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Buprenorphine Versus Methadone for Opioid Use Disorder

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Abstract

The purpose of this literature review is to analyze the use of Buprenorphine and Methadone for the treatment of opioid use disorder. Comparison of overall safety, efficacy, morbidity and mortality between the two treatment options is accomplished throughout this article. The literature review was performed using databases: PubMed, Clinical Key, Cochane and Uptodate. Results were limited to studies completed within the past 7 years. Methadone has been the treatment mainstay of opioid use disorder for decades. Buprenorphine has increased in popularity and prevalence for treatment of opioid use disorder, especially after receiving FDA approval for such use in 2002. Several benefits of Buprenorphine therapy were discovered including a significant reduction in overdose fatalities, more convenient dosing options and easier access to prescribing locations. Retention rates of those receiving Buprenorphine was found to be lower, sometimes quite significantly, than those who received Methadone therapy. A review of the literature showed that those receiving Methadone for the treatment of opioid use disorder have a higher likelihood of hospitalization or fatal overdose during the initiation of therapy. A significantly higher retention rate was shown in those receiving Methadone, in comparison to Buprenorphine. However, Methadone use was found to have an association with occurrences of neonatal abstinence syndrome in those taking the medication during pregnancy. A common negative theme throughout the literature review was the lack of a control population when comparing Buprenorphine and Methadone. Conclusively, neither Methadone nor Buprenorphine were found superior when used for treatment of opioid use disorder. Careful consideration must be given to the patient's personal situation, drug use history and likelihood of compliance.

Introduction

More than 67,000 Americans died from drug overdoses in the year 2018, this included illicit drugs and prescription opioids. Synthetic opioids, primarily Fentanyl and other similar compounds, accounted for 30,000 of the drug overdose deaths. Heroin was involved in nearly 16,000 deaths while roughly 15,000 deaths were attributed to prescription painkillers (Centers for Disease Control and Prevention, 2020). Medicinal treatment options for opioid use disorder has been limited, with Methadone being the mainstay. Recently, Buprenorphine has become a popular option for treatment of opioid use disorder as well. The purpose of this study is to determine whether overall morbidity and mortality is reduced more with Methadone or Buprenorphine in the treatment of opioid use disorder.

