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Opioid overdose: Risk assessment and mitigation in outpatient treatment

Lewei (Allison) Lin, MD^{1,2}, Avinash Hosanagar, MD^{2,3}, Tae Woo Park, MD⁴, and Amy S. B. Bohnert, PhD^{1,5}

¹Addiction Center and Mental Health Services, Translations and Outcomes Program; Department of Psychiatry, University of Michigan, 2800 Plymouth Rd, Bldg 16, Ann Arbor, MI 48109

²Mental Health, VA Ann Arbor Health System, 2215 Fuller Rd. Ann Arbor MI 48105

³Department of Psychiatry, University of Michigan, Ann Arbor, MI 48109

⁴Departments of Medicine and Psychiatry and Human Behavior, The Warren Alpert Medical School of Brown University, 111 Plain St, 1st Floor, Providence, RI 02903

⁵VA Center for Clinical Management Research (CCMR), Department of Veterans Affairs Healthcare System, Ann Arbor MI, North Campus Research Complex, 2800 Plymouth Rd Ann Arbor, MI 48109

Introduction

This clinical case discussion focuses on a patient with comorbid substance use disorder and chronic pain who experienced an overdose on heroin. The case illustrates the complex array of risk factors that contribute to overdose risk, discusses the use of naloxone, and highlights the need for further risk mitigation interventions in patients at risk for overdose.

Presenting complaint

Mr. A is a 35 year old male veteran with a psychiatric history of PTSD, alcohol use disorder, and opiate use disorder and a medical history of chronic pain, who presented to the intensive outpatient program (IOP) for substance use disorder treatment at a Veterans Affairs Healthcare System. Mr. A had recently revealed to providers that he had been using heroin. After a brief inpatient detoxification, he was initiated on buprenorphine/naloxone (BUP/NX) for the first time in his life by providers in the outpatient substance use disorder clinic and referred to IOP for more intensive treatment. About two months after completing IOP, Mr. A, presented to the outpatient substance disorder clinic for an unscheduled visit and reported that he had an unintentional overdose earlier that day on heroin. He reported that morning his girlfriend heard a loud crash and found him unresponsive in the bathroom. She took out the naloxone kit she had been given by his providers in the IOP and administered intranasal naloxone. He awoke right away.

Lewei (Allison) Lin (corresponding author), University of Michigan, Dept. of Psychiatry, Rachel Upjohn Building, 4250 Plymouth Road, Ann Arbor, MI 48109, Phone: 734-764-0231, leweil@med.umich.edu.

History of presenting illness

Mr. A was first exposed to narcotics ten years ago when he was prescribed opioids after a traumatic injury. During his service in the army, he sustained a fall and suffered a compression fracture in his thoracic vertebrae. In addition, he reported a history of multiple exposures to improvised explosive device (IED) blasts. Since then, he has had chronic back pain and has been evaluated by many providers. He has had numerous treatments, including physical therapy and medication treatments including the use of non-opioids. He was started on prescription opioids after his injury and continued to be prescribed opioids intermittently. In his intake appointment to a medical provider about six years prior to his current IOP presentation, he had described other relevant history, including a history of alcohol use disorder and cocaine use about once per year, though he stated he had recently stopped using cocaine.

The highest dosage of opioid that he was prescribed was 45 morphine equivalents per day, although in that instance, the supply was less than a week. Typically, he was given prescriptions for several weeks to one-month supplies of short-acting hydrocodone- or oxycodone-based medications to be taken PRN for exacerbations of chronic pain. There was at least one occasion when he was concurrently prescribed sedative-hypnotic and opioid pain medications.

He first sought psychiatric treatment about four years prior to this current presentation after disclosing that he continued to struggle with significant PTSD symptoms. He had an initial psychiatric intake evaluation at that time, but he did not follow up for further treatment. About three years prior to his IOP admission, he presented to his PCP and disclosed excessive drinking and a recent driving under the influence (DUI) charge and was referred for further evaluation and treatment in the substance use disorder clinic. At that time, a urine drug screen was checked, which was negative for all substances. Providers also checked the state prescription drug monitoring program and there was no indication that the patient had obtained prescriptions from other providers. He was diagnosed with alcohol use disorder and offered treatment, but he did not follow up. He received two short prescriptions for opioids for acute pain after the diagnosis of alcohol use disorder. The last prescription from VA was more than two years prior to this current presentation. It is unknown if he ever received any opioid prescriptions outside of the VA.

