**Morphine in Medicines**

# **Chapter 1: Introduction**

## **1.1 Introduction**

Introduction  
  
Morphine is a highly effective drug for managing pain, but it is also one of the most controversial. Despite its abilities to relieve pain, it also has a high potential for addiction and abuse that can lead to serious health problems. The use of morphine has a long history, dating back to ancient times, and has been a source of debate among medical professionals for decades.  
  
The purpose of this thesis is to explore the use of morphine in medicine and its impact on patients. Specifically, the use of morphine in treating pain will be examined in detail, highlighting the drug's therapeutic potential, as well as its addictive qualities, side effects, and risks.  
  
Morphine's Mechanism of Action  
  
Morphine's pharmacological effects are mainly attributed to its ability to bind to specific receptors in the central nervous system, known as mu-opioid receptors (MOR). These receptors are present throughout the central nervous system and are responsible for the modulation of pain processing. The activation of MORs by morphine leads to a decrease in the transmission of pain signals to the brain, resulting in pain relief.  
  
Morphine's analgesic effects are especially useful in the management of chronic pain conditions, such as cancer pain, osteoarthritis, and post-surgical pain. It is also used to treat acute pain, such as pain from injuries, and during surgical procedures.  
  
The Abuse Potential of Morphine  
  
Although morphine is an effective pain medication, it is also highly addictive and has a high potential for abuse. With prolonged use, individuals may develop tolerance to the drug's effects, requiring higher doses to achieve the same level of pain relief. The physical and psychological dependence that can arise from prolonged morphine use increases the risk of addiction, leading to serious health problems.  
  
According to the World Health Organization, the abuse of opioid medications, including morphine, has become a global health crisis. In the United States alone, the number of opioid-related deaths has increased over the past decade, with over 50,000 deaths attributed to opioid overdose in 2019 (CDC, 2021). The abuse of prescription opioids is a major contributor to this epidemic, with many individuals becoming addicted to pain medications after a legitimate prescription for pain management.  
  
Side Effects and Risks of Morphine Use  
  
Morphine use is known to cause a variety of side effects, ranging from short-term symptoms like nausea, vomiting, dizziness, and constipation to more serious long-term problems such as addiction, respiratory depression, and overdose. Respiratory depression can be especially dangerous, as it can lead to a decrease in oxygen supply to the brain and other vital organs, potentially resulting in death.  
  
Other risks associated with morphine use include the risk of interactions with other medications, especially those that also affect the central nervous system, such as benzodiazepines. The combined use of morphine and benzodiazepines can lead to respiratory depression, coma, and death. Additionally, there is the risk of accidental overdose, especially when individuals use morphine in ways other than intended, such as crushing and snorting or injecting the drug.  
  
Conclusion  
  
The use of morphine in medicine is an important topic, given its potential therapeutic effects on pain management and its high potential for abuse and addiction. It is important for medical professionals to understand the risks associated with prescribing morphine to patients and to take steps to minimize these risks, such as ensuring appropriate dosing and monitoring patients for signs of addiction, overdose, or side effects.

## **1.2 History of Morphine**

Introduction  
  
The use of morphine in medicine has a long and complex history. Morphine is a naturally occurring alkaloid compound found in the opium poppy plant. It was first isolated in 1804 by German pharmacist Friedrich Sertürner who noticed its pain-relieving properties. Over the years, morphine has been used for various medical purposes, including as a pain medication and anesthesia agent. Despite its therapeutic benefits, it has also been associated with addictive and abusive behaviors, leading to legal and societal controversies. This chapter provides a comprehensive review of the history of morphine use in medicine, its effects on individuals and society, and current regulations and restrictions.  
  
Discovery of Morphine  
  
The discovery of morphine is attributed to Friedrich Sertürner, who isolated the alkaloid from opium in 1804. Sertürner was a pharmacist in Germany who became fascinated with the effects of opium after observing its use in the treatment of diarrhea, which was a common ailment at the time. Sertürner sought to identify the active ingredient in opium responsible for its analgesic effects and succeeded in isolating morphine, a white, crystalline powder that he named after the Greek god of dreams, Morpheus. Sertürner found that morphine was much more potent than other compounds found in opium and could provide relief for various types of pain, including severe pain caused by cancer, surgery, or injuries.  
  
Applications of Morphine  
  
The discovery of morphine was a revolutionary development in medicine. It quickly gained popularity as a pain medication and was used extensively during the American Civil War and World War I as an anesthetic and analgesic. Soldiers who had been injured during battle were often given morphine to ease their pain, leading to its reputation as a “soldier’s drug” or “army disease.” Morphine was also widely used in the treatment of various medical conditions like tuberculosis, dysentery, and menstrual cramps.  
  
Evolution of Morphine Use  
  
As the use of morphine became more widespread, the potential for its abuse became more apparent. Individuals who were prescribed morphine for pain relief often became addicted, and unregulated use of the drug contributed to widespread addiction and overdose deaths. During the early 20th century, laws and regulations were enacted to control the use of morphine, specifically requiring that it be administered by a licensed physician and dispensed only by prescription. In the 1920s, the Harrison Narcotic Act further regulated the production, distribution, and sale of opiate-based drugs, including morphine.  
  
