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SUCCESSFUL TREATMENT WITH SLOW-RELEASE ORAL MORPHINE FOLLOWING A FENTANYL-RELATED OVERDOSE: A CASE REPORT

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Abstract

Background: Overdose deaths as a result of untreated opioid use disorder (OUD) pose a major public health concern across North America. Although slow release oral morphine (SROM) is increasingly used as an alternative option for the treatment of OUD, research on its efficacy among individuals exposed to illicit fentanyl or those with previous unsuccessful attempts with other opioid agonist therapies (OAT) is limited and controversial.

Case: We present a case of a 48-year-old male with severe OUD seeking treatment following a near-fatal fentanyl overdose. His previous treatment attempts with methadone and buprenorphine/naloxone-based OAT had been unsuccessful. As per local guidelines, he was started on SROM with subsequent cessation of opioid cravings and illicit drug use.

Discussion: This case report describes a patient entering early remission for OUD when treated with SROM following unsuccessful past treatment attempts on first-line oral medications. Future studies should seek to evaluate SROM-based OAT as a potential second-line treatment alternative for OUD.

Keywords

Opioid use disorder; opioid agonist therapy; slow release oral morphine; fentanyl; methadone; buprenorphine

INTRODUCTION

North America is facing an unparalleled public health emergency with skyrocketing opioid overdose related morbidity and mortality. In North America, more people are dying from

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accidental opioid related overdose than from motor vehicle accidents and homicides combined.¹ These deaths are primarily driven by untreated opioid use disorder (OUD) and the increasing contamination of the drug supply with illicitly manufactured fentanyl and other analogues.¹

The evidence strongly supports the use of opioid agonist therapies (OAT) (i.e., methadone and buprenorphine/naloxone) to decrease illicit opioid use and retain patients in care.² Retention in OAT, in turn, is associated with reduced morbidity, mortality and improved outcomes of related comorbidities such as HIV and hepatitis C.³ Unfortunately, studies indicate that less than half of the people who start OAT are retained in treatment at 6 months, severely undermining the public health impact of these therapies.² In this context, there is an urgent need to identify alternative strategies to attract patients into care, improve retention rates, and decrease opioid related deaths.

As part of a comprehensive approach to address the opioid overdose public health emergency, the province of British Columbia (BC) in Canada adopted a peer-reviewed provincial evidence-based guideline for the treatment of OUD.⁴ This guideline recommends buprenorphine/naloxone and methadone as first- and second-line treatment options, respectively. For patients who have been unsuccessful with these treatment options, the guideline suggests the use of slow release oral morphine (SROM) for non-pregnant adults on a cases-by-case basis. This recommendation is based on a growing evidence base suggesting that SROM may provide similar benefits to methadone-based OAT regarding illicit opioid use and retention in treatment, and with some additional advantages in terms of mental health and cravings.⁵ In BC, the delivery and monitoring of SROM-based OAT follows that of methadone-based OAT. In brief, patients typically receive ongoing clinical care for OUD, including prescriptions, from their treating physician, and self-administer the medication daily at a community pharmacy under witnessed ingestion from a pharmacist.⁴

Despite the emerging body of literature documenting the potential of SROM and increasing use of SROM-based OAT in some European jurisdictions, the clinical experience with this medication in North America is limited.⁴ We present a case of a patient who was placed on daily witnessed SROM for OAT, following failed treatment attempts with buprenorphine/naloxone and methadone. He subsequently showed dramatic improvement in functioning and cessation of all illicit substance use.

CASE PRESENTATION

A 48-year-old man with severe OUD according to DSM-5 (*Diagnostic and Statistical Manual of Mental Disorders, 5th Edition*) criteria presented to St Paul's hospital rapid access addiction clinic to discuss OUD treatment options following a recent overdose. The non-fatal opioid overdose event involved intravenous (IV) use of street "heroin" and resuscitation with naloxone in the field by a bystander. Urine drug testing at presentation to clinic was positive for fentanyl and negative for all other opiates, suggesting that the patient had consumed illicitly manufactured fentanyl rather than heroin, which may have contributed to his overdose event.

