

Heroin and Pain

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Pain Management in the Patient with Opioid Abuse

As the number of patients who are prescribed chronic opioid therapy for pain not related to cancer has grown so have the rates of opioid-related morbidity and mortality. In addition to a rise in prescription opioid use, there has also been an increase in the use of illicit opioids. In our region, the surge in heroin use has been particularly startling with steadily increasing rates of morbidity and mortality.¹ In the inpatient setting, providers may struggle to manage acute pain in individuals abusing opioids prior to admission, due to the challenge of balancing safety and adequate analgesia. Literature on the management of acute pain in patients on chronic prescribed opioid therapy is often used as a guide for treating patients that use opioids illicitly. There are, however, some factors that are unique those abusing opioids that further complicate their treatment. A few of the specific obstacles to achieving adequate analgesia include opioid tolerance, heightened pain sensitivity, comorbid psychiatric disease, risk of opioid withdrawal, and specific challenges related to their transition to the outpatient setting. In my personal experience as an inpatient pain management physician, I work to address all of these concerns and have found several strategies to improve the patient's overall analgesia while they are in the inpatient setting. Unfortunately, there are still barriers to the outpatient management of the patient's pain which have no straightforward solution.

Prevalence of Pain and Addiction

The use of opioids for chronic pain management was popularized in the 1990's when we believed that the use of opioids in the presence of painful stimuli would not lead to addiction. This belief was supported in part by early studies conducted by Portenoy and colleagues² and further encouraged by the pharmaceutical industry's aggressive advertising campaign. The conclusion that opioids were a safe and effective long-term pain management strategy contributed to the steady rise in opioid prescribing.

Subsequently, we have seen an increase in the misuse of both prescribed and illicit opioids. While determining precise rates of misuse and addiction have been difficult, due to inconsistencies in the definitions of dependence, misuse, and addiction used by researchers, attempts have been made to describe the epidemiology of the problem. Vowles and colleagues conducted a systematic review in 2015 which estimated the rates of opioid misuse to be between 21-29% and the rates of addiction to be between 8-12%.³ Another study published by Turk and colleagues in 2008 found that 30-40% of patients on prescribed opioids were misusing their medications based on urine toxicology results.⁴ These reported rates of misuse are staggering and have a major impact on our ability to provide effective treatment when these patients present with acute pain.

One of the primary difficulties in treating acute pain in individuals with an opioid addiction, specifically those patients abusing heroin, is achieving adequate analgesia in the face of opioid tolerance. We routinely utilize non-opioid adjuncts including acetaminophen, NSAIDs, gabapentanoids, and topical anesthetics as part of a multimodal analgesic plan, but opioids are often required. Finding the precise opioid dose needed to achieve adequate analgesia is difficult,

however, because there is significant interpatient variation in the amount of opioid used at baseline. Additionally, there is no standard conversion from heroin to oral or intravenous opioids. Researchers have attempted to measure the opioid dose increase needed for patients on chronic, prescribed opioid therapy to help guide treatment of acute pain. Two studies conducted in the postoperative setting found that opioid-tolerant patients undergoing various surgical procedures, using both epidural and patient-controlled analgesia, required up to three times the amount of opioid compared to the opioid-naïve patient.^{5,6} Even with the expectation that higher than typical doses of opioid will be required, the medications should be titrated carefully to effect for each patient as they remain at risk of oversedation and other opioid-related side effects.

