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Comparison in the Effectiveness of MAT in Patients with Oxycodone vs Heroin Opioid Use Disorders

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by

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Abstract

The purpose of this research and systematic literature review is to determine if there is a measurable difference of effectiveness in medication assisted treatment (MAT) in patients with oxycodone and heroin use disorders, retention in treatment, and sustained sobriety. In this review, the databases searched included CINAHL, Clinical Key, and Embase. A variety of key terms and MeSH terms were used to define a set of literature discussing the topic. The works chosen for review were published between 2015 and 2019 were peer reviewed, and included randomized control trials, pilot studies, and systematic reviews. Sources that were excluded, included those published prior to the year 2015, had poor study design or no useful statistical data. For this review, 16 resources were selected. Much of the research presented show proven evidence of the efficacy and usefulness in MAT for the treatment of opioid use disorder. However, much of the research does not seem to directly compare the statistical difference in effectiveness of MAT for oxycodone and heroin use disorders, rather they are both put together in one group. The differences become apparent when adjunctive therapies are added. These therapies include; inpatient and outpatient rehabilitation, the type of medication being used, and the addition of cognitive behavioral therapy (CBT). Consequently, more research is still needed to be done in order to definitively determine if MAT is more effective for treating oxycodone use disorder or heroin use disorder.

Keywords: medication assisted treatment, oxycodone, heroin, oxycodone use disorder, heroin used disorder, opioids, opioid use disorder.

Introduction

Opioid-use disorder is a major concern in the United States leading to an increased number of overdose deaths per year from both prescription and illegal opioids. Roughly half of opioid use deaths are attributable to prescription medications like oxycodone with other half from illegal drugs such as heroin. Over prescribing of opiates for pain management is one of the major contributors to opioid deaths. The ease of availability of illegal drugs like heroin has also added to the problem. Medication Assisted Treatment (MAT) was developed for this problem and the same medications can be used for both prescription and illegal opioid addiction. The purpose of this study is to compare the effectiveness of MAT programs at treating opioid-use disorders in both oxycodone and heroin users and determine if there is a difference in sustained sobriety and compliance.

Statement of the Problem

Medication assisted treatment programs have a negative stigma associated with them. Many providers believe that the use of medications like buprenorphine and naltrexone are merely substituting one opiate for another. MAT medications are opiates, but they are only partial agonists of the mu receptors compared with oxycodone and heroin which are complete agonists. The partial agonists activate the receptors without the euphoria from the complete agonists, and also satisfy cravings and withdrawal symptoms. MAT has been proven to be effective. Providers need to be informed on which patients are going to respond better to treatment with medications and which patients need alternate forms of treatment.

Research Question

In opioid addicted patients, is MAT a more effective therapy to achieve sobriety and compliance for patients addicted to prescription opioids, such as oxycodone, or more effective for those addicted to a street opioid, like heroin?

Research Methods

To prepare this article, the author searched CINAHL, Clinical Key, and Embase databases and selected articles to provide a broad overview of opioid use disorders, including which medications are used in treatment, how these medications are effective, and how using these medications along with other forms of therapy can be helpful in maintaining sobriety. The search included key terms and MeSH terms: medication assisted treatment, oxycodone, heroin, oxycodone use disorder, heroin used disorder, opioids, opioid use disorder. The search included articles from the past 4 years (2015-2019). Studies were included if they focused on safety and effectiveness of medication assisted treatment for both prescription opioids and illicit opioids to mainly focus on heroin as the illicit drug. Other studies included in this research encompassed, therapies to maintain sobriety once treatment with medication had begun. The literature focus of this investigation, because of their high quality, became the numerous newly published projects and studies.