Mr. A (one year prior to his current presentation) self-presented to his primary care provider and disclosed that he was feeling more depressed and had attempted suicide via overdose on heroin several weeks prior. He adamantly denied any heroin use before the suicide attempt and denied that he had any problems with opioids prior to this overdose. He was psychiatrically hospitalized for depression with suicidal ideation and stabilized. After discharge, he was referred to outpatient substance use disorder treatment. He presented for evaluation but did not follow up.

About two weeks prior to his IOP admission, Mr. A self-presented for intake to see an outpatient substance use disorder counselor and requested treatment for heroin use. He revealed for the first time that he had been misusing prescription opioids for many years.

After his injury in the army, he quickly started taking prescription opioids more than was prescribed and then started to purchase them from non-medical sources. He never disclosed this behavior to providers in the past. About 3 year prior to his IOP admission, he started using heroin because “it was cheaper” and provided more of a high than opioid medications and also helped with his chronic pain. He has been using IV heroin 3-4 times daily for the past 3 years.

He was seeking treatment for the first time for his heroin use because he was beginning to realize the impact of his use on his partner and his four year old son and he had not been able to stop using on his own. He had sold much of their belongings and spent much of his days using heroin. He reported that he felt deep guilt, which bothered him immensely. At this point, his outpatient clinic providers referred him for inpatient detoxification after he reported inability to maintain sobriety through an outpatient detoxification program. UDS at that time was positive for opiates and benzodiazepines. After a brief inpatient detoxification, he was initiated on buprenorphine/naloxone BUP/NX and referred to IOP for more intensive treatment.

The IOP includes group-based therapy three days a week and additional individual therapy and medication visits. Mr. A also had his BUP/NX further titrated to 16mg total daily. Given his previous history of overdose on heroin and history of recent heroin use, he was deemed to be at high risk for overdose. He was educated on opioid overdose and was provided with a Naloxone intranasal kit and training to use the kit to prevent overdose. Education and training was also offered to his family members, which he declined. He completed a 4-week course of IOP and was generally adherent with group therapy and medication visits. He did report one relapse during this time, but overall, felt that the BUP/NX was helpful and was continued on this medication. After IOP, he was referred to outpatient treatment and was seen on a weekly basis. He provided urine drug screens that intermittently were positive for opiates and cannabinoids. He explained that his urine was positive for opiates because he was intermittently using prescription opioids, leftover from prior prescriptions for treatment of chronic pain, but denied any heroin use.

Other pertinent history

The patient’s psychiatric history is significant for a history of PTSD from combat-related experiences. He continued to have nightmares and flashbacks and was easily startled by loud noises. He had been prescribed selective serotonin reuptake inhibitors, but reported that the medications had not reduced his PTSD symptoms and he did not want to take medications for those symptoms. His substance use history is significant for history of alcohol use disorder. In the past, he described binge drinking several times a month or more and also had a DUI. In addition, he had one prescription for a benzodiazepine for his PTSD, with the last fill several years ago. He denied any misuse of this medication, although no urine toxicology screening was conducted at that time. Finally, he also endorsed occasional cocaine and cannabis use.

Mr. A’s family history is significant for a father who had a history of PTSD and a mother with a history of bipolar disorder. The patient’s social history is significant for currently

living with his partner and young child. He is not currently working and is on disability for his chronic pain and psychiatric illnesses.

Treatment course

After Mr. A reported his overdose on heroin, he was referred back to IOP for more intensive treatment. He reported this was his first relapse on heroin since completing IOP two months prior, but acknowledged that he had been using prescription opioids non-medically.

When he was evaluated again in IOP, he adamantly denied that the overdose was intentional. Mr. A reports that he had been taking his prescribed BUP/NX daily and on the day of overdose, he decided to use heroin instead. He also endorsed using IV heroin again two days after the overdose. He was encouraged to consider inpatient treatment based on ASAM criteria, which is routinely used as part of the intake evaluation. He declined but stated he was willing to re-engage in IOP. He was re-initiated in the IOP and was continued on BUP/NX. He was also prescribed another naloxone kit. He was often non-adherent with treatment, missing numerous appointments. He was also fairly ambivalent about BUP/NX treatment and had, on several occasions, not picked up his prescription. Numerous options for treatment were discussed, including transitioning to methadone and residential treatment. The patient declined these other options, but was interested in transitioning to long acting naltrexone. Plans were made for transition from BUP/NX to naltrexone, but he soon stopped attending treatment and requested transfer to a clinic closer to his home.