Addiction and its Impact on Pain Perception

Beyond the difficulty with opioid dose titration due to tolerance in patients abusing opioids, other factors further complicate their analgesic management. One in particular is the phenomenon of opioid-induced hyperalgesia (OIH), which is characterized by a paradoxical response to opioids whereby opioids are believed to worsen the patient's pain rather than provide relief. Opioid-induced hyperalgesia has been recognized in patients on prescribed high-dose opioid therapy, those abusing heroin as well as individuals enrolled in medication-assisted opioid abuse treatment programs. Development of OIH is thought to be secondary to central sensitization of the neurons in the dorsal horn and dorsal root ganglion, similar to the pathophysiology of neuropathic pain.⁷ The pain is often characterized as increased intensity above the patient's baseline pain with a more widespread distribution. Studies involving quantitative sensory testing have demonstrated lower pain thresholds and tolerability in patients on chronic opioids for noncancer pain, those abusing heroin, and those enrolled in methadone maintenance.⁸ Additional studies have found that this hyperalgesic state can persist for months after opioid cessation.^{9,10}

The typical treatment for OIH is a reduction in dose or complete opioid cessation, but this is not usually possible in the case of a patient admitted with acute pain. There have been no studies done specifically on management of OIH in patients abusing heroin, but data pertaining to OIH due to other opioids can help guide treatment. Studies conducted by Lee et al in 2013 and Wu et al in 2015 investigated OIH secondary to the use of remifentanyl, a short-acting opioid most often used in the perioperative period. They found that pregabalin and NMDA-receptor antagonists such as ketamine, magnesium, and amantadine could reduce the development of OIH.^{11,12} These data can be extrapolated by providers to the opioid-abusing population, and both pregabalin and ketamine are routinely used in our hospital as well as nationwide as part of a multimodal analgesic plan in the care of patients admitted with acute pain and opioid tolerance.

Other factors may also contribute to increased pain sensitivity in patients abusing opioids, and one of those is the presence of comorbid psychiatric disease. It is well known that there are high rates of comorbid substance abuse among patients with mood disorders. Regier and colleagues reported that mood disorders were 4.7 times more prevalent in drug-dependent individuals than the general population. Most notably, those patients diagnosed with bipolar disorder had a 56% rate of substance use disorders.¹³ Kessler and colleagues reported similar findings where they found that those individuals with depression were twice as likely and those with bipolar disorder were seven times more likely to have a substance use disorder.¹⁴

In addition to the correlation between substance use and mood disorders, the literature also supports a connection between mood disorders and increased pain, and this may provide explanation for why opioid abusing patients, particularly those with comorbid psychiatric

conditions, having increased difficulty with analgesia. Taenzer et al found that depression was associated with increased postoperative pain scores as well as analgesic use¹⁵ and De Cosmo and colleagues reported similar results in patients with preoperative depression and anxiety.¹⁶ In my experience as an inpatient pain physician, I find that most of the patients I care for with acute pain and opioid abuse also carry psychiatric diagnoses including depression, anxiety, bipolar disorder, and posttraumatic stress disorder.

These conditions are not always easily addressed in the acute setting, but if I do feel that the patient is demonstrating a strong affective component to their pain, I will ask my colleagues in Psychiatry for assistance. I feel we should make every effort to improve the patient's perception of pain relief and addressing their psychiatric disease is one tool.

The Inpatient Pain Management Experience

In my work as an inpatient pain physician, I have personally witnessed the tremendous rise in the number of patients who suffer with both prescription as well as illicit opioid addiction. Our service is consulted when these patients are admitted with acute pain secondary to a variety of conditions including but not limited to multi-system trauma, cellulitis related to heroin injection requiring surgical debridement, and epidural abscesses from intravenous drug use necessitating surgical evacuation, etc. Beyond the complexities related to the pharmacologic management of the heroin-abusing patient, the interpersonal interactions between these patients and their providers can be equally complex and can have an even larger impact on their care.

The first step in developing a pain management plan with an opioid-abusing patient is establishing rapport. These patients often mistrust the medical system based on past experience or perceive that they will not receive good care due to their addiction. Healthcare workers must make a conscious effort to demonstrate to the patient an open mind and a desire to earn the patient's trust. These patients are acutely aware of the stigmas surrounding opioids and addiction and may become defensive and withdrawn if they feel "judged" in any way. Many healthcare providers mistakenly view the patient's requests for opioid medication to be "drug seeking behavior" rather than appropriate and normal pain relief-seeking behavior. Many of my patients have admitted a reluctance to request pain medication for fear of being labeled a "drug seeker" and thus suffer with pain as well as opioid withdrawal unnecessarily.

