

Opioid Use Disorder: Screening, Diagnosis, and Management

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Abstract

Over the past decade, the opioid crisis in Canada has been worsening. In 2019, over 3,800 people across Canada died due to an apparent opioid-related cause, which represents a 26% increase from just 3 years prior. Given North America's ongoing opioid crisis, and the contribution opioid-prescribing practices have had to date, a critical need exists to ensure that health care providers are not only educated about safe opioid prescribing but also are knowledgeable about how to effectively screen for, diagnose, and treat an individual with opioid use disorder.

Résumé

Au cours des dix dernières années, la crise des opioïdes au Canada n'a cessé de s'aggraver. En 2019, plus de 3 800 personnes au Canada sont décédées d'une cause apparemment liée à la consommation d'opioïdes, ce qui représente une augmentation de 26 % par rapport à seulement trois ans auparavant. Étant donné la crise des opioïdes qui sévit actuellement en Amérique du Nord et la contribution des pratiques de prescription d'opioïdes qui ont eu cours jusqu'ici, un besoin critique est à combler pour veiller à ce que les fournisseurs de soins soient non seulement formés sur la prescription sécuritaire des opioïdes, mais aussi bien informés sur le dépistage, le diagnostic et le traitement efficace d'un trouble lié à la consommation d'opioïdes.

Introduction

Canada is in the midst of an opioid crisis that has been progressively worsening. In 2019, over 3,800 Canadians died of an opioid-related cause, which represents a 26% increase from just 3 years prior in 2016.¹ Though British Columbia (BC) has been facing a disproportionate number of deaths per year, the opioid crisis is affecting communities from every province and territory across Canada, with similar trends being seen in the United States.²

While reasons for North America's recent increase in opioid-related deaths are certainly multifactorial, opioid-prescribing practices related to the treatment of acute and/or chronic pain

has previously been recognized as a significant contributor.³ Though Canadian data is lacking, prescription opioid misuse was found to be the second most common illicit drug used (after marijuana) in the previous month by surveyed Americans (aged 12 years or older) in 2018.⁴ Similarly, almost 20% of the 53 million Americans who reported past-year use of illicit drugs in 2018 reported the misuse of prescription opioids.⁴ While a significant proportion of individuals who misused prescription opioids did so to relieve physical pain (64%), the second most common reason cited was to feel good or get high (11%). Regarding the source of misused prescription opioids, approximately 51% were

given by, bought from, or taken from a friend or relative, while 37% obtained opioids directly through a prescription.⁴

Canada is now the second highest global opioid consumer, after the United States, with rates of pharmaceutical opioid use having tripled over the past decade alone.⁵ For many years, prescribers have been faulted for oligoanesthesia—the undertreatment of acute pain.^{6,7} To ensure pain was not dismissed and instead treated sufficiently, there was a push for physicians to treat pain more aggressively.⁸ In addition, pharmaceutical companies employed forceful, and sometimes deceiving, marketing strategies to increase opioid sales.^{9,10} Together, these influences have contributed to steep increases in opioid prescriptions over the past decade, in every province across Canada.¹¹ As recent evidence and guidelines are beginning to highlight, opioids have limited effectiveness in the treatment of chronic, noncancer pain.¹² Moreover, the risks of opioid use likely outweigh their potential short-term benefits when used to treat mild to moderate acute pain.¹³

Beyond increased rates of opioid prescribing, there is also evidence of high-risk prescribing practices. BC data, for example, demonstrate that among patients being prescribed methadone maintenance treatment for an opioid use disorder, approximately 35% also received a concurrent prescription for an additional opioid between 1996 and 2006.¹⁴ Furthermore, the number of opioid prescriptions per person per year nearly doubled within the same timeframe.¹⁴ Looking at the source of concurrent opioid prescriptions, the vast majority (74%) were prescribed to a patient by a physician that was not their methadone provider.¹⁴ Such a practice proves problematic as the co-prescription of opioids and methadone have important safety considerations as evidenced by the risk of fatal and nonfatal overdoses related to concurrent opioid use.^{15,16}