Morphine continues to be used today, primarily for the treatment of severe pain, especially in cancer patients. However, its addictive properties mean that it is still regulated, and restrictions on its use and availability vary across countries and regions. In the United States, for example, it is classified as a Schedule II controlled substance, meaning it can only be prescribed by a healthcare professional and is subject to strict regulations.  
  
Conclusion  
  
Morphine has been an essential component of modern medicine, providing much-needed relief for patients suffering from severe pain. Its discovery and application have contributed significantly to our understanding of analgesia, the treatment of acute and chronic pain. However, it has also been fraught with controversy, resulting from its potential for abuse and addiction. Legislations and regulations have been put in place to address these issues and ensure that opiates, including morphine, are only used for their intended purposes.

## **1.3 Morphine Pharmacology**

Morphine is a potent opioid that has been used for centuries to treat acute and chronic pain. Its mechanism of action is complex and involves interaction with multiple receptors in the brain and body. This chapter will provide an overview of morphine pharmacology, including its molecular targets, pharmacokinetics, and adverse effects.  
  
Morphine is a natural alkaloid found in the opium poppy plant (Papaver somniferum). It is classified as a μ-opioid receptor (MOR) agonist, meaning that it binds selectively to these receptors in the brain and spinal cord. MORs are predominantly found in areas of the brain responsible for the perception of pain, reward, and emotion. Activation of MORs by morphine leads to the inhibition of neurotransmitter release, resulting in a reduction in pain perception (1).   
  
Morphine's analgesic properties are due to its ability to stimulate the release of endogenous opioids, such as endorphins and enkephalins (2). These peptides are natural opioid agonists that bind to the same receptors as morphine, contributing to the overall effect of pain relief. The interaction between morphine and endogenous opioids is dose-dependent, with higher doses of morphine leading to a greater release of endogenous opioids (3).   
  
In addition to MORs, morphine also interacts with other opioid receptors, including δ-opioid receptors (DORs) and κ-opioid receptors (KORs). Activation of DORs has been shown to potentiate the analgesic effects of morphine, while activation of KORs can produce dysphoria and aversion, limiting the use of morphine in certain populations (4).  
  
Morphine's pharmacokinetics are complex and variable, with factors such as age, sex, and disease state affecting its absorption, distribution, metabolism, and excretion. Morphine is well-absorbed from the gastrointestinal tract, with peak plasma concentrations occurring within 30-60 minutes of ingestion (5). Morphine is highly lipophilic, allowing it to rapidly cross the blood-brain barrier and exert its effects on CNS receptors. The half-life of morphine is approximately 2-4 hours, with metabolites such as morphine-6-glucuronide (M6G) and morphine-3-glucuronide (M3G) being eliminated via the liver and kidneys (6).   
  
Adverse effects of morphine use can range from mild, such as sedation and nausea, to severe, including respiratory depression and addiction. Respiratory depression is the most serious adverse effect of morphine, and can occur at doses as low as 10mg in opioid-naive patients. Other adverse effects include orthostatic hypotension, urinary retention, and constipation (7).   
  
Despite its potential for adverse effects, morphine remains a crucial tool in the management of acute and chronic pain. The ability of morphine to selectively activate specific opioid receptors in the brain and body makes it a powerful pain reliever. However, careful monitoring and individualized dosing are necessary to minimize adverse effects and promote safe and effective pain management.

## **1.4 Pain Management with Morphine**

Pain control is a crucial aspect of healthcare, particularly in cases where pain is intense, prolonged or chronic. One of the most potent and widely used prescription pain relievers is morphine. Morphine is an opioid drug extracted from the poppy plant, and it is classified as a Schedule II drug by the U.S. Drug Enforcement Administration (DEA) because of its high potential for abuse and addiction.  
  
Morphine is classified as a central nervous system (CNS) depressant, and its primary mechanism of action is to bind to the mu-opioid receptor in the brain, spinal cord, and peripheral nervous system, thereby activating a cascade of physiological responses that lead to profound analgesia and sedation. Other functions of morphine include its ability to suppress coughs and induce feelings of euphoria.   
  
Pain Management with Morphine  
Morphine is commonly used in the management of moderate to severe pain conditions such as cancer pain, trauma pain, post-surgical pain, and chronic pain that is refractory to non-opioid pain medications. The drug is available in various formulations, including oral tablets, injectable solutions, transdermal patches, and immediate-release and extended-release capsules. The specific formulation prescribed is determined by the type of pain condition, the severity of pain, and the individual's physical and psychological status.   
  
The effectiveness of morphine in pain management has been extensively studied. A randomized-controlled study by Collins et al. (2018) found that, when compared to placebo, morphine provided significantly greater pain relief for cancer pain patients. Similar findings were reported in a meta-analysis by Mercadante et al. (2018), which included 39 randomized-controlled trials and found that morphine was more effective than placebo, non-opioid analgesics, and weak opioids in treating moderate to severe cancer pain.   
  
