Pacific Journal of Health

Volume 4 | Issue 1 Article 1

2021

Opioids and Dentistry

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Abstract

Dental professionals are among the leading prescribers of opioids in the United States and play a significant role in the current opioid epidemic. While dental professionals prescribe these potent pain killers to provide relief to patients, the serious implications of their prescription and distribution must be considered. This manuscript covers the science behind opioids, history of the opioid epidemic, the affliction it is currently causing in the U.S., the immense impact dentists have in providing opioid prescriptions along with gross over-prescription practices, and much more. Other topics discussed include alternative pain management, safe prescribing practices, naloxone, and how dentists can help patients with opioid use disorder (OUD).

Keywords

Opioids, Dentistry, Safe Prescribing, Alternative Pain Management, Naloxone

Section I: Opioids

I.A What are Opioids?

Opioids are a class of powerful analgesics that are often prescribed by health care professionals for the treatment of moderate to severe pain. Some of the commonly prescribed opioids include oxycodone, hydrocodone, morphine, and methadone[23]. Other forms of opioids exist such as fentanyl, which is a synthetic opioid up to 100x more potent than morphine[32]. Opioid prescriptions are often limited to a few days or a week due to the high risk of developing an addiction.

Opioids work by binding to opioid receptors. The three types of opioid receptors are mu, delta, and kappa. The binding of opioids to these receptors causes pre-synaptic Ca2+ channels to close and post-synaptic K+ channels to open, which reduces the chance for action potential propagation and decreases pain signals to the brain[24]. Depending on the type of opioid and its affinity to the different opioid receptors, these drugs can have various effects on the body. Side-effects of opioids include nausea, vomiting, hyperalgesia, constipation, dry mouth, and development of tolerance and physical dependence for the drug[23]. Other more serious side-effects of opioid use include immunosuppression, hormonal changes, and respiratory depression[4]. Respiratory depression is the most feared complication of opioid mis-use and can lead to subsequent death due to insufficient oxygen intake.

Knowing which opioids act as full agonists, partial agonists, antagonists, or with mixed activity is important to better understand their effects and potential for harm.

- Partial agonists have a “ceiling effect”, which means that there is a dosage above which additional drug administration does not produce additional analgesia or respiratory depression on the body.

- Full agonists do not have the protection of a “ceiling effect”, meaning that administering more of the drug induces additional analgesia and respiratory depression. The danger with full agonists is their increased likelihood of causing overdose and severe respiratory depression when taken at higher doses, leading to subsequent death.

- Opioid antagonists are competitive inhibitors for the opioid receptors and their binding reverses the effects of opioid agonists[33]. These antagonists can reverse an opioid-induced overdose and save lives if administered in time.

- Opioids with mixed activity include the agonist-antagonists. These opioids have properties from both agonists and antagonists which create varying effects depending on their interactions with the opioid receptors. One example of a mixed agonist-antagonist is nalbuphine, which acts as an agonist at kappa receptors, but as an antagonist at mu receptors[14]. The use of mixed agonist-antagonist opioids offers mild-moderate pain relief and a ceiling effect, reducing the number of negative side-effects and potential for abuse as compared to the full opioid agonists.

Table 1. Classification of opioid agonists and antagonists[36]

Full agonists	**Partial agonists**	**Mixed agonist-antagonists**	**Antagonists**
Morphine	Buprenorphine	Nalbuphine	Naloxone
Codeine	Meptazinol	Pentazocine	Naltrexone
Oxycodone		Nalorphine	Nalmefene
Hydrocodone		Butorphanol	Diprenorphine
Hydromorphone			
Levorphanol			
Methadone			
Heroin			
Fentanyl			
Tramadol			

Another interesting way to characterize opioids is whether they are made from naturally occurring sources, semi-synthetically, or purely synthetic methods. Table 2 summarizes the common opioids into these categories.

Table 2. Classification of naturally-derived and synthetic opioids[28]

Natural	**Semi-synthetic**	**Synthetic**
Morphine	Heroin	Fentanyl
Codeine	Oxycodone	Methadone
	Hydrocodone	
	Hydromorphone	
	Buprenorphine	

Section II: The Problem

II.A The Opioid Crisis

The opioid epidemic in the United States refers to the dramatic increase in abuse, overdoses, and deaths related to opioid misuse following the rise in opioid prescriptions in the 1990s. The history of this crisis can be described in three distinct waves.

