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HOSPITAL INITIATED INJECTABLE OPIOID AGONIST THERAPY FOR THE TREATMENT OF SEVERE OPIOID USE DISORDER

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Abstract

Background: Across North America, there is an unprecedented opioid overdose epidemic. Approximately 15% of individuals with severe opioid use disorder (OUD) do not benefit from opioid agonist therapy (OAT) such as buprenorphine/naloxone or methadone and are considered treatment refractory. Of those who inject, injectable OAT (iOAT), with hydromorphone or diacetylmorphine, offered in community settings has demonstrated improved retention to treatment and decreased nonprescription opioid use. This case series seeks to describe iOAT initiation and titration in a hospital setting for treatment refractory individuals with OUD and examine impacts of iOAT on leaving hospital against medical advice (AMA).

Methods: A retrospective chart review of 4 patients initiated on iOAT during hospitalization at St. Paul's Hospital in Vancouver, BC was completed between July 2017 to May 2018. Outcomes of interest included: (1) dose titration schedules of hydromorphone; and (2) reports of leaving hospital AMA; and (3) continuation of iOAT in community post-discharge.

Results: Of the 4 participants, 2 were female and the mean age was 42 years. Despite a history of AMA, all participants stayed until the recommended the discharge after iOAT initiation. The average total doses of intravenous hydromorphone used during titration were: day 1: 100mg and days 2 to 3: 200mg. All continued iOAT in the community and one participant was readmitted within 30 days post-discharge.

Interpretation: This case series describes a novel approach to the management of treatment refractory individuals with severe OUD during hospitalization. Prescribing iOAT in acute care settings is feasible and may reduce rates of leaving hospital AMA.

Keywords

acute care; injection drug use; opioid use disorder; opioids

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INTRODUCTION

Canada and the United States are in the midst of a drug overdose death epidemic. More than 150,000 people have died in both countries from a preventable overdose since 2016, largely secondary to the contamination of the street drug supply by fentanyl and its potent analogues.[1] Opioid use disorder (OUD) is a chronic, relapsing disease with significant morbidity and a crude mortality rate of 48.6 in 1000 person years.[2] Opioid agonist therapy (OAT; eg, buprenorphine/naloxone [BNX] or methadone) is the most efficacious treatment to prevent death and harms for those with OUD.[3] In the Canadian context, slow release oral morphine (SROM) is used as a treatment option for OAT.[4] For individuals with severe OUD who inject opioids and have not benefited from oral OAT, injectable opioid agonist therapy (iOAT) (eg, hydromorphone, diacetylmorphine) has been shown in community settings to reduce nonprescription opioid use and improve treatment retention when compared to methadone.[5] Refractory OUD is defined as ongoing nonprescription opioid use despite trials of standard OAT. Much of the literature on iOAT is with diacetylmorphine,[5] however, due to barriers with access in Canada and iOAT being a part of the spectrum of treatment of OUD, Health Canada has accordingly approved injectable hydromorphone. The literature supports the use of hydromorphone for iOAT as it has been shown to be non-inferior to diacetylmorphine.[6] However, research on iOAT has primarily been conducted in ambulatory care and has not been described in hospital settings with the exception of 1 case report.[7]

Hospitalization can be a challenging time for individuals with a severe OUD. For example, suboptimal pain or withdrawal management can result in individuals leaving hospital against medical advice (AMA), increasing their risk for morbidity and mortality. [8,9]

Despite this, hospital-initiated OUD treatment is associated with engagement in community, and self-reported decrease in nonprescription opioid use.[10,11]

Here, we report 4 cases of hospital-initiated injectable hydromorphone for the treatment of refractory, severe OUD to add to the limited current literature.

METHODS

Retrospective chart reviews were conducted of 4 participants who were offered iOAT titration as standard of care during an admission at St Paul’s Hospital, in Vancouver, BC. We utilized convenience sampling and selected out a list of who had already received iOAT and the first 4 to provide consent were enrolled in this study. Ethics board approval was obtained. Of all the OUD cases seen at our hospital, approximately 8% to 10% are iOAT starts or continuations. Each of the patients were started on low dose hydromorphone (4– 20 mg IV every 2 hours) and then quickly titrated to a suitable dose once tolerance was determined. Starting doses on average, are hydromorphone 15 mg IV every 3 hours regularly and 10 mg IV every hour as needed. Doses were titrated based on ongoing self-reported withdrawal, cravings or nonprescription opioid use. However, case 4 for example, was given a lower starting dose based on her tolerance history. Nurses administered the medication at the bedside with a postdose assessment at 5, 10, and 15 minutes for regular doses for the first 48 hours. SROM or methadone is also recommended as it provides a long-acting opioid

to prevent withdrawal in-between doses of iOAT. Here only 2 participants agreed to start oral OAT. All participants had trials of OAT in both inpatient and outpatient settings before this admission. None of these participants had tried iOAT before this admission.

