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INITIATION OF INJECTABLE OPIOID AGONIST TREATMENT IN HOSPITAL: A CASE REPORT

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Abstract

Uncontrolled opioid withdrawal and pain often drive inpatients with opioid use disorder to leave hospital against medical advice, resulting in suboptimal medical and addiction treatment. When oral opioid agonist treatments such as methadone and buprenorphine/naloxone fail for management of craving and withdrawal, injectable opioid agonist treatment may serve to retain patients in care and link them to addiction services. We describe the case of a 47-year-old man with a severe, active opioid use disorder and daily use of illicitly manufactured fentanyl, who was re-admitted to hospital for post-operative management after leaving against medical advice due to uncontrolled opioid withdrawal. Intravenous hydromorphone was used to retain him in care, allowing for completion of his antibiotics and enrolment in ongoing community injectable opioid agonist treatment.

Keywords

opioid-related disorders; opioid substitution therapy; intravenous injections; diacetylmorphine; opioid addiction

INTRODUCTION

Injectable opioid agonist treatment (iOAT) is a high-intensity therapy along the continuum of care for patients with opioid use disorder (OUD) [1]. Prescription injectable diacetylmorphine is offered as an established standard of care for refractory OUD in several European countries [2,3]. In patients who have not benefitted from oral opioid agonist treatment (OAT), injectable diacetylmorphine is effective in reducing non-medical opioid use while improving overall health and social functioning in comparison to methadone [4,5]. In Canada, injectable diacetylmorphine is only available for a small number of patients, as stringent regulation and cost limit further expansion. As a lower-cost, more accessible

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alternative, providers have increasingly prescribed intravenous (IV) hydromorphone since 2016 based on results of the SALOME trial, which demonstrated non-inferiority of IV hydromorphone compared to IV diacetylmorphine for retention in treatment, safety, and reductions in street opioid use [6]. Patients enrolled in iOAT programs attend specialised clinics to inject diacetylmorphine or hydromorphone two to three times daily under direct medical supervision, thereby ensuring safety while mitigating diversion.

Though guidelines exist on outpatient iOAT initiation [1], little is known about the utility of initiating iOAT in the hospital setting. We speculate that providers may hesitate to start iOAT in hospital due to unfamiliarity with dosing and management, concerns regarding overdose or perceived facilitation of drug-seeking behaviours. Community iOAT is also a limited resource, so providers may be unsure of who may optimally benefit.

Prior studies associate inadequate management of opioid withdrawal with an increased risk of patients leaving hospital against medical advice (AMA) [7,8]. Treatment in hospital with oral OAT, such as methadone, has been shown to reduce the risk of AMA discharges [9]. Among patients inadequately managed on conventional oral OAT in hospital, iOAT may be a valuable tool to engage patients in treatment for both their OUD and acute medical illnesses [4,5,10–15]. Here we present the case of a patient with a severe, active OUD with daily use of a high potency synthetic opioid (illicitly manufactured fentanyl), admitted to hospital for post-operative antibiotics after leaving AMA due to inadequately managed opioid withdrawal. Initiation of hydromorphone iOAT in hospital enabled him to complete his antibiotics and facilitated a transition to community iOAT.

CASE REPORT

A 47-year-old man with no fixed address and a severe, active OUD presented to a hospital in downtown Vancouver, Canada, with a two-day history of right lower quadrant pain. Physical examination was significant for an elevated blood pressure of 161/75, diffuse abdominal tenderness and a positive McBurney's sign. His white blood cell count was elevated at $13.2 \times 10^9/L$. Imaging showed mildly thickened appendix walls. The consulting General Surgery team suspected acute appendicitis and performed an emergent laparoscopic appendectomy.

To manage the patient's pain and OUD, the surgical team administered 50 mg of morphine orally (PO). Post-operatively, two additional doses of morphine 50 mg PO and one dose of morphine 10 mg IV were given, which unfortunately proved to be insufficient. The next morning, the patient left AMA to use illicit fentanyl as he felt his pain and withdrawal were inadequately managed.

He returned that evening with worsening abdominal pain and nausea. He remained mildly hypertensive with a respiratory rate of 24 and diffuse abdominal tenderness. He was re-admitted to hospital and started on ceftriaxone 1 g IV daily, metronidazole 500 mg IV twice daily and hydromorphone 10–20 mg IV every 1 h as needed (PRN) by General Surgery. Despite being administered roughly every 80 min, this hydromorphone regimen was insufficient to prevent withdrawal and left the patient feeling embarrassed requesting

medication so often. The Addiction Medicine Consult Team was then consulted for pain and withdrawal management.

The patient recounted a 30-year history of IV opioid use. He used heroin initially before transitioning to fentanyl, and was injecting one to 2 g of illicitly manufactured fentanyl per day. He also injected crystal methamphetamine approximately twice per week. He reported no other current substance use. He had experienced five previous opioid overdoses requiring reversal with naloxone and had previously contracted hepatitis C, which cleared with treatment. He had formerly been prescribed several forms of OAT including sublingual buprenorphine/naloxone, methadone, slow-release oral morphine (SROM) and hydromorphone iOAT, but continued to use illicit opioids daily. His most recent treatment was a one-month course of daily supervised SROM 1300mg that he had stopped 3 weeks prior to hospitalisation because it was ineffective for managing cravings. He cited positive effects of his intravenous heroin and fentanyl use including managing cravings, controlling withdrawal, producing euphoria, decreasing his sense of self-hatred and suppressing traumatic memories from childhood.

