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Research Article

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Cannabis Use is Associated with Depressive Symptoms Among Pregnant Women Receiving Buprenorphine for Opioid Use Disorder

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Abstract

Background and aims

Previous studies have evaluated various effects of cannabis use on depression and opioid agonist therapy (OAT) outcomes; however, to date, there is no research focused on pregnant women with opioid use disorder (OUD) receiving OAT. This study examined the associations between cannabis use, and OAT outcome measures (retention and opioid use) and depressive symptoms in pregnant women treated with buprenorphine for OUD.

Methods

121 pregnant women with OUD in an outpatient clinic were included in a retrospective chart review. At each clinic visit, Beck Depression Inventory (BDI-II) and urine drug screens (UDS) were collected. Women were categorized into two groups, cannabis use (>1 UDS positive for cannabis) and non-use (all UDS negative for cannabis). Retention was defined as total weeks in treatment and opioid use was defined by the percent of positive UDS for opioids and compared between groups. To evaluate depression symptoms, the mean Beck Depression Inventory-II score over the course of treatment was calculated and compared between the groups.

Results

There were no significant differences among retention ($p=0.67$) or use of opioids ($p=0.14$) between those who did or did not use cannabis. Women who used cannabis during treatment had a higher BDI-II mean score compared to women without cannabis use (16 vs 9.3, $p<0.001$) over the course of treatment. Cannabis use continued to be associated with elevated depressive scores when controlling for opioid use (rho=0.252; $p=0.006$), and prescribed antidepressants (rho=0.269; $p=0.003$).

Conclusion

Cannabis use among pregnant women receiving buprenorphine for opioid use disorder was not correlated with retention or opioid use. However, cannabis use was associated with higher levels of depressive scores despite opioid use or prescribed antidepressant.

Introduction

During the past decade, the prevalence of cannabis use in the U.S. has doubled, while its perceived health risks have simultaneously declined (1). This is especially worrisome when considering vulnerable populations, such as pregnant women. Recent epidemiologic data from the National Survey on Drug Use and Health denotes an estimated increase in past-month perinatal cannabis use in the United States of as much as 106% from 2002 to 2017 (2).

This increase prompted the release of the Surgeon General report in August 2019 that recommended "no amount of marijuana use in pregnancy or adolescence is known to be safe… it is critical to educate women… about the risks of marijuana" (3). Despite the recent Surgeon General report, evidence-based research evaluating the obstetrical, neonatal and child outcomes following in utero marijuana exposure remains limited. Additionally, cannabis is the second most common (7.0%) used non-opioid drug among pregnant women with opioid use disorder second only to tobacco (53.5%) (4). For pregnant women diagnosed with opioid use disorder (OUD), OAT- either buprenorphine or methadone, is the mainstay treatment recommendation (5-7). For these treatment modalities, the main outcome measures include retention in treatment and lapse to opioid use among others (8). The effect of cannabis use on retention among pregnant women receiving buprenorphine remains unclear. Some have suggested that cannabis use has an adverse impact on retention in patients engaged in OUD treatment while others found no association in non-pregnant populations. Although there are numerous studies addressing the prevalence of opioid use and treatment recommendations in pregnant women with OUD, to our knowledge, there are no studies examining the effect of co-occurring cannabis use on retention in OAT or opioid use relapse among pregnant women with OUD in treatment with buprenorphine (9-12).

Previous studies have shown a positive correlation between cannabis use and depression in the general population (13-15). Additionally, research has indicated a high prevalence of mood disorders among individuals enrolled in OAT as well as a correlation between depression and higher levels of illicit drug use (16-20). The association of depression and cannabis use is important when considering pregnant women with OUD as perinatal substance use has been associated with an increased risk of fetal growth restriction, abruptio placentae, preterm labor, and death (21). In addition, untreated depression has profound effects on both maternal and fetal outcomes (22-23). Although the impact of cannabis use on OAT treatment outcomes and depressive symptoms has been studied in non-pregnant populations, to our knowledge, there are no data on the impact of cannabis use among pregnant women.

