Difficult Decisions: Managing Chronic Neuropathic Pain With Opioids

John D. England, MD, FAAN; Gary M. Franklin, MD, MPH, FAAN

ABSTRACT

The decision to use opioids to treat chronic neuropathic pain is complex and somewhat controversial. Although opioid therapy may be appropriate for some patients with chronic neuropathic pain, physicians must implement strategies to reduce opioid abuse, addiction, and diversion. The decision to use chronic opioids should be made proactively with institution of best practices to ensure safe and effective use. As with all aspects of chronic pain management, better education of both health care providers and patients is necessary. Fortunately, specific recommendations for the safe and effective use of opioids are now available in several recently published guidelines. The best practices embodied in these guidelines should be considered for widespread adoption by both individual providers and health care systems.

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Case

A 38-year-old man with type 2 diabetes mellitus and apparent painful diabetic polyneuropathy presented to a neurologist as a new patient. He stated that he had had ''personality conflicts'' with his previous neurologist. He was taking several medications for pain, including pregabalin 75 mg orally twice daily, duloxetine 30 mg orally twice daily, and oxycodone controlled-release 40 mg orally twice daily. He denied a history of mental illness or substance abuse but stated that he did go through a period of depression when he lost his job several years ago. He described ''deep aching,'' ''burning,'' and ''stabbing'' pain in his feet. He rated his average pain as 6 to 7 out of 10 and his average functional impairment as 4 out of 10. Examination demonstrated reduced pinprick and cold temperature sensibility in both feet, moderately reduced vibration sensibility at the toes, and absent ankle reflexes. The patient provided a copy of recently performed nerve conduction studies showing bilaterally absent sural sensory action potentials and bilaterally decreased peroneal nerve motor amplitudes with normal distal latencies, normal conduction velocities, and normal F wave latencies. He provided no additional medical records. He had refills for all of his medications except for oxycodone, and he requested a new prescription for oxycodone.

Address correspondence to Dr John England, LSUHSC School of Medicine, 1542 Tulane Avenue, Room 763, Department of Neurology, New Orleans, LA 70112, *jengla@lsuhsc.edu*.

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DISCUSSION

The treatment of painful diabetic neuropathy is often challenging, and most patients do not obtain complete pain relief with any combination of medications. A recent AAN evidence-based guideline on the treatment of painful diabetic neuropathy reviewed the available options.[1] On the basis of Class II evidence, the opioids morphine sulfate, tramadol, and oxycodone controlled-release were judged to be probably effective in lessening the pain of painful diabetic neuropathy. The guideline recommended that these agents be considered for the treatment of painful diabetic neuropathy (Level B); however, the effectiveness of opioids for pain relief is usually moderate, and there is no substantial evidence that opioids maintain a significant degree of pain relief for more than a few months. Additionally, opioids have many adverse effects, and chronic use can lead to tolerance, dependence, abuse, and overdose.[2] For these reasons, the administration of opioids for chronic nonmalignant pain must be carefully considered, and they should not be a first-line treatment. In addition, the decision to use chronic opioids should be made proactively, with institution of best practices to ensure safe and effective use.

Recommendations for the use of opioids must also take into account the significant and escalating public health problems of opioid abuse, addiction, and deaths from opioid overdose.[3–5] In the United States, unintentional opioid-related deaths increased from approximately 3,000 to 12,000 between 1999 and 2007.[5] Opioid overdose is now second only to motor vehicle accidents as the leading cause of accidental death in the United States.[5] These statistics prompted the Centers for Disease Control and Prevention (CDC) to issue a statement calling pharmaceutical opioid overdose a national epidemic. A recent study documented a ninefold increased risk of overdose with opioid doses exceeding 100 mg/d morphine equivalent dose (MED) compared to doses below 20 mg/d MED for patients with chronic noncancer pain.[6] In a Veterans Health Administration study, the risk of opioid overdose death was directly related to the maximum prescribed daily dose of opioids, and the risk of opioid overdose increased when doses exceeded 50 mg/d MED.[4] In a recent Canadian study, risk increased threefold at doses greater than or equal to 200 mg/d MED.[7] Opioid-mediated respiratory depression is likely a prominent factor in unintentional poisoning.[8] It is likely that tolerance for euphoria and analgesia precedes tolerance for respiratory depression.[9] Other contributing factors include use of other prescribed drugs that, in combination with opioids, may exacerbate respiratory depression. For this reason, it is recommended that sedative-hypnotics and benzodiazepines not be used regularly with chronic opioid therapy.

Acknowledging that some patients with chronic noncancer pain probably benefit from opioid therapy, physicians must recognize the importance of implementing strategies for reducing opioid abuse, addiction, and diversion. Current best practice involves consideration of all of these factors when prescribing opioids. Several recently published guidelines may help physicians prescribe opioids in a safe and effective manner. The most comprehensive are those released by the American Academy of Pain Medicine,[10] the CDC (*www.cdc.gov/HomeandRecreationalSafety/Poisoning/brief.htm*), and the State of Washington (*www.agencymeddirectors.wa.gov*). The guideline from the State of Washington is especially thorough and includes validated instruments to track

pain and function; validated tools to screen for alcohol abuse, substance abuse, and depression; and advice about instituting and monitoring treatment, including targeted urine drug testing (UDT). Specific recommendations for prescribing chronic opioid therapy include (1) screen for substance abuse and mental illness; (2) discuss benefits versus risks supported by a treatment agreement; (3) discuss treatment goals, which must include improvements in pain and function while minimizing adverse effects; (4) schedule frequent follow-up visits with monitoring of opioid dose, pain, and function; and (5) administer random UDT. Both the CDC and the State of Washington guidelines have identified an opioid dose of 120 mg/d MED as a ''yellow flag'' dosage. If a patient's dose has reached 120 mg/d MED (**Practice Table 1**) or more without substantial improvement in pain and function, the provider should seek consultation with a pain specialist. The best practices embodied in these guidelines should be considered for widespread adoption in both individual practices and in large health care systems.[11]