- The first wave began in the late 1990s with the increase in opioids prescribed by doctors at the recommendation of pharmaceutical companies, who assured the medical community that patients would not become addicted to these opioid pain relievers[26].
- The second wave began in 2010 and was marked by rapid increases in overdose deaths involving heroin[34].
- The third wave began in 2013 with the rise of synthetic opioids, such as fentanyl, which can be dangerously more potent than previous opioids such as morphine.

The CDC estimates that between 1999-2017, more than 702,000 people have died from a drug overdose with opioid-related overdoses accounting for 68% of these deaths. On average, 130 Americans die every day due to opioid overdoses[2].

The tragic loss of human life caused by the opioid crisis is compounded by a massive economic debt. In a report published by the Society of Actuaries in 2019, the estimated total economic burden in the U.S. caused by the opioid crisis between 2015-2018 was $631 billion[6]. Excess healthcare spending ($205 billion), mortality costs ($253 billion), criminal justice ($39 billion), assistance programs ($39 billion), and lost productivity ($96 billion) were included in this estimate. 29% of the total economic burden was estimated to be borne by the federal, state, and local governments while the remaining 71% was borne by the private sector and individuals.

Clearly, the consequences of the opioid crisis extend far beyond those directly involved with addiction.

The opioid epidemic undoubtedly affects every state in the US, however some states seem to be affected more severely than others. Fig. 1 below illustrates the overdose death rates involving opioids across states in the US in 2018. A closer look into the data reveals that states with higher opioid prescription rates do not always have proportionally high rates of death due to opioid overdoses. For instance, while West Virginia lead the country in highest death rate due to opioid overdose (42.4%) with an equally high rate of opioid prescriptions (69.3%), Mississippi showed a relatively low opioid death rate (6.1%), yet its opioid prescription rate was reported to be (76.8%), even higher than West Virginia's. This finding suggests that the opioid crisis in America is a complex issue with various contributors to its lethal outcomes. Each state is faced with unique challenges, socioeconomic differences, governmental involvement, assistance, and policies that all play a part in how each population is affected by the opioid crisis. While many disparities exist and contribute to the opioid crisis, the extremely high rates of opioid prescriptions distributed in the US is an issue that must be addressed.

