AMA Journal of Ethics

March 2015, Volume 17, Number 3: 202-208

ETHICS CASE

# Opioids for Nonmalignant Chronic Pain

Commentary by Anna Woodbury, MD

Dr. Belay is an anesthesiologist and board-certified pain management specialist in a thriving private practice. She has grown concerned over the past month since hearing that a well-respected colleague came under scrutiny for "troubling prescribing patterns" based on the percentage of his patients prescribed long-acting opioids.

Dr. Belay receives a refill request for morphine from her patient Mr. Flora. He is a law professor at the local university who sustained a severe back injury six years earlier while replacing the catalytic converter in his award-winning antique car. Although he underwent spine surgery for the injury the same year, he has since suffered chronically worsening back pain that is frequently accompanied by a sharp pain that radiates along the leg. Before seeking the care of his pain specialist, he saw numerous orthopedic surgeons, chiropractors, physiatrists, neurologists, and physical therapists.

Dr. Belay informs him he is due for an appointment before she can provide a refill. During his appointment, Dr. Belay discusses her long-term plans of reducing Mr. Flora's reliance on opioid therapy by supplementing it with adjuvants, injection therapy, and possibly a spinal cord stimulator. She offers him a trial of the spinal cord stimulator, explaining that, if successful, it would reduce the amount of oral medication needed, pose fewer side effects, and provide better long-term control of his chronic pain.

Mr. Flora is aghast. He cries, "Cutting my back open is what caused this pain in the first place! And now you're telling me you want to cut me again to fix it?"

Dr. Belay tells him about the benefits and good outcomes for other patients who received spinal stimulation therapy, but Mr. Flora remains unwilling to consider these options and says he only wants a refill of his morphine.

## Commentary

Often, patients with chronic pain have undergone multiple evaluations and treatments prior to seeing a pain management physician. These patients typically are frustrated with the medical system and feel like they have tried it all. If they have found something that works for them, they logically want to continue that regimen. In the case of opioids, this often leads to behaviors that can be misunderstood and misinterpreted as addiction with the desire for dose escalation. Although it is inappropriate to label all patients on opioids as addicts, physicians must also be cautious of the potential for overdose, abuse, and diversion of prescription drugs [1].

Is a Patient Who Demands Opioids an Addict?

A patient who is seeking opioid therapy is not necessarily an addict. There is a phenomenon known as pseudoaddiction that physicians must keep in mind when dealing with any chronic pain patient. Addiction results in a compulsive state of seeking out and using a substance despite harm to personal health and relationships. It is characterized by intense cravings, inability to quit, and continued use despite harmful effects. In pseudoaddiction, on the other hand, the patient is seeking opioid medications for pain relief, not with the intent of abuse. Because pain is primarily a subjective complaint, it is often difficult to determine whether a patient is seeking substances for abuse or simply seeking better pain control. In some ways, the medical field has created addicts by exposing patients to narcotic medications and by prescribing short-acting, euphoric, and addictive medications so freely. Diversion of these medications—often when children of the patients gain access to them and use them recreationally—leads to a rise in overdoses [2]. According to the Centers for Disease Control and Prevention, deaths from drug overdoses continue to rise, with 36,000 deaths in 2008 and most of these from prescription drugs [3].

However, the pendulum often swings too wildly in both directions whenever awareness is raised about a controversial issue. At some point in the last few decades, pain became "the fifth vital sign" to ensure that clinicians were not ignoring patients' pain complaints. That response could have contributed to the current predicament of overprescribing opioid medications without fully assessing or addressing the pain complaint [4, 5]. Knowing when opioid therapy is going to be beneficial rather than harmful involves a precarious balancing act. If physicians become too wary of prescribing pain-relieving medications, they could leave patients in chronic pain to suffer with no alternatives. Psychiatric comorbidities and chronic pain are often linked, and it is hard to tell which came first. Depression can lead to an increased perception of pain, but untreated, chronic pain can lead to depression. I have heard patients say, "If I don't have my fentanyl patch, I'm in so much pain that I want to die." And that statement can never be taken lightly. However, patients who are suicidal should not be prescribed opioid medications or other pharmaceutical agents that could potentially cause a fatal overdose. The complex interplay between the effects of pain, addiction, depression, and other comorbid conditions requires assessment on a case-by-case basis.

Prior to prescribing opioids, it is prudent, therefore, to administer the opioid risk tool (ORT) or a similar assessment to screen patients for the likelihood of prescription drug abuse [6]. The opioid risk tool examines five domains, including family history of substance abuse, personal history of substance abuse, age, history of preadolescent sexual abuse, and psychological disease. Patients are scored and fall into low-, moderate-, or high-risk groups. In general, patients between 16 and 45 years old with a strong history of family or personal substance abuse, psychiatric illness, or childhood sexual abuse tend to be at higher risk of prescription drug abuse and addiction. It would not be prudent to prescribe opioids to a high-risk patient given the potential for overdose, whether accidental or intentional.

