furthermore, compared with other payers, Medicare experienced the biggest average annual increase in the number of opioid-related hospital inpatient stays it covered. In 2012, Medicare covered nearly 30% of such hospitalizations—more than double its 1993 share.

An Important Public Health Issue

"We certainly have a situation where we have an overreliance on opioids, particularly for long-term painful conditions," said Wilson Compton, MD, deputy director of the National Institute on Drug Abuse (NIDA), part of the National Institutes of Health (NIH). "This is an important public health issue, and the elderly are a major part of the population that's impacted."

So do the numbers signify a real increase in overuse of opioids in older patients?

On the one hand, as people age they're more likely to have chronic pain and less-likely to abuse prescription painkillers. "The overdose rate drops way off after age 65," said Leonard Paulozzi, MD, a medical epidemiologist at the Centers for Disease Control and Prevention. On the other hand, older individuals are also more likely to experience adverse effects from opioids.

"At the same equivalent dose, an older person is much more likely to experience falls, liver impairment, cardiac toxicity, and, in particular, cognitive impairment," Compton said. "Even in the 65- to 84-year-olds, what you're dealing with are patients with multiple comorbidities and a body that has less resilience."

In the AHRQ brief, "overuse" was defined by a range of 16 diagnostic codes that covered opioid abuse, opioid dependence, opioid poisoning, and adverse effects from therapeutic use of opioids. The authors noted that the average number of secondary diagnoses per hospital discharge nearly tripled during the period they analyzed. That suggests the increase in opioid-related hospitalizations could be due in part to an increase in diagnoses, as opposed to an increase in actual cases, said Daniel Solomon, MD, MPH, a Harvard rheumatologist.

"One has to be a bit cautious in interpreting the data," Solomon said, adding, "I wouldn't

sciencesource.com

A recent report from the Agency for Healthcare Research and Quality on hospitalizations related to use of prescription opioid painkillers found the largest increases occurred among older patients.

Copyright 2014 American Medical Association. All rights reserved.

claim that this is all artifact. I think that what they're noting is a real rise in misuse."

Whether the increase in prescribing opioids to older people is appropriate or not is difficult to ascertain, especially from an analysis of diagnostic codes, Paulozzi said. "There may indeed be situations where people are prescribed opioids too soon, where they could have tried other things," such as acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), or physical therapy, he said.

"You really need very detailed data to know whether the prescription was appropriate," such as the duration and intensity of the pain and whether an opioid was the last resort, said Paulozzi. "You really need to go into the clinical records and examine cases to see whether or not it's appropriate," he said.

What's Fueling Opioid Prescribing?

Several factors have combined to fuel the increase in opioid prescribing, Solomon said. "There's been a great push to make pain the 'fifth vital sign,' and there's a great push among medical educators to educate doctors about treating pain in all patients." In addition, he said, concerns have been raised about the safety of acetaminophen, NSAIDs, and selective NSAIDs, or COX-2 inhibitors. Yet a study of older arthritis patients concluded that opioid users had an increased relative risk of many safety events compared with NSAIDs other than COX-2 inhibitors (Solomon DH et al. *Arch Intern Med*. 2010;170[22]:1968-1976).

Paulozzi and other observers speculate that the guidelines from the American Geriatrics Society (AGS) also might have helped to stoke the increase in opioid prescribing among older patients. "We know that prescribing has gone up," said Paulozzi, who studies drug overdoses, especially those associated with prescription drugs. "The guidelines might have encouraged that."

Indeed, the most recent AGS clinical practice guideline on the use of medication to manage persistent pain, published in 2009, suggests that in most cases, "all patients with moderate to severe pain, pain-related functional impairment, or diminished quality of life due to pain [should] be considered for opioid therapy," and nonselective NSAIDs and COX-2 selective inhibitors "may be considered rarely, with caution, in highly selected individuals" (http://bit.ly/1weybTj). This advice, the document's executive summary noted, was "a significant departure" from the society's 2002 guideline (http://bit.ly/1tHoE9c).

Joseph Hanlon, PharmD, of the University of Pittsburgh School of Medicine, coauthored a critique in *Pain Medicine* of the AGS guideline shortly after its publication (Hanlon JT et al. *Pain Med*. 2009;10[6]:959-961). "While the purpose of the guidelines is to present recommendations on the use of pharmacological agents for frail older adults, it is precisely these individuals for whom pharmacotherapy should be used only when absolutely necessary and virtually always prescribed along with evidence-based non-systemic medication treatment options," Hanlon and his 3 physician coauthors wrote.

