National Institutes of Health Study Shows Benefit of Emergency Department Use of Buprenorphine in Opiate Withdrawal

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As the patient presents himself in the emergency department (ED), he is sweating and agitated. He won’t even sit in a chair and can’t meaningfully answer questions. In other words, the patient is exhibiting symptoms of opiate withdrawal.

No single treatment will suffice. Most emergency physicians would give the patient a cocktail of medicines for high blood pressure, anxiety, and muscle aches, and some brochures for treatment programs. Sometimes this works, sometimes not.

Gail D’Onofrio, MD, MS, chairman of the Department of Emergency Medicine at Yale University, thought there must be a better way to treat the increasing numbers of patients who come into the ED and are dealing with opioid withdrawal. Not only was there the challenge of trying to control their immediate problems but also many of the same patients kept coming back.

“Opiate dependence and overdose really are prevalent problems, and we’re really seeing an escalation,” D’Onofrio said. “Emergency physicians often just treat the immediate issue in the emergency department, and so we know there’s a huge gap between patient needs and patients actually getting services. We wanted to try and find an innovative way of identifying patients and getting them into treatment.”

One of D’Onofrio’s colleagues at the Yale School of Medicine, an internist named David Fiellin, MD, had been treating opioid dependence with buprenorphine for more than 10 years, with considerable success. At about the same time D’Onofrio was looking for better tools to treat opioid dependence in the ED, Dr. Fiellin was looking to expand treatment with buprenorphine in the ED.

In 2009, they began studying the use of buprenorphine compared with brief interventions and referrals. The medicine that had worked so well for internists performed similarly well in the ED, increasing engagement in addiction treatment and reducing self-reported illicit opioid use.

A study describing the results was published in the April 28, 2015, issue of the Journal of the American Medical Association.

“I was extremely surprised by the results,” D’Onofrio said. “It is an amazing thing when you see a patient that is so compromised from acute withdrawal, that within 20 minutes of giving them medicine they have normal vital signs. Now you can actually talk to them about their issues, or find out if they have underlying problems.”

Long an issue just below society’s radar, opiate addiction is rapidly becoming recognized as a major problem facing the United States. Although it’s early in the 2016 presidential campaign, mental health and drug addiction have already surfaced as major issues. Former Secretary of State Hillary Clinton has heard about these problems during several meetings with voters in Iowa and New Hampshire.

“When I started running, when I started thinking about this campaign, I did not believe I would be standing in your living room talking about the drug abuse problem, the mental health problem, and the suicide problem,” she said during a campaign visit to Mason City, IA, in May. “But I’m now convinced I have to talk about it. I have to do everything I can in this campaign to raise it, to end the stigma against talking about it.”

Clinton has told her campaign aides to develop policy solutions to opiate addiction, and Republican candidates have likewise been talking about the issue during visits to early primary and caucus states.

Just as public access to prescription opioids such as hydrocodone, oxycodone, and fentanyl has increased significantly during the last 2 decades—from an estimated 76 million prescriptions in 1991 to 207 million in 2013—so too have cases of fatal overdoses. According to Centers for Disease Control and Prevention (CDC) data, the number of overdose deaths has quadrupled, from 4,030 in 1999 to more than 16,000 in 2010. By the late 2000s, opioid accidental deaths were exceeding those of motor vehicle crashes.
But the problem goes much farther than deaths, and addiction has placed an incredible burden on the US health care system, with EDs on the front line. The CDC reports that for every overdose death caused by opioids, 9 people are admitted to substance abuse treatments and there are 35 visits to the ED.

Additionally, opioid abuse is a gateway to heroin use. In October 2014, the CDC reported in its Morbidity and Mortality Weekly Report that a study of death certificates in 28 states found that deaths related to heroin use had doubled from 2010 to 2012. The federal agency believes 2 factors drove the increase in heroin deaths, widespread prescription opioid exposure and increasing rates of opioid addiction, and increased heroin supply. Although a majority of opioid users do not become heroin users, the study found, about three quarters of all new heroin users said they had abused prescription opioids before using heroin.

“Reducing inappropriate opioid prescribing remains a crucial public health strategy to address both prescription opioid and heroin overdoses,” said CDC Director Tom Frieden, MD, at the report’s release. “Addressing prescription opioid abuse by changing prescribing is likely to prevent heroin use in the long term.”

The federal government has finally begun responding to the burgeoning crisis. In March 2015, US Health and Human Services Secretary Sylvia M. Burwell announced an initiative to reduce prescription opioid- and heroin-related overdose, death, and dependence. President Obama’s fiscal year 2016 budget added $133 million in new funding to provide training for physicians to address overprescribing of opioids, increasing the use of naloxone to reduce the number of deaths associated with opioid and heroin overdose, and expanding the use of medication-assisted treatment to treat substance abuse disorders.

States have not waited for the federal government to act. Maryland, for example, formed a task force in February 2015 to identify ways of addressing the state’s increasing heroin and prescription opioid crisis.