If in the course of treatment it becomes apparent that Mr. Flora is truly addicted, then it would be appropriate for Dr. Belay to express her concerns about dependence and

recommend that he consult an addictionologist. These professionals are typically psychiatrists who specialize in drug or alcohol-related addiction.

Informing Patients about the Efficacy and Side Effects of Opioids

If addiction is not a concern, attention turns to finding the most effective and least harmful treatment. When nonaddicted, rational patients with the capacity to make decisions for themselves are presented with detailed information about the efficacy and side effects of opioid treatment, they might make an educated decision to discontinue opioid therapy themselves. Many patients are aware only of the potential for addiction or overdose and believe that they are not at risk for these behaviors. However, when given thorough information regarding the risks of long-term opioid therapy, patients often see the value of exploring other options rather than believing their physicians are avoiding prescribing narcotics simply for fear of litigation or regulatory action.

So, are opioids a good therapeutic choice for chronic pain? Unless a patient has been sustained on low-dose opioids with little or no need for escalation over time, the answer is no. While opioids do provide short-term benefit and can be helpful when the pain will resolve (e.g., following a fracture or immediately after surgery), there is no evidence of long-term benefit. In fact, studies suggest that many patients develop a tolerance to the medication over time, leading to the need for dose escalation with inadequate pain relief, more side effects, poor quality of life, and, often, long-term unemployment [7]. In one study, for example, opioid use was associated with greater disability than non-use after six months, despite adjusting for confounding factors [8]. While opioid rotation, which staves off tolerance, can sometimes help maintain a lower total necessary dose, eventually patients still tend to become resistant to the analgesic effects and experience worsening pain. In addition to the well-known potential for physical and psychologic dependence with long-term opioid use, which can progress to addiction, other negative effects include:

- *Opioid-induced hyperalgesia*. This increased sensitivity to pain—related to decreased endocytosis of the mu-opioid receptor and increased excitatory mechanisms such as N-methyl D-aspartate (NMDA) receptor activation [2, 9]—typically occurs with higher doses of opioids but can happen at lower doses as well. The preferred treatment, which usually works, is to cut the opioid dose by 50 percent [10, 11].
- *Constipation.* Opioids also act on mu-opioid receptors in the gastrointestinal tract, leading to decreased peristalsis and resulting in constipation.
- *Sexual dysfunction*. This occurs in at least 80 percent of both men and women on oral opioid therapy, due to drops in testosterone and estrogen levels that can decrease libido and cause erectile dysfunction and hypogonadism, even in those with intrathecal pumps [12-15].
- *Weight gain, decreased energy, and moodiness*. Dysregulation of both the hypothalamic-pituitary axis and thyroid hormone release can affect all three of these areas [15-19].
- *Lower-extremity edema*. Vasopressin dysfunction affects water retention [14, 15, 20].
- *Withdrawal syndrome*. If a physiological dependence is established (regardless of whether psychologic dependence is present), stopping opioid use abruptly can lead

to anxiety, agitation, diarrhea, nausea, and vomiting, among other unpleasant symptoms.

Recommendations

In addition to their side effects, opioids may not even be particularly effective for Mr. Flora's condition. His pain is likely due to post-laminectomy syndrome, but worsening of his symptoms could indicate either progressive disease or tolerance to morphine; opioids, while they can be used for the treatment of neuropathic and radicular pain syndromes such as his, are not first-line treatment [21, 22]. This is important information for him to know.

Dr. Belay should explain to Mr. Flora that neuropathic pain is classically hard to treat, but many medications specific to this condition are available, each one acting through a different mechanism. Sometimes it is a process of trial and error, and it may take a particular medication or a combination to adequately treat neuropathic pain. Neuropathic pain medications include anticonvulsants, tricyclic antidepressants, serotonin norepinephrine reuptake inhibitors, and even oral local anesthetics [21]. She must convey to him that it might be a long process to find the optimal therapy for him, but that opioids are not typically the best option for neuropathic pain given their high risk-benefit ratio [1].

Dr. Belay should ask whether Mr. Flora has tried gabapentin and at what dose. It may be worth trying again, depending on the dose used previously. Often, starting on too high a dose can cause adverse side effects and lead the patient to abruptly discontinue the medication. Similarly, starting on too low a dose without informing the patient that the medication will require slow dose increases to minimize side effects while working up to effectiveness can lead the patient to perceive that the medication doesn't work.