While opioid-prescribing practices have undoubtedly contributed to North America's opioid crisis, the presence of fentanyl (and its potent analogues) in the illicit drug supply cannot be ignored. In 2019, 77% of accidental, apparent opioid-related deaths in Canada involved fentanyl or one of its analogues compared to only 54% of apparent opioid-related deaths in 2016.^{1,17} The use of nonmedical prescription opioids, however, has previously been identified to be a risk factor for subsequent illicit opioid use (with some studies citing up to a 40-fold increased risk for the development of a heroin use disorder among those with a nonmedical prescription opioid use disorder compared to those without).^{18–24} More specifically, a 2013 national US study demonstrated that among individuals with both nonmedical prescription opioid use and heroin use in the preceding year, 77% reported their heroin use was concerned with nonmedical prescription opioids.²⁵ Accordingly, given North America's ongoing opioid crisis and the contribution opioid-prescribing

practices have had to date, a critical need exists to ensure health care providers are not only educated about safe opioid prescribing but also are knowledgeable about how to effectively screen for, diagnose, and treat an individual with opioid use disorder.

Opioid Use Disorder: Screening and Diagnosis

Historically, there has been a lack of focus on pain management or addiction medicine training in medical education (both in Canada and the United States). Accordingly, screening patients for either substance misuse or addiction is not routinely integrated into many clinician's existing workflows. Though Canadian data are lacking, one national survey of primary care physicians in the United States demonstrated 94% of respondents (n = 648) reported being unable to identify a substance use disorder among their adult patients.²⁶ Accordingly, being able to accurately screen for and diagnose opioid use disorder is of critical importance.

The Rapid Opioid Dependence Screen (RODS) is an eight-item survey that can provide targeted screening for opioid dependence (as defined by the Diagnostic and Statistical Manual of Mental Disorders [DSM], Fourth Edition) in either a clinical or research setting.²⁷ The instrument, on average, takes less than 2 minutes to administer and can be done individually or as part of a more thorough assessment. The RODS has demonstrated good-to-strong sensitivity (97%) and specificity (76%), among newly incarcerated HIV-infected individuals.²⁷ An individual screens “positive” if they respond “yes” to at least three questions. A “positive” screen should then be followed up with a formal diagnosis of opioid use disorder using the 11-item criteria from the DSM-Fifth Edition. The severity of opioid use disorder can further be classified as mild (score: 2–3), moderate (score: 4–5), or severe (score ≥ 6). Additional screening tools have been validated in various populations, for example, the Mini International Neuropsychiatric Interview (MINI) and the National Institute on Drug Abuse Modified Alcohol, Smoking, and Substance Involvement Screening Test (NMASSIST).²⁸ As each screening/ diagnostic tool has specific benefits and drawbacks in relation to reliability, validity, and time of administration, it is important to carefully consider the most appropriate choice dependent on the population at hand. Most importantly, any individual diagnosed with an opioid use disorder should be offered and initiated on evidence-based treatment in a timely fashion by either the patient's primary care provider or referral to a practitioner with expertise in addiction medicine.

Opioid Use Disorder: Management

In the spring of 2018, a national Canadian guideline for the treatment of opioid use disorder was published.²⁹ The guideline describes the need for the treatment of opioid use disorder to occur along a continuum, with treatment intensity matched

to disease severity. Furthermore, a need exists for ongoing reassessment to ensure a patient's treatment needs (which may evolve over time) are consistently being met. Harm reduction strategies (e.g., take-home naloxone kits, safe injection, or overdose prevention education) and/or psychosocial interventions (e.g., counselling, group therapy, residential treatment) should span the entire treatment continuum and be offered to all patients as standard practice.

