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Methadone-Maintained Pregnant Patients and Current Mood Disorder: Delivery and Neonatal Outcomes

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Abstract

Methadone-maintained pregnant patients with mood disorders have compromised treatment outcomes (1). This study examined the relationship between the presence of mood disorders and delivery and neonatal outcomes. Participants were categorized into two groups: no current mood disorder ($n=30$) or primary mood disorder ($n=38$). The mood disorder group reported more serious lifetime and current depression than did the no current mood disorder group. Neonates from mothers with mood disorders had a longer length of stay in the neonatal intensive care unit than the no current mood disorder group. Findings emphasize the need to treat mood disorders in methadone-maintained pregnant patients.

Introduction

Mood disorders in pregnancy

Depression during pregnancy often goes unnoticed and untreated (2). A systematic review reported that prevalence rates of depressive symptoms in pregnancy were 7.4%, 12.8% and 12.0% for the first, second, and third trimesters, respectively (3). If left untreated, mood and other psychiatric disorders are associated with increased pregnancy and neonatal related morbidity and mortality (4,5).

Substance use disorders in pregnancy

The largest study focusing on the prevalence of substance use during pregnancy was the National Study on Pregnancy and Health conducted in 1993 by the National Institute on Drug Abuse (6). Based on this study, it was estimated that each year approximately 53,400 babies born in the U.S. have been exposed in utero to heroin or the non-medical use of other analgesics. Since the conduct of this study, both heroin abuse and the non-medical use of analgesics has increased in the U.S., with the number of admissions to treatment for heroin use increasing from 168,000 in 1992 to 245,984 in 2006 (7).

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Mood disorders in substance-abusing pregnant women

Rates of depression among pregnant women with a substance use disorder are higher than among pregnant women without a co-morbid substance use disorder. Depression is estimated to affect 56-73% of substance-dependent pregnant women (1,8).

The recognition of the co-occurrence of depression in pregnant women with substance-use disorders is important because depression has been associated with negative maternal drug-treatment outcomes. For example, cocaine-using pregnant women enrolled in drug abuse treatment were less likely to complete treatment if they had current mood disorders (9). Moreover, depressive symptoms in a sample of pregnant methadone-maintained women were associated with lower rates of clinic attendance (10).

Adverse obstetrical and birth outcomes observed in women with mood disorders

Depression during pregnancy is associated with adverse pregnancy outcomes such as prematurity, lower birth weight, and neonatal behavioral effects (4,11-12). Research has consistently reported that prenatal depression is associated with more neonatal crying (13-15), greater newborn inconsolability (15), less verified sleep behavior, and more activity and movement (13-14).

Adverse obstetrical and birth outcomes in pregnant women with substance use disorders

Opioid dependence during pregnancy has close associations with a plethora of biological, medical, and environmental factors that can contribute to adverse prenatal and neonatal outcomes. Some of the adverse consequences associated with opioid use include premature delivery, high rates of infection, and low birth weight (an important risk factor for later developmental delay) (16-17). Literature limitations notwithstanding, the published research suggests that children born to opioid-dependent women may be at risk for less-than-optimal developmental outcomes. The elevated adverse outcome risk may be due to not only illicit drug exposure, but also to alcohol and tobacco exposure as well as numerous factors related to the caregiver environment (18).

Compared to heroin dependence, methadone maintenance treatment during pregnancy has been associated with greater compliance with prenatal care and drug treatment attendance, decreased risk of HIV infection and reduced risk of pre-eclampsia (19-21). Additionally, methadone maintenance in the context of comprehensive care has been associated with reduced fetal mortality, increased fetal growth, and an increased likelihood of the infant being discharged to his/her parents (19,22).

Purpose of the present study

While it has been shown that expectant mothers with current mood disorders have higher rates of illicit drug use compared to those without a current mood disorder (1), it is not known if the delivery and/or neonatal outcomes of these patients are also compromised. The present study addresses two unanswered research questions: do pregnant women with a primary mood disorder have poorer 1) delivery and 2) neonatal outcomes than women without a current mood disorder? Answers to these questions can help build an evidence-based framework for determining the best treatment approaches for opioid-dependent pregnant patients with mood disorders.