Safety and Efficacy of Medication Assisted Treatment

Opioid use disorder (OUD) has become a major epidemic and has affected many populations across the United States and especially in rural areas, where there are not as many healthcare facilities to provide service (Kawasaki, 2019). The medications used in treatment are buprenorphine, naltrexone, and methadone. Medication assisted treatment (MAT) is medical treatment used to help individuals with opioid use disorder. Unfortunately, the number healthcare providers participating in the treatment programs is very low, likely because they have a negative stigma surrounding it. Primary care providers are on the front lines of the overdose epidemic, but the demand for treatment far exceeds the capacity to treat. Certain projects, like project ECHO, were developed for this supply and demand problem. The mission was to provide and expand comprehensive, patient-centered and innovative evidence-based treatment to individuals with substance use disorders by using four core principles: (1) use technology to leverage scarce resources; (2) share best practices to reduce disparities; (3) employ case-based learning to master complexity; (4) monitor outcomes to ensure benefit (Kawasaki, 2019).

The project connected primary care sites and hospital systems in rural areas through a combination of Hub and spoke, bridge clinic services provided at the Hub, peer recovery services, and layered emergency departments. To investigate the efficacy, a study was conducted to review medications used in the treatment and to determine retention rates. The initial trial had 180 patients with 127 started on buprenorphine, 9 on extended-release naltrexone, and 30 on methadone treatment. The first 6 months showed a treatment retention rate of 43% of the buprenorphine patients, 11% of the extended-release naltrexone patients, and 63% of the methadone patients (Kawasaki, 2019).

This study along with the development of project ECHO, had many other components other than merely the medications the patients were prescribed. It is recognized that in order for treatment of OUD to be successful, four key components were necessary. These components are comprised of; pharmacological therapy, psychosocial services, integration of care, and education and outreach (Kawasaki, 2019).

In another article by Oesterle et al. (2019), a comparison of all three FDA-approved medications for treatment of OUDs (buprenorphine, naltrexone, and methadone) appear to offer evidence of efficacy. One study found that individuals randomly assigned to either methadone or buprenorphine showed that 33.2% had achieved 5-year abstinence from heroin, only 20.7% had remained abstinent from both heroin and other opioids. The two treatment groups were compared and showed that after 5 years, opioid use at follow-ups were higher among participants randomized to buprenorphine, relative to methadone. However, both groups were more successful than the no-treatment group, and mortality was not different between the 2 groups. Unfortunately, there was no data available from the naltrexone group for the 5-year follow-up (Oesterle, 2019).

Opioid use disorder treatment is a long-term commitment which can take years and, in some cases, indefinite medication and cognitive assistance to remain abstinent. For those who become pregnant while suffering from OUD, continuing with MAT is a risk versus reward scenario. Opioids have an effect on the fetus and after delivery can cause neonatal abstinence syndrome (NAS) after delivery. MAT medications when compared to heroin and oxycodone have much lower opioid receptor agonist activity but hold a higher affinity to the receptor as well. This means, cravings will be satisfied without the euphoria felt with complete opioid receptor agonists.

In a study by Gala et al. (2019), 257 pregnancies were followed after having antenatal exposure to buprenorphine from 2015-2018. The study was performed at a single center to determine the relationship between buprenorphine dose and neonatal abstinence syndrome incidences. Buprenorphine has been the preferred medication for opioid maintenance therapy in pregnancy in comparison with other medications. No major congenital anomalies occurred during the study. Doses at delivery were divided into three groups: low (0-10 mg), medium (11-20 mg), and high (>20 mg) dose groups. Correlations between delivery dose and neonatal outcomes of interest were analyzed. A statistically significant increase in NAS duration was found in the high dose group (P¼0.06) and decrease in birthweight in the medium dose group (P¼0.002) were noted in neonates of mothers with positive urine drug screens at delivery. No statistically significant difference was seen among other neonatal outcomes, such as APGAR scores and gestational age at delivery by buprenorphine dose and urine drug screen status. Similar trends, in the small dose group, were noted by not statistically significant (Gala, 2019). No major complications occurred in the study and at lower doses, lower incidences of NAS were observed. It was found that if the dose is gradually decreased prior to delivery, the incidence of NAS also lowers making it safer for the neonate (Gala, 2019).

Patients with Opioid Use Disorder Involving Oxycodone

A large number of individuals who suffer from opioid use disorder involving prescription pain medication, such as oxycodone, have chronic pain. There are also a lot of individuals that use prescription pain medications recreationally including adolescents. Along with the recreational use of prescription opioids, there is a high correlation with mental health issues, such as depression and anxiety.