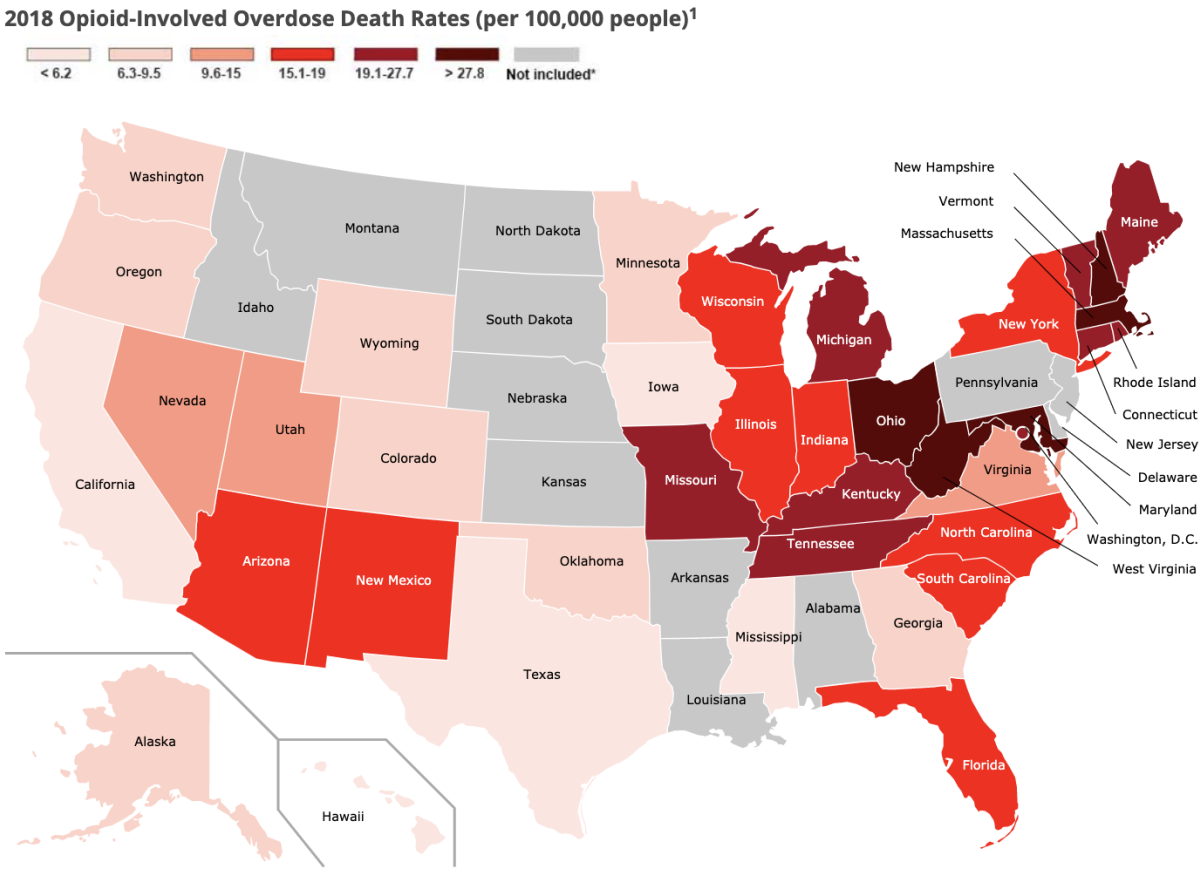

Figure 1. Opioid-Involved Overdose Death Rates in the United States in 2018[21]

II.B Dentistry's Impact

In the United States, dental professionals are among the leading prescribers for immediate release opioids, such as hydrocodone and oxycodone, which are frequently abused and used nonmedically. A 2011 study found that dentists prescribed 12% of immediate release opioids in the US, only slightly behind family physicians at 15%[7]. A comparative study found that in 2016, dentists in the US wrote 11.4 million opioid prescriptions while dentists in England wrote only 28,082. Dentists in the US wrote a greater proportion of opioid prescriptions (35 prescriptions per 1000 people) while English dentists only wrote 0.5 prescriptions per 1000 people.

Additionally, US dentists wrote a greater variety of opioids with stronger potentials for abuse, such as oxycodone, compared to dentists in England who solely prescribed dihydrocodeine (less-potent opioid)[30]. This study calls attention to the stark contrast of prescribing practices between the United States and England despite having similar patterns of dental care, oral health quality indicators, and incidence of dental disease. Another study conducted by Suda et al. found that 29% of opioids prescribed by dentists exceeded the recommended morphine equivalents and 53% exceeded the 3-day supply for management of acute pain as recommended by the CDC[31].

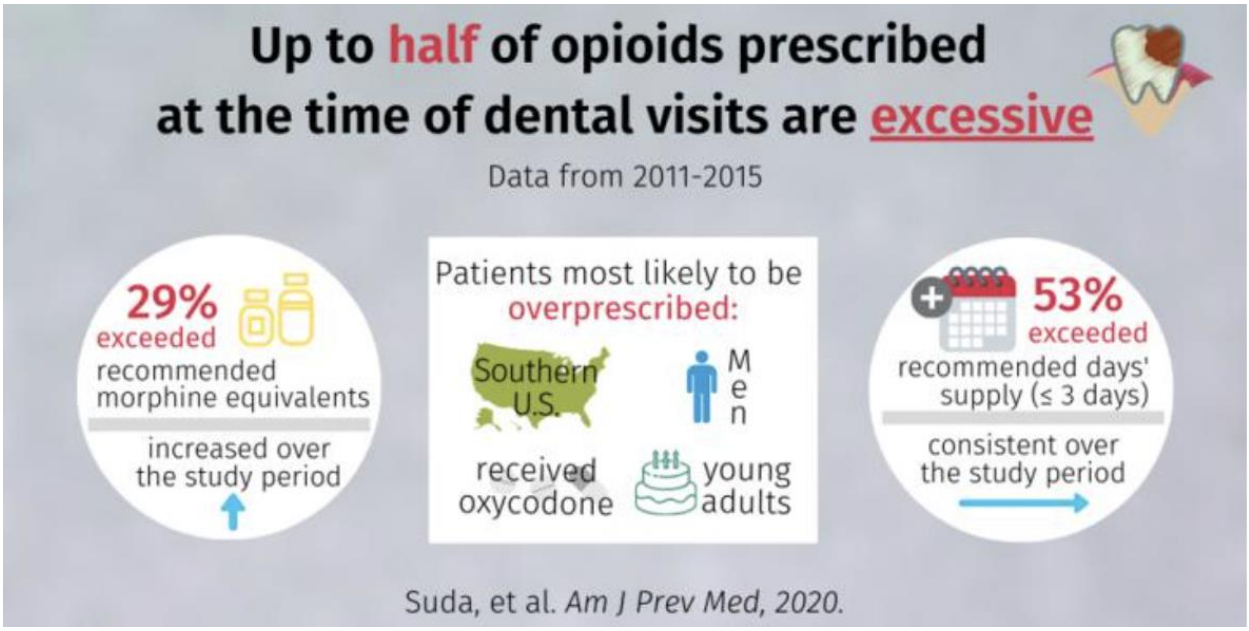

Figure 2. Opioid prescriptions from dentists inconsistent with CDC guidelines[38]

