

Buprenorphine Rescue in Acute Opioid Toxicity: An Alternative to Naloxone Infusion

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Abstract

Following an opioid overdose, repeated doses of naloxone are often administered in the Emergency Department (ED) for recurrent opioid toxicity. Naloxone infusions are often started after several doses of naloxone, which are challenging to titrate, can lead to sustained periods of precipitated withdrawal, and often result in hospital admission. In this case report, we use initiation of buprenorphine as an alternative to a naloxone infusion following acute opioid toxicity in the ED while also demonstrating the transition of care of Opioid Use Disorder (OUD) in the ED setting to long-term outpatient management. Currently, we see high rates of recurrent opioid toxicity post naloxone administration in this setting, emphasizing the need for an alternative approach.

Keywords

Naloxone Infusion, Buprenorphine Initiation, Opioid Overdose, Repeat Naloxone Doses, Opioid Toxicity, Long-Acting Injectable Buprenorphine

1. Case Summary

A 36-year-old woman with Opioid Use Disorder (OUD), methamphetamine use disorder, Post-traumatic stress disorder (PTSD), and housing instability was found unresponsive by a friend who called 911. Emergency Medical Services (EMS) found her unresponsive, with slow, shallow breaths and pinpoint pupils. They administered 4mg of intranasal (IN) naloxone, which showed a good response. She became agitated and restless and developed nausea with vomiting and subsequently received 2mg of intravenous (IV) lorazepam.

Upon arrival to the ED, she increasingly displayed signs of opioid withdrawal syndrome—*anxiety, diaphoresis, nausea, emesis, piloerection, and myalgia*. Vital signs on presentation were: heart rate 110 beats per minute, respiratory rate 20 breaths per minute, blood pressure 146/90 mmHg, temperature 37.3°C, and oxygen saturation 95% on room air. Her Clinical Opiate Withdrawal Scale (COWS) was 20, indicating moderate withdrawal symptoms.

Initially, treatment focused on non-opioid management of opioid withdrawal symptoms. She was administered 1 mg of IV lorazepam, 4 mg of oral ondansetron, 2 mg of oral loperamide, and 0.2 mg of oral clonidine over 10 minutes. She became more alert and comfortable and was able to provide a history. She endorsed daily injection of fentanyl and methamphetamine, typically 5 - 6 times per day. This pattern has been consistent for 2 - 3 years. She currently has unstable housing and lives by “couch-surfing” with friends. She intermittently uses cannabis and tobacco, but denies use of alcohol, benzodiazepines, hallucinogens, or supplements. She has not been medically prescribed methadone or buprenorphine for OUD, but did try buprenorphine off the street and subsequently became very sick.

Eighty minutes after arrival at the ED, she began to display signs of recurrent opioid toxicity. She became progressively somnolent with bradypnea. She again received naloxone (0.1 mg IV), which improved her symptoms. The Addiction Medicine Consult Service was then consulted.

Two hours and ten minutes after arrival and fifty minutes after naloxone was given, the cycle repeated itself with signs of recurrent opioid toxicity and subsequent 0.1 mg of IV naloxone administration. Post-naloxone administration, she again developed symptoms of opioid withdrawal (*mydriasis, rhinorrhea, piloerection, nausea, and myalgias*).

Addiction Medicine then recommended buprenorphine as an alternative to starting a naloxone infusion for preventative treatment of recurrent opioid withdrawal and admitting her to the hospital. She received a total of 4 mg of IN naloxone (10% - 90% bioavailability) and 0.2 mg IV naloxone over 2.5 hours. Buprenorphine profoundly outcompetes naloxone at the mu opioid receptor (MOR), making this transition suitable, regardless of the total naloxone dosing.

Through shared decision making with a patient-centered approach, she agreed to starting sublingual (SL) buprenorphine by doing a rapid, high-dose buprenorphine initiation with a subsequent follow-up appointment the next day with Addiction Medicine. Chronic opioid users have a profound opioid tolerance; this makes the theoretical risk of oversedation or respiratory suppression when combining higher doses of opioids and other sedatives lower. In addition, the partial agonist effects of buprenorphine make these outcomes less likely compared to full agonist opioids. Buprenorphine is also not dosed by weight, but rather by clinical effect. Higher doses are used to saturate central MOR's, thereby maximizing downstream signaling [1]. She received 16 mg SL buprenorphine/naloxone (suboxone) and her objective and subjective symptoms began to improve, but did not fully resolve. Forty minutes after her first dose of SL buprenorphine, she received

another 16 mg of SL buprenorphine with further improvement. She endorsed that she was feeling better, albeit with mild nausea and fatigue, and would like to be discharged.