In an article by Clayton et al. (2019), a survey of 14,765 high school students in grades 9-12 was performed in 2018. A questionnaire was released to assess the lifetime, nonmedical use of prescription opioids (NUPO) with the responses listed as “zero times” or “one or more times”. This questionnaire was paired with health behaviors and experiences such as substance use, violence victimization, suicidal thoughts and behaviors, sexual behavior and others, to determine if there was a correlation between those factors and NUPO. The overall prevalence of NUPO among high school students was 14%. The prevalence of NUPO varied significantly by grade ($p<0.0001$) and sexual identity ($p<0.0001$). In each of the adjusted models, students who engaged in NUPO had a significantly greater likelihood of also engaging in each substance use behavior, than students without NUPO (Clayton, 2019).

Students who engaged in NUPO were significantly more likely also to have reported being bullied on school property or threatened or injured with a weapon on school property than students without NUPO. Students who engaged in NUPO also were more likely to experience each of the three suicide behaviors than students without NUPO (ranging from seriously considering suicide to attempting suicide). Students who engaged in NUPO were more likely to be at increased risk for sexual behaviors ranging from not using a condom, nor a highly effective hormonal contraceptive method during last sexual intercourse, to having 4 or more sexual partners. It was also found that students who engaged in NUPO were 5-6 times more likely to have poor academic performance and more likely to have experienced persistent feelings of sadness and hopelessness (Clayton, 2019).

A study was performed from June 2015 to June 2016 in an article by Gardner et al. 2019, to predict opioid use disorder in patients with chronic pain presenting to an emergency department. The goal was to categorize these individuals for chronic pain issues as either “opioid

use disorder" or "nonopioid use disorder" patients. This was determined by a series of questions, physical exams and past medical histories that were performed on 89 patients to help categorize the participants. The results found that 45 of the 89 participants had OUD. Those 45 participants also had a higher proportion of documented or reported psychiatric diagnoses ($p=0.049$), preference of opioid treatment ($p=0.005$), current oxycodone prescription ($p=0.043$), borrowed pain medicine ($p=0.004$) and non-authorized dose increase ($p<0.001$). The state prescription monitoring database revealed the OUD group to have increased number of opioid prescriptions ($p=0.005$) and pills ($p=0.010$). Participants who borrowed pain medicine and engaged in non-authorized dose increase were 5.2-6.1 ($p=0.025$), ($p=0.001$) times more likely to have OUD. Ultimately, it was determined that patients with chronic pain categorized as having an OUD have distinguishable characteristics and associated mental health behaviors (Gardner, 2019).

Patients with chronic pain and their severity of the pain can be hard to judge and patients with OUD become even more sensitive to pain after a period of time, making treatment and stopping opioids a tough battle. A pair of studies by Paulus et al. (2019), discussed pain severity and prescription opioid misuse among individuals with chronic pain and the moderating factor of alcohol use. The goal of the studies was to examine the relationship between pain and prescription opioid misuse and the moderating role of alcohol use severity, using data from online samples of individuals with chronic pain. Both studies revealed that the association, between pain severity and opioid misuse was significant for those with high alcohol scores. The findings suggest that alcohol use severity exacerbates the pain-opioid association such that pain is positively associated with opioid misuse only among those with relatively greater alcohol use. Other factors were also considered in the studies which included age, level of education, and depressive symptoms. Including the interaction term of average pain severity and alcohol use in

step three significantly improved model fit (F (7356) =29.00, p < .001, ΔR^2 =.03), and the interaction term was a significant predictor (B = .16, SE = .04, p < .001). Examining the simple slopes revealed that those with high AUDIT total scores (+1SD; B=1.50, SE =.38, p =.001), but not low (-1 SD; B=-.26, SE = .33, p =.430) evidenced a statistically significant association between average pain severity and opioid misuse. The JN technique revealed that the effect of pain severity on opioid misuse was significant only for those with an AUDIT of 4.84 or greater (34.34% of the current sample). It was revealed that greater depressive symptoms related significantly and strongly to greater opioid misuse in both samples (Paulus, 2019).