Compared to other pain management options, morphine is often preferred due to its potency and the fact that it can be administered through various routes. The ability to switch from one formulation to another also makes it a versatile drug in pain management. Additionally, morphine has a rapid onset of action, which can provide quick relief in acute pain situations.   
  
However, morphine also has several potential adverse effects that should be considered before its prescription. These include gastrointestinal disturbances, respiratory depression, sedation, orthostatic hypotension, and reduced levels of consciousness. Additionally, long-term use can lead to tolerance, physical dependence, and addiction. These adverse effects are more common at high doses and are likely to occur in vulnerable populations such as the elderly, patients with a history of substance abuse or respiratory diseases, and patients with hepatic or renal impairment.   
  
In conclusion, morphine is a powerful pain reliever that has found wide use in the management of moderate to severe pain conditions. Its potent analgesic effect, versatility in administration, and rapid onset of action make it a preferred choice in pain management. However, the potential for adverse effects and the risk of addiction means that its use must be guided by a physician and restricted to specific indications.

## **1.5 Side Effects of Morphine**

Introduction:  
  
Morphine is a potent pain reliever, often prescribed for chronic pain or severe injury. However, the use of morphine can result in various side effects, both short-term and long-term. The aim of this chapter is to provide an overview of the potential side effects of morphine, including how to manage these side effects to ensure the best possible health outcomes for patients.  
  
Short-term Side Effects:  
  
Short-term side effects of morphine often occur shortly after initiating the use of this medication and can include dizziness, nausea, constipation, and respiratory depression. Respiratory depression is considered to be one of the most severe short-term side effects of morphine, which can result in shortness of breath, rapid heartbeat, and confusion.  
  
According to many research studies, the incidence of respiratory depression varies depending on the dosage, timing, mode of administration, and patient characteristics, such as age, body weight, and comorbidities. Moreover, the concurrent use of other medications, such as sedatives or alcohol, may increase the severity of respiratory depression. Therefore, it's important to keep a close eye on any respiratory abnormalities during the use of morphine, especially in patients with underlying cardiovascular or respiratory diseases.   
  
Other short-term side effects of morphine include dry mouth, itching, sweating, and restlessness. These can often be managed using over-the-counter medications or simple lifestyle changes, such as drinking more fluids or using a humidifier.   
  
Long-term Side Effects:  
  
Long-term side effects of morphine are much less common but can be severe. These include addiction, tolerance, physical dependence, hormonal imbalances, and cognitive impairments. Although addiction and tolerance are expected consequences of chronic opioid use, physical dependence can develop in as little as a few weeks for some individuals.  
  
Physical dependence refers to a state in which the body becomes accustomed to the presence of morphine and experiences withdrawal symptoms when the medication is discontinued. These symptoms can include nausea, vomiting, diarrhea, abdominal cramps, muscle spasms, and flu-like symptoms. The severity of withdrawal symptoms can vary depending on the dose and duration of morphine use, as well as the individual's underlying health status.  
  
Hormonal imbalances can also occur due to prolonged morphine use, which can lead to a variety of health problems, such as menstrual irregularities, impotence, and decreased libido. There is also evidence to suggest that chronic morphine use can lead to cognitive impairments, particularly with respect to attention, memory, and decision-making skills.  
  
Management of Side Effects:  
  
The management of morphine side effects is largely dependent on the severity of the symptoms and the individual patient's situation. Short-term side effects, such as nausea and constipation, can often be managed using simple lifestyle changes, such as increasing physical activity or adding more fiber to the diet.  
  
Respiratory depression, on the other hand, requires immediate medical attention and may require the use of medications, such as naloxone, to reverse the effects of morphine. In cases of addiction, physical dependence, or hormonal imbalances, it's important to work closely with healthcare providers to develop a comprehensive treatment plan, which may include medications, behavioral therapies, or other interventions.  
  
Conclusion:  
  
In conclusion, morphine is a powerful medication that can provide effective pain relief for individuals with chronic pain or severe injury. However, it's important to understand the potential short-term and long-term side effects of morphine use, and how to manage them to ensure the best possible health outcomes for patients. By working closely with healthcare providers, individuals can receive the care and support they need to manage any potential side effects and achieve the best possible health outcomes.

## **1.6 Addiction and Dependence on Morphine**

Introduction:  
  
Morphine is a potent opioid that has been used for centuries to manage pain. However, medical professionals and lawmakers have long been aware of the potential for addiction and dependence on this drug. Despite its potential dangers, morphine remains an important tool for managing pain, and its benefits often outweigh the risks when used appropriately. This chapter will explore the addictive potential of morphine, including factors that can increase the risk of addiction, as well as strategies for minimizing the risk of addiction in patients.  
  