Putting all of this information into perspective, what would be a reasonable approach to managing the patient in the case presented at the beginning of this article? Our recommended approach to this patient is to perform a comprehensive history and examination and document the current level of pain and function; however, he should be informed that oxycodone cannot be prescribed at the initial visit because all of his relevant medical records are not available. He should be notified that a signed release of information form is required prior to prescribing opioids. If necessary, contacting the previous provider for information on the patient should be considered. At this initial visit, a baseline UDT should be ordered and a return visit scheduled when the patient's medical records and UDT results are available. On the return visit, if medical records show improved pain and function with oxycodone and no history of substance abuse, substantial depression,

PRACTICE TABLE 1 **Morphine Equivalent Dose for Selected Opioids**

Opioid	Approximate Equianalgesic Dose (oral and transdermal)[a]
Morphine (reference)	30 mg
Codeine	200 mg
Fentanyl transdermal	12.5 μg/hr
Hydrocodone	30 mg
Hydromorphone	7.5 mg
Methadone	Chronic: 4 mg[b]
Oxycodone	20 mg
Oxymorphone	10 mg

[a]Adapted from Veteran Affairs/Department of Defense. Opioid therapy for chronic pain. Clinical Practice Guidelines June 2003. www.oqp.med.va.gov/cpg/cpg.htm and from US Food and Drug Administration labeling.
[b]Equianalgesic dosing ratios between methadone and other opioids are complex, thus requiring slow, cautious conversion (Ayonrinde OT, Bridge DT. The rediscovery of methadone for cancer pain management. Med J Aust 2000;173(10):538.).

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or drug-seeking behavior, then it would be reasonable to consider prescribing oxycodone. Before providing a prescription, the following steps should be taken:

1. Check the patient's recent prescription opioid history through the State Prescription Drug Monitoring Program, which is available in 48 states (*www.namsdl.org/presdrug.htm*).
2. Screen for substance abuse and mental illness.
3. Obtain an opioid agreement signed by both the clinician and the patient.
4. Establish clear treatment goals including improvements in pain and function.
5. Establish clear expectations for patient behavior related to opioids (eg, take only as prescribed, one prescriber, one pharmacy, no drug sharing, etc.).
6. Establish a follow-up plan to monitor treatment (eg, regularly scheduled follow-up visits, random UDT, etc.).

Further guidance and recommendations are available from the CDC and State of Washington websites. In addition, 4 hours of free CME specifically related to the Washington guidelines and new rules can be found on the Washington site. It is likely that state and federal requirements for education related to opioid use for chronic noncancer pain will increase in the near future.[12]

REFERENCES

1. Bril V, England J, Franklin GM, et al; American Academy of Neurology; American Association of Neuromuscular and Electrodiagnostic Medicine; American Academy of Physical Medicine and Rehabilitation. Evidence-based guideline: treatment of painful diabetic neuropathy: report of the American Academy of Neurology, the American Association of Neuromuscular and Electrodiagnostic Medicine, and the American Academy of Physical Medicine and Rehabilitation. Neurology 2011;76(20):1758–1765.
2. Dworkin RH, O'Connor AB, Audette J, et al. Recommendations for the pharmacological management of neuropathic pain: an overview and literature update. Mayo Clin Proc 2010;85(3 suppl):S3–S14.
3. Franklin GM, Mai J, Wickizer TM, et al. Opioid dosing trends and mortality in Washington State workers' compensation, 1996-2002. Am J Ind Med 2005;48(2):91–99.
4. Bohnert ASB, Valenstein M, Bair MJ, et al. Association between opioid prescribing patterns and opioid overdose-related deaths. JAMA 2011;305(13):1315–1321.
5. Volkow ND, McLellan TA. Curtailing diversion and abuse of opioid analgesics without jeopardizing pain treatment. JAMA 2011;305(13):1346–1347.
6. Dunn KM, Saunders KW, Rutter CM, et al. Opioid prescriptions for chronic pain and overdose: a cohort study. Ann Intern Med 2010;152(2):85–92.
7. Gomes T, Mamdani MM, Dhalla IA, et al. Opioid dose and drug-related mortality in patients with nonmalignant pain. Arch Intern Med 2011;171(7):686–691.
8. Walker JM, Farney RJ, Rhondeau SM, et al. Chronic opioid use is a risk factor for the development of central sleep apnea and ataxic breathing. J Clin Sleep Med 2007;3(5):455–461.
9. White JM, Irvine RJ. Mechanisms of fatal opioid overdose. Addiction 1999;94(7):961–972.
10. Chou R, Fanciullo GJ, Fine PG, et al; American Pain Society-American Academy of Pain Medicine Opioids Guideline Panel. Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. J Pain 2009;10(2):113–130.
11. Trescott CE, Beck RM, Seelig MD, Von Korff MR. Group Health's initiative to avert opioid misuse and overdose among patients with chronic noncancer pain. Health Aff (Millwood) 2011;30(8):1420–1424.
12. White House Office of National Drug Control Policy. Epidemic: responding to America's prescription drug abuse crisis, 2011. *www.whitehousedrugpolicy.gov/prescriptiondrugs*. Accessed August 15, 2011.