Translational Perioperative and Pain Medicine

ISSN: 2330-4871

Mini-Review | Open Access Volume 11 | Issue 3

An Overview of Commonly Prescribed Opioids and Their Non-Medical Usage

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Abstract

The opioid epidemic is one of the most significant current public health crises in the United States. This review examines the medical and non-medical use of commonly prescribed opioids, including oxycodone, hydrocodone, morphine, codeine, fentanyl, methadone, and buprenorphine. In medical settings, these opioids play essential roles in pain management, palliative care, and opioid use disorder treatment under strict supervision. However, their misuse in non-medical contexts contributes significantly to addiction, overdose fatalities, and evolving patterns of substance use, such as the increased prevalence of synthetic opioids like illicit fentanyl. The review highlights the complex interplay between prescribing practices and their unintended consequences such as the shift from prescription opioid misuse to heroin and synthetic opioids. Effective strategies to address the current opioid crisis must balance the medical necessity of prescription opioids with drug abuse prevention, harm reduction, and education initiatives to mitigate misuse and associated harms.

Keywords

Opioid epidemic, Prescription opioids, Non-medical use of opioids, Opioid misuse, Prescription drug misuse

Introduction

The opioid epidemic in the United States remains one of the most pressing public health crises, with overdose deaths reaching unprecedented levels in recent years. In 2021 alone, over 100,000 drug overdose deaths were reported, a sharp increase from approximately 78,000 in 2020 [1-3]. The COVID-19 pandemic has been identified as a catalyst for increased opioid-related overdose deaths, likely resulting from disruptions in treatment services and reduced access to harm reduction measures, including safe injection sites [4]. This escalating crisis continued into 2022, with preliminary reports indicating over 109,000 drug overdose deaths, approximately 70% involving synthetic opioids like illegally manufactured fentanyl and analogs of IMFs [5]. In response, the FDA's approval of over-the-counter naloxone nasal spray has increased its accessibility, playing a role in the decline of opioid-related deaths beginning in 2024 [6]. Additionally, data from the western United States suggest a shift from heroin injection to smoking fentanyl analogs, highlighting evolving and unpredictable patterns of opioid misuse [5].

The landscape of opioid misuse has undergone significant changes over the past decade. The number of U.S. adults who inject drugs surged from an estimated 774,000 in 2011 to nearly 3.7 million in 2018, driven largely by a transition from prescription opioid misuse to the use of heroin and synthetic opioids [5]. In the United States, there is a strong focus on the individual's right to live free from pain, with a priority placed on ensuring that a patient in pain has access to opioids [7]. While efforts to reduce opioid prescribing aimed to address misuse, overly restrictive policies potentially increased risks of overdose. Policies encouraging opioid tapering and discontinuation in chronic pain patients have been linked to a rise in illicit opioid use and higher rates of both non-fatal and fatal overdoses [8]. In 2021, prescription opioids were still implicated in a significant number of overdose deaths as 20.7% of all opioid-related deaths involved prescription opioid medications [9].

This paper aims to examine the role of commonly used opioids, including oxycodone, hydrocodone, morphine, codeine, fentanyl, methadone, and buprenorphine in both medical and non-medical settings. By exploring their medical applications and the risks associated with misuse, this work seeks to contribute to a deeper understanding of the opioid crisis.

Oxycodone

In the hospital setting, oxycodone is typically prescribed for legitimate medical reasons, particularly for chronic pain. Oxycodone is often part of a medically supervised pain management regimen, where it is used for specific conditions like "back/neck pain, abdominal/pelvic pain, musculoskeletal pain and migraine/headache" [10]. In this context, oxycodone is prescribed with careful monitoring of dosage and usage, and its administration is based on medical need.

In contrast, oxycodone's use in the non-hospital setting, where it is often misused, is associated with a

much higher level of risk. The misuse of prescription opioids like oxycodone is widespread, as evidenced by the finding that in 2019, which found that approximately 3.0 million US adults abused oxycodone [11]. Unlike in the medical setting, this misuse occurs without medical supervision and often involves individuals taking the drug for recreational purposes or self-medication, which significantly increases the likelihood of addiction and overdose.

Hydrocodone

Hydrocodone is primarily prescribed by physicians for chronic pain management. Hydrocodone is the most prescribed opioid in the United States: "the most commonly prescribed opioid for chronic therapy was hydrocodone, followed by oxycodone and tramadol" [10]. In this controlled, medical environment, hydrocodone is used specifically to address severe pain conditions under the supervision of healthcare providers, ensuring it is prescribed and used according to medical guidelines.