Patients with Opioid Use Disorder Involving Heroin

The opioid use disorder epidemic has become a major problem in the last few decades. The number of individuals that need treatment greatly outnumbers the capacity of healthcare providers that can supply the necessary services. Heroin use has been a major issue in the opioid epidemic and an article by Brighthaupt et al. (2019), studied the trends in adolescent heroin use in some of the largest urban cities in the United States from 1999-2017. The goal of the study was to determine if the trend of heroin use has remained low and stable or has increased (Brighthaupt, 2019).

The study was conducted by surveying high school students in grades 9-12 regarding the use of heroin, using logistic regression to test for linear and quadratic trends. It included nine of the largest cities in the U.S. The study identified increases in heroin use over time in the majority of the cities over time, which suggests the use among adolescents is increasing (Brighthaupt, 2019). With the increase in heroin and other opioids, MAT treatment with medication alone

cannot solve the problem. Many other factors contribute to the success MAT and incorporating those aspects is where success will be found.

In a study by Colledge et al. (2017), exercise was assessed to monitor the feasibility and acceptance as an adjunctive therapy in patients receiving outpatient treatment for heroin use disorder. The study was a pilot randomized trial of 50 were selected but only 24 individuals willing to take part in the study. The results revealed 92.3% of the participants were compliant or semi-compliant with the exercise condition and were able to exercise at a high intensity level. The other 7.7% of the participants did not follow through with the exercise. Although the sample size was small and participants were allowed to freely select the type and intensity of exercise triggering a number of variables, it was concluded that exercise intervention is a feasible and accepted supplementary therapy to heroin-assisted therapy. The mental aspect, however, specifically mood was increased in all the participants that took part in any type of exercise. Mood is a very important factor to consider in patients in treatment for opioid use disorder.

Along with the mental aspect of MAT, dose adjustments need to be monitored closely to assess how well other symptoms are being controlled such as pain, cravings, and withdrawal symptoms. In an article by Mannaioni et al. (2018), a randomized clinical trial was used to assess how methadone dose adjustments and monitoring of the plasma r-methadone levels of heroin users can be used for therapeutic outcomes. The goal was to determine if there was a significant improvement in retention and therapeutic outcome in patients being treated with methadone, by adjusting the oral methadone dose in order to reach a target plasma r-methadone level of 80-250 ng/mL (Mannaioni, 2018).

A total of 308 patients already in methadone maintenance treatment for heroin use disorder were participants in the study. Participants were randomized into two groups: the first

(controls) received a daily methadone dose, which was previously selected and adjusted on clinical basis by the specialist physician in charge in each participating center. The second group (treated patients) had their daily methadone dose adjusted on the basis of plasma r-methadone concentrations. The belief was that if the patient's plasma r-methadone level was stabilized by constantly changing the daily dose to remain at a certain level it would result in higher retention and better therapeutic outcomes. After six months of the study, 91% of the control group and 81% of the treated patient group were still participating in treatment, indicating that, the constant dose adjustments to stabilize the plasma r-methadone level did not improve retention in treatment. After 12 months there was no significant differences between the two groups. When retention in therapy was evaluated, both groups reported a significant decrease in heroin use. Although the constant dose adjustment theory was not a success, it was determined that patients with optimal plasma r-methadone levels at the beginning of study achieved higher retention rates and therapeutic outcomes than those patients with levels outside the optimal range.

Compliance and Sobriety During and After Treatment

Compliance of MAT and maintaining sobriety is not just simply taking the prescribed medication appropriately. There are many factors that need to be taken into account and it can be an everyday battle for some people. In an article by Huhn et al. (2017), a study was performed to look at the relationship between treatment accessibility and preference amongst out-of-treatment individuals who have an opioid use disorder. The study had 357 participants that were surveyed regarding demographics, insurance status, attitudes toward OUD and self-reported symptoms of OUD. The treatment options participants were most likely to use during their recovery were one-on-one counseling (53.8%) 12-step groups (41.2%) and physician visits (32.8%) (Huhn, 2017).