Materials and Methods

Setting

The Center for Addiction and Pregnancy (CAP), a comprehensive care setting located on the Johns Hopkins Bayview Medical Center campus in Baltimore, Maryland, provides addiction counseling, methadone maintenance, and medically-assisted withdrawal for opioid-dependent patients refusing methadone or those not meeting current opioid dependence criteria. Additional services include case management, obstetrical care, psychiatric evaluation and pharmacotherapy, pediatric care, and on-site child care.

Participants and sampling

Participants selected for this secondary data analysis were 68 methadone-maintained pregnant patients enrolled in a larger behavioral study conducted at CAP for whom drug treatment outcomes have been reported (1). All participants signed written informed consent to participate in the larger study. Johns Hopkins Bayview Medical Center's Institutional Review Board approved the larger study and found this study exempt from review. Also included in this study and not included in Fitzsimons et al. (2007) was one additional participant who did not have a current mood diagnosis. Excluded from this report was one participant who had a current mood disorder but had too little maternal and neonatal data to be included. Participants were categorized into two groups according to the primary current SCID diagnoses: (1) no current mood disorder ($n=30$); or (2) primary mood disorder ($n=38$). While 44% of the participants with a current mood disorder also met criteria for a current anxiety disorder, the participants were classified by their *principal* diagnosis by the SCID interviewer following assessment administration.

Measures and Data Sources

All data were collected using interview assessments or abstracted from maternal and neonatal hospital charts.

Structured Clinical Interview for the DSM-IV (SCID)—Participants typically completed the Structured Clinical Interview for DSM-IV (SCID, 23) during the first week of treatment. The SCID is a semi-structured interview for assessing current and lifetime axis I diagnoses. For this study, diagnoses from Module A: Mood Disorders were examined. Additionally, all participants met criteria for opioid dependence based on Module E: Substance Use Disorders. SCID interviewer training and ongoing inter-rater reliability assessment has been previously reported (1).

Maternal delivery and neonatal data—Maternal and neonatal delivery data were collected from documents completed by clinical staff during the care of the patient. All neonatal data were tracked from delivery until hospital discharge.

Data Analysis

To compare the primary mood disorder group to the no mood disorder group, one-way analysis of variance was used for continuous outcome measures and a X^2 goodness-of-fit test was used for binary outcome measures.

Results

Demographic and pre-treatment characteristics

The groups did not differ on demographic variables or on current drug use (Table 1). Overall, the sample had a mean age of 30 years ($SD=5.9$) and 10.8 years of education

($SD=1.7$). Seventy-four percent were African American and 93% were unemployed. On average, participants entered treatment in the second trimester of pregnancy. Self-reported drug use in the 30 days prior to intake included heroin (93%), methadone from another program (7%), cocaine (76%), nicotine (97%), and alcohol (to intoxication) (22%).

As expected, the groups differed on psychiatric status, with five times as many participants in the primary mood disorder group reporting current symptoms of serious depression and three times the rate of lifetime serious depression compared to participants in the no current mood disorder group. A total of 67% of primary mood disorder participants received psychiatric treatment for their disorder during their pregnancy.

Delivery and neonatal outcomes

The groups did not differ on delivery outcomes (Table 2). Eighty two percent of the sample delivered vaginally and 55% received an epidural. Thirty four percent of the sample had a positive drug screen at delivery. The mean length of maternal hospital stay was 2.8 ($SD=1.1$) days.