CASES

Case 1

A 39-year-old female was hospitalized with a severe neck abscess. Past medical history included: anxiety, depression, hypertension, and cellulitis. Her substance use began 15 years prior and at the time of hospitalization was using 1 g/d of intravenous (IV) fentanyl and heroin and 1/2 g/d of IV crystal methamphetamine (CM). Her urine drug screen (UDS) was positive for fentanyl, opiates, and amphetamines. The patient had left hospital AMA twice in the 3 months before this admission. Previous treatment attempts with both methadone and BNX had been unsuccessful and the patient declined oral OAT during this admission. She was started on IV hydromorphone (see Table 1 for titration). She reported significant pain and withdrawal relief, self-reported no non-prescription substance use during hospitalization, and completed her antibiotic treatment. Her nonprescription opioid use decreased to 1/10 g IV every other day, at 3 weeks post-discharge, based on chart review from her outpatient clinic. She was discharged to a community iOAT program and the discharge dose was hydromorphone 110mg BID IV. She declined any oral OAT with her iOAT during this admission.

Case 2

A 47-year-old man was hospitalized with lower extremity cellulitis. Past medical history included: HIV on treatment, hepatitis C spontaneously cleared in 2017, osteomyelitis, and drug-induced psychosis. His substance use began at the age of 13 years. At the time of hospitalization, he was using 1/2 g/d of IV fentanyl and heroin and IV CM 1 to 2 times/wk. His UDS was positive for fentanyl, cocaine, opiates, and amphetamines. His OUD had been refractory to both methadone (maximum 200 milligrams [mg]/d) and SROM (maximum 560 mg/d). He had experienced frequent overdoses and had left AMA 3 times in the last three months before this admission. He was started on IV hydromorphone (see Table 1 for titration) for OUD treatment. The patient subsequently self-reported no nonprescription opioid use during hospitalization and completed his antibiotic treatment. He was discharged to a community iOAT program on hydromorphone 110 mg IV BID and SROM 200 mg.

Case 3

A 52-year-old man was hospitalized for spinal osteomyelitis. Past medical history included: untreated hepatitis C, and previous cellulitis. He left hospital AMA once in the 3-month period before this admission. At the time of hospitalization, he was using 1/2 g/d of IV fentanyl and heroin. His UDS was positive for fentanyl, opiates, and amphetamines. Previous addiction treatment included BNX, methadone (maximum 180 mg/d) and SROM (maximum 1000 mg/d). He had not had sustained abstinence from nonprescription opioids in many years. The patient was started on IV hydromorphone (see Table 1 for titration) for OUD treatment. The patient completed antibiotic treatment and had no reported

nonprescription opioid use in hospital. He was discharged to a community iOAT program on hydromorphone 150mg IV BID. He declined continuing methadone upon discharge.

Case 4

A 32-year-old female was hospitalized with diabetic ketoacidosis (DKA). Past medical history included: type 1 diabetes and numerous drug overdoses. Her opioid use began 15 years prior. At the time of hospitalization, she was using 1/2 g/d of IV fentanyl and heroin and 1/2 g/d of IV CM. Her UDS was positive for fentanyl, opiates, and amphetamines. The patient had left hospital AMA once in the 3 months before this admission. Previous addiction treatment included residential treatment, BNX (maximum 32 mg/d), methadone, and SROM (maximum 400 mg/d). The patient was initiated on injectable hydromorphone (see Table 1 for titration) for severe OUD treatment. The patient successfully completed medical treatment and she subsequently had fewer hospital admissions for DKA. There was ongoing nonprescription substance use however she reported it was less than before along with less overdoses and more stabilization of the diabetes. She was discharged to a community iOAT program on hydromorphone 50 mg IV BID. She did experience readmission within 30 days of discharge for ongoing management of DKA.

DISCUSSION

These cases suggest injectable hydromorphone may be an effective treatment for individuals with severe, refractory OUD in an acute care setting. All patients remained in hospital (despite previous episodes of leaving hospital AMA) and successfully completed their medical treatment following iOAT initiation. Further 2 individuals were able to cease all nonprescription opioid use during hospitalization and no one experienced any adverse events with iOAT, that is, sedation or overdose. Following discharge, all patients were connected with a community iOAT and primary care provider and all participants continued treatment post-discharge. One participant was readmitted within 30 days of discharge.

