

Original Article

The Pharmacologic Differences that Causes Opioids to be the Number One Cause of Deaths

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Abstract

With the increasing prevalence of opioid related deaths in North America, there is a need to understand the pharmacologic differences that explain why opioids are the leading causes of death among individuals who consume opioids. The opioid receptors in the brain, spine, as well as the gut are responsible for the observed analgesia after the administration of the opioids. For many patients, an opioid overdose depresses the respiratory system and compromises the functioning of organs due to the greatly reduced respiration. A literature review was conducted with the purpose of identifying relevant articles that explain the pharmacologic basis of opioids. From the electronic search of articles, ten were identified as the most relevant for the literature review. In the results and discussion sections is an overview of the pharmacologic basis of opioids and an explanation of how an overdose of opioids leads to death.

Keywords: Opioids; Pharmacology; Mechanisms of action; Opioid receptors; Opioid overdose

Introduction

North America registers an increasing rate of opioids related deaths. The United States has registered an alarming increase of the fatal overdoses of pharmaceutical opioids [1]. However, North America is one of the regions that have registered the highest opioids related deaths in the recent years. Specifically, North America represents the leading consumer of opioids across the globe. As expected, the region experiences the highest death rates due to opioid abuse. Notably, North America registered opioid dispensing rates of 30,540 in defined daily doses by 2014. The marketing strategies that pharmaceutical companies have adopted in North America serve as the main reason for the alarming increase of opioid related deaths and consumption [2]. A critical analysis of the pharmacology of opioids helps in understanding why they are the leading drugs attributable for causing death in cases of overdose. Notably, opioids represent the treating treatment

approach in the management of acute and chronic pain.

With the increase of chronic illnesses such as cancer, patients with excessive pain have to rely on opioids as a way of increasing their quality of life. Some of the opioid drugs include morphine and fentanyl. Unfortunately, the alarming rates of opioid related deaths are a significant issue that requires the attention of leaders in the healthcare sector. The overdose of opioids leads to death due to the impact of the drugs on the respiratory system [3]. The pharmacological basis of opioids involves the activation of the opiate receptors in the central nervous system. Although the therapeutic activity of opioids is desirable in pain management, the adverse effects of an overdose through the depression of the respiratory system and other undesirable outcomes. The main symptoms of the opioid overdose include pinpoint pupils, respiratory depression, and unconsciousness. The lack of immediate response in patients with an opioid overdose results in death [4]. The fatal overdoses of opioids majorly result from respiratory depression. In North America, the fatal overdoses of opioids have become a regular occurrence that needs a critical analysis.

Methodology

In order to understand the pharmacological differences that explain why opioids are a leading cause of death, there was a need to access recently published articles with evidence on the pharmacological basis of opioids. Specifically, a literature search on the EBSCO database helped in identifying relevant articles that explain the pharmacology of opioids. The literature search focused on identifying recent articles that explain the causes of death in opioid related overdoses. The keywords for the search were; namely, opioids, pharmacology, mechanisms of action, opioid receptors, opioid overdose, and fetal opioid overdose. The electronic search yielded 10 articles that contained critical information regarding the pharmacology of opioids and the mechanism of action involved in opioid related deaths.

Results

Opioids are chemical substances whose mechanism of action involves the binding to opioid receptors. Opioid receptors are located in the central and peripheral

nervous system as well as in the gastrointestinal tract. The main purpose of prescribing opioids is to reduce the pain threshold and eliminate an individual's attachment to pain [5]. Opioids register analgesic effect such as sedation, respiratory depression, constipation, as well as euphoria. The analgesic effects of opioids result from the mediation of the opioid receptors. Specifically, different studies have demonstrated that the activation of opioid receptors occurs because of the presence of opioids taken in different dosages. For the analgesic effects to occur, a complex series of neuronal interactions takes place. There are three types of opioid receptors; namely, μ (μ), δ (δ) and κ (κ) [6]. Each of these receptors has an impact on the spinal code triggering analgesia. The binding to the μ receptor, which are present at the GABAergic neurons, is the first step in the activation of the various receptors. The GABAergic neurons serve to project to the descendant inhibitory neurons available in the brainstem leading to their inhibition [7]. When opioid analgesics initially bind to the μ receptors, the inhibition of the GABAergic neurons takes place because of the resulting mechanisms. Additionally, the descendant inhibitory serotonergic neurons undergo activation and are responsible for the resulting analgesia. In the spine, there is the inhibition of pain mediator pathways resulting in the desired analgesic effect. Morphine and fentanyl represent analgesic opioids that serve as full agonists that bind to the μ receptors.

