

A Case of Opioid Overdose and Subsequent Death After Medically Supervised Withdrawal: The Problematic Role of Rapid Tapers for Opioid Use Disorder

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Background: Relapse to opioid use is common after rapid opioid withdrawal. As a result, short-term tapers of opioid agonist/partial agonist medications, such as methadone and buprenorphine/naloxone, are no longer recommended by recent clinical care guidelines for the management of opioid use disorder. Nonetheless, rapid tapers are still commonplace in medically supervised withdrawal settings.

Case summary: We report a case of an individual with opioid use disorder who was prescribed a rapid buprenorphine/naloxone taper in a medically supervised withdrawal facility and who had a subsequent opioid overdose and death after discharge.

Discussion: The fatal outcome in this case study underscores the potential severe harms associated with use of rapid tapers. Given the

increased overdose risk, tapers should be avoided and continuing care strategies, such as maintenance pharmacotherapy, should be initiated in medically supervised withdrawal settings.

Key Words: buprenorphine, detoxification, opioid agonist therapy, overdose, taper

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North America is in the midst of an overdose crisis. According to the Centers for Disease Control and Prevention, drug overdose deaths nearly tripled from 1999 to 2014 in the United States, with the majority of overdose deaths due to opioids (Rudd et al., 2016). The number of deaths due to illicit drug overdose increased by 78% in 2016, compared with the previous year in British Columbia—the Canadian province most affected by the overdose epidemic (British Columbia Coroners Service, 2017). As a result, efforts to implement and scale-up evidence-based strategies to treat opioid use disorder and prevent overdose are urgently underway in multiple jurisdictions across North America (British Columbia Centre on Substance Use, 2017).

Medically supervised withdrawal (ie, “detoxification”) is 1 health systems approach for the management of opioid use disorder (Wines et al., 2007). To manage the acute symptoms of withdrawal arising from cessation of illicit opioid use, rapid tapers with medications including the full agonist methadone and partial agonist buprenorphine/naloxone over the course of several days are commonly prescribed in these settings (Darke and Hall, 2003; Wines et al., 2007). However, rapid tapers have been associated with increased potential for fatal overdose risk due to loss of tolerance after rapid tapers in these settings (Wines et al., 2007). In addition, rates of short-term abstinence from medically supervised withdrawal alone are low, between 20% and 40% (Carroll et al., 2009).

Given the high relapse rates and increased risk for overdose associated with medically supervised withdrawal alone, the approach to care has shifted in some settings that have traditionally offered medically supervised withdrawal for opioid use disorder to focus on facilitating transition to ongoing substance use disorder care, including initiation and stabilization on a opioid agonist therapy, defined as a stable dose of a long-acting medication such as methadone or buprenorphine/naloxone. Recent clinical practice guidelines reflect this shift by recommending against rapid tapers in the

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absence of ongoing treatment for opioid use disorder (Dunlap and Cifu, 2016). However, despite these evolving recommendations for treatment of opioid use disorder, rapid tapers remain a frequent practice in medically supervised withdrawal settings. Here, we present a case of an individual who underwent a rapid taper of buprenorphine/naloxone in a medically supervised withdrawal setting and suffered an opioid overdose with subsequent death in the weeks after discharge from the facility.

CASE PRESENTATION

A 28-year-old male was admitted to an inpatient medically supervised withdrawal facility in Vancouver, Canada, for management of comorbid opioid and stimulant use disorders. He was not in contact with his family and had a history of homelessness. Before admission, the patient was living in a shelter and supported by income assistance. His past medical history was significant for schizoaffective disorder, which was treated by a psychiatrist with medications including olanzapine, quetiapine, lorazepam, and trazodone. The patient was both HIV and hepatitis C negative. He had a history of attending inpatient medically supervised withdrawal on numerous previous occasions. He had a brief 2-week period of methadone maintenance therapy 2 months before, up to a maximum daily dose of 50 mg, which he had abruptly discontinued for unclear reasons. The patient had never previously been prescribed buprenorphine/naloxone treatment.