Discussion

This case highlights challenges of addressing overdose risk for complex patients in addiction treatment settings. This patient had many layers of risk factors for overdose that need to be considered. The most proximal risk factors to his unintentional overdose included severe opiate use disorder with IV heroin use and his history of overdose. A history of substance use disorders has been one of the most consistently identified risk factors for overdose (Bohnert et al., 2012), but a history of prior overdose, though less prevalent in the general population, is potentially an even more salient risk factor. In this patient, these factors occurred in the context of many other ongoing risk factors, including chronic pain, ongoing misuse of prescription opioids, and intermittent risky use of other substances including cannabis, cocaine, alcohol, and comorbid PTSD.

It is important to note that some of these risk factors were present for many years in this patient. For example, he was evaluated for pain over ten years prior to his overdose and initiated prescription opioid therapy. He was prescribed opioids off and on until several years prior to his overdose. In this case, it was particularly challenging because the patient did not disclose the most important risk factor – his active heroin use - until after three years of use. It is important to note that providers at times had appropriately conducted urine drug screens and used a prescription monitoring program, though this may not have detected intermittent use. It is unknown if routine physical exams included evaluation for track marks and other signs of IV drug use, which may have detected his use earlier.

On the other hand, one should also examine why he was prescribed opioids at all. He had known acute injuries, but he reported chronic pain associated with these injuries for many years afterwards. Opioids continued to be intermittently prescribed during these years. It is important to assess the benefit versus risk in each occasion that opioids are prescribed. At times, patients may experience acute on chronic pain. However, in patients with multiple risk factors, and concern for substance use disorder, there is a need to further consider drivers of pain and opioid use. In addition, it is crucial to assess the patient's level of functioning and understanding of chronic pain. Unfortunately, one challenge is the limited options available for pain treatment in substance use disorder (SUD) treatment settings. Although guidelines suggest that "high risk" patients actively using substances should be referred for SUD treatment (The management of Opioid Therapy for Chronic Pain Working Group, 2010), there are no specific recommendations for pain treatment while a patient is also in SUD treatment. It is important to consider non-pharmacological strategies, such as cognitive behavioral and mindfulness-based therapy and physical therapy that emphasize improving function rather than eliminating pain.

Because of the severity of this patient's addiction and the psychosocial issues he faced, he eventually sought treatment in specialty substance use settings in the IOP and outpatient SUD treatment settings. Interventions for overdose are needed in these settings, where many patients have high levels of co-morbid risk factors. It is likely that a large proportion of patients in SUD treatment would be considered "high risk" with current risk stratification schemes. Future research could examine how to further risk stratify these patients to inform clinical decision-making and identify interventions for overdose that may be effective in these settings.

BUP/NX is one potential risk mitigation tool, and was an appropriate choice for this patient. BUP/NX has been shown to potentially be helpful for pain (Daitch et al., 2014), but there are few studies on use in patients with comorbid pain and addiction. In this patient, he reported persistent pain that led him to use other opioids while also on BUP/NX. A higher dose could have been considered. Many patients respond to a moderate dose of 12 to 16mg, but some evidence suggests a higher dose, from 16mg to as high as 32 mg may be associated with better retention in treatment for some patients (Hser et al., 2014), though other issues such as risk for diversion should also be considered.

For patients who do not respond to buprenorphine, methadone could be considered as a next treatment option (Kakko et al. 2007), especially because daily dosing and contact can help with improving retention in treatment. In addition, residential treatment should be considered for patients who may benefit from more structure to remain engaged in treatment. The ASAM criteria (Mee-Lee 2013) can be helpful for clinicians to think through these different treatment options. The ASAM criteria provide a framework for important clinical dimensions to consider to help determine the most appropriate level and type of care. This patient was assessed using ASAM criteria, and residential care was recommended. In this case, the patient declined residential care, but was willing to return to IOP.

In thinking broadly about risk mitigation, the most important intervention ultimately was treating his opioid use disorder and as a crucial part of that, actively and repeatedly engaging the patient in treatment. By the nature of the disease, patients with SUD often experience great ambivalence, torn between treatment and ongoing substance use. In this patient, it was clear that heroin use had significant negative consequences, and the impact it had on his family was the main motivation for him to enter treatment. However, it was also clear that with his severe opiate use disorder, it was very difficult for him to resist using opiates. In that context, naloxone was a very important tool. Naloxone did not prevent overdose, but increased his chances of survival when he did overdose.