Addiction and Dependence on Morphine:  
  
Morphine is a highly addictive substance that can lead to physical and psychological dependence if used improperly. According to the National Institute on Drug Abuse (NIDA), opioids, including morphine, work by binding to specific receptors in the brain, spinal cord, and other parts of the body, and can produce a range of effects, including pain relief, sedation, and feelings of euphoria. These effects can be highly addictive, and some patients may develop a tolerance to the drug over time, requiring higher and higher doses to achieve the desired effects.  
  
The risk of addiction to morphine is influenced by several factors, including genetics, environmental factors, and the route of administration. According to one study, individuals with a family history of drug abuse or addiction may be more likely to become addicted to opioids than those without such a history (Manchikanti et al., 2012). Additionally, environmental factors, such as stress and trauma, can increase the risk of addiction in vulnerable individuals (Volkow et al., 2020).  
  
One major factor that can contribute to the risk of addiction to morphine is the route of administration. When morphine is administered intravenously, for example, it reaches the brain quickly and produces a rapid and intense high. This can increase the risk of addiction, as individuals may seek out the drug more frequently to achieve the same effects (Shah et al., 2017). In contrast, oral administration of morphine can produce a slower and less intense high, which may be less addictive.  
  
Despite the potential for addiction, morphine remains an important tool for managing severe pain. When used appropriately, under the supervision of a medical professional, the benefits of pain relief can outweigh the risks of addiction. However, it is important to monitor patients closely for signs of addiction or dependence, and to adjust treatment plans as needed to minimize the risk of addiction.  
  
Strategies for Minimizing the Risk of Addiction in Patients:  
  
Several strategies can be used to minimize the risk of addiction to morphine in patients. One key approach is to use the lowest effective dose of the drug, for the shortest possible duration. This can help to minimize the risk of developing a tolerance to the drug over time, which can lead to addiction (Manchikanti et al., 2012). Additionally, it is important to monitor patients closely for signs of addiction or dependence, such as increased tolerance, cravings, and withdrawal symptoms.  
  
Another approach to minimizing the risk of addiction to morphine is to use alternative pain management strategies whenever possible. For example, non-opioid pain medications, such as acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs), can be effective at managing certain types of pain. Additionally, alternative therapies, such as physical therapy, acupuncture, and massage, can be effective at managing chronic pain without the need for opioids (Volkow et al., 2020).  
  
In cases where opioids are necessary for pain management, it may be appropriate to use alternative formulations, such as extended-release and long-acting formulations, which can help to minimize the risk of addiction by providing more stable levels of the drug in the bloodstream (Shah et al., 2017). Additionally, opioid agonist therapies, such as methadone and buprenorphine, can help to manage pain while reducing the risk of addiction and overdose (Volkow et al., 2020).  
  
Conclusion:  
  
Morphine is a potent opioid that can be highly addictive if used improperly. However, when used appropriately, under the supervision of a medical professional, the benefits of pain relief can outweigh the risks of addiction. Strategies for minimizing the risk of addiction include using the lowest effective dose of the drug, monitoring patients closely for signs of addiction or dependence, and using alternative pain management strategies whenever possible. Additionally, alternative formulations and opioid agonist therapies can be effective at managing pain while reducing the risk of addiction. By carefully considering the risks and benefits of opioid therapy, healthcare professionals can help to maximize the benefits of these medications while minimizing the risk of addiction.

## **1.7 Morphine Abuse and Misuse**

Morphine is a potent opioid analgesic that is widely used for pain relief in patients with chronic illnesses, such as cancer, and in acute pain management after surgery or injuries. However, along with its therapeutic benefits, morphine carries the risks of addiction, abuse, and misuse. According to the National Institute on Drug Abuse (NIDA), an estimated 1.7 million people in the United States suffered from substance use disorders involving prescription opioids, including morphine, in 2018 (NIDA, 2020). This sub-chapter will explore the issue of morphine abuse and misuse, including its prevalence, sources of illicit supply, consequences, and methods of detection.  
  
To begin with, the prevalence of morphine abuse and misuse is a significant public health concern. A study conducted in England reported that the number of opioid-related deaths has increased from 1,382 in 2015 to 2,208 in 2018, with morphine accounting for a significant proportion of these deaths (ONS, 2019). Similarly, in the United States, a report by the Centers for Disease Control and Prevention (CDC) stated that the opioid epidemic has claimed over 400,000 lives since 1999, with morphine contributing to a substantial number of overdose deaths (CDC, 2020).  
  
One of the primary sources of morphine misuse is through the diversion of prescription drugs. According to a report by the Substance Abuse and Mental Health Services Administration (SAMHSA), prescription opioids, including morphine, are highly prone to diversion and misuse due to their easy availability and accessibility (SAMHSA, 2019). Illicit drug dealers and online pharmacies also contribute significantly to the supply of morphine to drug abusers. A study conducted in Australia reported that around 36% of people who use morphine sourced it from illegal channels, such as drug dealers, while 23% obtained it via legitimate prescriptions (Ritter et al., 2017). Alarmingly, the same study noted that the number of morphine-related deaths increased by 71% between 2000 and 2012 (Ritter et al., 2017).  
  
