Acute Pain Management in Opioid-tolerant Individuals

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ABSTRACT

Opioids have been used widely since the late 1990s to treat chronic pain. In the last 15 years, prescription opioid drug abuse has been escalating and more individuals are receiving medication-assisted treatment for addiction. Individuals utilizing opioids to treat chronic pain or addiction or those actively abusing opioids may require acute pain management. Nurse practitioners must possess the skills to assess and manage pain in this population.

Keywords: acute pain management, chronic opioid therapy, medication-assisted treatment, multimodal analgesia, opioid tolerant, opioid use disorder

BACKGROUND

Over 100 million adults in the United States are living with chronic pain.[1] These individuals may not have responded to non-opioid treatments and thus receive chronic opioid therapy (COT). Recent guidelines suggest that COT may not be the first-line treatment for people with chronic pain and may have long-term effects, including increased risk for abuse and dependence.[2] However, prescribing of opioids has been widespread and patients receiving COT for pain are treated in the acute care setting.

In 2015, 27 million (1 in 10) Americans $\geq$ 12 years of age used an illicit drug within the previous month. The nonmedical use of opioid pain relievers was second only to marijuana as the most commonly used drug (3.8 million).[3] The number of overdose deaths secondary to opioids was 3 times greater in 2015 ($>$ 15,000) than in 2000, and the number of heroin overdose deaths (13,000) in 2015 was 4 times greater than in 2010.[4] An emerging problem is the use of illicitly manufactured fentanyl, which is more potent than pharmaceutical fentanyl and is contributing to the rising morbidity.[5]

In 2015, $>$ 2 million individuals sought treatment for a substance use disorder (including opioids).[3] Treatment often included medication-assisted treatment (MAT) with methadone, buprenorphine, or naltrexone. The number of people receiving MAT is expected to increase as a result of the Comprehensive Addiction and Recovery Act legislation in 2016, which allows nurse practitioners (NPs) and physician assistants to complete 24 hours of training and become certified and registered to prescribe buprenorphine for MAT.[6] NPs would still be subject to state rules that may require specific types of supervision.

Acute pain relief may be complicated for individuals with opioid tolerance. Two recent, large, retrospective studies addressed associations between opioid dependence/abuse and inpatient morbidity, mortality, and resource utilization for individuals who underwent major elective orthopedic surgery. In both studies, those with opioid use/dependence had increased mortality, postoperative complications, and increased resource utilization.[7,8]

Pain and opioid dependence are related clinical conditions. Patients on methadone maintenance have reported higher pain scores, use more postoperative opioid analgesia, and a need for more anxiolytics than opioid-naive individuals.[9] Individuals in MAT programs or those actively using heroin have demonstrated increased pain sensitivity and lower pain tolerance than opioid-naive individuals.[10] For those who have a prolonged opioid abstinence, pain tolerance may improve, but these individuals may still experience abnormal hypersensitivity to pain.[11]

Treatment by NPs skilled in acute pain management in those who are opioid tolerant can improve the experiences and outcomes of these patients. In what follows we provide an overview of acute pain management in this population. We highlight the case of a patient with active substance use disorder. Many patients with chronic pain who are compliant with prescribed COT may face similar issues in terms of pain experiences and responses to treatment. Thus, many of the suggestions for management would be applicable to this population.

Case: *A 29-year-old man, with no past medical history, sustained significant injuries in a motorcycle crash and required a below-the-knee amputation. Intraoperatively he received intravenous (IV) fentanyl 700 μg and hydromorphone 2 mg. In the postanesthesia care unit he was alert and rated his pain severity as 10/10. In 1 hour, he received IV morphine 16 mg, IV hydromorphone 6 mg, and IV midazolam 2 mg. IV patient-controlled analgesia (PCA) of hydromorphone was started at 0.4 mg with a 10-minute lock-out interval. The patient reported he was on methadone maintenance therapy of 130 mg/day and also used marijuana, 1 bundle (10 bags) of heroin, and 10 mg of alprazolam daily.*

ACUTE PAIN MANAGEMENT OVERVIEW

Acute pain management is a priority for all patients. Initial patient evaluation includes a thorough assessment to establish a pain diagnosis, medication use, prior response to analgesics, concurrent psychiatric conditions, chronic opioid use, or opioid use disorder (OUD).[12] Ideally, this assessment should be conducted in the outpatient or pre-admission testing setting. Checking the state prescription drug monitoring program is a prudent step before any analgesic administration. NPs should be aware of signs and symptoms of opioid withdrawal. Use of a tool such as the Clinical Opioid Withdrawal Scale may ensure adequate treatment to avoid opioid withdrawal.[13]

NPs face challenges treating opioid-tolerant individuals, including those who take opioids chronically for pain, are actively using opioid class substances for nonmedical use, or are in MAT programs. According to the United States Food and Drug Administration (FDA), individuals who are opioid tolerant have received the equivalent of at least 60 mg/day of oral morphine for $\geq$ 1 week.[14] Others who may be opioid tolerant are those with OUD. Individuals with OUD are actively engaged in nonmedical use of opioids or use of opioids other than as prescribed, on MAT, or are in recovery.[15]

Opioid tolerance is a phenomenon that develops with repeated opioid exposure, resulting in a decrease in analgesic effect or side effects of opioids, thus requiring an increase in opioid dose to achieve adequate pain relief.[12] Opioid tolerance involves complex, not completely understood mechanisms. Generally, the higher the daily opioid requirement and the longer the duration of exposure, the greater the opioid tolerance. However, in some cases, acute tolerance may develop abruptly after a single dose (remifentanil) or a few doses of opioids, within a short period of time.[12] However, some individuals are maintained on stable doses of opioids for years.

Opioid-induced hyperalgesia is an abnormal sensitivity to pain, and may be associated with long-term use of opioids. In contrast to tolerance, where escalating doses of opioids improve pain relief, in opioid-induced hyperalgesia, escalating doses of opioids worsen the pain. Controversy exists about this phenomenon, and the exact mechanism that induces hyperalgesia is unknown.[16] In individuals with possible opioid-induced hyperalgesia and those with increased tolerance to opioids, it is essential for the NP to utilize multimodal analgesia techniques to control the pain.

MULTIMODAL ANALGESIA

The use of multimodal analgesia for postoperative pain is supported by high-quality evidence and strongly supported by the American Pain Society, the American Society of Anesthesiologists, and American Society for Pain Management Nursing.[17,18] As pain is a complex and multidimensional phenomenon, it is thought that the use of combinations of analgesics of different classes that act on different target sites in the pathways may provide better pain relief while reducing opioid requirements and the risks of adverse effects.[17]

Multimodal analgesia includes the use of a variety of analgesic agents, perioperative interventions, and nonpharmacologic modalities.[17] Pharmacologic agents include opioids, acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), anticonvulsants, *N*-methyl D-aspartate receptor antagonists, serotonin