On history, the patient reported initial use of prescription opioids for pain following multiple musculoskeletal injuries to his back and knees in his youth. His opioid use rapidly escalated, and by age 20 he had transitioned to daily intravenous (IV) heroin use. At the time of this consultation, the patient was using IV heroin daily, IV cocaine 2–3 days per week, and smoking 15 cigarettes per day. He did not report use of alcohol or other substances. Apart from his opioid and stimulant use disorder, other relevant medical history included benign prostatic hypertrophy, osteoarthritis, gastroesophageal reflux, depression, anxiety and a past transient ischemic attack. His current medications included tamsulosin, ranitidine, paroxetine and rivaroxaban.

Prior to this consultation, the patient had a number of unsuccessful OAT attempts. He initially tried buprenorphine/naloxone, but reported ongoing pain and cravings. Subsequently the patient tried methadone, but had a number of side effects as well as cravings with ongoing heroin use. In 2012, he attended residential addiction treatment that resulted in one year of reported opioid abstinence before relapse.

During the current presentation, the patient was recommended another trial of buprenorphine/naloxone or methadone, including split dosing for possible improved analgesia, which he declined given his past negative experiences with these medications. In line with the BC guideline, and with the patient's consent, it was decided to initiate SROM 100 mg once daily, dispensed via daily witnessed ingestion at a local pharmacy. Follow-up clinical visits were scheduled bi-weekly to assess response and tolerability. SROM dose was up titrated by 50–100 mg per visit, up to a stabilized dose of 500 mg daily at week ten. From the second week on SROM, the patient reported decreasing cravings, better self-reported feelings of wellbeing, and improvement of chronic pain symptoms. After three weeks on SROM his urine drug tests were negative for illicit drugs. Ten weeks after initiation of SROM he was transferred from the stabilization clinic to a community provider on a stable dose of 500 mg daily, with no illicit opioid or stimulant use. He had returned to work as a chef after an extended period on social assistance. Up to his last consultation six months following initiation of treatment, SROM had been well tolerated with only mild constipation that managed with diet and over-the-counter medications.

Written consent was obtained from the patient.

DISCUSSION

We presented a case of a patient with severe and treatment refractory OUD, who did exceptionally well on SROM-based OAT, stopping all illicit drug use and returning to full time employment within ten weeks of SROM treatment initiation.

Strong evidence supports the use of methadone and buprenorphine/naloxone for the treatment of OUD. However, not everyone benefits from these two treatment options, with data showing that less than half of individuals initiating OAT with methadone or buprenorphine/naloxone are retained in treatment at six months.⁶ This is concerning as discontinuation of OAT has been consistently associated with heightened mortality risk;⁷ risk that is greatly augmented in an era with increasing contamination of the illicit drug supply with fentanyl.

In this context, SROM has emerged as an attractive alternative treatment option, with accumulating evidence suggesting that SROM might be as effective as methadone in reducing opioid use, with a similar safety profile.^{8–10} Some studies have also shown additional advantages of SROM such as shorter QT intervals¹¹ and improvements in patient-reported outcomes, including lower opioid craving,¹² better treatment satisfaction,¹³ and improved mental health.¹³ Future research should seek to elucidate the psycho-physiological pathways underlying these differences in patient-reported outcomes.

Although available evidence suggests that SROM may be a promising treatment option for OUD, it is important to note that only four clinical trials have evaluated its efficacy in this context (mostly compared to methadone), with high heterogeneity across studies. In addition, none of them have been conducted among individuals who have failed other treatment options, highlighting the urgent need for research in this area.¹⁴ If the evidence base for SROM as an alternative oral OAT agent grows, anticipating and addressing regulatory and systemic barriers that affect medication access and development of clinical guideline recommendations regarding this medication for treatment of OUD will be important for facilitating an expanded continuum of care for OUD.¹⁴

In conclusion, this case provides evidence that SROM may be an effective and acceptable treatment option for treatment refractory OUD, and should be further investigated in this context. In particular, given the significant mortality risk associated with untreated opioid use disorder in the fentanyl era, clinical studies confirming the potential of SROM as OAT should be an urgent public health priority.

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