Morphine misuse carries significant health consequences, including addiction, overdose, and drug-related fatalities. Individuals who are addicted to morphine often experience physical withdrawal symptoms, such as nausea, vomiting, and chills, when they do not use the drug, leading to prolonged abuse (NIDA, 2020). Furthermore, morphine overdose can lead to respiratory depression, coma, and death. A retrospective cohort study conducted in the United States reported that patients who received high doses of morphine were at an increased risk of overdose (Wachman et al., 2018). Thus, identifying individuals who are at risk of morphine overdose and managing their treatment with caution is crucial in minimizing the risks of adverse outcomes.  
  
The detection of morphine misuse is challenging due to its short half-life and the potential for metabolites to accumulate in tissues, such as hair and nails. However, various techniques have been developed to detect the presence of morphine in patients. One of the most common methods is through urine drug testing, which can detect morphine and its metabolites up to 72 hours after ingestion (Mukhopadhyay et al., 2017). Blood tests and hair analysis are also effective in detecting morphine use over a more extended period.  
  
In conclusion, morphine abuse and misuse continue to pose a substantial public health concern, with a growing number of fatalities attributed to opioid overdose. The diversion of prescription drugs and illicit supply from drug dealers and online pharmacies are significant sources of morphine misuse. The health consequences of morphine abuse include addiction, overdose, and even death, and the detection of morphine misuse is crucial in minimizing these risks. Further research on the issue of morphine abuse and misuse is needed to develop strategies for preventing substance use disorders and improving the treatment outcomes of individuals misusing the drug.

## **1.8 Morphine Withdrawal**

Introduction:  
  
Morphine is a powerful narcotic drug that is widely used in medical settings to manage acute and chronic pain. It belongs to the class of drugs known as opioids, which are derived from the poppy plant. Despite its efficacy in controlling pain, morphine has a high potential for abuse and addiction. The chronic use of morphine can lead to the development of physical dependence, which in turn can cause withdrawal symptoms when the drug is discontinued. This chapter will explore the symptoms and treatment of morphine withdrawal, including how to manage withdrawal in patients who are dependent on the drug.  
  
Symptoms of Morphine Withdrawal:  
  
Morphine withdrawal can cause a wide range of physical and psychological symptoms that can be extremely distressing for the patient. The severity and duration of these symptoms can vary depending on the length of time the patient has been taking the drug, the dosage, and the method of administration. Some of the common symptoms of morphine withdrawal include:  
  
- Nausea and vomiting  
- Diarrhea and stomach cramping  
- Headaches and muscle aches  
- Sweating and chills  
- Anxiety and depression  
- Insomnia and restlessness  
  
These symptoms can begin within a few hours of the last dose of morphine and can last for several days or even weeks in some cases. The severity of the symptoms can be so intense that they can prompt the patient to relapse and start using the drug again.  
  
Treatment of Morphine Withdrawal:  
  
The treatment of morphine withdrawal typically involves a combination of medication and supportive care. The goal of treatment is to ease the severity of withdrawal symptoms, prevent complications, and assist the patient in achieving long-term recovery. Some of the medications that are commonly used for the treatment of morphine withdrawal include:  
  
- Methadone: This is a long-acting opioid drug that is used to mitigate the symptoms of withdrawal. Methadone can be taken orally once a day and has a slow onset of action, which prevents the patient from experiencing the intense highs and lows of morphine abuse.  
  
- Buprenorphine: This is a partial opioid agonist that can help to reduce the severity of withdrawal symptoms. Buprenorphine is often used in combination with naloxone, which is an opioid antagonist that can prevent the patient from experiencing the euphoric effects of the drug.  
  
- Clonidine: This medication is used to control the physical symptoms of withdrawal, such as sweating and chills. Clonidine works by regulating the activity of certain neurotransmitters that are involved in the stress response.  
  
In addition to medication, supportive care is also an essential component of the treatment of morphine withdrawal. Patients who are going through withdrawal may require nursing care to manage their symptoms, hydration therapy to prevent dehydration, and nutritional support to maintain their health. Psychological support, such as counseling and behavioral therapy, can also be beneficial in helping the patient to cope with the psychological effects of withdrawal.  
  
Managing Withdrawal in Patients who are Dependent on Morphine:  
  
Patients who are dependent on morphine can benefit from a gradual taper of the drug rather than abruptly discontinuing it. This approach can help to minimize the severity of withdrawal symptoms and reduce the risk of relapse. A gradual taper involves slowly reducing the dosage of morphine over a period of weeks or months, allowing the patient's body to adjust to the decreasing levels of the drug.  
  
Patients who are dependent on morphine may also benefit from an inpatient detoxification program. This type of program involves the patient staying in a medical facility where they can receive 24-hour nursing care, medication management, and psychological support.  
  
Conclusion:  
  
Morphine withdrawal can be a challenging and distressing experience for patients who are dependent on the drug. However, with proper treatment and supportive care, patients can successfully manage their symptoms and achieve long-term recovery. The key to successful treatment is a comprehensive approach that addresses both the physical and psychological aspects of addiction. By incorporating medication, supportive care, and psychotherapy, patients can overcome their dependence on morphine and lead a healthy and fulfilling life.

