

A Comparison of Suboxone and Methadone in the Treatment of Opiate Addiction

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Abstract

Background: The rate of drug dependence and abuse is a growing problem in the United States. Since 1990, the rate of death from drug overdoses has tripled. According to the Center for Disease Control, for every one drug overdose there are 130 people that abuse or are dependent on drugs. Opiates are the primary drug class that is abused and there is a great need to identify effective treatment options.

Method: A review of the literature was conducted using articles regarding opiate addiction and treatment that were published between 2009-2014 in peer-reviewed journals.

Results: Suboxone and methadone are both proven to be effective treatment options. Both medications have unique risks and benefits, and the research does not indicate that one medication is a better option than the other. This decision must be based on an individual basis after reviewing important patient factors such as health status and access to the medication.

Conclusion: Suboxone and methadone each have their own advantages and disadvantages. When choosing an appropriate medication, many factors must be considered, such as dosing schedule, side effects, risk of abuse and overdose, and cost. The choice must be made as a collaborative effort between the provider and the patient to choose the most appropriate and effective medication.

Keywords: Suboxone; Methadone; Buprenorphine; Naloxone; Opiate addiction

Introduction

A comparison of suboxone and methadone in the treatment of opiate addiction

The rate of opiate addiction and dependence is growing exponentially in the United States. Since 1990, the rate of drug overdoses have more than tripled and the majority of these are caused by opiates [1]. Opiates are a class of medication defined as a psychoactive substance that is derived naturally or synthetically but has similar effects to morphine. This includes medications such as codeine, oxycodone, heroin, and even methadone and buprenorphine [2]. Opiates are legally prescribed to patients for pain management of acute, chronic, or surgical pain. Patients taking these medications long term often develop a tolerance, or need for increased dosages to achieve analgesia. This can further develop into an opiate dependence, in which the patient requires continued dosages to prevent withdrawal symptoms. However, some people also develop an addiction to opiates, which is defined as the inappropriate use of medication for purposes other than those it was prescribed for and despite medical, legal, and social consequences. Addiction is frequently associated with psychological attributes while dependence and tolerance are more physiological, but addiction and dependence are often coexistent. Addiction and dependence can occur in any person and is regularly the result of taking more than the prescribed opiate dose or obtaining opiates illegally so the user can experience desired effects such as analgesia or euphoria. As a result of the analgesia and euphoric effects, there is a high addiction potential for many individuals, which is why opiate addiction and dependence is such a widespread problem [3].

The growing incidence of opiate addiction and dependence necessitates that effective treatment is developed to treat addiction and prevent overdose. Currently, treatment for opiate addiction is a difficult, complicated, and a multifocal process. Addiction is a complicated disease and has many physical and psychological components that need

to be addressed in order for treatment to be effective. Addressing the psychological components of addiction are key in long term success of treatment, but helping the patient end their dependence on the opiate and preventing them from restarting use of the drug is very difficult. Today, medication is being used by many treatment programs to help patients manage their addiction with the hope that they can one day achieve opiate abstinence. Methadone has been used for this purpose for decades and more recently a combination drug of buprenorphine and naloxone (Suboxone) was introduced. These medications share many similarities but differ greatly in side effects, cost, and other areas. This literature review will examine both medications and compare and contrast their use in the treatment of opiate addiction [4].

Suboxone

Suboxone is a combination of the medications buprenorphine and naloxone. Buprenorphine was discovered in the 1960's and was used throughout the years in several different forms for the treatment of opiate addiction. In the 1970's, pharmaceutical companies were working hard to discover medications and combinations that could provide a 'cure' for addiction and the focus continually shifted from opiate agonists, like buprenorphine, and opiate antagonists, like naloxone. There were many forms and combinations of these treatment medications and eventually buprenorphine and naloxone