Participants were asked which types of treatment they would refuse or which treatments they felt did not work. The three treatments assessed least negatively were: sober living/half-way houses (33.1%), methadone clinics (32.2%), and 12-step groups (26.6%). The least endorsed option was one-on-one counseling (5.6%). When put into two groups; one being with insurance and two without insurance, the results of treatment options varied. The cost of medication was the largest deciding factor and participants without insurance endorsed less perceived availability for treatment options compared to participants with insurance. It was determined that out-of-treatment opioid users were particularly interested in counseling-based services and medical care that could be attained from a primary care provider. Results suggest that insurance coverage and perceived access to OUD treatment modalities influences where out-of-treatment opioid users might first seek treatment. Understanding the factors that shape treatment preferences is critical in designing early interventions to effectively reach each of these populations (Huhn, 2017).

In another article by Ober et al. (2018), a study was done to assess patient predictors of substance use disorder treatment initiation in primary care. In clinics that had recently implemented motivational-interviewing and cognitive behavioral therapy (CBT) – based brief treatment and MAT for patients identified with an OUD were involved in the study. The major questions that were asked were: What predisposing, enabling/inhibiting resources and need/severity factors predict initiation of CBT for an OUD in primary care (Ober, 2018).

In the multivariate model examining factors associated with initiation of CBT, being "other" or "multiple" races compared with being White, being homeless and having been arrested within 90 days of baseline, were associated with significantly lower odds of initiating CBT. Greater self-stigma, and having received the collaborative care study intervention were associated with higher odds of initiating CBT. In the multivariate model examining patient

factors associated with initiating MAT include; older age, female gender, having a diagnosis of heroin use disorder compared with having a diagnosis of alcohol dependence only and having received at least one session of CBT were associated with higher odds of initiating MAT (Ober, 2018). Mental health is one of the biggest factors that affect individuals with OUD and even just one session of counseling has shown to improve outcomes.

An article by Prieto et al. (2019), assessed over 3200 patients with an OUD that were receiving MAT to measure engagement and adherence to treatment. The results showed that 32% were in the medication assisted treatment stage, and of those, 60% were adherent to treatment. In another group 78.4% adhered to treatment for at least 90 days and 52.3% for more than one year. Among patients who received MAT, less than one third were adherent for more than one year (Prieto, 2019). The treatment was working, but MAT alone cannot maintain sobriety. Many more factors must be in place for MAT to be successful for long-term sobriety.

Medicated assisted treatment works better when it is combined with a structured facility like a 12-step based professional treatment center. An article by Klein et al. (2019), examined the feasibility of and initial impact of combining these 2 models for individuals with OUDs. The study sought to determine whether patients self-selecting into a treatment program based on a 12-step philosophy would elect to use MAT and if so, what initial outcomes might result (Klein, 2019).

Additionally, researchers tracked patients to determine which recruited participants were successfully inducted on either form of naltrexone or buprenorphine, or no medication; and among patients who took buprenorphine, which patients continued taking it as a maintenance medication beyond the withdrawal period. Injectable naltrexone patients had a higher follow-up rate (92%) than buprenorphine patients (76%), the oral naltrexone patients (67%) and the no

medication patients (62%) ($p<0.001$). Of those patients, 81% reported compliance with their medications. Injectable naltrexone compliant patients were significantly more likely to be abstinent at 6 months than oral naltrexone compliant, buprenorphine compliant, and all other patients (Klein, 2019).

A significant difference emerged for the total number of co-occurring mental health disorders; buprenorphine patients and oral naltrexone patients had a significantly higher number of mental health disorders than the no medication patients. Buprenorphine patients had significantly higher scores on the desire and intention to drug use scale than injectable naltrexone patients and no medication patients. Patients who ultimately chose to maintain on buprenorphine reported significantly higher levels of craving than both naltrexone groups and the no medication group at treatment admission ($p<0.001$) (Klein, 2019).