In community iOAT programs, doses are given 2 to 3 times daily based on hours of operation of the clinics.[12] There is a standard titration schedule used however, in these cases, with the available acute care resources, we were able to provide more frequent iOAT doses, therefore reaching a therapeutic dose faster. Also, in the community, patients self-administer their doses under nursing supervision however, due to hospital regulations, doses were administered by the nurses. Only 2 out of 4 participants agreed to use oral long-acting OAT as per their preference and only 1 took a prescription for oral OAT upon discharge.

iOAT has been shown to be a cost effective intervention compared to methadone for those with treatment refractory OUD in community settings.[13,14] Further, Bansback et al showed iOAT with hydromorphone is as cost effective as iOAT with diacetylmorphine.[15] As an extension, it may have significant cost savings in acute care settings because leaving hospital AMA has higher readmission and mortality rates.[9,16] Important considerations before initiating hospital iOAT is to ensure an after-care plan is in place for treatment continuation following discharge. Albeit, some patients may not be interested in treatment once discharged therefore using iOAT as harm reduction while in hospital can be considered. As outlined in the recently published national clinical guidelines on iOAT, treatment of OUD

should follow a multiprong approach, which includes both pharmacological and non-pharmacological treatment options including harm reduction, tailored to the needs of the patient.[12]

More research is required to assess feasibility and impact of iOAT on hospitalized patients. Some limitations include selection bias as a consequence of a case series design, lack of generalizability and the inability to comment on efficacy due to a small sample size. Also, only 2 of the participants received oral OAT as the rest declined therefore, they cannot be accurately defined as treatment refractory at these particular admissions however, multiple previous attempts signaled the need for treatment intensification.

In the wake of the opioid crisis, a critical need exists to ensure all evidence-based treatment options are available to individuals with OUD in acute care settings. Providing higher intensity treatment for those who need it may prevent patients leaving hospital AMA, reduce nonprescription opioid use while in hospital and improve completion of medical therapy.

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Table 1.

Hospital-initiated Injectable Hydromorphone: Titration Schedule

	Scheduled Intravenous (IV) Hydromorphone	IV Hydromorphone PRN (Total Used in 24/h)	Scheduled Oral Opioid Agonist Therapy*
Case 1			
Day 1	5mg q3h	1–2mg q1h prn (3mg)	—
Day 2	10mg q3h	1–2mg q1h prn (1mg)	—
Day 3	15 mg q3h	1–2 mg q1h prn (10 mg)	—
Day 4	20 mg q3h	1–2 mg q1h prn	—
Day 5	50mg q6h	5mg IV q2h prn	—
Discharge prescription Hydromorphone IV 110 mg BID			
Case 2			
Day 1	—	10–20–20 mg q2h PRN (80 mg)	SROM 200 mg
Day 2	40 mg q4h	10–20 mg q2h PRN (20 mg)	SROM 200 mg
Day 4	60 mg q4h	10–20 mg q2h PRN (20 mg)	SROM 200 mg
Day 5	110mg BID	—	SROM 200 mg
Discharge prescription Hydromorphone IV 110 mg BID, SROM 200 mg			
Case 3			
Day 1	25mg q3h	10 mg q3h PRN (30 mg)	Methadone 10 mg TID
Day 2	25mg q3h	10 mg q1h PRN (60 mg)	Methadone 10 mg TID
Day 4	25mg q3h	10 mg q2h PRN (70 mg)	Methadone 10 mg TID
Day 9	65mg TID	10 mg q2h PRN (90 mg)	Methadone 10 mg TID
Day 10	100mg TID	10 mg q2h PRN (10 mg)	Methadone 10 mg TID
Discharge prescription Hydromorphone IV 150 mg BID			
Case 4			
Day 1	4mg Q3H	2–4mg Q1H PRN (2mg)	—
Day 2	10mg Q3H	2–4mg Q1H PRN (8mg)	—
Day 3	12mg Q3H	2–4mg Q1H PRN (12mg)	—
Day 4	50mg twice daily	—	—
Discharge prescription Hydromorphone IV 50 mg BID			

*Oral OAT is often provided in combination with iOAT to alleviate withdrawal symptoms over night.

h, hours; mg, milligrams; PRN, as needed; q, every; QID, 4 times per day; SROM, slow release oral morphine; TID, 3 times per day.