Withdrawal management

Withdrawal management (e.g., detox) is considered merely symptom management in the realm of treatment modalities for opioid use disorder and, therefore, should not be used as a treatment option without additional support. Methadone and buprenorphine/naloxone can be used as a taper to reduce symptoms of opioid withdrawal, albeit with certain risks.³⁰ For example, many patients did not complete treatment and there were high rates of relapse during and after tapers, which results in the potential of overdoses and deaths.^{30,31}

In addition, although alpha₂-adrenergic agonists (e.g., clonidine) tend to relieve opioid withdrawal symptoms faster than a methadone taper and usually require a shorter length of treatment, they may also be associated with certain side effects including sedation, dry mouth, and/or hypotension.³² Conversely, buprenorphine/naloxone provides more rapid symptom relief for opioid withdrawal and its use is associated with higher rates of withdrawal management completion when compared to a methadone taper.¹⁹ Furthermore, compared to alpha₂-adrenergic agonists, buprenorphine/naloxone is more effective at relieving opioid withdrawal symptoms.³³ Regardless of which medication is used, it is important to note that withdrawal management should never be offered in isolation (e.g., without transition to ongoing maintenance therapy) as such an approach is associated with higher rates of relapse,²¹ HIV infection and transmission,²⁰ and increased morbidity and mortality.³⁴ In addition, pairing psychosocial interventions with medical management appears to be a helpful adjunct in the context of opioid withdrawal management.³⁵

Opioid agonist therapy

First-line treatment for opioid use disorder is opioid agonist therapy. Given its improved safety profile (and decreased risk for diversion), buprenorphine/naloxone is currently recommended as first-line therapy for opioid use disorder treatment. Buprenorphine is a partial opioid agonist, and confers a lower risk for sedation and respiratory depression, as well as a sixfold decreased risk for overdose when compared to methadone.^{36,37} Furthermore, the medication has few drug-drug interactions and is not associated with prolongation of the cardiac QT interval.³⁷

Compared to placebo, buprenorphine/naloxone is associated with increased rates of treatment retention (buprenorphine daily dose >2 milligrams [mg]) and suppression in illicit opioid use (buprenorphine daily dose ≥16 mg).³⁸ Therapeutic dosing of buprenorphine/naloxone can be achieved within 24–72 h, and given its safety profile, the medication can be prescribed for take-home dosing earlier than methadone. Moderate to severe withdrawal from full opioid agonists (either prescribed or illicit) must be achieved for a period of time prior to induction to prevent the occurrence of precipitated withdrawal. While more novel induction techniques (e.g., the Bernese method of buprenorphine/naloxone microdosing) can be successful without the need for the patient to experience opioid withdrawal, such an approach is currently off-label.³⁹ Specific details regarding how to prescribe buprenorphine/naloxone for opioid use disorder treatment can be found in province-specific guidelines.^{12,40–42}

Methadone, a full opioid agonist, has been available as a treatment option for opioid use disorder since 1965. Accordingly, its efficacy is supported by a large body of literature, spanning various countries, jurisdictions, and socioeconomic settings.^{43,44} Compared to placebo, methadone maintenance therapy has been shown to be significantly more effective in addiction treatment retention, suppression of illicit opioid use,⁴³ reduction in mortality (2.6 versus 12.7 per 1000 person years),⁴⁵ and reduction in HIV infection.⁴⁶ When buprenorphine/naloxone and methadone are compared, both medications (when prescribed at medium or high doses [≥ 7mg daily buprenorphine/naloxone, ≥ 40mg daily methadone]) have proven equally efficacious for retention in addiction treatment and reduction in illicit opioid use.³⁸ Given the prolonged half-life of methadone, dose adjustments are currently recommended every 3 to 7 days (depending on specific provincial guidelines and risk of patient methadone toxicity).^{12,47} Accordingly, it can take weeks or even months to achieve a therapeutic dose. During this period, it is not uncommon for patients to discontinue treatment, experience adverse events, or overdose.⁴⁸ Specific details regarding how to prescribe methadone for opioid use disorder treatment can be found in province-specific guidelines.^{12,40,49–53}