She was then discharged home with a two-week supply of SL buprenorphine/naloxone 8 mg three times daily, with a plan to transition to long-acting injectable buprenorphine (sublocade) the following week. She was also given the option of inpatient psychosocial therapy, but declined, opting only for medication management and outpatient follow-up in the clinic. Her outpatient Addiction Medicine provider would provide details on her subsequent outpatient psychosocial treatment options.

2. Discussion

Naloxone is a short-acting opioid antagonist used to reverse acute opioid toxicity. Given its short half-life, repeated doses of naloxone are often administered for recurrent opioid toxicity following an opioid overdose, particularly because the specific opioid and amount used are unknown. A Naloxone infusion transiently reverses opioid toxicity and prevents ensuing respiratory depression but does not address withdrawal or treat the underlying OUD [2] [3]. Patients often return to habitual use post-ED visit, leading to exceptionally high rates of morbidity and mortality. Notably, naloxone also precipitates opioid withdrawal in opioid tolerant individuals, leading to intense patient discomfort, impaired decision-making, and decreased treatment retention [4]. Experiencing precipitated withdrawal, which can be prolonged in the case of a naloxone infusion, can harm patient-provider relationships, adversely affect their view of our healthcare system, and decrease the chance of coming to the ED for care in the future. Simply put, continued naloxone infusion limits the treatment of OUD beyond immediate stabilization [5]. Starting a patient on the partial opioid agonist buprenorphine reduces the risk of overdose and decreases all-cause mortality for those with OUD by 3-fold. Post naloxone administration, buprenorphine alleviates symptoms of opioid withdrawal as a result of its net agonist effect. Its pharmacologic properties, namely its long half-life and strong binding affinity for and slow dissociation from the MOR, prevent recrudescence of opioid toxicity, regardless of the full agonist opioid that initially caused toxicity (fentanyl, heroin) [6]. Moreover, the withdrawal state induced by naloxone is an ideal time to initiate buprenorphine using a rapid, high-dose induction. It rapidly alleviates withdrawal symptoms and quickly achieves a therapeutic buprenorphine dose, which is the most important variable to prevent a return to use, increase treatment retention, and decrease mortality [7] [8]. Importantly, buprenorphine, when given in the setting of moderate opioid withdrawal, is highly unlikely to precipitate withdrawal [9]. To avoid precipitated withdrawal, patients need to be on the spectrum of opioid withdrawal, which can be done by ensuring there is a COWS score of at least 8 [10]. If precipitated withdrawal does occur, it is often benign and treated with additional buprenorphine [11].

Early initiation of buprenorphine in the ED has been shown to reduce future overdose risk, lead to fewer ED visits, and lower healthcare costs while improving outcomes [8]. In addition, providing patient-centered care through interventions utilizing shared decision making has been shown to improve outcomes by bridging the gap to increased outpatient adherence. Bridging ED buprenorphine initiation to outpatient follow-up is vital in working towards adherence [12]. One study showed that hospitals participating in an incentive plan to provide improved care through focused interventions had increased rates of filled prescriptions thirty days later [13]. Patients have also emphasized the need for peer recovery specialists as part of a treatment regimen [14]. Treatment engagement is significantly increased post-ED discharge in patients who are started on buprenorphine in that setting [15]. Also worth noting, reducing the rate of precipitated withdrawal through the use of buprenorphine in the field by EMS has been shown to improve outcomes [5] [16].

In our case, the patient was initiated on SL buprenorphine, but ultimately transitioned to long-acting injectable (LAI) buprenorphine. LAI buprenorphine has the benefit of ensuring medication adherence, and has been shown to improve treatment retention compared to SL buprenorphine alone [17]. Moreover, another study showed that LAI buprenorphine led to reduced ED visits and a decrease in inpatient visits related to mental health or substance use. This same study demonstrated that a large proportion of people who stopped their treatment were due to high prices and loss of insurance [18].

Case studies lack generalizability in populations due to their single patient nature and lack of statistical significance. Case reports are prone to bias, confounding variables limiting causal relationships, and difficulty in reciprocation. Our case study highlights a specific patient circumstance, emphasizing the need for controlled studies comparing buprenorphine rescue with naloxone infusions.

3. Conclusion

Initiating rapid high-dose buprenorphine inductions following naloxone-induced reversal of an opioid overdose in the ED is a viable alternative to administering repeated doses of IV naloxone or starting a naloxone infusion. This approach can eliminate the need for hospital admission, decrease hospital length of stay, and improve patient comfort and their overall experience while also reducing rates of morbidity and mortality due to recurrence of opioid use post ED discharge. Transitioning to LAI buprenorphine when possible improves treatment retention and reduces further ED visits.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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