At admission to the facility, he reported that he had been using intravenous heroin and crystal methamphetamine for 3 years and had no prior overdoses. He self-reported the injection of, on average, 0.3 g of heroin daily and 0.1 g of crystal methamphetamine 3 days per week. He also reported occasional smoked cannabis use. His last reported use of all substances was the day before presentation at the medically supervised withdrawal facility. Corroborating this history, his initial urine drug screen was positive for opiates, amphetamines, and tetrahydrocannabinol.

The attending physician assessed the patient on the day after admission and documented multiple objective signs of opioid withdrawal, including frequent yawning, piloerection, and dilated pupils at 6 mm diameter. A plan for buprenorphine/naloxone taper was initiated to manage the acute symptoms of opioid withdrawal. An initial dose of buprenorphine/naloxone 8 mg/2 mg was to be tapered by 2/0.5 mg daily to discontinuation over 4 days. The patient was also prescribed trazodone, clonidine, quetiapine, and dimenhydrinate as needed to treat any residual opioid withdrawal symptoms. The patient was discharged from the facility back to a shelter after completion of the 4-day buprenorphine/naloxone taper. There was no mention of naloxone provision and further linkage of care based on patient's record.

Three weeks later, the patient was found by a bystander in a public bathroom in downtown Vancouver unresponsive and without a pulse. The records from emergency rescue services noted that there was a needle in the right antecubital fossa when he was found. Cardiopulmonary resuscitation was initiated at the scene, and also administration of intramuscular naloxone at a dose of 0.4 mg and a second dose of 0.8 mg. After this, the patient had a return of spontaneous respiration.

He was then transferred to a local hospital where he was intubated and ventilated, and admitted to the intensive care unit (ICU). His urine drug screen on arrival at the hospital was positive for opiates and amphetamines.

The patient failed to regain consciousness after several days in the ICU. Subsequent brain magnetic resonance imaging was consistent with severe anoxic brain injury. After discussion with the family, a decision was made to transfer the patient to a palliative care unit, and the patient died after 10 days in the unit.

DISCUSSION

We have presented a case of opioid overdose and subsequent death after discharge from inpatient medically supervised withdrawal facility for a patient with comorbid opioid and stimulant use disorders. The patient had been prescribed a buprenorphine/naloxone rapid taper. Several weeks later, the patient had an opioid overdose and suffered an anoxic brain injury that resulted in death.

Risk factors for fatal overdose include co-ingestion of central nervous system depressants such as benzodiazepines and alcohol, use of illicit opioids, particularly by injection, past nonfatal overdose, and recent periods of abstinence from opioids (Darke and Hall, 2003; Coffin et al., 2007). The patient had several aforementioned risk factors for opioid overdose, including co-ingestion of benzodiazepines, illicit injection opioid use, and recent abstinence in a medically supervised withdrawal facility with a rapid opioid agonist therapy taper. Darke and Hall (2003) have described loss of tolerance to opioids after a period of abstinence, as in this case, to be a major risk factor for heroin overdose. One study documented a high mortality rate of 30 per 100 person-years in the first 4 weeks after inpatient medically supervised withdrawal (Ravndal and Amundsen, 2010). Overdose risk increases with abstinence because physiological tolerance is reduced, rendering a previously tolerated dose potentially fatal in the event of relapse to opioids. Loss of tolerance commonly occurs in incarceration, hospitalization, and medically supervised withdrawal settings (Darke and Hall, 2003). Additional risk factors for overdose also include this patient's recent homelessness, which is thought to be a risk factor for overdose, in part, due to the necessity for rushed injection drug in public spaces (Kerr et al., 2007), and concurrent mental illness where lack of social support, relationship dissatisfaction, and feelings of hopelessness are associated with increased substance use risk behaviors (Burns et al., 2004).