In summary, little is known about the potential impact of cannabis use on treatment retention, opioid use, and depression symptoms among pregnant women receiving buprenorphine. This is an important knowledge gap to fill as the relatively high prevalence of cannabis use in this population could be negatively impacting these outcomes and could be a targeted area of treatment in addition to OUD. Therefore, the present study attempts to fill this gap by conducting a retrospective analysis of pregnant women with OUD receiving OAT. In doing so, we examined, separately, associations between cannabis use and treatment retention rates, opioid use, and depression symptoms in this population. Given findings from prior studies, we hypothesized that cannabis use would decrease treatment retention as well as increase percent of positive UDSs for opioids and depression symptoms in this population.

Methods

Participants

Pregnant women with OUD followed in an ambulatory clinic were included in a retrospective chart review from their intake appointment during pregnancy to three months postpartum. The Women's Mental Health Program (WMHP) at the University of Arkansas for Medical Sciences provides psychiatric care for pregnant and postpartum women and has a dedicated clinic for the treatment of substance use disorders during pregnancy that includes observed urine drug screens, group and individual therapy, and medication management for psychiatric illness including buprenorphine for OUD when indicated. This study included participants that were seen in the clinic from November 2014 to August 2018. The study was approved by the Institutional Review Board at UAMS (IRB # 206852). Women were included if they met the clinical diagnosis of OUD, were prescribed buprenorphine, and gave consent for their data to be used for future research purposes. Women were excluded if they were postpartum or hospitalized at intake appointment, in a subsequent pregnancy with the clinic, younger than eighteen years old, or had missing data (i.e., UDS result or BDI score).

Measures

Demographic information including age, level of education, marital status, housing situation, addiction history, insurance, and race were collected from the medical record. Total weeks in treatment from their intake appointment to three months postpartum was calculated and used for determination of retention. Observed urine drug screen (UDS) data was collected from the medical record from each clinic visit with attention given to positive results for THC or opioids. Opioid use was defined by percent of positive UDSs for opioids during the study period. The Beck Depression Inventory-II (BDI-II) was administered at intake and each visit as part of clinical care; higher scores indicate greater depression (21 items, total score range 0-63 with scores > 20 indicating moderate depression) (24). The mean BDI-II score across all visits was used to determine impact of cannabis on depression symptoms. In addition to these variables, antidepressant use was defined by at least one prescription for an antidepressant during treatment.

Data analysis

Women were categorized into two groups: 1) cannabis use, defined as those with at least one positive UDS for cannabis and 2) non-use, defined as all UDSs negative for cannabis. We calculated the mean values of each variable for every woman across all weeks of treatment and then obtained the average of these means for each group. We used t-test with SigmaPlot analyses to determine if there is a significant difference between two groups when calculating weeks in treatment, opioid use, mean BDI score, and age of women. A p-value of <0.05 was considered statistically significant. We used z-test to assess for possible differences between the two groups in antidepressant use and demographics (aside from age). Spearman partial correlations in Matlab v2018b was used to evaluate any associations between the variables while controlling for possible confounding variables (lapse to opioid use or antidepressant prescription); Spearman correlations were chosen due to non-normal distributions of variables, specifically percent positive UDS results. Additionally, Wilcoxon rank-sum test was utilized to investigate opioid lapse during treatment due to this non-normal distribution.

Results

Of the 188 women treated in the clinic during the study period,

121 met study criteria. 22 participants were excluded due to lack of consent, 15 subjects were not prescribed buprenorphine, 15 subjects were in their subsequent pregnancy, 8 subjects were excluded from the study for missing information (UDS or BDI at intake), 6 subjects were postpartum during the intake, and 1 subject was excluded due to being hospitalized at the time of the first appointment (Figure 1). The average age of subjects was 29 +/- 4.60 years old with 79.5% of the participants being Caucasian. The average estimated gestational age at enrollment was 22 +/- 8.87 weeks. Additionally, the average duration of treatment was 15 +/- 7.01 weeks and around half of the cohort (48.8%) was prescribed an antidepressant during at least one appointment throughout treatment. The final cohort of women was divided into 35 (28.9%) women in the cannabis use group and 86 (71.1%) in the group without cannabis use. Table 1 presents the demographics for the total cohort and both groups. There were no significant differences in demographics between those using cannabis and those not aside from age (27.0 vs 29.5, p= 0.006), respectively.