Regarding neonatal outcomes (Table 2), the groups differed on the length of stay at the neonatal intensive care unit (NICU). Infants of women with a current mood disorder remained in the NICU 6 times longer than infants of women without a current mood disorder diagnosis [3.1 ($SD=1.6$) v. 0.5 ($SD=0.4$) days, respectively; $p = .05$]. Although they did not reach conventional levels of statistical significance, a number of tendencies existed in the data suggesting poorer neonatal outcomes for infants of women with a primary mood disorder. These infants tended to be born at an earlier EGA week ($p = .16$) and larger percentages tended to be born premature ($p = .11$) and to be admitted to the NICU ($p = .12$) compared to infants of women without a mood disorder diagnosis. The groups did not show evidence of differences on other neonatal outcomes examined. Overall, infants weighed 2741 ($SD=114$) grams at delivery, with 43% classified as low birth weight. The total length of infant stay was 10.3 ($SD= 2.9$) days, with an average of 7.5 ($SD= 1.8$) of the days in the newborn nursery. Sixteen percent of the infant sample had a positive urine drug test at delivery and 42% of the sample was treated for NAS.

Discussion

The present study aimed to address unanswered research questions regarding the maternal and neonatal impact of having a mood disorder in a sample of opioid dependent pregnant women. It is important to note that the outcomes examined in the present study were those of methadone-maintained pregnant women. Prior reports have indicated that psychiatric and substance use disorders, both separately and combined, are associated with poorer neonatal outcomes (e.g., 24). However, it is unclear what proportion of women in these studies was receiving treatment for either or both conditions. Of particular interest is whether pregnant drug dependent women diagnosed with a co-occurring mood disorder have worse delivery and neonatal outcomes. Because psychiatric symptoms often resolve with treatment stabilization (e.g., 25), it is unclear whether substance abuse treatment alone might improve both conditions sufficiently to ameliorate expected differences in neonatal outcomes. The present study addresses two primary questions, namely whether there are poorer maternal delivery and neonatal outcomes among women with a primary mood disorder compared to women without a current mood disorder.

Regarding the first question, the maternal delivery outcomes examined did not differ between women with and without a mood disorder. However, regarding the second question, infants of women with a mood disorder had longer NICU stays compared to infants of women without a diagnosis. In addition, a number of related neonatal birth outcomes,

including EGA week at delivery, % of infants premature, and % of infants admitted to the NICU, were suggestive of poorer outcomes among infants of women with a mood disorder diagnosis.

Although the overall length of hospital stay for the neonates did not differ significantly between the two groups, infants of women with a mood disorder diagnosis spent more of their hospital stay in the NICU. The current cost of a 24-hour stay with routine observation in the NICU located in our hospital is \$1417 compared to \$330 for the same length of time in the newborn nursery. This difference in costs multiplied by the mean 2.5-day difference between groups in length of NICU stay works out to a \$2717 increase in cost overall. This observation underscores the possible cost-effectiveness of assessing and treating co-occurring mood disorders in pregnant substance abusers.

There are several limitations of this study that should be noted. First, data were collected as part of a secondary observational study. A prospective trial designed to compare the delivery and neonatal outcomes of methadone-maintained patients with and without a current mood disorder could include more comprehensive measures and yield results supporting stronger conclusions. However, current results do support the conclusion that heroin-dependent pregnant patients with co-morbid mood disorders have neonates with increased complications resulting in longer, more costly hospital stays. The present data can inform the design of other direct comparisons between the most effective co-morbid psychiatric treatments for this patient population. Second, the sample sizes of the groups are modest and limit the power to detect differences. This limitation is tempered by the fact that differences in the expected direction were observed on a neonatal outcome measure. A larger sample size would allow for patients with current mood disorders to be further categorized as treated and untreated and may yield interesting information on the effect of treatment and no treatment on delivery and birth outcomes in this population. Third, while the present sample is similar to other samples of patients with substance use disorders (9,10) the extent to which the outcomes observed in this sample generalize to the larger population of methadone maintained patients is unknown.

The present study provides initial data examining the relationship of mood disorders on delivery and neonatal outcomes in a group of pregnant women stabilized on methadone. Results suggest that poorer neonatal outcomes may persist among women diagnosed with a mood disorder and emphasize the need to assess and treat mood disorders among substance abusing pregnant women.