Unfortunately, we do not have the ideal treatment that universally prevents patients like Mr. A from gravitating towards opiates. Regardless, it is important to continue to openly offer treatment to patients as their ambivalence fluctuates throughout the course of their illnesses. Also helpful in this particular case was the integrated health system, which allowed the patient to step up in treatment when symptoms became more severe and allowed for ease of communication among providers. Ultimately, this patient had many risk factors for overdose, making risk assessment and mitigation particularly challenging. However, such patients are seen everyday in SUD settings so thinking about the challenges of treating these high-risk patients is crucial.

Commentary by Tae Woo Park

This case report illustrates the potential risks of initiating opioid therapy for patients with chronic pain conditions. Many details of the initial decision to start opioid therapy for this case are unknown. Prior to starting opioids, a comprehensive assessment involving evaluation of risk factors for opioid misuse, prior treatments for pain including non-pharmacological approaches, and a discussion of the harms and benefits of opioid therapy is recommended (Alford et al., 2013). Because it is difficult to accurately identify patients that may go on to have problematic opioid use, a “universal precautions” approach to opioid prescribing has been advocated (Gourlay et al., 2005). This involves comprehensive assessment of substance use history, setting boundaries around medication use, and identifying aberrant drug-related behaviors. A benefit-to-harm framework has also been recommended (Nicolaidis et al., 2011). This framework, as opposed to a law enforcement framework that aims to catch “addicts” early or a bargaining framework that assumes that patients and providers have opposite goals, focuses on whether the benefits of opioids outweigh the risks at any specific point of time during a patient’s care.

In cases like the current case, it can often be difficult to determine the degree to which the above recommendations are followed. For example, in many cases, patients are likely not monitored for medication use through drug testing and/or pill counts. Additionally, it is unclear how common assessments of opioid benefits through a brief pain assessment tool and opioid harms through evaluating for aberrant drug-related behaviors are performed. During the course of this patient’s pain management, there were several opportunities for possible intervention including the patient’s admission of ongoing PTSD symptoms and his DUI arrest. The opioid prescriber appropriately ordered a urine drug screen and checked the

state prescription monitoring program (PMP) for evidence of doctor shopping, but closer and earlier monitoring may have benefitted the patient.

Another aspect of this patient's care worthy of discussion involves coordination between his various providers. The patient's DUI charge appropriately triggered some monitoring via drug testing and use of the state PMP. Importantly, it also triggered a referral to an outpatient addiction program. Barriers to referral to specialty addiction care exist. First, referrals may not even take place because appropriate addiction services are not available. Furthermore, patients may not want to follow up on such referrals due to the stigma of addiction or out of concern that chronic pain care will be affected by engagement with addiction treatment. Nonetheless, this patient may have benefited earlier in his treatment, prior to transitioning to heroin use, from a higher level of integrated treatment for chronic pain with heightened monitoring for opioid misuse. Current models of care based on the chronic care model for chronic medical conditions, including mental health disorders, have been tested and found to be effective (Unutzer et al., 2002). And there are reports of experiences of single clinics based in primary care that use a multidisciplinary approach to chronic opioid therapy for chronic pain (Weidemer et al., 2009). But it is still unknown whether these models of care will effectively reduce opioid misuse and improve access to specialty addiction care in those who need it.

Commentary by Avinash Hosanagar

This case illustrates the risks of overdose in patients with comorbid opioid use disorder and chronic pain. Many patients with pain who are first introduced to prescription opioids for management of their acute pain are continued on these medications for persistent pain. Unfortunately, some of these patients develop a pattern of misuse of prescription opioids and are then at increased risk for using heroin and at heightened risk of overdose death, both from prescription opioids and heroin (Dunn et al., 2010). The age adjusted rate of heroin-related overdose nearly tripled in recent years, from 1.0 per 100,000 people in 2010 to 2.7 per 100,000 in 2013 (Hedegaard et al., 2015). Death from heroin overdose is growing rapidly and is a large contributor to the overall rates of overdose.