Statement of the Problem

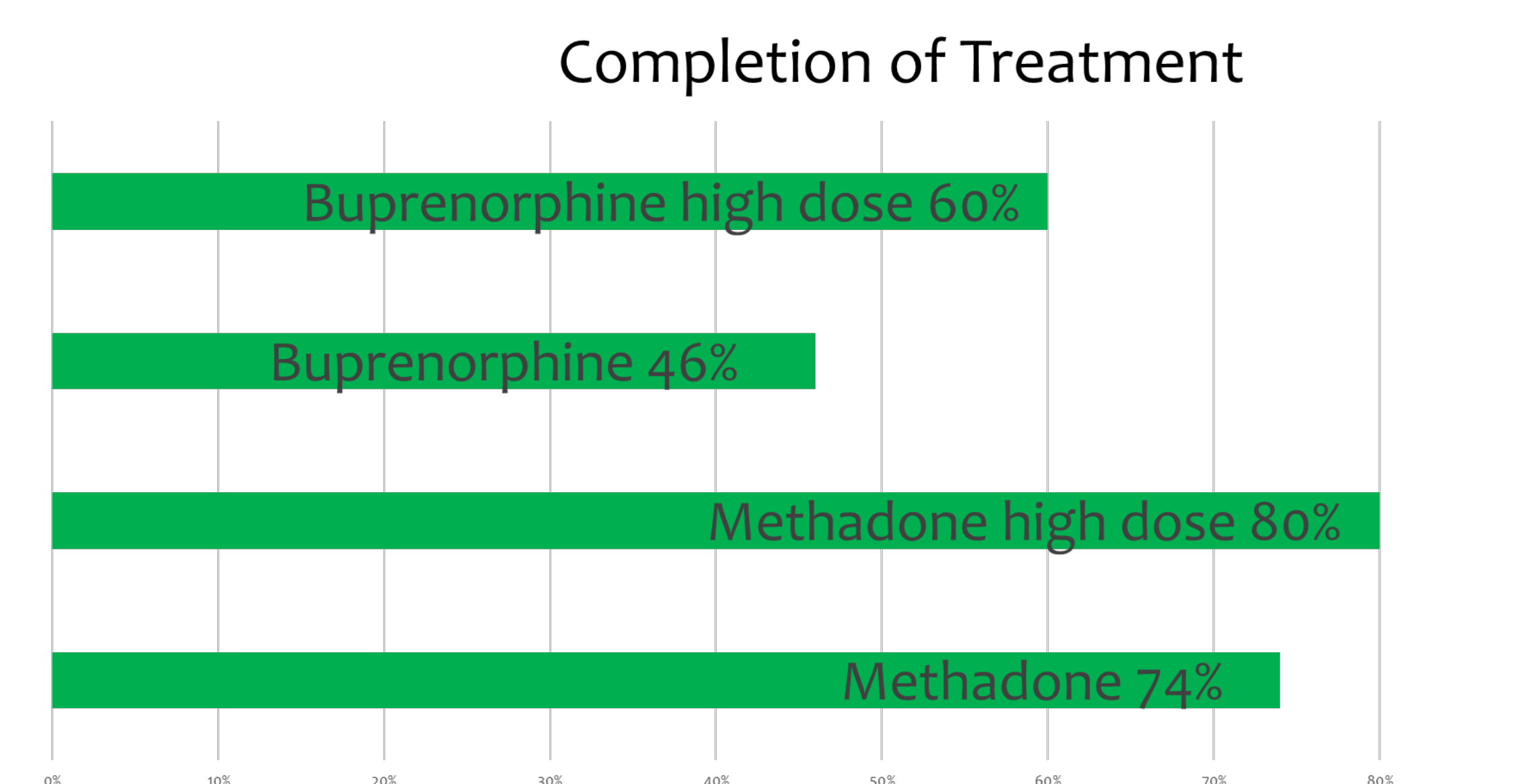
Methadone, FDA approved for treatment of opioid addiction in 1972, is a full agonist which activates opioid receptors. This mechanism of action has successfully aided in the treatment of opioid addiction, however, also allows for abuse potential. For this reason, methadone treatment must take place in a specialized, highly structured clinic, often requiring daily in-clinic dosing. Buprenorphine is a partial agonist which activates opioid receptors but produces less of a response. Therefore, it reduces abuse potential while still offering successful treatment of opioid addiction. Due to the decreased likelihood of abuse, buprenorphine is the first medication used to treat opioid use disorder in a physician office, and was FDA approved for such use in 2002, however, this comes at a cost nearly triple that of methadone.

Research Question

In patients with opioid use disorder, does treatment with buprenorphine in comparison to methadone lead to overall decreased morbidity and mortality?

Literature Review

- Fernandez et al. (2019) concluded methadone treatment is associated with increased antenatal care, improved fetal growth, decreased mortality and fewer complications compared to ongoing opioid use. However, the majority of neonatal abstinence syndrome is caused by maternal methadone exposure. Buprenorphine treatment led to an approximately seven-day shorter hospital stay and approximately five-day shorter duration of treatment for neonatal abstinence syndrome. Buprenorphine treatment was also shown to have less fetal cardiac and movement suppression, improved neonatal growth parameters and less severe neonatal abstinence syndrome symptoms.
- For adolescents, methadone is recommended mostly due to the significantly increased treatment retention rate compared to buprenorphine. On average, methadone retained individuals for 354 days while buprenorphine retained individuals for only 58 days, showing that the potential for positive outcome in adolescents is drastically higher in the methadone category. Srivastava, Kahan, and Nader (2017)
- There were no fatal overdoses in the buprenorphine group during the induction phase of treatment (first 28 days) while high rates of fatal opioid overdoses were observed in patients treated with methadone in the induction phase. Buprenorphine also had significantly lower hospital admissions for non-fatal opioid poisoning ($p=0.018$) than methadone. Kely and Hulse (2017)
- Results confirmed the methadone group had 74% completion of treatment and the Buprenorphine group had 46% completion of treatment. However, when the maximum methadone dose reached or exceeded 60mg/day, completion rate reached 80%. When doses of buprenorphine reached 30-32mg/day, completion rates reached 60%. Hser et al. (2013)