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Table 1
Demographic and pre-treatment characteristics of drug-dependent pregnant women

	Total sample (N = 68)	No Current Mood Diagnosis (n = 30)	Current Mood Diagnosis (n = 38)	Test Statistic $\chi^2(df)$ or F(df, df)	Significance (p value)
Demographics					
Age, <i>M</i> (<i>SD</i>)	30 (5.9)	30 (6.0)	31 (5.8)	$F(1, 66) = .00$	0.97
% African American	74	80	68	$\chi^2(1) = 1.15$	0.28
Education, in years, <i>M</i> (<i>SD</i>)	10.8 (1.7)	10.6 (0.3)	10.9 (0.2)	$F(1, 66) = .41$	0.53
% unemployed [N=59]	93	97	90	$\chi^2(1) = 1.00$	0.32
Drug use (% reporting use in past 30 days) [N=59]					
Heroin	93	90	97	$\chi^2(1) = 1.15$	0.28
Cocaine	76	72	80	$\chi^2(1) = .47$	0.49
Nicotine	97	100	93	$\chi^2(1) = 2.00$	0.16
Alcohol to intoxication	22	17	27	$\chi^2(1) = .76$	0.38
Psychiatric status [N=59]					
% with serious depression, past 30 days	58	14	70	$\chi^2(1) = 19.08$	<.01
% with serious depression, lifetime	49	24	77	$\chi^2(1) = 16.28$	<.01

Table 2

Delivery and neonatal birth outcomes

	Total sample (N = 68)	No Current Mood Diagnosis (n = 30)	Current Mood Diagnosis (n = 38)	Test Statistic $\chi^2(df)$ or F	Significance (p value)
Pregnancy Loss					
% with spontaneous abortion [N = 63]	10	7	12	$\chi^2(1) = .54$	0.46
Delivery					
% receiving epidural [N = 33]	55	55	55	$\chi^2(1) = .96$	0.33
% with vaginal delivery [N = 65]	82	86	78	$\chi^2(1) = 1.49$	0.22
% with urine sample (+) at delivery for any illicit drug [N = 61]	34	29	38	$\chi^2(1) = .05$	0.82
Maternal LOS, in days, <i>M (SD)</i> [N = 62]	2.8 (1.1)	2.6 (0.7)	2.9 (1.3)	$F(1, 22) = 1.27$	0.27
Neonatal					
EGA at delivery, in weeks, <i>M (SD)</i> [N = 67]	37.3 (0.6)	38.2 (0.9)	36.5 (0.8)	$F(1, 59) = 2.29$	0.16
% premature (≤ 35 weeks) [N = 67]	21	13	27	$\chi^2(1) = 2.58$	0.11
Birth weight, in grams, <i>M (SD)</i> [N = 67]	2741.1 (114.4)	2845.5 (166.6)	2638.5 (139.8)	$F(1, 59) = 1.02$	0.32
% low birth weight (≤ 2500 grams) [N = 67]	43	33	51	$\chi^2(1) = 1.00$	0.32
Total infant LOS, in days, <i>M (SD)</i> [N = 28]	10.3 (2.9)	8.2 (4.0)	12.9 (3.3)	$F(1, 20) = .76$	0.39
LOS nursery [N = 25]	7.5 (1.8)	8.2 (3.1)	6.8 (1.7)	$F(1, 17) = .18$	0.68
LOS NICU [N = 34]	1.2 (0.7)	0.5 (0.4)	3.1 (1.6)	$F(1, 26) = 4.11$	0.05
% NICU admission [N = 34]	41	23	52	$\chi^2(1) = 2.43$	0.12
% with urine sample (+) for any illicit drug at delivery [N = 61]	16	8	22	$\chi^2(1) = 1.12$	0.42
% treated for NAS [N = 26]	42	50	38	$\chi^2(1) = .12$	0.73
% with meconium staining [N = 31]	3	9	0	$\chi^2(1) = 1.88$	0.17
% Child Protective Services Referral [N = 50]	48	38	56	$\chi^2(1) = 156$	0.21