Novel and emerging treatments

Slow-release oral morphine (SROM) is a 24-h, extended release formulation of morphine that can be prescribed as an alternative treatment option to either methadone and/or buprenorphine/naloxone for opioid use disorder. Although a 2013 Cochrane review did not show conclusive results in treatment retention or effectiveness of SROM, it is important to note that only three studies were available at the time and thus included in the review.^{54,55} Since then, data have emerged demonstrating the efficacy of SROM (when compared to methadone) with regard

to similar rates of addiction treatment retention,⁵⁶ a reduction in illicit opioid use and cravings,⁵⁵ as well as no interaction with the cardiac QTc interval.⁵⁶ If buprenorphine/naloxone or methadone is unsuccessful or contraindicated for the treatment of opioid use disorder, SROM should be considered. Of note, a portion of the studies investigating SROM have been uncontrolled, pointing to a need for more robust trials. Therefore, SROM is not recommended as a first-line treatment option for opioid use disorder. Health care providers should seek expert consultation from an addiction medicine specialist prior to prescribing.^{12,57}

Injectable opioid agonist therapy (iOAT), such as diacetylmorphine (DAM), the active ingredient in heroin, has been offered as a treatment for severe opioid use disorder in several European settings for decades.^{58,59} Individuals who have experienced treatment failure with oral opioid agonist therapy (e.g., buprenorphine/naloxone, methadone, SROM) may be considered for treatment with iOAT, which has demonstrated efficacy in improving addiction treatment retention, reducing illicit opioid and stimulant use, ensuring decreased criminal activity, and improving social functioning.⁶⁰ In Canada, injectable DAM is currently only available through the federal Special Access Program, which greatly limits its availability as a treatment option.⁶⁰ In 2015, injectable hydromorphone was found to be noninferior to injectable DAM in a Vancouver-based randomized controlled trial.⁴¹ Subsequent to this, injectable hydromorphone was approved as a treatment option for severe opioid use disorder among Canadian adults in the spring of 2019. A few months later, Canada adopted national iOAT guidelines for the treatment of opioid use disorder.⁶¹ Of note, however, prescribing of iOAT for the treatment of opioid use disorder is limited to health care providers with appropriate training and expertise.

Antagonist therapies

Naltrexone is an opioid antagonist that binds to opioid receptors and blocks the effects of other opioid agonists. Oral naltrexone has been evaluated as a treatment option for opioid use disorder, but compared to placebo or no treatment, the medication demonstrated no significant difference in treatment retention or abstinence rates in a 2011 meta-analysis.⁶² Compared to its oral counterpart, extended-release naltrexone has been shown to increase adherence to therapy, partially attributed to its intramuscular route of administration.⁶³ In addition to decreased opioid cravings when compared to methadone, patients who use extended-release naltrexone for OUD have improved treatment retention and reduced illicit opioid use overall, when compared to placebo.⁶⁴ In contrast to the United States, extended-release naltrexone is not available to Canadians unless it is approved through Health Canada on a case-by-case basis. In addition to

the hurdle of availability, patients are required to pay for it, as it does not fall under provincial medical coverage.

Conclusion

Over the past decade, the opioid-related death toll has continued to increase, prompting a public health emergency in both Canada and the United States. Though reasons for the current opioid crisis are multifactorial, health care providers' opioid-prescribing practices and the prevalence of fentanyl and other potent analogues in the illicit drug supply have been highlighted as significant contributors. Moving forward, if we are ever to turn the tide on the opioid epidemic a critical need exists to ensure health care providers are not only educated about safe opioid prescribing but also are knowledgeable about how to effectively screen for, diagnose, and treat an individual with opioid use disorder. Furthermore, opioid agonist treatment (e.g., buprenorphine/naloxone, methadone) should be routinely offered to any patient identified to have an opioid use disorder to prevent the negative consequences associated with ongoing use.

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