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were combined to create Suboxone, which received Federal Drug Administration approval in 2002 [5]. To fully understand how Suboxone can be effective, it is important to understand opiate receptors and Suboxone's effect on the receptors. There are three main opiate receptors in the brain, specifically the mu, kappa, and delta receptors. These are the same receptors affected by endorphins, which can produce a sense of euphoria and are the main catalysts for creating habits. These receptors are often called "reward centers" because the release of endorphins onto these receptors causes pleasant sensations, or rewards, and thus increase the likelihood of the person performing the same actions repeatedly to release more endorphins. This is the same concept that happens when a person exercises; they are often rewarded with a feeling of satisfaction after the exercise is complete so that they will be more willing to repeat that act. The use of artificial opiates, such as heroin or oxycodone, affects the opiate receptors in the same way as endorphins, however the effects are often magnified and the person can experience intense feelings of euphoria or high. These intense feelings often make it easy for a person to develop a habit that will continually act on the receptors to replicate those feelings. This is how the process of opiate addiction and dependence is developed [6].

In the battle against opiate addiction, medications that are opiate agonists, such as methadone and buprenorphine, are often used. Opiate agonists block opiate receptors by binding to them, preventing other opiates, such as heroin or oxycodone, from binding. Although opiate agonists can also produce a feeling of high, the effects are less than other artificial opiates and can be used in tapering doses to help decrease a person's desire for opiate medications. Buprenorphine is a unique opioid agonist that works at the mu receptor, but it is the only medication considered a partial agonist. This means that it still effectively blocks the opioid receptor but has a lower euphoric effect. Actually, once a patient reaches the stabilization dose of therapy, it is difficult for them to obtain feelings of intoxication due to the partial blocking of receptors. Naloxone is an opioid antagonist, which binds to opioid receptors but produces no effect on them. This means that the receptor is blocked but not stimulated, which produces no euphoric effects, and blocks other opiates from stimulating the receptors. Naloxone is added to Suboxone to help block receptors to lessen euphoria but to also help prevent abuse of the drug. Since the buprenorphine can create euphoric feelings similar to other opiates, it is sometimes dissolved in water and injected, similar to heroin. However, the antagonist effect of naloxone intravenously is very strong and will block the receptors, putting the patient into opiate withdrawal and discouraging this practice. Naloxone is fast acting and is often used in cases of opiate overdose and the withdrawal symptoms, such as vomiting, chills, and tremors, it produces are definitely unwanted by the opiate addict. Suboxone is very effective in reducing artificial opiate cravings due to its unique combination of an agonist and antagonist, however, it has been used in the treatment of addiction for a relatively short time compared to other medications and the decision to use it must be made very carefully based on the patient's medical and social qualities [6].

Methadone

Methadone has been used in the treatment of opiate addiction for many decades. It was first used and marketed in 1939 in Germany as an effective painkiller. In the early 1950's, the use of methadone began in the United States as a treatment for patients detoxing from heroin, however, it was not until 1972 that the FDA approved the drug as a daily medication to treat patients with opiate addiction. Since then, methadone has been clinically shown to reduce the number of those addicted to opiates with limited long term side effects. Like

buprenorphine, methadone is an opiate agonist that affects the mu receptors. Unlike other opiate medications, methadone achieves a stabilization dose without tolerance; meaning that once the patient reaches their stabilization dose, they have relief of symptoms (pain or addictive cravings and withdrawal) but do not develop a tolerance and need to continually increase the dose. In addition, methadone binds to approximately 30% of the mu receptors, leaving the other 70% free to perform their normal physiological functions such as regulating pain, pleasure, and reward. Since methadone is a strong opioid agonist, it is also very effective in pain management and is often used for patients with chronic pain. It is because of these strong effects that it is an effective drug in the treatment of opiate addiction. Methadone gives opiate addicts a satisfactory fulfillment of their craving for opiates like heroin, but it is much easier to monitor and taper the doses to decrease the patient's dependence on the medication, and eventually remove them from the medication completely. Since methadone is an opioid agonist, there is a period of withdrawal once a patient stops the medication and the period of withdrawal is typically longer than with other opiates, but the symptoms are significantly less severe. This makes the medication more attractive to those opiate addicts seeking help that do not want to go through the painful withdrawal symptoms of heroin and other opiates. Over the years, methadone has proven to be an effective medication for some patients in both pain control and the treatment of opiate addiction, however it may not be safe or effective for other patients and other therapies may be required [7,8].