She should also consider that, while Mr. Flora has been to multiple specialists, he has not seen a cognitive behavioral therapist or psychiatrist. It is possible that life stressors are aggravating his pain symptoms. A cognitive behavioral therapist can help Mr. Flora learn to manage his pain through techniques such as distraction and meditation. Biofeedback can also be helpful in self-management of physiological responses to stress and pain. So can acupuncture; evidence supports its effectiveness in the treatment of some chronic pain conditions [23, 24]. Of course, Dr. Belay cannot force Mr. Flora to go to a specialist. However, she can express her concerns for his dependence on morphine and his refusal to try alternative treatment modalities, and she can recommend that he see an addictionologist to determine whether or not it would be appropriate for him to continue opioid use.

If, in the course of speaking with Mr. Flora, it becomes apparent that he has truly exhausted all conservative medical options (physical therapy, heat, ice, massage, anti-inflammatory medications, neuropathic pain medications, cognitive behavioral therapy, biofeedback, acupuncture, and minor interventional pain procedures such as epidural steroid, trigger-point, or facet injections) and is stable on an opioid regimen without concerns for increased risk based on the ORT or comorbidities such as obstructive sleep apnea, then it is reasonable to continue this class of medication.

One long-acting opioid medication that can be particularly beneficial in the treatment of chronic pain, including neuropathic pain, is methadone. Because methadone works not only through the opioid receptors but also through NMDA antagonism, it can be more potent than other opioids. Additionally, because of its pharmacokinetics, methadone does not provide the rush of euphoria and the roller-coaster effects of shorter-acting, fast-onset narcotics. These characteristics of methadone tend to make it less addictive than other opioids.

If Dr. Belay is uncomfortable in continuing to prescribe certain narcotics for Mr. Flora, she is within her rights to refuse to do so. However, Dr. Belay must balance her moral obligations to "do no harm" and to relieve suffering, and she should not abandon this patient. If Mr. Flora is an appropriate candidate for opioid therapy and, after a thorough discussion of the risks, benefits, and alternatives to opioid therapy, he insists that morphine is the only therapy he will accept, Dr. Belay could provide a list of physicians who are more comfortable prescribing it.

If Dr. Belay does decide to take on the responsibility of prescribing opioids for Mr. Flora, she will need to follow local and federal regulations regarding the prescribing of narcotic medications. Regulations may include a pain contract to discuss risks and benefits of opioid therapy and discourage patients from obtaining opioids from multiple sources and random urine drug screens to assess whether patients are taking the medications as prescribed or abusing any other substances. She will also need to monitor him regularly for any aberrant behavior.

And what about the stimulator? Ultimately, if the patient has adequate decision-making capacity, patient refusal is an absolute contraindication to any procedure. Although Dr. Belay may feel that spinal cord stimulation is a more appropriate long-term treatment for Mr. Flora's pain, ultimately it is Mr. Flora's choice what is done to his body. And any patient undergoing implantation of a spinal cord stimulator or intrathecal pump would require a psychological evaluation prior to placement of the device; Mr. Flora is clearly not psychologically ready for this procedure [25].

Mr. Flora clearly has attributed his chronic pain to his previous surgery and is skeptical of further surgery. And that is not necessarily unreasonable—surgery comes with its own set of risks. There is a risk of infection, bleeding, and nerve damage with every procedure. The stimulator could stop working due to lead migration or battery failure. Even an intrathecal pump that delivers opioids to the spinal opioid receptors, which minimizes systemic effects, does not completely eliminate them and tolerance can still develop. Furthermore, there are risks of pump malfunction or leakage, which could lead to a need for repeat surgery or a fatal overdose. An implantable device is not necessarily the best option. As with any treatment, the risks and benefits must be weighed for each individual patient.

However, Mr. Flora may not be opposed to trying other adjuvants or injections for his pain. Dr. Belay should assure Mr. Flora that no procedure will be performed on his body without his consent and focus more on discussing other interventions with him. Over time, as trust builds between the two, the possibility of spinal cord stimulation for his pain could be readdressed.