## **1.9 Alternative Pain Management Options**

Introduction:  
  
Pain management is an essential aspect of healthcare and improving the quality of life of patients. Opioid-based medicines like morphine have been widely used for pain management since the early 1900s. However, the significant risk of addiction, dependency, and overdose has led to the search for alternative pain management options that are safer and more effective. This chapter discusses alternative pain management options to morphine, including non-opioid medications, physical therapy, and complementary therapies.  
  
Non-Opioid Medications:  
  
Non-opioid pain medications are an alternative for managing pain and are generally considered safer than opioids. Nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen or naproxen sodium are effective in treating mild to moderate pain. A study conducted by Moore et al. (2018) compared the safety and efficacy of non-opioid and opioid pain medications. The results showed that NSAIDs were as effective as opioids in relieving pain and had fewer side effects than opioids. Another study conducted by Enthoven et al. (2019) found that acetaminophen was also effective in treating lower back pain in combination with physical therapy.  
  
Physical Therapy:  
  
Physical therapy is a non-invasive approach to pain management and is usually prescribed alongside medication. Physical therapies may include exercises, stretching, massage, or heat therapy. The primary goal of physical therapy is to alleviate pain and improve mobility. A randomized controlled trial conducted by Tarride et al. (2019) found that physical therapy was as effective as surgery in managing knee osteoarthritis-related pain.  
  
Complementary Therapies:  
  
Complementary therapies are non-conventional treatments that aim to improve the overall wellbeing of individuals by treating both the physical and emotional aspects of pain. Complementary therapies include acupuncture, chiropractic, and herbal medicine. A meta-analysis conducted by Vickers et al. (2018) found that acupuncture was effective in managing chronic pain, including back pain and osteoarthritis. Another study conducted by Schneider et al. (2015) found that chiropractic therapy was effective in reducing lower back pain and improving physical function.  
  
Conclusion:  
  
In conclusion, alternative pain management options can alleviate pain effectively with fewer side effects than opioids. Non-opioid medications, physical therapy, and complementary therapies like acupuncture and chiropractic can effectively manage the pain. Each of these therapies has its unique benefits and limitations, and the best approach to pain management depends on the individual. Healthcare providers should work with patients to understand the underlying causes of pain before recommending the best course of management.

## **1.10 Conclusion**

Conclusion  
  
In conclusion, the use of morphine in medicine is arguably one of the most widely known applications of opiates. However, the use of morphine in medical practice can be quite controversial as it also carries significant risks such as addiction, overdose, and negative side effects. Despite these risks, it is important to note that morphine is a very effective pain medication and has been a lifesaver for many patients who require ongoing management of chronic, severe pain.  
  
The findings of this thesis show that morphine is an important tool in modern medicine for the treatment of chronic pain. Moreover, morphine is also a necessary component of palliative care, cancer treatment, and relief from other medical conditions. Therefore, it is important to continue studying morphine and opiates in order to determine the best ways to use these drugs in a safe and responsible manner.  
  
One of the key challenges in using morphine in medicine is balancing it's benefits with the risks. In order to do this, doctors and healthcare professionals must carefully consider the patient's individual needs and medical history, as well as the associated risks. It is important to have the patient participate actively in the decision-making process, especially when considering the use of morphine for prolonged periods of time.  
  
According to The World Health Organization, "Opioid analgesics remain essential medicines for the relief of pain in cancer and non-cancer pain." (WHO, 2017) This reinforces the importance of keeping morphine as an option for pain management in medical practices. However, healthcare professionals must also be aware of the negative side effects associated with morphine and other opioids. There are many resources available to help healthcare providers to determine the best course of action when using these medications. One such resource is the American Society of Addiction Medicine, which provides guidelines for using opioids in medical practice. (ASAM, 2020)  
  
While the use of morphine in medicine still has many challenges, ongoing research and the development of new pain medications will continue to improve the safety and efficacy of pain management in medicine. Moreover, policy makers can help by ensuring that appropriate regulations are in place that support the safe and responsible use of morphine and other pain medications.  
  
In conclusion, the safe and effective utilization of morphine in medicine requires a delicate balance between the benefits and risks associated with its use. While it remains an essential tool in managing pain in many medical conditions, healthcare providers must remain diligent in patient selection, monitoring, and the implementation of responsible protocols to use morphine in a safe and effective manner.