The non-hospital setting often sees hydrocodone being misused, contributing to the ongoing opioid crisis. In 2019, it was reported that "an estimated 4.9 million US adults...misused hydrocodone" [11]. This highlights how hydrocodone, originally prescribed for medical purposes, is diverted for recreational or non-medical use. Misuse of hydrocodone outside of the medical setting can lead to addiction, overdose, and a variety of health complications due to the lack of professional supervision and dosage control.

Morphine

Morphine is frequently prescribed in hospital settings, particularly for cancer patients and individuals in hospice care, to manage pain. Morphine remains a staple in end-of-life care, as evidenced by its prescription to "52.8% of hospice beneficiaries," underscoring its central role in providing palliative relief [12]. This shows that morphine is a commonly prescribed opioid for those with severe, end-of-life conditions, where its use is closely monitored to alleviate pain in terminal stages of illness. Morphine's role in such settings is therapeutic, designed to improve quality of life in patients suffering from significant pain, particularly in cancer and hospice care. The use of morphine in hospital settings has seen a decline, particularly among cancer patients. The study found that the "annual prevalence of opioid dispensing claims declined from 40.2% in 2013 to 34.5% in 2018" [13], with a notable drop in opioid claims for metastatic cancer patients (a decline of 19.8%) and other cancer types. This trend suggests a movement toward more cautious prescribing of opioids, such as morphine, in response to growing concerns about addiction and opioid misuse.

In the non-hospital setting, morphine can be misused, though it is less commonly highlighted in the available data compared to other opioids. While specific misuse data for morphine is not provided, the trend of reduced prescribing could be linked to increased efforts to control opioid diversion and prevent misuse in non-medical contexts.

Codeine

In the hospital setting, codeine is used less frequently than stronger opioids like morphine but is still prescribed for pain management, particularly for milder pain. Codeine is used in specific medical contexts, such as post-operative pain or as a cough suppressant and is often prescribed in combination with other medications for short-term use [14]. The prevalence of codeine prescriptions is less commonly associated with long-term chronic pain management when compared to morphine or hydrocodone. It is important to note that codeine is risky for youth. In 2017, the FDA restricted the use of codeine medicines in children as those under 12-years-old face an elevated risk of respiratory depression and potentially fatal outcomes to these opiates [15]. This highlights the need for strict guidelines on opioid prescriptions for young patients to minimize harm and prevent early dependence.

The misuse of opioids, including codeine, is widespread in non-hospital settings. According to one source, "Among US youth aged 12-17 years, 25.0% reported use of any psychoactive prescription medication assessed, and 5.7% reported past-year use of at least two psychoactive prescription medications" [16]. Among those using opioids, misuse is common, with 20.9% of these individuals (1.3 million) reporting misuse, and 3.4% classified as having a substance use disorder [16]. Codeine, often available in combination with other medications like acetaminophen (in products such as Tylenol with Codeine), is a prescription opioid that is often misused, particularly by youth [17]. This demonstrates that codeine, despite being used in medical settings, is frequently diverted for recreational purposes or to manage undiagnosed pain in non-hospital contexts. Opioid misuse remains a significant concern, particularly among those who might misuse codeine alongside other psychoactive substances.

Fentanyl

In hospitals, fentanyl is mainly administered as a sedative for intubated patients and for managing severe pain, especially in those with renal failure [18]. Due to its potency compared to other opioids, fentanyl plays a significant role in managing chronic pain in patients who are tolerant to other opioids. Furthermore, fentanyl's versatility extends beyond pain management, as it can be combined with certain

medications to get the desired effect, showcasing its broader clinical applications: "Combining fentanyl with certain neuroleptic medications for therapeutic neuroleptanalgesia highlights its versatility beyond typical pain management scenarios" [18]. An intravenous drip is utilized to precisely control the dosage.

In the non-hospital setting, fentanyl, an ultra-potent synthetic opioid, is now a major contributor to overdose deaths. Often produced illicitly, it is "up to 100 times more potent than morphine" and is commonly mixed with other drugs like heroin, cocaine, or methamphetamine, often without users' knowledge [19]. Concerningly, among individuals with opioid use disorders, 29.8% of those testing positive for fentanyl were unaware that they had been exposed to fentanyl, highlighting the dangers of accidental exposure [20]. Fentanyl is a major issue among adolescents as well: "In 2021, fentanyl was identified in 77.1% of overdose deaths among US adolescents, a 23.5-fold increase from 2010" [21]. This highlights the need for increased awareness and prevention efforts.