An even more alarming statistic is that dentists are the leading prescribers of opioids to adolescents, who are at increased risk of developing opioid addiction. In 2009, dentists wrote 31% of opioid prescriptions for adolescents aged between 10 to 19 years old[37]. A study conducted by Gupta et al. found an acute increase in the opioid prescriptions given by dentists

for patients aged 11 through 18 between the years of 2010 (99 per 1000) to 2015 (165 per 1000). Of these opioid prescriptions written, 31% were prescribed after nonsurgical dental visits[15]. One study of high school seniors and nonmedical use of opioids found that approximately 27.1% of misused opioids were obtained from leftover personal prescriptions given by their dentist[18]. A study conducted by the University of Michigan found that patients who received opioids after wisdom teeth extractions were 2.7 times as likely to refill their opioid prescription months after their procedure, indicating a use beyond what is needed for post-op pain[16]. The potential for abuse and development of addiction to opioids is evident and dental professionals must carefully consider these consequences before writing a prescription for opioids.

Figure 3. Likelihood of refilling an opioid prescription after wisdom teeth extractions[35]

Section III: The Solution

III.A Alternative Pain Management

The next practical topic to discuss is how to manage moderate to severe pain without the use of opioids. The use of NSAIDS such as ibuprofen to effectively control post-op pain has been studied for decades with comparisons to acetaminophen as a common pain relief alternative. These studies provide evidence that ibuprofen is superior to acetaminophen in relieving pain in cases involving inflammatory processes. One study found that 400mg ibuprofen produced greater peak effect and duration of action for pain relief as compared to 1000mg acetaminophen in patients who had undergone dental impaction surgery[5].

A likely explanation for this finding is based on the mechanism of action of ibuprofen, which is a non-steroidal anti-inflammatory drug (NSAID)[13]. NSAIDs specifically inhibit the enzyme cyclooxygenase (COX) which typically produces prostaglandins. Prostaglandins are involved in the inflammation process which can trigger the sensation of pain when excessive prostaglandins are produced. Ibuprofen, an NSAID, inhibits prostaglandin synthesis and effectively relieves pain caused from inflammation that occurs during healing processes or acute infections. Acetaminophen has analgesic and antipyretic effects; however, it lacks the anti-inflammatory properties of NSAIDs[12].

A Cochrane systematic review published in 2014 evaluated the efficacy of ibuprofen and acetaminophen in pain management after wisdom teeth extractions. This review found that 400mg ibuprofen produced at least 50% of maximum pain relief in 47% more patients compared to patients who received 1000mg acetaminophen[3]. A combination drug containing both 400mg ibuprofen and 1000mg acetaminophen achieved this same level of pain relief in 77% more

patients than either drug alone. Other studies have found similar results regarding improved pain relief when ibuprofen and acetaminophen are taken simultaneously to control post-op pain[19]. One study directly comparing the efficacy of ibuprofen to ibuprofen combined with various dosages of oxycodone found evidence to suggest that ibuprofen alone is just as effective for pain relief [8]. The study found that when 400mg ibuprofen was compared to 400mg ibuprofen + 2.5mg, 5mg, and 10mg oxycodone, only the 10mg oxycodone group showed faster onset of pain relief. The groups taking oxycodone experienced more adverse effects such as nausea, drowsiness, and vomiting.

The main take away from these studies is that even moderate to severe pain can be successfully managed with non-opioid medications such as ibuprofen (NSAIDS) and acetaminophen.

Suggested post-op pain management:[22]

- 600mg ibuprofen taken up to 4x/day, first dose taken immediately following extraction or surgery.
    - Additional acetaminophen taken as needed respecting the 4g/day maximum dose.

Cases of more severe pain or contraindication for ibuprofen:[22]

- Vicodin 5/500, 7.5/500, 7.5/750 (hydrocodone/acetaminophen) can be prescribed (max daily dose is 8, 6, and 5 tabs, respectively). Limit to 2-3 day supply.
    - Additional ibuprofen 600mg can be taken up to 4x/day except when contraindicated.

III.B Safe Prescribing

If opioids are to be prescribed, it is important to use safe prescribing practices.