Dosing and length of therapy

Suboxone is often used as outpatient treatments to help patients addicted to opiates reduce their cravings and need for the medications. The goal of treatment is to find the lowest dose possible of Suboxone, which reduces cravings for other opiates without producing symptoms of withdrawal. Dosages can range from 2 mg buprenorphine/0.5 mg naloxone to 12 mg buprenorphine/3 mg naloxone and the dose is dependent on the stage of treatment. The first phase of treatment is called the induction phase and typically the patient is started on higher doses of Suboxone when symptoms of withdrawal begin to show during this phase. The Suboxone helps lessen the symptoms and blocks any use of other opiates, so the patient cannot supplement with more drugs. The stabilization phase begins after about 1 week and lasts 1-2 months. The patient in this phase usually shows no signs of withdrawal, has minimal side effects, and has greatly reduced cravings for other opiates. At the end of the stabilization phase, the patient is probably on a lower dose of Suboxone and this dose will be maintained during the maintenance phase. This phase varies and can last from a few months to a lifetime. The decision to continue to taper the Suboxone dose or eliminate therapy altogether is a decision made by the patient and the provider and depends on the patient's symptoms, tolerance, and mental state. The length of the maintenance also varies based on the patient's opiate of choice. If they abused drugs, such as hydrocodone, then their therapy is often shorter than those who used illicit drugs, such as heroin [9,10]. Identifying the appropriate dose and length of treatment for Suboxone can be difficult, and for this reason not all providers are able to prescribe the medication. There are special training programs and certifications that providers must complete prior to prescribing and then there are strict regulations on how many patients on Suboxone the provider can manage. This can be from 30-100 patients depending on certain criteria. The dosing and timing of Suboxone can be very complicated and requires commitment by the patient and provider but unique makeup of the medication makes it an effective treatment for opiate abuse in many patients [6].

Methadone has a similar dosing scheduling to Suboxone. In the

induction dosing of oral methadone, the dose should not exceed 30-40 mg a day due to the risk of adverse events such as respiratory depression. In the induction phase it is recommended that the dose increases by 5-10 mg every 3-5 days. This phase typically lasts until a steady state of methadone as verified by blood test is achieved. After the initial induction phase, there is a stabilization and maintenance dose. Regular serum methadone levels are drawn during the maintenance therapy. If levels are less than 200 ng/mL they are most likely sub-therapeutic and may experience withdrawal symptoms. Optimal levels are often considered between 400-500 ng/mL. Dosages are often adjusted based on serum results to help the patient avoid withdrawal symptoms. Methadone dosages are titrated based on these results; however, the amount of titration will be dependent on each patient's symptoms and history in addition to their serum levels. Once the patient is stabilized on methadone therapy, the ultimate goal is normally to taper the doses until the patient can eventually stop taking the medication [11]. This may take anywhere from weeks to years depending on the patient. Like Suboxone, it takes special providers to be able to prescribe methadone and monitor patient therapy. There are many methadone clinics where this is done and methadone is more likely to be prescribed in a clinic setting rather than in the office like Suboxone [6].

Side effects

One of the major risks of these medications is their abuse potential. Methadone is a full opiate agonist, which means that it can produce greater feelings of euphoria than the partial opiate agonist used in Suboxone. The addition of naloxone also helps prevent the abuse of Suboxone, because the medication cannot be diluted and injected intravenously like methadone. Studies show that methadone users also have a higher risk of overdose on the drug, in part because it does not include an opiate antagonist like Suboxone [6,12,13]. Both medications have shown to have a fairly low side effect panel for serious side effects. According to Reckitt Benckiser Pharmaceuticals Inc. [10], common side effects of Suboxone include chills, fever, abdominal pain, vasodilation, withdrawal syndrome, constipation, nausea, vomiting, diarrhea, insomnia, and anxiety. The risk of respiratory depression or overdose is considered minor with Suboxone. The minor side effects of methadone are similar and include drowsiness, headache, nausea, vomiting, constipation, anorexia, abdominal pain, insomnia, and dry mouth. However, methadone has been shown to have more serious cardiovascular side effects. Several studies have shown a significant increase in the potentially fatal cardiac rhythm, torsades de pointes. There is also a higher risk of overdose and respiratory depression than with Suboxone. A significant difference related to mortality rates between Suboxone and methadone use has not been found. The side effects and risks of serious adverse events must be considered when deciding between the two medications [6,12,14,15].