“The goal of this emergency task force is to shine a light on heroin and the havoc it is causing in Maryland,” said Lt. Governor Boyd Rutherford. “From preventing our kids from using heroin in the first place to increasing and improving access to treatment services for those in recovery, this task force will employ every resource available to take a holistic approach to address this public health emergency.”

The research conducted by D’Onofrio and Dr. Fiellin was supported by a grant from the National Institute on Drug Abuse. Dr. Fiellin said the federal institute was primarily interested in the efficacy of screening, brief interventions, and referral to training to improve long-term treatment of individuals addicted to opioids. Dr. Fiellin said he believed that this approach may work for individuals with low levels of opioid use but that it would not prove effective for people with deeper addictions.

D’Onofrio and colleagues got permission to expand their study of 329 opioid-dependent patients treated in an ED to include a group that received buprenorphine. The first group received screening and referral to treatment; the second group received screening, brief intervention, and facilitated referral to community-based treatment services; and the final group received screening, brief intervention, and treatment with buprenorphine or naloxone in the ED, and referrals. Of the patients in the buprenorphine group, 78% were engaged in addiction treatment 30 days later. Only 37% of patients in the referral group and 45% of patients in the brief intervention group were similarly engaged after 30 days.

Some physicians have questioned the study because the rate of urine samples that tested negative for opioids did not differ statistically across groups. However, D’Onofrio said the urine test could specify only whether opioids had been used during the previous 72 hours, not whether a person had ingested the drugs once or 10 times a day. She said she wouldn’t have expected patients to give up opioid use right away.

Regardless of the urine aspect of the study, some EDs are already moving to more widely adopt the use of buprenorphine.

“There’s been a lot of interest in the work,” Dr. Fiellin said. He acknowledged it’s only a proof-of-concept study and that some institutions will want to see a larger study. But he said the buprenorphine approach is better than what EDs are currently doing.

There is one difficulty with wider adoption of buprenorphine treatment, however. Federal regulations allow emergency physicians to provide only one 24-hour dose of buprenorphine during a patient’s stint in the ED. To prescribe the medication for a longer duration for up to 30 patients, a physician must complete an 8-hour training course and submit this paperwork to the Drug Enforcement Agency. After a year, the number of patients a physician could prescribe the medication to would increase to 100.

“I want people to understand that this isn’t as difficult as it seems,” D’Onofrio said.

And it may be worth the effort. It seems increasingly important for emergency physicians to take some ownership of this problem because they are part of the group being...
blamed for writing excess prescriptions for opioids. A study in the March 2014 issue of Academic Emergency Medicine found that between 2001 and 2010, the percentage of overall ED visits during which any opioid was prescribed increased by 49% to 31% in 2010, whereas the percentage of pain-related visits increased by only 8% during the same time. Authors of the study said several factors contributed to the increase, including a sense that pain was going untreated and pressure to make patients feel satisfied with their care. Some hospitals tie pay incentives to patient satisfaction surveys.

In addition, Medicare payments are linked to patient satisfaction surveys. Concern that prescriptions are being written to increase these scores, US Senators Chuck Grassley of Iowa and Dianne Feinstein of California wrote to Administrator Marilyn Tavenner of the Centers for Medicare & Medicaid Services in 2014: “There is growing anecdotal evidence that these surveys may be having the unintended effect of encouraging practitioners to prescribe opioid pain relievers unnecessarily and improperly, which can ultimately harm patients and further contribute to the United States’ prescription epidemic,” Grassley and Feinstein wrote.

Regardless of the extent of blame that emergency physicians bear for the increase in prescriptions written for opioids in the United States, they appear to be well positioned to do something about the problem.

“One message I have from our study is that we need to do something,” D’Onofrio said.

She noted that emergency physicians often initiate treatment for chronic diseases, such as diabetes, and help link patients to follow-up services. Doing the same kind of thing for opioid addicts, providing them with medication to ease withdrawal symptoms and helping to find specialized substance abuse treatment centers in their communities, is really no different.

But some emergency physicians have questioned the notion of excess prescriptions being written in the ED. Noting that earlier studies had relied on national survey extrapolation or prescription databases, the authors of a study published in April 2015 by Annals observed 19 ED sites across the country during 1 week in October 2012. The authors found that only 17% of discharged patients were prescribed opioid pain relievers and that the majority of the prescriptions had small pill counts.

She is working to develop a multicenter trial and make it easier for emergency physicians to prescribe buprenorphine.

“I hope it won’t take too long because the risks of this are very small compared to the benefits,” D’Onofrio said. “If we had to wait for 10 years for this to be widely adopted, that would be very unfortunate. Substance abuse can be a revolving door. I know it’s complicated and money is tight, but it’s in the best interest of everyone to get patients into treatment, not just patch them up and send them out.”

Section editor: Truman J. Milling, Jr, MD

Funding and support: By Annals policy, all authors are required to disclose any and all commercial, financial, and other relationships in any way related to the subject of this article as per ICMJE conflict of interest guidelines (see www.icmje.org). The author has stated that no such relationships exist.

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http://dx.doi.org/10.1016/j.annemergmed.2015.08.010