1. Only dispense as many pills as needed for expected pain duration
2. Utilize the prescription drug monitoring program (PDMP)
3. Encourage proper disposal of unused/extra pills

-"Providers should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioid pain relievers (3 or fewer days will usually be sufficient)." [20]

It sounds reasonable to only prescribe as many pills as needed, however patients are routinely given excessive amounts of opioids for procedures that should only require a few days of pain medication. An alarming statistic reported from the CDC found that in 2012, health care providers wrote 259 million prescriptions for opioids, enough for every adult in the United States to have a bottle of pills[10]. A study analyzing the prescribing practices of dentists between 2011-2015 found over half of the opioid prescriptions exceeded the recommended limit of 3 days[31]. This study also found that 29% of opioids were prescribed after procedures expected to produce only mild post-op pain. Overprescription of opioids is prevalent among both medical and dental providers and must be addressed through education, advocacy, and policy.

PDMPs

In an effort to reduce the diversion and misuse of opioids and other prescription drugs, prescription drug monitoring programs (PDMP) are being utilized across the U.S. PDMPs are statewide electronic databases that track controlled substance prescriptions and allow authorized providers access to data such as types and dosages of prescriptions dispensed to patients. PDMPs can improve patient safety by identifying patients receiving opioids from multiple providers, calculating total opioids prescribed per day (in MME/day), and keeping track of other prescribed substances which may have dangerous interactions, such as opioids and benzodiazepines. While states vary on requirements, the CDC recommends providers check PDMPs every 3 months and before any opioid prescription[29]. Ultimately, PDMPs supply providers with information to help identify patients who may suffer from drug addiction and allow for discussions with patients to express concern and sincere interest in their safety.

Disposing of unused opioids

Given the overprescription practices seen in the U.S., it is no surprise that having unused or extra prescription pills is common. People often hold on to these extra pills in case they need them in the future, however the risk this poses can be devastating. Individuals who abuse opioids often use leftover pills that were originally prescribed for friends and family. Even more severe consequences can occur if children or pets ingest these leftover prescription pills, leading to death in some cases. The FDA recommends proper disposal of leftover prescription drugs as soon as possible to avoid these serious consequences.

Options for proper disposal include take-back events hosted by public health departments, disposal by mail to pharmacies, and secure collection receptacles located throughout communities. If these options are unavailable, some medications such as opioids may be disposed of by flushing down the toilet. Traces of prescription drugs have been found in the environment such as in lakes and streams, however the FDA claims that most of these come from the urine and feces of individuals taking these prescription drugs. The toll flushing prescription drugs has on the environment is considered negligible when compared to the harm unused opioids cause through accidental or illicit use[9].

One study conducted at a university-affiliated oral surgery clinic found a 22% absolute increase in behavioral intention to utilize the recommended pharmacy-based opioid disposal program simply by informing patients of its existence[17]. Dentists can help educate patients about these options for prescription drug disposal after prescribing opioids to help encourage proper discarding of extra pills.

III.C Naloxone

Naloxone, also known by its brand name Narcan, is a rescue medication designed to reverse an opioid overdose. Naloxone is an opioid antagonist that works by binding to opioid receptors to block the effects of opioids on the body[27]. If administered in time, naloxone can successfully restore normal respiration in a person suffering from respiratory depression due to opioid overdose. The U.S. Surgeon General published an advisory in 2018 emphasizing the importance of naloxone as a life-saving medication. In this advisory, the importance of knowing how to use naloxone and keeping it within reach is highlighted.

I, Surgeon General of the United States Public Health Service, VADM Jerome Adams, am emphasizing the importance of the overdose-reversing drug naloxone. For patients currently taking high doses of opioids as prescribed for pain, individuals misusing prescription opioids, individuals using illicit opioids such as heroin or fentanyl, health care practitioners, family and friends of people who have an opioid use disorder, and community members who come into contact with people at risk for opioid overdose, ***knowing how to use naloxone and keeping it within reach can save a life.***

BE PREPARED. GET NALOXONE. SAVE A LIFE.

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Health care practitioners, including dentists, should carry naloxone in their offices for emergency situations of opioid overdoses and be properly trained on how to administer the medication.

III.D Managing Patients with Opioid Use Disorder (OUD)

Dentists, as health care providers, have access to sensitive health information of their patients and will inevitable come across individuals with opioid use disorder (OUD). Although dentists will not be specifically treating the opioid use disorder of their patients, it is their responsibility as health care providers and within their scope of practice to educate and refer patients with OUD to the proper resources to obtain help.

Some resources dentists can suggest include recovery centers (abstinence), medicated assisted treatment, and harm reduction organizations. Dentists can play a key role in helping their patients access these resources by simply offering the information and encouragement to pursue treatment.

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