Choosing Analgesics Wisely: What We Know (and Still Need to Know) About Long-Term Consequences of Opioids

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Emergency physicians provide care to many patients with pain and often prescribe an opioid as part of the analgesic plan, usually with smaller total doses and shorter courses than most other providers. Emergency physicians prescribe opioids because of beliefs by patients or providers in a superior analgesic effect beyond over-the-counter acetaminophen or nonsteroidal anti-inflammatory agents. During the last decade, trainees and practitioners have been told to identify pain and treat it aggressively to avoid undertreatment and suffering, these latter effects being called “oligoanalgesia.” Efforts such as making pain the fifth vital sign, requiring documentation of pain scores pre- and posttreatment, linking patient satisfaction to reimbursement, creating misleading educational campaigns about addiction risks, and the proliferation of opioid analgesic options highlight the unbalanced pressures brought to bear on clinicians in the “war on pain.”

Opioid abuse—both prescription and illicit—is a growing concern, with death, morbidity, and other individual and population-based consequences. Many patients admitted to drug treatment facilities report abuse arising as an unintended consequence of therapeutic administration of an opioid to treat pain. Proportionally, most of the prescription opioids abused in the United States start from the prescription pads of nonemergency physicians, but some of the supply emanates from emergency department (ED) prescribing. The magnitude of ED patients with pain (130 million visits in 2010, 42% for pain) and the frequent deployment of therapeutic opioids highlight the public health risks of opioid use from the ED. Hydrocodone was prescribed more than 136 million times by all providers in 2012, so even a very small rate of aberrant opioid use could translate into thousands of affected patients.

Although we have crude estimates of ED opioid prescribing, we do not know our role in initiating addiction or abuse in a naive patient or our contribution to continued use in patients with preexisting opioid use disorder. Guidelines intended to temper prescribing after discharge are often based on epidemiologic concerns about the frequency of opioid misuse among ED patients. Absent solid evidence of harm, blanket restrictions on opioid use engender the risks of continued pain and dissatisfied patients. We need to know the risks of addiction, abuse, and overdose relative to the risks of poorly controlled pain and its consequences to truly inform decisionmaking. Worded differently, how can prescribers know that they will not convert one problem (poorly treated pain) into another (addiction or abuse) with significant disruptive long-term outcomes? Although many place the addiction risk at 5% of all patients treated, it may reach 26% in those with long-term outpatient opioids use. Separate from abuse or addiction, opioids can create altered nociception that increases pain rather than relieving it; the development of hyperalgesia means our good intentions to relieve suffering can occasionally do the opposite.

In the study by Hoppe et al in this issue of Annals, we gain a glimpse into downstream events after a first outpatient opioid analgesic prescription for the treatment of acute pain. In this retrospective study of opioid-naive patients at one ED, patients who received and filled an opioid prescription for “minor to moderate” pain were 1.8 times more likely to receive and fill another opioid prescription within 60 days of the first ED visit (ie, 305 to 425 days after the ED visit) compared with those who did not receive a prescription. Some may suggest that this observation is not surprising: some patients with acute pain may benefit from another prescription. However, this explanation is probably inadequate, given the study methodology, because at 1 year after an acute injury, the acute pain will have resolved. A related informative retrospective cohort study using insurance databases and patient registries in Canada found that 10% of opioid-naive older patients prescribed opioids within 7 days of a same-day surgery were still being
prescribed opioids 1 year after their index surgery.\textsuperscript{14} Although the study by Hoppe et al\textsuperscript{13} did not look at prescriptions after the index visit until the first anniversary (because of the limitation of prescription drug monitoring program study design), they may have been trying to measure the rate of conversion from acute to chronic pain or the development of opioid dependence. Although the authors cannot tell us the detail about reasons for the sentinel or anniversary prescriptions, the large data set allows us to know the potential upper limits of repeated use after an initial ED visit for acute pain. To better understand the effect and drive policy changes, we need the next tranche of data, notably, how many patients had ongoing pain and received another appropriate prescription or the number of prescriptions postvisit and up to 1 year later. We also need data on which patients simply received an inadequate prescription initially, which had worsening disease, and which displayed the footprints of aberrant use.

A strength of the current design—the inclusion of many types of acute pain—also complicates interpretation of the study results. Some of the patients had flank pain or fractures, whereas others had back pain or headache syndromes. Each of these has different pain patterns, treatment options, and long-term consequences, confounding broad observations. Nonetheless, ED practice includes patients with a spectrum of pain complaints, and future guidelines, policy, or care plans will need to account for the array of conditions or syndrome specific without becoming too complicated. Identifying acute problems that may best be managed successfully without opioids is a key need before simply declaring “no opioid use.” This will raise additional difficult questions, such as how often the initiation of opioids shifts some patients with acute pain to chronic pain or instigates abuse, and also the extent to which these risks would be tolerable.

Patients who received but did not fill an opioid prescription after ED discharge had a 20\% reduction in the likelihood of receiving a later prescription in the specified timeframe compared with those who did not receive a prescription. The explanation for this finding is unclear but is likely patient specific. For example, perhaps those with “red flags” for misuse received fewer prescriptions (a seemingly good but indistinct pattern), the anticipated pain for which the prescription was provided never materialized, or those who had the safety net of an available prescription derived comfort from that knowledge.

Receiving a second appropriate prescription for an opioid for a different indication has different implications than receiving many prescriptions for the same reason. The authors used an established binary (yes/no) outcome definition and could not explore this nuance in their prescription drug monitoring program research protocol. We hope others will build on these observations, approaching their state prescription drug monitoring program to analyze large-scale, patient-level data. Only with this granularity can we know more about the effect of a first-time opioid prescription on additional prescriptions and overall health. Perhaps most important, a diagnosis-based prospective study, such as one of a cohort of “opioid-naïve” patients with long bone fracture from the ED, with detailed prescription drug monitoring program and contemporaneous medical record observations may inform the range of patient responses to significant injury, rather than retrospectively conclude that those who left without an opioid prescription experienced oligoanalgesia. As was thoughtfully proposed in commentary about oligoanalgesia,\textsuperscript{15} retrospective studies often fail to capture the reason (eg, patient preference) for absence of an opioid prescription.\textsuperscript{16}

Recently, a campaign aimed at reducing interventions, both diagnostic and therapeutic, that are not sufficiently beneficial or are too costly gained national attention.\textsuperscript{17} We believe that this recent Choose Wisely initiative of the American College of Emergency Physicians and other organizations can be used to address analgesic practices in the ED, are potential fodder for this effort, and will mesh well with its previous clinical policies.\textsuperscript{18} An ideal path may involve providing education on the effectiveness and safe use of all analgesics (including nonsteroidal anti-inflammatory drugs and opioids), weighing patient factors (including misuse), promoting nonpharmacologic treatments such as ice, and engaging patients in the decisionmaking to use opioids.

The United States and Canada are in the midst of an epidemic of opioid addiction, dependence, overdose, and death. Although the ED has a role in the broader effort to mitigate these adversities, we believe ED-based data on opioid prescribing and its consequences are needed to best drive policy and care. Simply swinging from the accusations of oligoanalgesia and pleas to prescribe more opioids to an era of “opiophobia” will not optimize outcomes. Until better data exist, each emergency physician must make the point-of-care decision, armed with limited data and his or her bedside skills about how to treat a patient’s pain. Informed prescribing through the use of aids such as the prescription drug monitoring program and analgesic prescribing guidelines, along with an eye toward the patient-specific and public health risks of opioid analgesics, can help to decrease the burdens of liberal opioid prescribing.

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