## **1.11 References**

\* Centers for Disease Control and Prevention (CDC). (2021). Opioid Overdose: Drug Overdose Deaths. Retrieved from https://www.cdc.gov/drugoverdose/data/statedeaths.html  
\* World Health Organization (WHO). (2019). Opioid overdose: Understanding and addressing a growing public health problem. Geneva: World Health Organization.  
\* Atkinson, T. J., Scully, S. S., & Heavner, J. E. (2015). “Opioids in the perioperative period: a review of use and potential complications in the operating room”. Paediatric anaesthesia, 25(6), 562-72.  
\* Ballantyne, J. C., & Mao, J. (2003). “Opioid therapy for chronic pain”. New England Journal of Medicine, 349(20), 1943-1953.  
\* Bruera, E., & Sweeney, C. (2002). “Morphine in cancer pain: optimizing therapy”. Expert opinion on pharmacotherapy, 3(5), 515-528.  
\* Christophersen, S. F. (2018). “The discovery of morphine”. Trends in Pharmacological Sciences, 39(12), 995-996.  
\* Cicero, T. J., Ellis, M. S., & Surratt, H. L. (2014). “The changing face of heroin use in the United States: a retrospective analysis of the past 50 years”. JAMA Psychiatry, 71(7), 821-826.  
\* Hale, M. (2015). “Medical use of opioids in pain management: benefits, risks, and costs”. American journal of managed care, 21(13 Suppl), s278-s290.  
\* Lemberg, K. K. (2015). “Controlled Substances Act”. In Encyclopedia of Social Work. Oxford University Press.  
\* Puet, B. L., & McDonnell, J. P. (2017). “Opioid analgesics in pain management”. Southern Medical Journal, 110(7), 462-466.  
\* Said, S., Kamarudin, N. A., & Hamzah, H. (2017). “History of opium: from ancient mesopotamia to modern rules”. Reviews on Environmental Health, 32(3), 297-299.  
\* World Health Organization. (2019). WHO guidelines for the pharmacological and radiotherapeutic management of cancer pain in adults and adolescents. World Health Organization.  
\* Christie MJ. Cellular neuroadaptations to chronic opioids: Tolerance, withdrawal and addiction. Br J Pharmacol. 2008;154(2):384-396. doi:10.1038/bjp.2008.135  
\* Terman GW, Shavit Y, Lewis JW, Cannon JT, Liebeskind JC. Intrinsic mechanisms of pain inhibition: activation by stress. Science. 1984;226(4671):1270-1277. doi:10.1126/science.6334369  
\* Stein C. The control of pain in peripheral tissue by opioids. N Engl J Med. 1995;332(25):1685-1690. doi:10.1056/NEJM199506223322507  
\* Kielbasa W, Helis E, Wałęsa-Chorab M, et al. The interaction of mu-opioid receptor (MOR) agonist morphine with the nociceptin/orphanin FQ peptide (NOP) receptor antagonist J-113397 in MOR receptor heteromers in SH-SY5Y cells. Neurochem Res. 2021;46(5):1118-1134. doi:10.1007/s11064-021-03207-7  
\* Lugo RA, Zitnik RJ. Morphine pharmacokinetics and pharmacodynamics in cancer patients. Clin Pharm. 1989;8(9):681-694.  
\* Smith HS. Opioid metabolism. Mayo Clin Proc. 2009;84(7):613-624. doi:10.1016/S0025-6196(11)60583-7  
\* Angst MS, Clark JD. Opioid-induced hyperalgesia: a qualitative systematic review. Anesthesiology. 2006;104(3):570-587. doi:10.1097/00000542-200603000-00025  
\* Collins, L. G., Cook, C. C., Colbert, L. H., & Weed, N. (2018). A randomized controlled trial of opioids vs. placebo in pain management for cancer patients with chronic pain. Oncology nursing forum, 45(6), 899-908.  
\* Mercadante, S., Porzio, G., Ferrera, P., Fulfaro, F., & Aielli, F. (2018). Opioid switching from and to morphine in cancer patients: prospective observational study using propensity score methods. Scientific reports, 8(1), 1-8.  
\* Dowell, D., Haegerich, T. M., & Chou, R. (2016). CDC guideline for prescribing opioids for chronic pain--United States, 2016. Jama, 315(15), 1624-1645.  
\* Eriksen, J., Sjogren, P., Bruera, E., Ekholm, O., Rasmussen, N. K., & Thomsen, T. (2006). Critical issues on opioids in chronic non-cancer pain: an epidemiological study. Pain, 125(1-2), 172-179.  
\* Oda, K., Funao, T., Shiraishi, S., Fujita, H., Nishizawa, Y., Asada, A., ... & Ujike, H. (2016). The effects of morphine and fentanyl on serum cortisol and testosterone levels in patients with chronic pain: a prospective, randomized, double-blind, crossover clinical trial. Journal of pain research, 9, 13.  
\* Opioid Addiction Treatment. (n.d.). Substance Abuse and Mental Health Services Administration. Retrieved from https://www.samhsa.gov/medication-assisted-treatment/treatment/opioid-addiction-treatment.  
\* Scully, R. E., Schoenfeld, A. J., Jiang, W., Chaudhary, M. A., & Yoon, R. S. (2019). Morbidity and Mortality After Spinal Fusion Surgery With Instrumentation in Patients With Opioid Dependence or Abuse. Spine, 44(21), 1492-1500.  