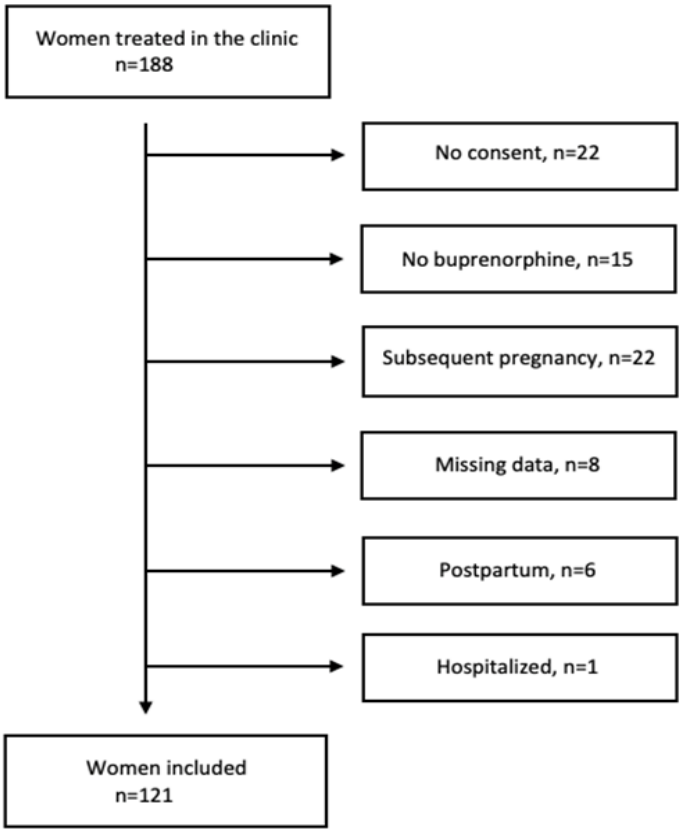

Figure 1: Flow diagram showing selection of participants.

Table 1: Characteristics, mean Beck Depression Inventory (BDI) score, percent of opioid use and average weeks in treatment for women in the cannabis user and non-cannabis user groups. SD, standard deviation. Bold indicates p value of <0.05.

	Total (n = 121)	Non-Cannabis (n = 86)	Cannabis (n = 35)	P value
Age, mean (SD)	28.8 (4.60)	29.5 (4.79)	27.0 (3.58)	0.006
Education, n (%)				
<12 years	20 (16.5)	15 (17.4)	5 (14.3)	0.88
>12 years	101 (83.5)	71 (82.6)	30 (85.7)	0.88
Relationship, n (%)				
Single	84 (69.4)	55 (64.0)	29 (82.9)	0.07
Married	37 (30.6)	31 (36.1)	6 (17.1)	0.07
Ethnicity, n (%)				
Caucasian	97 (80.2)	71 (82.6)	26 (74.3)	0.43
African American	11 (9.09)	7 (8.14)	4 (11.4)	0.82
Other	13 (10.7)	8 (9.30)	5 (14.3)	0.63
Insurance, n (%)				
Medicaid	69 (57.0)	48 (55.8)	21 (60.0)	0.83
Private	47 (38.8)	35 (40.7)	12 (34.3)	0.65
None	5 (4.13)	3 (3.49)	2 (5.71)	0.96
BDI score,				
mean (SD)		9.31 (8.31)	16.0 (12.2)	<0.001
Opioid use,				
n (percent of UDS)		13.4 (131/1239)	16.5 (67/529)	0.14
Retention, weeks				
mean (SD)		14.4 (6.92)	15.0 (7.32)	0.67

Associations with cannabis use and OAT outcome measures and depressive scores appear in Table 1. Retention in treatment by weeks did not significantly differ between those using cannabis (mean=15.0 weeks) and those not using cannabis (mean=14.4; two-tailed t-score=0.424; p=0.672). Cannabis use was not significantly correlated with percent of positive UDSs for opioids during treatment (16.5% vs 13.4%; rank sum=2379; z=1.47; p=0.143).

Participants using cannabis had significantly higher BDI scores across treatment (mean=16.0) than those without cannabis use (mean=9.3; t-score=3.46; p<0.001). This difference persisted when using partial correlation to control for potential confounders including opioid use (Spearman rho=0.252; p=0.006) and being prescribed an antidepressant (rho=0.269; p=0.003).