Unfortunately, not only do uncontrolled pain and untreated withdrawal lead to a miserable hospital stay, both factors have also been associated an increased likelihood of abuse relapse.

To gain trust, I typically approach the first interview with as much transparency as possible and openly discuss the patient's opioid abuse including their drug of choice, the route administered, and their average daily use. While there are no specific guidelines for opioid dosing in patients abusing heroin or other illicit opioids, knowledge of their pre-admission use can provide some frame of reference for their degree of opioid tolerance. I establish very early that my primary goals are providing safe and effective analgesia as well as withdrawal symptom management. I employ a multimodal analgesic regimen with scheduled use of non-opioids, and I also utilize opioid medications if needed. Given the degree of injury and pathology in the patients I see, opioid analgesics are typically required. I explain to the patient that complete relief of their pain may not be possible but I will do my best to make it manageable. Establishing realistic expectations as well as setting functional rather than numeric pain score goals allows for more constructive discussion and analgesic adjustments. Specifically, I work towards an acceptable

pain level that will allow the patient to participate in self-care, physical therapy or other in-hospital treatments.

I also begin discussing the patient's discharge analgesic plan early in the hospitalization as I have found this to be one of the most challenging aspects of the patient's care. Many of the patients seen by our inpatient service are left with new, painful conditions at the time of discharge when most were using opioids exclusively for recreation prior to admission. Although it can seem cruel to discharge a patient home with a new painful condition and no opioid analgesics, particularly when they have been given as an inpatient, I feel that the risks of prescribing these medications outweigh the potential benefits. I fear it would be tremendously difficult for the opioid-addicted patient to regulate their opioid use appropriately, and most of these patients have no more than a few follow up visits with their healthcare providers after discharge. There is currently no system in place for the kind of very close follow up these patients would require such as a clinic where they could be seen every few days or every week with procedures in place to help monitor their outpatient opioid use such as pill counts and urine drug screening.

I do recommend that the patient continue their non-opioid adjuncts at discharge as these can provide a great deal of relief. Some of these medications such as gabapentin or pregabalin are initiated at lower doses during their admission due to the risk of sedation but these can be further titrated as an outpatient for ongoing pain. In anticipation of stopping opioids completely at discharge, I begin weaning the patient's dose as early as possible to help reduce or eliminate the risk of opioid withdrawal after discharge. As previously stated, untreated withdrawal symptoms are a major risk factor for relapse in opioid abuse so I often offer these patients a prescription for clonidine, a common medication used in withdrawal, to be used at home.

Just as I begin formulating a discharge analgesic plan as early as possible, I also open the discussion of substance abuse treatment early in the patient's hospitalization. We are very fortunate to have a robust substance abuse treatment program at our institution, which offers support and guidance to those patients wishing to enter recovery. This liaison program presents the various outpatient options for substance abuse treatment available to the patient, taking into account where they live, their financial situation, as well as their ability to get to and from the clinic each day. Although entry into these programs is based on the presence of addiction, both of the commonly used treatment medications, methadone and buprenorphine, have analgesic properties so they may provide a dual benefit for the addicted patient with a new painful condition. Not all patients elect to enter treatment but many do as they see treatment as an opportunity to get healthy as well as have some analgesia while they continue to heal. I strongly encourage them to consider treatment since their analgesic options are more limited than those of a patient who does not suffer with addiction. It is established that poorly controlled pain is a risk factor for relapse so any effort we can make to control their pain can be helpful to maintaining their recovery.