Medical comorbidities included untreated chronic pain secondary to a jaw injury sustained in a motor vehicle collision, attention-deficit/hyperactivity disorder and an unspecified anxiety disorder. He was no longer taking any regular medications and had no allergies.

The Addiction Medicine Consult Team started hydromorphone 20 mg IV every 3 h regularly and 300 mg SROM once daily, as well as a 5 mg/mL, 0–20 mL/h ketamine infusion. These orders were added to the PRN IV hydromorphone initially prescribed by General Surgery and resulted in the patient decreasing his PRN use from once every 80 min to approximately once every 3 h.

Over his admission, doses were gradually up-titrated (Table 1) based on national iOAT guidelines [1]. For the first three hydromorphone injections after a dose adjustment was made, nurses documented level of consciousness and respiratory rate pre-injection, and 5, 10 and 15 min post-injection. For all subsequent injections they documented level of consciousness and respiratory rate pre-injection and 30 min post-injection. Medications were to be held if the patient was not easily rousable.

Ketamine was discontinued on day 5 as the patient's pain had abated. By day 7, he was no longer experiencing cravings or withdrawal, and was not requiring any supplemental opioids. He still expressed a preference for IV diacetylmorphine over hydromorphone. Based on his preference and previous unsuccessful trial of community hydromorphone iOAT, the Addiction Medicine Consult Team advocated for switching to diacetylmorphine iOAT on discharge. Of note, diacetylmorphine was not available on the hospital formulary due to regulatory restrictions.

While on iOAT in hospital, the patient successfully completed his course of antibiotics, recovered from his operation and eliminated his consumption of non-prescribed opioids. He was discharged on day 9 to a community diacetylmorphine iOAT program. He was counselled on harm-reduction practices and given a take-home naloxone kit. Post-discharge out-patient follow up was arranged with his surgical, psychiatric and social work teams. Six

months later, he continued to be on IV diacetylmorphine at a dose of 330 mg for the first two daily doses and 340 mg for the third daily dose, along with 700mg of oral SROM daily.

DISCUSSION

We described the case of a 47-year-old male with a severe OUD refractory to oral OAT who was successfully retained in treatment through initiation of hydromorphone iOAT and SROM in hospital. Receiving both iOAT and SROM, which he had not previously received in combination, may explain his success on this occasion. For inpatients with OUD it is important to note that their opioid requirements are often two-fold; they require opioid replacement to manage baseline cravings and withdrawal, and additional opioids and non-opioid therapy such as ketamine to manage pain. A long-acting opioid such as SROM in addition to the short-acting IV hydromorphone helps to reduce the severity of withdrawal symptoms by providing background 24 h opioid receptor saturation. Therefore, flexible doses of oral opioid agonists, such as SROM or methadone, are commonly provided as part of iOAT programs to prevent withdrawal overnight [1,4].

It is important to acknowledge that even in jurisdictions such as Vancouver where community iOAT is available, spots are often extremely limited. As of February 2019, there were approximately 300 iOAT spots in Vancouver, while in most other Canadian provinces iOAT is not available at all. Referrals are therefore made judiciously, often after unsuccessful trials of oral OAT. Priority may be given to hospitalised patients in order to facilitate successful transition to the community upon discharge. Outside of Canada, iOAT is available in several European countries. Switzerland is the largest of these programs, with 1600 patient spots available for iOAT [16].

In jurisdictions with limited or absent community iOAT availability, there is a risk of initiating iOAT in hospital without being able to provide continuing iOAT after discharge. Upon discontinuation of iOAT there is often a return to pre-treatment levels of illicit opioid use [3,17]. Therefore, it is recommended that hospital-based inductions be done in coordination with an outpatient prescriber who agrees to continue care following discharge [1]. If a spot cannot be secured, oral OAT is recommended while they are placed on the waiting list. However, in some exceptional cases such as a patient not willing to engage in oral OAT, iOAT could still be considered in hospital to help foster engagement in medical care and treat opioid cravings and withdrawal, although further study is warranted.

CONCLUSION

Oral OAT, while effective for many patients with OUD, will fail to benefit some patients. Therefore, for select patients, iOAT is a further treatment option that can be considered. As shown in this case, initiation of iOAT can be considered in the inpatient setting to improve medical outcomes and engage patients in long-term OUD treatment.

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Table 1.

Opioid medication orders for the patient during the first 7 days of his hospital admission

Day of admission	Scheduled IV HM (mg)	PRN IV HM (mg)	SROM (mg)
1	–	10–20 q1h	–
2	20q3h	10–20 q1h	300 daily
3	40q4h	10–30 q1h	400 daily
4	60q4h	20–0 q1h	400 daily
5	80q4h	10–20 q1h	600 daily
6	80q4h	10–20 q1h	600 daily
7	160 TID	20–30 q1h	600 daily

HM, hydromorphone; IV, intravenous; PRN, as-needed; q#h, every # hours; SROM, slow-release oral morphine; TID, three times per day.

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