Through the effect of the opioid analgesics, the pain threshold in the spine increases significantly. For this reason, individuals will only experience pain if exposed to a more intense stimulus. In the limbic system, numerous opioid receptors are responsible for altering a patient's subjective evaluation of pain [7]. Particularly, the effect of opioid analgesics on the limbic system leads to the emotional detachment from pain. The effect of opioids is also evident in the constriction of the pupils in the eyes. The pinpointed pupils occur because of the impact of opioids in the receptors present in the brain stem. Notably, the brain stem is responsible for regulating the diameter of the pupils [7]. For this reason, treatment with opioids affects the size of the pupils due to the binding of the drug on the receptors located in the brainstem. Additionally, the pharmacology of

opioids results in constipation due to the opioid receptors located in the gastrointestinal tract. In many instances, individuals taking doses of opioids may need the help of laxatives to trigger a relief of the resulting constipation.

Different studies have demonstrated that an overdose of opioids leads to a significant impact on the respiratory system. Specifically, the overdose increases the adverse effects associated with the use of opioids. Depending on the age, organ function, as well as the administration of other drugs, some patients may experience fatal adverse effects of opioids [6]. The most prevalent adverse effects have been characterized as respiratory depression, sedation, vomiting, constipation, and nausea. Some individuals may experience confusion, nightmares, dizziness, dysphoria, and urinary retention. Respiratory depression is the most undesirable adverse effect that can trigger other serious effects such as death. Notably, an overdose of opioids depresses the respiratory system, thereby, increasing the accumulation of carbon dioxide in different body parts [5]. The depression of respiration alters respiratory activities such as the rate, the volume in each minute, as well as tidal exchange. Respiratory depression is the leading cause of death in cases of opioid overdose. For this reason, there is a need to understand the best approaches of addressing the respiratory depression before the patient becomes unconscious.

Discussion

Different opioid receptors are responsible for the mediation of the analgesic effect that occurs after the administration of opioids. Through the action of the opioid receptors, the drugs lead to an increased threshold of pain in the spine as well as emotional detachment that leads to a limited subjective evaluation of the pain experienced [8]. In North America, opioids are the most popular pain relievers used in different healthcare facilities. The prescription of opioids has increased significantly in recent years a factor that has led to increased cases of fatal overdoses. Notably, an overdose of opioids leads to a highly depressed respiratory system that eventually compromises the organ function of the patient [7]. Increased cases of fatal opioid overdose result among individuals who are not used to the increased consumption of opioids. Unfortunately, North Americans are likely to consume a combination of opioids a

factor that increases their effect on the respiratory system. There is emerging evidence that the overdose death toll in North America has become an issue of concern. The pharmaceutical industries underestimate the addictive potential of opioids leading to an increased prescription of opioids to many patients [9-10]. More people have increased access to prescribed opioids a factor that triggers the opioid use disorder.

In the United States, about 2.1 million people exhibited opioid use disorder. In the Canadian provinces, opioid use disorder was more prevalent. Between 2010 and 2016, British Columbia registered three times increase in seizures related to the use of heroin. The main problem in North America is that opioids such as heroin are available in the streets a factor that explains the increased chances of opioid overdose [1]. To understand opioid overdose in North America, it is imperative to compare the overdose rates in the United States and Canada. Differences provinces in Canada have significantly high opioid overdose rates. In the last two decades, the prevalence rates of opioid overdose have increased significantly.