Pain in the Setting of Medication-assisted Substance Abuse Treatment

In addition to offering entry into treatment for patients with active substance abuse disorders, our consult service has also seen a rise in the number of patients admitted with acute pain who are already receiving medication-assisted treatment. The two most commonly used medications are methadone and buprenorphine, and there are several unique challenges in managing pain in these patients as well as several misconceptions. Methadone acts as a full opioid agonist much like

typical opioid medications while buprenorphine is a partial agonist, which binds tightly to the receptor and prohibits the binding of other opioids. For patients with mild to moderate pain, they can often be managed with continuation of their methadone or buprenorphine, since both of these medications have analgesic effects, and receive supplementary analgesia with non-opioid adjuncts. In patients with more severe pain, however, additional opioid therapy is often required. Like those who are actively abusing opioids, patients on methadone and buprenorphine are considered opioid tolerant and often require higher opioid doses to achieve adequate analgesia.

In patients on methadone maintenance with severe pain, the most commonly used strategy for treating pain is to continue the patient's baseline daily dose, use scheduled non-opioid adjuncts, and carefully titrate opioids for breakthrough pain. Like patients on chronic prescribed opioid therapy, we are unable to predict precisely what breakthrough dose will be needed based on the maintenance dose so we titrate carefully based on the patient's pain and clinical status.

Individuals taking buprenorphine for medication-assisted treatment present a unique challenge due to the medication's mechanism of action. In patients on buprenorphine maintenance, there are several options for management. One method is to continue buprenorphine and also use full opioid agonists to treat breakthrough pain. This often requires aggressive opioid titration to overcome the tight receptor binding of the buprenorphine.

Another option, the one I employ most often, involves discontinuation of buprenorphine followed by careful titration of full opioid agonists for breakthrough pain. In both cases, I anticipate higher than average opioid dose requirements to achieve pain relief. In the case of discontinuation of buprenorphine, the increased requirement due to buprenorphine binding may dissipate 24-48 hours after the last dose as the medication slowly dissociates from the receptor.

In addition to the difficulties in achieving adequate analgesia in patients on medication-assisted maintenance therapy for opioid addiction, there are a few misconceptions regarding this type of treatment, which can impact the patient's care. One common misconception is the belief that the patient's maintenance dose is adequate for analgesia which can lead to the inaccurate assumption that the patient should not require additional opioid dosing. Patients in maintenance therapy have established opioid tolerance and thus may require higher doses to achieve an analgesic response. Additionally, they most commonly receive only once daily dosing which is insufficient for pain relief based on the pharmacokinetics of the medication. The analgesic half-life of both methadone and buprenorphine is only four to eight hours while the suppression of withdrawal symptoms lasts 24-48 hours.^{16,17} As mentioned, the continuation of once daily dosing is a common strategy, but some have proposed dividing the daily dose into every six to eight hours which may provide enhanced relief by taking advantage of the analgesic half-life. There is emerging data on buprenorphine specifically that suggests that patients do better if the buprenorphine is continued in divided doses during the treatment of acute pain before resuming once daily dosing at discharge.^{18,19}

A second common misconception regarding pain management in the opioid-abusing patient in recovery is that any opioid administration will trigger a relapse. While this concern is understandable, untreated pain is also a risk for relapse so these patients should have their pain managed commensurate to their medical conditions with judicious and intelligent use of opioids.⁸ It has been suggested that intravenous opioids present more of a threat for relapse than oral opioids based on the more rapid rate of absorption and peak concentration so an early transition to oral medications should be sought.²⁰

There are many challenges in caring for patients with both active opioid abuse as well as those in recovery who present with acute pain. The difficulties are related to their opioid tolerance, heightened pain sensitivity, as well as the challenges related to making the transition to outpatient care. The strategic use of opioids along with non-opioid analgesics during their hospitalization can effectively manage these patients' acute pain, but there is much room for improvement in the way we manage their pain in the outpatient setting. Not all institutions have inpatient pain and addiction medicine specialists, but consulting with an expert can provide valuable guidance in the management of these challenging patients.

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