- Duration of treatment was shown to have a direct correlation between relapse and overall morbidity and mortality. Therefore, average duration of treatments in each group weighed significantly on the final outcomes. For injection opioid users, methadone is recommended since treatment retention rates are significantly higher. Methadone was also found to be more effective at reducing withdrawal symptoms and cravings, given its full opioid agonist effects. For oral prescription opioid users, buprenorphine is recommended for socially stable individuals for two reasons; its safer side effect profile and higher likelihood of treatment retention due to a more stable and supportive social environment. Srivastava, Kahan, and Nader (2017)
- Overall, it appears buprenorphine therapy has significant positive results for those who remain in treatment but has an alarming rate of dropout early in the treatment process. Demetrovics et al. (2009)
- Conclusions included buprenorphine treatment having a lower all-cause mortality in each treatment category. After adjustment for confounding variables, there was evidence of reduced drug-related mortality at initiation of treatment with buprenorphine when compared to methadone. Hickman et al. (2018)

Discussion

- After significant review of the literature, a common theme presented, methadone and buprenorphine treatment are both effective treatment modalities for opioid use disorder. However, when comparing methadone treatment to buprenorphine treatment for opioid use disorder, there is no evidence of buprenorphine being superior to methadone for treatment of opioid use disorder as expressed by Potter et al. (2013). Consideration must be given to the patient and the situation to determine the most appropriate treatment plan. Close follow up and constant reevaluation should also be considered during therapy to monitor for a need in treatment alteration.
- A concern associated with opioid use disorder treatment is overall treatment retention, further supported by Srivastava et al. (2017) discovering a direct correlation between relapse and overall morbidity and mortality. Demetrovics et al. (2009) found a 22% treatment dropout rate within the first month of buprenorphine treatment. This high dropout rate must be considered when placing a patient on buprenorphine therapy. Srivastava et al. (2017) recommended buprenorphine treatment for socially stable individuals who have a supportive social environment which increases likelihood of treatment retention. For injection opioid users and those with a less-stable social environment, methadone is recommended as treatment retention rates are significantly higher than that of buprenorphine. However, the higher dropout rate of buprenorphine can likely be mitigated by promptly placing the patient on methadone if indicated. Medication dosage should also be considered for effective treatment. Saxon et al. (2013) found an increase of retention from 46% to nearly 60% when buprenorphine dosages reached 30-32mg/day. Therefore, higher doses should be considered for those with higher likelihood of treatment attrition.
- Reduction of all-cause mortality must be considered when prescribing medication assisted treatment for opioid use disorder. Reduction or elimination of opioid use is the goal of both methadone and buprenorphine treatment. However, without a correlating reduction in morbidity and mortality, treatment may not be considered effective. Hickman et al. (2018) found buprenorphine to have a lower all-cause mortality in several treatment groups including: first four weeks of treatment, remainder of time in treatment and four weeks following end of treatment. More so, Kely and Hulse (2017) discovered there was a statistically significant reduction in rates of opioid poisoning which required hospitalization in patients who were treated with buprenorphine. No fatal overdoses were observed in the buprenorphine group during the induction phase while high rates of fatal opioid overdoses were observed in patients treated with methadone during the induction phase. Overwhelmingly, it seems buprenorphine is the safer option when prescribing for medication assisted treatment of opioid use disorder.
- It cannot be ignored that a drawback to most available studies for buprenorphine and methadone treatment is the lack of a control population. Due to the nature of opioid use dependence, the ability to gather data on a population attempting to discontinue opioid use in the absence of formal treatment or medication is limited.
- In conclusion, neither methadone nor buprenorphine treatment were found to be overall superior. Consideration must be given to each patient and their individual situation to select the correct treatment modality.



<https://www.livescience.com/44036-heroin.html>

Applicability to Clinical Practice

The information provided within this literature review will allow medical providers to guide those suffering from opioid use disorder to the most effective treatment modality. It will also allow providers to give a clear and informed explanation to patients pursuing medical treatment for opioid use disorder including, associated risks, success rates, therapy delivery methods and more.

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