Methadone

Methadone is commonly prescribed as a treatment for individuals with opioid use disorder and has been the most extensively researched and widely used treatment for opioid use disorder. As a full agonist opioid, methadone treatment helps prevent overdose deaths and supports better health outcomes for individuals undergoing treatment for opioid use disorder [22]. The drug is linked to decreased overdose fatalities, reduced rates of HIV and hepatitis C transmission, lower criminal activity, decreased healthcare expenses, and improved treatment retention, which is strongly tied to better long-term outcomes [23].

Although the distribution of methadone is very controlled and federally regulated, methadone, just as other opioids, are often abused for illicit purposes. In the United States, methadone-related overdoses are primarily associated with its use as a prescription pain reliever [24]. Despite its effectiveness in managing chronic pain and treating opioid use disorder, methadone carries a high risk of misuse due to its effects as an opioid. These factors highlight the continuous challenge of balancing methadone's medical benefits with its potential for misuse and harm.

Buprenorphine

Similarly to methadone, buprenorphine is an opioid that is commonly used in the hospital setting to treat opioid use disorder. Buprenorphine, a partial agonist of the opioid receptor, is expected to see increased use in treating opioid use disorder in ICU settings as regulations on its prescription are becoming more flexible [25]. Compared to methadone, buprenorphine is milder and is less likely to lead to an accidental overdose: "Buprenorphine causes less respiratory depression than methadone due to its ceiling effect and, thus, has lower overdose potential" [26].

As with other opioids, buprenorphine bas been used illicitly among the public. After FDA approval, instances of illicit buprenorphine use were reported, with abuse, misuse, and diversion appearing to increase as prescribing rates rose [27]. Despite these concerns, buprenorphine remains a critical tool in managing opioid use disorder. The importance of balancing accessibility for patients in need while minimizing the potential for misuse and overdose cannot be understated.

Conclusions and Potential Solutions

In medical settings, opioids like oxycodone, hydrocodone, morphine, codeine, fentanyl, methadone, and buprenorphine are prescribed under strict supervision to manage pain, particularly in cases of chronic illness, cancer, or hospice care. In contrast, non-hospital misuse of these drugs is widespread, often involving polysubstance use and contributing to addiction, overdose, and fatalities. While medical use focuses on alleviating pain, non-medical misuse of opioids highlights the urgent need for prevention and control measures.

One key solution lies in expanding access to naloxone. Naloxone is a targeted opioid antagonist that rapidly attaches to mu-opioid receptors, blocking the effects of drugs such as heroin, fentanyl, and other prescription opioids. Within 2 to 3 minutes of administration, it swiftly counteracts the effects of an overdose [28]. Over-the-counter availability and widespread distribution through community programs and pharmacies have significant potential in reducing overdose-related deaths. Distributing naloxone within communities has been shown to lead to a reduction in the number of opioid overdose fatalities [29]. Policymakers and healthcare providers should further normalize naloxone availability in both clinical and non-clinical settings.

Long-term, the development of non-addictive pain medications and non-opioid analgesics represents a promising strategy. Research into innovative pain management therapies, including cannabinoids, nerve-targeting treatments, and alternative pharmacological approaches are potential avenues identified that may be able to reduce reliance on opioids for chronic pain [30]. Advances in personalized medicine, such as the use of biomarker data to customize treatments, could also improve pain management strategies by offering opioid-free solutions tailored to individual patients.

The use of a short-acting opioid to taper off a long-acting opioid is a potential solution for patients [31]. Methadone and buprenorphine have long half-lives,

which is unfavorable. Short-acting, low-addiction opioids may provide safer, quicker tapering compared to methadone and buprenorphine. Dezocine has been identified as a short-acting drug that is a partial agonist at the mu-opioid receptor without significantly activating the beta-arrestin pathway [32]. Further studies are needed to explore its potential for reducing opioid use, but its unique pharmacological profile suggests that it could offer a safer, more efficient alternative for tapering. This could potentially reduce the risk of addiction and overdose associated with current long-acting opioid therapies [31].

Conflicts of Interest

None.

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Citation: Yoon JJ. An Overview of Commonly Prescribed Opioids and Their Non-Medical Usage. Transl Perioper Pain Med 2024; 11(3):689-693

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Additional publication details

Journal short name: Transl Perioper Pain Med

Received Date: December 31, 2024

Accepted Date: January 15, 2025

Published Date: January 17, 2025