Discussion

The safety and efficacy of medicated assisted treatment medications has been proven to be safe and effective. Buprenorphine, in the more commonly prescribed form, has naloxone combined with it, which induces withdrawals if taken any other way than how it is prescribed, which is orally. The naloxone prevents patients from experiencing euphoria when injected and patients are less likely to try to abuse the medication other than for its prescribed purpose. There is still a negative stigma about the effectiveness of the medications of many providers. They believe that MAT is merely substituting one opioid for another. MAT has shown to be effective and the providers that are against it, likely need more education about the subject to understand what MAT really incorporates. Buprenorphine has also been shown to be effective during pregnancy. The doses should be lowered as much as possible but remain high enough so it is still

effective for the mother. Studies have shown, no major birth defects from buprenorphine. The newborn may go through withdrawals for a period of time after birth but using buprenorphine is much safer than a full agonist drug like heroin or oxycodone (Gala, 2019).

Patients with opioid use disorders involving oxycodone or heroin share many characteristics. A large proportion of this population will use whichever opioid they can obtain to satisfy cravings or relieve pain and become addicted. For these patients, it has been found that most of them suffer from mental health issues as well, such as depression and anxiety. The use of heroin and oxycodone only increase these behaviors compounding the issue (Tsui, 2016).

Medication assisted treatment can be effective for both types of OUD from prescription medications to heroin. The transition from using to recovery with a change in medication can be the hardest for the patient, and finding the right dose to start with is precarious. Most patients choose to start with buprenorphine as it is convenient and easily administered over naltrexone or methadone. Methadone is very effective but is not convenient for the patient. Methadone is administered once a day but the patient needs to go to the clinic every day for the dose to be administered. For those who utilize this method and stay adherent to it, they do very well, but most choose to stop going. This typically ends in relapse or the patient may find another route to get prescribed buprenorphine or naltrexone.

The research question asked if there is a measurable difference in the effectiveness of MAT comparing oxycodone and heroin users and achieving sobriety and compliance in MAT programs. From the research that was found and utilized, there does not seem to be a measurable difference. The research revealed that many other factors contribute such as homelessness, age, race, depression and anxiety, level of education and others. Almost all patients who suffer from OUD have some level of mental health behavior like depression. MAT is effective for both types

patients, including patients suffering from chronic pain. There does not appear to be a significant statistical difference of effectiveness between drugs.

In order for a patient with OUD to be successful with MAT and achieve long-term sobriety, each patient must be treated as an individual case. Each situation is different and there are more factors than solely treating an addiction with a medication. Some patients need more structure like an inpatient treatment facility to begin their recovery and others do well with just outpatient to start. It has been revealed that almost all patients with OUD however, do better in the long-term if they receive some sort of cognitive behavioral therapy. CBT improves adherence to therapy and maintenance of sobriety past the 1-year mark (Klein, 2019).

In order for all individuals suffering from OUD and want to start treatment, demographics, location, cost of medication, and even having a car or some mode of transportation are important factors that need to be reconciled. Many patients in rural areas that need to see a primary care provider must travel up to 2 hours or more to get to their provider who participates in MAT programs. These are barriers that patients face every day, which complicate and contribute to the opioid crisis. More providers need to utilize MAT programs. There is a large population of patients with unmet needs which could be met if more MAT programs were available. With all the information provided through research, it is ultimately up to the patient, whether or not all the treatment modalities provided will help. If the patient does not want to be treated, MAT will not work until they reach the point of wanting help.

Applicability to Practice

The information gathered with this research is very valuable as a provider. MAT is a great way to help reduce the opioid crisis and will help in making better choices, and be more conscientious about prescribing opioids to patients who need them and what to watch out for. MAT is also another tool to build your patient numbers and help the healthcare facility bring in more patients and money.

If more providers participated in MAT programs, at their healthcare facilities, the patients would have another option for their required care. By seeing these types of patients, it will become easier to identify the patients that come in requesting painkillers, if they are seeking opioids or if they really are in pain and need help. Asking astute questions and assessing patients with a thorough history and physical is key to identifying these patients and also being able to identify if they have any mental health behaviors that are contributing to their situation. The research and information included, will make each provider a better provider and add to their abilities to treat these patients appropriately and provide the quality medical treatment including mental health specialist referrals when required.

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