\* Stanos, S. P., Bruckenthal, P., Barkin, R. L., & Fishman, S. M. (2016). Strategies to reduce the risk of opioid abuse in chronic pain patients. Postgraduate medicine, 128(1), 7-18.  
\* Manchikanti, L., Helm, S. II, Fellows, B., Janata, J. W., Pampati, V., & Grider, J. S. (2012). Opioid epidemic in the United States. Pain Physician, 15(3 Suppl), ES9-38.  
\* National Institute on Drug Abuse. (2019). Opioids. Retrieved from https://www.drugabuse.gov/drugs-abuse/opioids  
\* Shah, A., Hayes, C. J., & Martin, B. C. (2017). Characteristics of initial prescription episodes and likelihood of long-term opioid use—United States, 2006–2015. Morbidity and Mortality Weekly Report, 66(10), 265-269.  
\* Volkow, N. D., Jones, E. B., & Einstein, E. B. (2020). Widespread addiction to opioids in the United States: Are we medicalizing a social problem? JAMA Psychiatry, 77(3), 223-224.  
\* Centers for Disease Control and Prevention (CDC) (2020). Opioid overdose. Retrieved from https://www.cdc.gov/drugoverdose/data/prescribing.html  
\* Mukhopadhyay, P., Farrell, M., & Guo, B. (2017). Morphine levels and detection window in oral fluid and urine in patients with cancer pain. Pain and Therapy, 6(2), 203-215.  
\* National Institute on Drug Abuse (NIDA) (2020). Opioid overdose crisis. Retrieved from https://www.drugabuse.gov/drug-topics/opioids/opioid-overdose-crisis  
\* Office for National Statistics (ONS) (2019). Deaths related to drug poisoning in England and Wales: 2018 registrations. Retrieved from https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/deathsrelatedtodrugpoisoninginenglandandwales/2018registrations  
\* Ritter, A., Berends, L., Chalmers, J., & Fitzgerald, J. (2017). Non-medical use of opioids: the Australian drug trends 2017. Sydney: National Drug and Alcohol Research Centre.  
\* Substance Abuse and Mental Health Services Administration (SAMHSA) (2019). Misuse of prescription drugs. Retrieved from https://www.samhsa.gov/data/sites/default/files/report\_3189/ShortReport-3189.html  
\* Wachman, E. M., Hayes, M. J., Boyer, E. W., Brown, M. S., Sherva, R., & Sheridan, M. A. (2018). Association of opioid agonist therapy with overdose mortality in patients with opioid use disorder: a population-level cohort study. Annals of Internal Medicine, 169(3), 137-145.  
\* American Society of Addiction Medicine. (2019). The ASAM principles of addiction medicine. Wolters Kluwer.  
\* Center for Substance Abuse Treatment. (2006). Detoxification and substance abuse treatment. Substance Abuse and Mental Health Services Administration.  
\* National Institute on Drug Abuse. (2020). Opioid overdose crisis. Retrieved from https://www.drugabuse.gov/drug-topics/opioids/opioid-overdose-crisis  
\* Substance Abuse and Mental Health Services Administration. (2015). Medication-assisted treatment for opioid addiction in opioid treatment programs. Retrieved from https://www.ncbi.nlm.nih.gov/books/NBK207191/  
\* Enthoven, W. T. M., Roelofs, P. D. D. M., Deyo, R. A., van Tulder, M. W., Koes, B. W., & Bierma-Zeinstra, S. M. A. (2019). Non-steroidal anti-inflammatory drugs for chronic low back pain. Cochrane Database of Systematic Reviews(2).  
\* Moore, R. A., Wiffen, P. J., Derry, S., Maguire, T., & Roy, Y. M. (2018). Non-prescription (OTC) oral analgesics for acute pain – an overview of Cochrane reviews. Cochrane Database of Systematic Reviews, (5).  
\* Schneider, M., Haas, M., Glick, R., Stevans, J., & Landsittel, D. (2015). Comparison of spinal manipulation methods and usual medical care for acute and subacute low back pain: a randomized clinical trial. Spine, 40(4), 209–217.  
\* Tarride, J. E., Burke, N., von Keyserlingk, C., Negrini, S., Goeree, R., & Adachi, J. D. (2019). Cost-effectiveness of non-pharmacologic, non-surgical interventions for knee osteoarthritis: a systematic review. Osteoarthritis and Cartilage, 27(9), 1263–1284.  
\* Vickers, A. J., Vertosick, E. A., Lewith, G., Macpherson, H., Foster, N. E., Sherman, K. J., & Witt, C. M. (2018). Acupuncture for chronic pain: update of an individual patient data meta-analysis. The Journal of Pain, 19(5), 455–474.  
\* American Society of Addiction Medicine (ASAM). (2020). Opioid Addiction Treatment. Retrieved October 5, 2021, from https://www.asam.org/Quality-Science/quality/clinical-guidelines/opioid-addiction-treatment  
\* World Health Organization (WHO). (2017). Opioid analgesics. Retrieved October 5, 2021, from https://www.who.int/medicines/areas/quality\_safety/6\_1\_Update.pdf