In addition to increased overdose risk, rapid taper strategies have been found to be associated with very low rates of cessation of illicit opioid use; a study conducted by Nosyk et al. (2012) showed that methadone tapers had a 13% success rate, and individuals who underwent short-term tapers (less than 12 weeks) were approximately 7 times less likely to succeed than individuals on long-term tapers (more than 52 weeks). This is in contrast to maintenance pharmacotherapy with methadone or buprenorphine/naloxone, which have been shown to be effective for treatment of opioid use disorder in several Cochrane systematic reviews and meta-analyses, including treatment retention (relative risk 0.33) (Mattick

et al., 2003, 2014; Nielsen et al., 2016). Moreover, previous studies indicated that successful abstinence after medically supervised withdrawal was associated with engagement in ongoing substance use disorder treatment, including long-term opioid agonist therapy and residential treatment (Mattick et al., 2003, 2014; Strang et al., 2003; Nielsen et al., 2016). Most relapses after medically supervised withdrawal resulted from patients being discharged without any follow-up or without continuation of opioid agonist therapy in outpatient settings (Strang et al., 2003; Carroll et al., 2009).

In this patient's case, although the rationale was not documented, the decision to initiate a buprenorphine/naloxone taper could have been patient-initiated. Some clinical practice guidelines suggest that patients who opt for a taper be counseled regarding relapse risk after rapid opioid tapers and overdose education and naloxone distribution should also be a part of the standard practice (Tzemis et al., 2014). Guidelines suggest that patients who decide to taper be initiated on a slow outpatient taper rather than a fast taper in a medically supervised withdrawal facility to reduce overdose risk (British Columbia Centre on Substance Use, 2017). Those who decide to initiate a rapid taper despite these recommendations may preferentially be prescribed buprenorphine/naloxone over methadone, given superior efficacy for alleviating withdrawal symptoms and relatively lower overdose risk, particularly in people with comorbid benzodiazepine use (Dunlap and Cifu, 2016). In addition, until the overdose crisis was declared in British Columbia, naloxone was not a routine part of care in medically supervised withdrawal settings and was not provided in this case; however, it is now recommended in the most recent provincial guidelines (British Columbia Centre on Substance Use, 2017).

Despite this knowledge, like in our case, rapid tapers without linkage to ongoing care are common (Carroll et al., 2009). There remain several barriers to accessibility of opioid agonist therapies, including paucity of trained prescribers, medication cost, and negative attitude towards opioid agonist therapies by both patients and healthcare providers. Continuing education and adequate medication cost coverage for opioid agonist therapies are needed to help address these barriers (Volkow et al., 2014). Linkage with additional treatment options should also be considered and include psychosocial intervention, intensive outpatient treatment, residential treatment, access to long-term opioid agonist therapy, or antagonist treatment, such as naltrexone (British Columbia Centre on Substance Use, 2017).

There are several limitations to this case report. First, the lack of information for the 3 weeks after the patient's discharge limits a clear conclusion of abstinence and loss of opioid tolerance. Regardless, we believe that a death this proximal to the medically supervised withdrawal, combined with the known association between reduced tolerance with rapid tapers and overdose risk, makes this case illustrative of the potential harms associated with the practice of rapid tapers in medically supervised withdrawal settings. Second, this patient died after withdrawal of care after anoxic brain injury subsequent to a nonfatal overdose event; though this case is not a typical fatal overdose presentation in which death immediately follows opioid exposure; it underscores

downstream impacts of initial nonfatal overdose presentations that may not be initially apparent, and includes, for instance, a surge in organ transplantation in British Columbia related to increased severe nonfatal overdoses that ultimately result in withdrawal of care and death (Fayerman, 2017). Third, the patient had several aforementioned risk factors for opioid overdose, and also concurrent mental health illness and more information on his previous unsuccessful substance use disorder treatment with his psychiatric comorbidities would help identify the cause of death. Though comorbid mental health conditions and multiple substance use are common in patients with substance use disorders requiring treatment (Burns et al., 2004; Kerr et al., 2007), this patient had limited engagement with the healthcare system, and medical documentation was limited.