An investigation by the *Milwaukee Journal Sentinel* in 2012 raised concerns that the AGS guideline authors were biased in favor of opioid therapy, noting potential financial conflicts of interest for some of the guideline authors (http://bit.ly/1ugCiz3). At the time the guideline was issued, at least 5 of its 10 authors had financial ties to opioid companies as paid speakers, consultants, or advisers, according to the newspaper. The guideline chairman was listed as a paid speaker for an opioid company a year later, according to the newspaper.

American Geriatrics Society spokesperson Carol Goodwin said in an e-mail in early September that her organization at present has no plans to revisit its guideline. "The judicious use of opioids can be an effective approach to treating moderate to severe persistent pain in medically complex, frail older adults when alternatives such as acetaminophen or COX-2 inhibitors and… nonpharmacological approaches are not effective in managing pain," wrote Goodwin. But physicians need to weigh the risks vs the benefits and screen and monitor patients to prevent harm and misuse, she said.

Monitoring older adults who are prescribed opioids is important, agreed Louis Trevisan, MD, an associate clinical professor of psychiatry at the Yale School of Medicine and associate chief of psychiatry at the Veterans Affairs Connecticut Healthcare System. "You can't just give them the medications and walk away," he said.

However, Compton said, many physicians "are poorly informed about the treatment of pain" and are not up to the task. Unlike with younger people, "we tend not to be automatically suspicious of elderly individuals who request pain medications," he said.

"One of the things we've been doing at NIDA is to promote medical education on these issues," Compton said. As many as 100 000 physicians have taken NIDA's online courses on pain management (http://1.usa.gov/1pp3LYM), he said.

Research Gap

Medical education on pain management can only do so much, however, because there's a dearth of research about the risks and benefits of long-term opioid use in older patients, Compton and Hanlon said.

"It's really tricky using these drugs in older people," Hanlon said. "They're more sensitive to them to begin with. The dosing is sort of your best guess. They're usually not in trials. There's not a lot of long-term data."

In late September, Hanlon spoke about adverse drug reactions in older individuals taking opioid painkillers at an NIH workshop on the role of opioids in treating chronic pain (http://1.usa.gov/1pJv3JC).

"There has not been adequate testing of opioids in terms of what types of pain they best treat, in what populations of people, and in what manner of administration," according to background information from the NIH. "With insufficient data, and often inadequate training, many clinicians prescribe too much opioid treatment when lesser amounts of opioids or nonopioids would be effective. Alternatively, some health care providers avoid prescribing opioids altogether for fear of side effects and potential addiction, causing some patients to suffer needlessly."

Andrew Kolodny, MD, cofounder of the group Physicians for Responsible Opioid Prescribing, echoed the thought that some physicians are prescribing excessively large doses of opioids, especially to older patients. "The medical community isn't simply overprescribing… but they tend to be prescribing aggressive doses of these medications," said Kolodny, chief medical officer of Phoenix House, a chain of substance abuse treatment centers. And with the elderly, in particular, it's important to "go very low and very slow," he said.

No matter the dose, physicians should not prescribe any opioid to elderly patients if it hasn't been studied in their age group, Hanlon said. That includes codeine, methadone, and oxymorphone, he said. "Here's what I tell people: don't use that drug. You're doing an experiment on that person every time you use it."

Little is known about the relative safety of the various opioid painkillers for treating

Copyright 2014 American Medical Association. All rights reserved.

noncancer pain in older adults, Solomon said. He led a study that used health care utilization data for Medicare beneficiaries starting opioid therapy for noncancer pain to try to help answer that question (Solomon DH et al. *Arch Intern Med*. 2010;170[22]:1979-1986).

The study, published in 2010, was devised "somewhat in response to the AGS guideline," Solomon said. Granted, he said, research had raised concerns about the safety of NSAIDs, but AGS "moved too far, perhaps, to embrace the potential benefits of opioids."