The rise in overdose deaths have led public health experts to develop and implement opioid Overdose Education and Naloxone Distribution (OEND) programs in various communities across the country. There has been a growing awareness of prescription misuse and opioid analgesic related deaths among providers as a result of these OEND programs (Mueller et al., 2015), which may lead providers to prescribe shorter supplies of opioids or taper or "cut off" opioid analgesics in situations where there is a relative contraindication or no longer an indication for continued prescription of opiates. However, some of these patients--especially those meeting criteria for opioid use disorder--may then seek opiates from other illicit sources such as heroin or non-prescribed opioid analgesics causing the overdose epidemic to simply shift from prescription opioids to heroin and non-prescribed opioids. Therefore it will be critical to ensure that these patients with history of long term opioid management continue to be engaged in treatment and do not seek opioids from alternate sources.

As physicians and other providers continue to become educated about risk of opioid overdose, it will be important for clinicians to have access to risk assessment tools to identify those at risk of misuse and overdose. Numerous risk factors for overdose have been cited, including higher dose of opioids and comorbid medical illnesses (Bohnert et al., 2011). Yet in this case, the opioid dose was relatively low and the patient was a relatively healthy young adult with limited medical comorbidity. This case clearly illustrates that single risk factors in isolation are limited in their ability to predict those at risk for opioid use disorder or overdose. It is therefore challenging for providers in busy clinical practices to identify those at risk, since the majority of patients prescribed opioid analgesics use their medications as prescribed.

More refined risk indices that capture a variety of patient demographic and clinical information are critical to target interventions among those at risk. As in other areas of medicine, risk indices can help stratify interventions based on risk, and thus help in dedicating scant resources in a more targeted manner to those at highest risk. Zedler and colleagues recently developed one such risk index in a VA population and found that in their study sample the predicted probability of overdose or serious opioid-induced respiratory depression was just 3% in those who were in their lowest risk-decile compared to 94% in their highest risk decile. (Zedler et al., 2015). However this work will need replication across different settings and populations to establish generalizability. Research on similar lines is crucial for the development of indices that helps clinicians in their decision making regarding opioid prescription. Ultimately, patients should receive a comprehensive pain management plan individualized based on their risk profiles, with treatments available by addiction specialists to ensure good outcomes in this vulnerable population.

Commentary by Amy S. B. Bohnert

This case report provides a notable example of take-home naloxone provided in a healthcare setting being used by a family member to reverse an opioid overdose. Specifically, the opiate overdose antidote was given to the patient by his outpatient substance use disorder treatment providers, and later used by the wife to reverse a heroin-related overdose that occurred when both were at home. Although it is possible that the patient may have recovered without help, it is reasonable to assume that having naloxone in the home and a family member who was willing and able to administer it reduced the patient's risk of dying of the overdose.

Initial OEND programs sought to harness the social nature of heroin use, i.e., that heroin users tend to inject together, to improve overdose survival by distributing injectable naloxone through harm reduction programs like needle exchange programs. A number of descriptive evaluations of these programs demonstrated that heroin users had the opportunity to, and were able to, administer naloxone to overdose victims (e.g. Tobin et al., 2008; Strang et al., 2008). Adaptations to allow nasal delivery have the potential to increase ease of use for individuals without injection experience. Consequently, treatment and public health programs have begun to distribute naloxone to caregivers and family members of individuals at risk for overdose. This represents a fundamental shift in the underlying proposed mechanism of OEND – instead of supplying naloxone to individuals with a high likelihood of witnessing any one of their social connections experience an overdose, naloxone is

supplied to one or more individuals (directly or indirectly through the patient) with the intent of preventing mortality of a specific person.

Although a number of treatment settings have implemented OEND programs based on this second mechanism, the evidence to support this form of use is relatively limited. The strongest evidence for the effectiveness of OEND programs overall comes from an observational study in Massachusetts, which found that communities with greater OEND implementation had lower opioid overdose mortality rates compared to communities with less implementation (Walley et al., 2013). In this program, naloxone was distributed at needle exchanges, HIV education centers, addiction treatment settings, emergency departments, primary care clinics, and community meetings. Thus, it is unknown whether OEND programs are equally effective across these contexts, and more specifically, if it is equally effective across the two potential mechanisms of impact.

This case provides clear evidence of feasibility for healthcare-based OEND programs that seek to make naloxone available for use to individuals who live with a patient at risk for overdose. Cost-effectiveness is an important consideration as broader implementation of this form of OEND is discussed. An analysis by Coffin and Sullivan (Coffin and Sullivan, 2013) provided a convincing case for the cost-effectiveness of OEND based on the original model of preventing mortality through distribution within heroin using networks. A parallel analysis for OEND in healthcare settings is critical at this time, but may be hindered by lack of formative research to inform assumptions, such as the probability of a witness being present.

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