In this report, we have illustrated a case, which is consistent with a phenomenon apparent in clinical practice, where rapid tapers are still used in medically supervised withdrawal settings, despite its related morbidity and mortality. It is essential to pay more attention to this outdated but common practice, especially in the context of the overdose crisis in North America. Avoidance of rapid tapers is a key measure that can prevent unintentional overdoses due to rapidly reduced tolerance after taper completion. Continuing care, including initiation of opioid agonist therapy and bridging to residential and outpatient substance use disorder treatment, should be a key focus in medically supervised withdrawal settings.

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REFERENCES

- British Columbia Centre on Substance Use. A Guideline for the Clinical Management of Opioid Use Disorder. February 2017. Available at: http://www.bccsu.ca/wp-content/uploads/2017/02/BC-OU-D-Guidelines_FINAL.pdf. Accessed March 13, 2017.
- British Columbia Coroners Service. Illicit Drug Overdose Deaths in BC, January 1, 2007-January 31, 2017. February 2017. Available at: <http://www2.gov.bc.ca/assets/gov/public-safety-and-emergency-services/death-investigation/statistical/illicit-drug.pdf>. Accessed March 13, 2017.
- Burns JM, Martyres RF, Clode D, et al. Overdose in young people using heroin: associations with mental health, prescription drug use and personal circumstances. *Med J Aust* 2004;181(7 suppl):S25–S28.
- Carroll CP, Triplett PT, Mondimore FM. The intensive treatment unit: a brief inpatient detoxification facility demonstrating good postdetoxification treatment entry. *J Subst Abuse Treat* 2009;37:111–119.
- Coffin PO, Tracy M, Bucciarelli A, et al. Identifying injection drug users at risk of nonfatal overdose. *Acad Emerg Med* 2007;14:616–623.
- Darke S, Hall W. Heroin overdose: research and evidence-based intervention. *J Urban Health* 2003;80:189–200.
- Dunlap B, Cifu AS. Clinical management of opioid use disorder. *JAMA* 2016;316:338–339.
- Fayerman P. Organ Transplants Surge in B.C. Because of Fentanyl-Overdose Deaths. 2017. Available at: <http://vancouver.sun.com/news/local-news/organ-transplants-surge-in-b-c-because-of-fentanyl-overdose-deaths>. Accessed July 12, 2017.
- Kerr T, Fairbairn N, Tyndall M, et al. Predictors of non-fatal overdose among a cohort of polysubstance-using injection drug users. *Drug Alcohol Depend* 2007;87:39–45.
- Mattick RP, Breen C, Kimber J, et al. Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence. *Cochrane Database Syst Rev* 2003;CD002209.

- Mattick RP, Breen C, Kimber J, et al. Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. *Cochrane Database Syst Rev* 2014;CD002207.
- Nielsen S, Larance B, Degenhardt L, et al. Opioid agonist treatment for pharmaceutical opioid dependent people. *Cochrane Database Syst Rev* 2016;CD011117.
- Nosyk B, Sun H, Evans E, et al. Defining dosing pattern characteristics of successful tapers following methadone maintenance treatment: results from a population-based retrospective cohort study. *Addiction* 2012; 107:1621–1629.
- Ravndal E, Amundsen EJ. Mortality among drug users after discharge from inpatient treatment: an 8-year prospective study. *Drug Alcohol Depend* 2010;108:65–69.
- Rudd RA, Seth P, David F, et al. Increases in drug and opioid-involved overdose deaths: United States, 2010–2015. *MMWR Morb Mortal Wkly Rep* 2016;65:1445–1452.
- Strang J, McCambridge J, Best D, et al. Loss of tolerance and overdose mortality after inpatient opiate detoxification: follow up study. *BMJ* 2003; 326:959–960.
- Tzemis D, Al-Qutub D, Amlani A, et al. A quantitative and qualitative evaluation of the British Columbia Take Home Naloxone program. *CMAJ Open* 2014;2:E153–E161.
- Volkow ND, Frieden TR, Hyde PS, et al. Medication-assisted therapies: tackling the opioid-overdose epidemic. *N Engl J Med* 2014;370:2063–2066.
- Wines JD, Saitz R, Horton NJ, et al. Overdose after detoxification: a prospective study. *Drug Alcohol Depend* 2007;89:161–169.