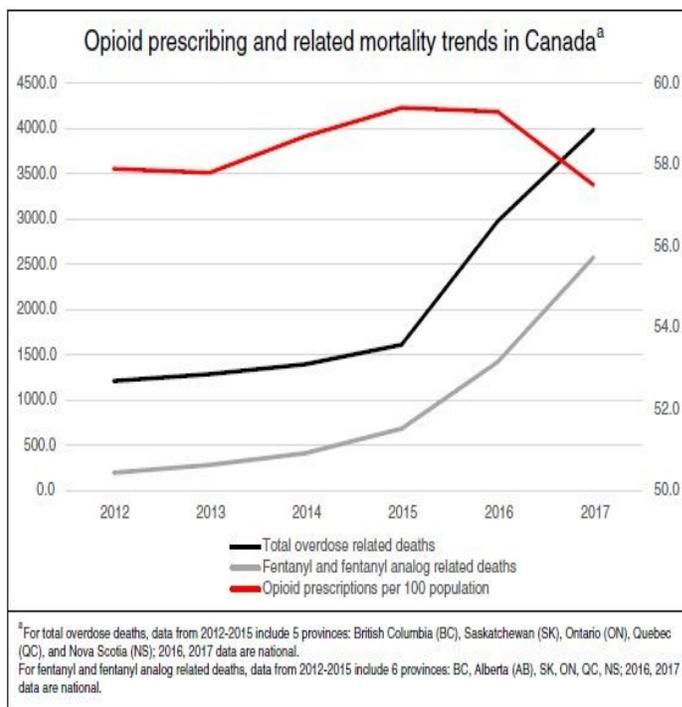


Figure 1: Showing opioid prescribing and related mortality trends in Canada [9-10].

Synthetic opioids are easily accessible in North America and people can access them in the streets [2]. Fentanyl caused about 66% of opioid related deaths in British Columbia and Alberta in 2016. In 2017, British Columbia registered more than 1,400 fatal overdoses with 80% of them involving fentanyl. Fentanyl analogs are also available in North America a factor that affects the statistics of fatal overdoses.

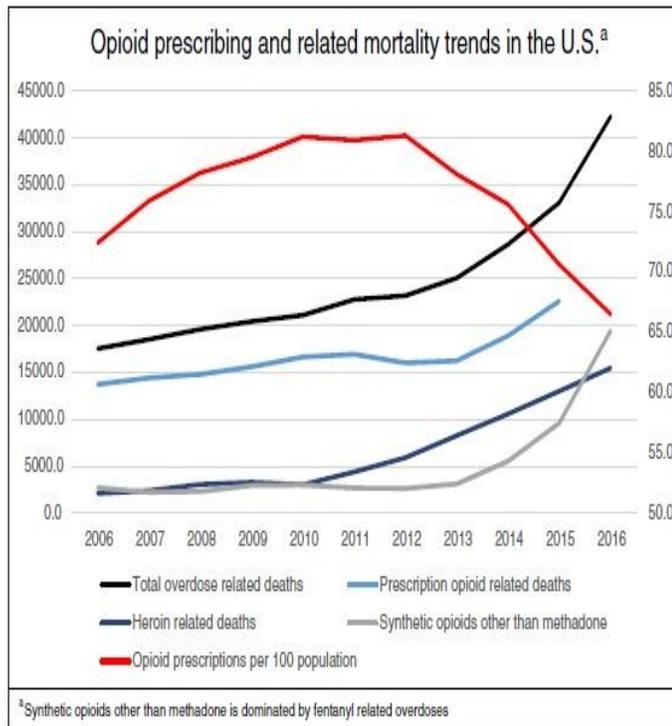


Figure 2: Showing opioid prescribing and related mortality trends in US [9-10].

All these undesirable effects result from the described adverse effects of opioids due to their action in depressing the respiratory system.

Conclusion

North America presents alarming rates of opioid-related deaths. Specifically, British Columbia and Alberta are two of the provinces that researchers have closely studied with the core objective of understanding people's likelihood to register an opioid overdose. The prescription rates of opioids in North America are significantly higher than in other parts of the world. North Americans can easily access opioids due to the extensive marketing of pharmaceutical companies as

well as the availability of the opioids in the streets. The fatal overdoses of opioids result from respiratory depression, which is an adverse effect of consuming opioids.

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