## References


1. Franklin GM; American Academy of Neurology. Opioids for chronic noncancer pain: a position paper of the American Academy of Neurology. *Neurology*. 2014;83(14):1277-1284.
2. Williams JT, Ingram SL, Henderson G, et al. Regulation of mu-opioid receptors: desensitization, phosphorylation, internalization, and tolerance. *Pharmacol Rev*. 2013;65(1):223-254.
3. Centers for Disease Control and Prevention. Vital signs: overdoses of prescription opioid pain relievers—United States, 1999-2008. *MMWR Morb Mortal Wkly Rep*. 2011;60(43):1487-1492.
4. Caudill-Slosberg MA, Schwartz LM, Woloshin S. Office visits and analgesic prescriptions for musculoskeletal pain in the US: 1980 vs. 2000. *Pain*. 2004;109(3):514-519.
5. Mularski RA, White-Chu F, Overbay E, Miller L, Asch SM, Gazini L. Measuring pain as the 5th vital sign does not improve quality of pain management. *J Gen Intern Med*. 2006;21(6):607-612.
6. Chou R, Fanciullo GJ, Fine PG, Miaskowski C, Passik SD, Portenoy RK. Opioids for chronic noncancer pain: prediction and identification of aberrant drug-related behaviors: a review of the evidence for an American Pain Society and American Academy of Pain Medicine clinical practice guideline. *J Pain*. 2009;10(2):131-146.
7. Sjøgren P, Grønbæk M, Peuckmann V, Ekholm L. A population-based cohort study on chronic pain: the role of opioids. *Clin J Pain*. 2010;26(9):763-769.
8. Ashworth J, Green DJ, Dunn KM, Jordan KP. Opioid use among low back pain patients in primary care: is opioid prescription associated with disability at 6-month follow-up? *Pain*. 2013;154(7):1038-1044.
9. Lee M, Silverman SM, Hansen H, Patel VB, Manchikanti L. A comprehensive review of opioid-induced hyperalgesia. *Pain Physician*. 2011;14(2):145-161.
10. Angst MS, Clark JD. Opioid-induced hyperalgesia: a qualitative systematic review. *Anesthesiology*. 2006;104(3):570-587.
11. Lee SH, Cho SY, Lee HG, Choi JI, Yoon MH, Kim WM. Tramadol induced paradoxical hyperalgesia. *Pain Physician*. 2013;16(1):41-44.
12. Rhodin A, Stridsberg M, Gordh T. Opioid endocrinopathy: a clinical problem in patients with chronic pain and long-term oral opioid treatment. *Clin J Pain*. 2010;26(5):374-380.
13. McWilliams K, Simmons C, Laird BJ, Fallon MT. A systematic review of opioid effects on the hypogonadal axis of cancer patients. *Support Care Cancer*. 2014;22(6):1699-1704.
14. Paice JA, Penn RD, Ryan WG. Altered sexual function and decreased testosterone in patients receiving intraspinal opioids. *J Pain Symptom Manage*. 1994;9(2):126-131.
15. Xenidis M, Pandya N, Hames E. Effects of intrathecal opioid administration on pituitary function. *Pain Med*. 2013;14(11):1741-1744.
16. Vuong C, Van Uum SH, O'Dell LE, Lutfy K, Friedman TC. The effects of opioids and opioid analogs on animal and human endocrine systems. *Endocr Rev*. 2010;31(1):98-132.

17. Gold PW, Extein I, Pickar D, Rebar R, Ross R, Goodwin FK. Supression of plasma cortisol in depressed patients by acute intravenous methadone infusion. *Am J Psychiatry*. 1980;137(7):862-863.
18. Grossman A. Brain opiates and neuroendocrine function. *Clin Endocrinol Metab*. 1983;12(3):725-746.
19. Oltmanns KM, Fehm HL, Peters A. Chronic fentanyl application induces adrenocortical insufficiency. *J Intern Med*. 2005;257(5):478-480.
20. Chaney MA. Side effects of intrathecal and epidural opioids. *Can J Anaesth*. 1995;42(10):891-903.
21. O'Connor AB, Dworkin RH. Treatment of neuropathic pain: an overview of recent guidelines. *Am J Med*. 2009;122(10)(suppl):S22-S32.
22. Moulin D, Boulanger A, Clark AJ, et al. Pharmacological management of chronic neuropathic pain: revised consensus statement from the Canadian Pain Society. *Pain Res Manag*. 2014;19(6):328-335.
23. Lam M, Galvin R, Curry P. Effectiveness of acupuncture for nonspecific chronic low back pain: a systematic review and meta-analysis. *Spine*. 2013;38(24):2124-2138.
24. Deare JC, Zheng Z, Xue CC, et al. Acupuncture for treating fibromyalgia. *Cochrane Database Syst Rev*. 2013;5:CD007070.
25. Nagel SJ, Lempka SF, Machado AG. Percutaneous spinal cord stimulation for chronic pain: indications and patient selection. *Neurosurg Clin N Am*. 2014;25(4):723-733.

Anna Woodbury, MD, is an anesthesiologist and pain management physician at the Veterans Affairs Medical Center and an assistant professor of anesthesiology at Emory University School of Medicine in Atlanta. Her scholarly interests include research in integrative medicine and non-narcotic pain management.

Related in AMA Journal of Ethics
The Importance of Good Communication in Treating Patients' Pain, March 2015

Drug Seeking or Pain Crisis? Responsible Prescribing of Opioids in the Emergency Department, May 2013

Diagnosing Acute Low Back Pain, April 2011

Objectifying Chronic Pain: From the Patient to Diagnostic Metrics, May 2013

Education to Identify and Combat Racial Bias in Pain Treatment, March 2015


ISSN 2376-6980