Discussion

This study focused on the impact of cannabis use on retention, use of opioids, and depression symptoms in pregnant women with OUD receiving buprenorphine through an ambulatory psychiatric clinic. Cannabis use was not associated with retention in OAT or use of opioids; however, cannabis use was correlated with higher depressive scores throughout treatment. Previous research has evaluated the prevalence of cannabis use in non-pregnant patients receiving treatment for OAT with one study showing that 55.1% of patients in methadone maintenance treatment used cannabis while another reported as high as 79% of participants using cannabis (25-26). This elevated prevalence has also been seen in buprenorphine treatment. Of our cohort, 28.9% of the women tested positive for cannabis at least once during treatment, which is lower than the percent of cannabis use seen in non-pregnant populations enrolled in OAT. These results are consistent with previous research indicating pregnant women use cannabis at half the rate of non-pregnant women (27).

Several studies have evaluated the effects of cannabis use on treatment outcomes for non-pregnant patients enrolled in OAT and the results have been inconclusive with some indicating negative effects on retention and lapse to opioid use (28). Our results in pregnant patients provides additional support that there is no association between cannabis use and retention or lapse to opioid use (29-30). This is the first study, to our knowledge, that has found increased depressive symptoms in relation to cannabis use in pregnant women in treatment for OUD. Perinatal cannabis use continued to be associated with higher depressive scores even when controlling for opioid and antidepressant use. Complications of untreated depression during pregnancy include elevated rates of preeclampsia, spontaneous abortion, premature delivery, low birthweight, and fetal growth retardation. Additionally, depression in pregnancy is associated with poor attendance with perinatal care, decreased nutrition, increased risks of smoking, alcohol and substance abuse which also have negative effects on fetal development. These are the same adverse outcomes correlated with perinatal illicit drug use (31). Our results showed that women who use cannabis during pregnancy expose their newborn to adverse effects of perinatal cannabis use as well as untreated depression.

A key finding of this study was that women with perinatal cannabis use reported elevated depressive scores when controlling for prescribed antidepressants and it may be reasonable to consider cannabis and its potential negative impact on treatment response. Given our results, adverse effects of untreated depression and concerns about exposures during pregnancy, these patients may benefit from close clinical management such as psychoeducation about risks of cannabis use on worsening depression and pregnancy as well as in-depth conversations about risks, benefits and side effects of adding an antidepressant with continued cannabis use.

Strengths and Limitations

There are limitations that should be considered when interpreting our findings. First, there are restraints when testing for cannabis use including the lag time between cannabis cessation and a negative UDS. Secondly, antidepressant use was based on self-report and medical record data which is unreliable as it cannot account for adherence to the medication. Third, although we screened for other substance use disorders and demographics at intake, this is a retrospective chart review and we were unable to include possible confounding variables during the study such as nicotine use, alcohol use, poverty, and partner violence that could also impact outcomes. Another possible limitation is questionnaire burnout causing false BDI-II scores over time. Lastly, we used mean values of each variable which may overly simplify causation between our variables.

While our focus on pregnant women with OUD may have limited generalizability to other populations; we view our emphasis on this highly vulnerable population as a strength given the growing prevalence of marijuana use during pregnancy. Our study offers a moderate sample size, enhancing the power of the study effect. Numerous studies have evaluated the effects of prenatal cannabis use on fetal health; however, far fewer studies have evaluated the impact of cannabis use on the health of pregnant women. Although we cannot fully account for possible confounding variables, our results suggest that cannabis may be more harmful than expected for participants using cannabis for improvement in mood. These results could be used to expand the information available for pregnant patients with cannabis use disorder so they can make a more informed decision about their healthcare. This is especially important as there is minimal information available for pregnant patients in a time where the perceived risk of cannabis use is decreasing, and prevalence is increasing.

Conclusion

Cannabis use was not associated with retention or opioid use among pregnant women receiving treatment for opioid use disorder. Conversely, cannabis use was associated with higher levels of depressive scores over course of treatment despite controlling for antidepressant use. Our findings reiterate the importance of screening for and treating depression and cannabis use in pregnant patients enrolled in treatment for OUD.

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