Patients that are pregnant or may become pregnant add another level of concern to providers when choosing appropriate opiate addiction treatment. Suboxone is ranked as a pregnancy category C, meaning that there have been studies that showed negative fetal effects in rats and rabbits but not in humans. There have not been any significant and well controlled studies to date to verify the safety of Suboxone during pregnancy, so the use of Suboxone during pregnancy must be based on a careful risk/benefit ratio [10]. Methadone is also ranked as a pregnancy category C. However, it has been in use longer and more studies have been conducted on its safety during pregnancy. Due to this, it is generally chosen as the best treatment of opiate addiction during pregnancy [16]. Based on these studies, the choice between the two medications may be dictated based on potential side effects in the patient, especially if they are at risk for cardiovascular problems or high

chance of pregnancy. The decision between methadone and Suboxone must be carefully weighed based on the side effect profile and patient's pregnancy status [13,16].

Cost

Accessibility should also be considered when comparing the two medications. The cost of both methadone and Suboxone is quite substantial and may be the deciding factor for treatment choice based on the patient's financial situation. The price of Suboxone often varies depending on pharmacy, insurance and dosage but typically the tablet form of medication ranges from approximately \$430 to \$640 for 60 tablets, which in most patients is about a month's supply [17]. The cost of providing methadone is approximately \$42-\$166 per week with an average of \$91. The average cost per year is typically \$5250 if the patient remains in consistent treatment. The cost and accessibility of these medications can make them difficult for patients to obtain. For these reasons it is very important for the provider and patient to discuss the patient's best option and provide any resources to help obtain the medications. Methadone is typically less expensive than Suboxone and this may be the deciding factor when the physician is trying to choose between methadone and Suboxone for patients [18].

Long term success

There are many studies that have examined the long term effects and success of methadone since it has been used for many years for treatment of addiction. There are some studies on Suboxone but significantly fewer than on methadone due to its more recent use in addiction. As of now, there are not many studies that compare the long term use of Suboxone or methadone directly [12]. However, a systematic review by Mattick, Breen, Kimber, and Davoli [13] did compare several aspects of methadone and Suboxone based on self-report and statistics. Criminal activity is often associated with the use of heroin and the review examined the rates of crime in areas with more Suboxone and methadone treatment. The review showed that there were no differences in the reduction of criminal activity or heroin use by self-report when comparing the effectiveness of Suboxone and methadone in regards to these areas.

One of the most important aspects of opiate addiction treatment is the ability to retain patients in the treatment program long enough to create a successful outcome. Since methadone has been in use significantly longer, there are many more studies in regards to its treatment retention rates over those of Suboxone. Retention rates in the first year of methadone treatment are typically 70-80%, compared to 56.9-90% for the first year of Suboxone treatment. All studies examined for methadone outcome success found a significant reduction in illicit drug use, risky behaviors, and health problems. However, one study found that there was a significant reduction in the percentage of opioid found on urine drug screens of patients receiving Suboxone therapy over those receiving methadone. These studies all show that both methadone and Suboxone are effective treatment modalities for opiate addiction, however the choice between the two depends on many factors, including patient's health status, cost, and availability [19,20].

Conclusion

Opiate addiction is a serious and growing worldwide problem. Due to the vast impact of opiate addiction, all medical professionals need to be familiar with effective treatment options. It is important to identify and utilize the most effective treatment options to prevent opiate overdoses and reduce the addiction rates. The two most common medication choices for this treatment are Suboxone and methadone.

Much research has been conducted on these medications and both have proven to be effective, however each medication comes with its own risks and benefits. Methadone has been used for decades and is well-known and established, making it the easy choice for some providers. Suboxone has been used for a shorter time frame and there is less research available but it shows promising success in the treatment of addiction. The decision between these two medications is a difficult one to make and many factors must be considered including their dosing schedule, side effects, risk of abuse and overdose, cost, and long term effects. Overall, both medications can be effective in reducing the rates of opiate addiction, but the choice of medication must be made as a collaborative effort between the provider and patient while considering all the above factors.

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