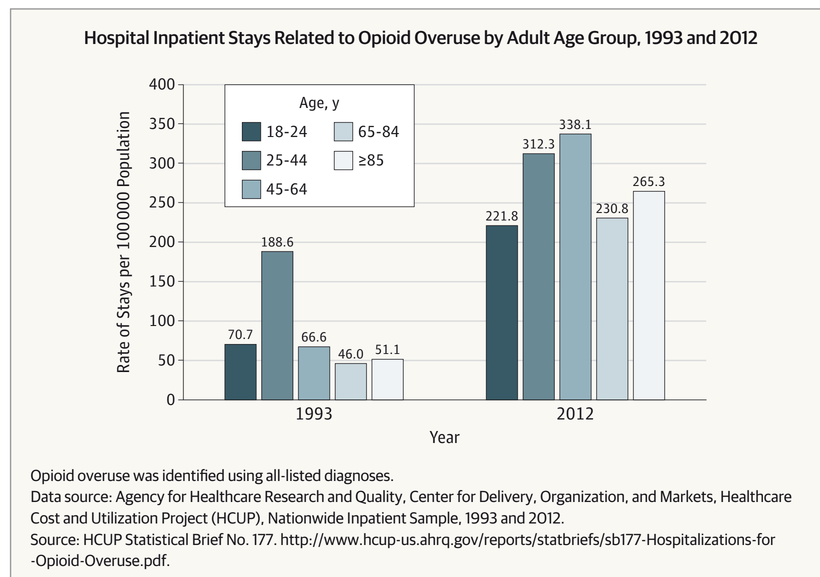
Solomon's study found that the rates of adverse events varied, depending on the opioid and the duration of treatment. For example, the risk of cardiovascular events increased for codeine users after 180 days of use. And the risk of death from all causes increased after only 30 days for users of oxycodone or codeine. "This study's findings do not agree with a commonly held belief that all opioids are associated with similar risk," Solomon and his coauthors wrote.

As the baby boomers age—the oldest are now aged 68 years, the youngest nearly 50 years—overuse of opioids is expected to increase. With their history of experimentation with drugs, the baby boomers as a group may be more likely to seek and abuse opioids than members of their parents' generation, Trevisan said.

Westley Clark, MD, JD, MPH, director of the Center for Substance Abuse Treatment at the Substance Abuse and Mental Health Services Administration, cited a 2006 report, coauthored by Compton, that projected the number of elderly individuals using drugs for nonmedical reasons in 2020 (Colliver JD et al. *Ann Epidemiol*. 2006;16[4]:257-265). By 2020, the nonmedical use of psychotherapeutic drugs, which includes opioid painkillers, was expected to reach 2.4%, nearly 2.7 million, among the population of US individuals 50 years or older, Compton and his coauthors wrote. That compares with 1.2%, or 911 000 people, in that age demographic in 2006.

Although the AHRQ statistical brief can't prove that opioid overuse played a substantial role in the increase in US hospitalizations among older individuals, Clark said, he views the document as a "cautionary tale."

"I see it as opening the door for greater inquiries," he said. "It is consistent with a number of other observations being made about the use of prescription opioids." ■



In the past 2 decades, the rate of hospital stays related to overuse of prescription opioids increased more than 5-fold for individuals aged 45-64 years, 65-84 years, or 85 years or older.

CDC to Clinicians: Be Alert for Children With Poliolike Illness

Joan Stephenson, PhD

Clinicians should be on alert for pediatric patients who present with an acute neurologic illness that features focal limb weakness and abnormalities of the spinal cord gray matter on magnetic resonance imaging (MRI), according to a health advisory issued September 26 by the Centers for Disease Control and Prevention (CDC).

The advisory (http://1.usa.gov/1BwY167) was prompted by the CDC's investigation with Colorado health authorities of a cluster of cases of this illness involving 9 pediatric patients aged 1 to 18 years. The patients were identified with this neurologic syndrome August 9 to September 27; most of them had a respiratory illness with fever in the 2 weeks before they developed neurologic symptoms.

Noting that the United States was also currently experiencing a nationwide outbreak of enterovirus D68 (EV-D68) associated with severe respiratory disease, the CDC said that the "possible linkage of this cluster of neurologic disease to this large EV-D68 outbreak is part of the current investigation."

The illness is characterized by acute focal limb weakness and findings from MRI of the spinal cord that show nonenhancing lesions largely restricted to the gray matter, the CDC advisory said. None of the patients experienced altered mental status or seizures.

All but 1 of the children were up-to-date on polio vaccinations. Tests of cerebrospinal fluid were negative for West Nile virus and enteroviruses (including poliovirus). Nasopharyngeal specimens were positive for rhinovirus/enterovirus in 6 of 8 patients who were tested; 4 of the 6 positive specimens were typed as EV-D68 (typing results were pending for the other 2 specimens).

The CDC said clinicians should contact their state and local health departments if they encounter patients aged 21 years or younger with acute onset of focal limb weakness on or after August 1 and an MRI showing a spinal cord lesion largely confined to gray matter. ■

Copyright 2014 American Medical Association. All rights reserved.