CSAM-SMCA Journal Club

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ORIGINAL RESEARCH

A Retrospective Cohort Study Examining the Utility of Perinatal Urine Toxicology Testing to Guide Breastfeeding Initiation

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Background

14. Pregnant women on opioid agonist treatment should be encouraged to breastfeed regardless of the maternal dose, in the absence of an absolute contraindication (II-2B). Women with active substance use should be encouraged to discontinue alcohol or other drug use while breastfeeding, and the risks and benefits of breastfeeding versus breast milk exposure to substances should be discussed (II-2B).

JOGC Journal of Obstetrics and Gynaecology Canada / Journal d'obstétrique et gynécologie du Canada

Breastfeeding should be encouraged because it can delay the onset and decrease the severity of withdrawal symptoms as well as decrease the need for pharmacological treatment [32]. HIV-negative mothers who are stable and on opioid maintenance treatment with either methadone or buprenorphine should be encouraged to breastfeed [9]. Breastfeeding provides optimal nutrition, promotes maternal–infant attachment and facilitates parenting competence. Mothers with a dependency who wish to breastfeed may require extra support as they are less likely to initiate breastfeeding successfully and more likely to stop breastfeeding early [33].

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- Maternal opioid use disorder (OUD) affects 6.5 per 1000 live births in the United States
- Breastfeeding has positive effects for maternal and neonatal health, especially in OUD/Neonatal abstinence syndrome (NAS)
- Breastfeeding rates vary between 17-81% for women with OUD in North America and Europe
- Urine drug testing (UDT) is used to measure adherence and stability in OUD
- Study objective: Assess the correlation between non prescribed use on prenatal and postpartum UDT findings

ABM Clinical Protocol #21: Guidelines for Breastfeeding and Substance Use or Substance Use Disorder, Revised 2015

General (Circumstances contraindicated or requiring more caution)

Counsel women under any of the following circumstances not to breastfeed (III):

- Not engaged in substance abuse treatment, or engaged in treatment and failure to provide consent for contact with counselor
- Not engaged in prenatal care
- Positive maternal urine toxicology screen for substances other than marijuana at delivery [see (b) above]
- No plans for postpartum substance abuse treatment or pediatric care
- Women relapsing to illicit drug use or legal substance misuse in the 30-day period prior to delivery
- Any behavioral or other indicators that the woman is actively abusing substances
- Chronic alcohol use.

Evaluate carefully women under the following circumstances, and determine appropriate advice for breastfeeding by discussion and coordination among the mother, maternal care providers, and substance abuse treatment providers (III):

- Relapse to illicit substance use or legal substance misuse in the 90–30-day period prior to delivery
- Concomitant use of other prescription medications deemed to be incompatible with lactation
- Engaged later (after the second trimester) in prenatal care and/or substance abuse treatment
- Attained drug and/or alcohol sobriety only in an inpatient setting
- Lack of appropriate maternal family and community support systems
- Report that they desire to breastfeed their infant in order to either retain custody or maintain their sobriety in the postpartum period.

Methods

- Retrospective cohort of women that delivered at Boston Medical Center engaged in Project RESPECT (Recovery, Empowerment, Social Services, Prenatal Care, Education, Community, and Treatment) between January 2006 and December 2015

- Inclusion:
  - DSM 4 or 5 OUD diagnosis
  - Receiving methadone or buprenorphine
  - Completed one third trimester and one post partum UDT

Methods

Primary Outcome

- Any non prescribed substance in the first 6 months after delivery in postpartum women with OUD

Explanatory variable

- Non prescribed use between 90-31 days before delivery, between 30 days before and delivery, and at time of delivery
- UDT results per trimester

Methods

Statistical analysis

- Descriptive statistics used to summarize non prescribed use during various time periods
- Student t-test for continuous variables and Pearson-Chi squared test for categorical variables to examine association between demographic characteristics and postpartum non prescribed use
- Sensitivity, specificity, positive and negative predictive values (PPV, NPV) of non prescribed use prenatally

	Disorder	No Disorder
Positive Test Result	True Positive (TP)	False Positive (FP)
Negative Test Result	False Negative (FN)	True Negative (TN)

Sensitivity = TP/(TP+FN)
Specificity = TN/(TN+FP)
PPV = TP/(TP+FP)
NPV = TN/(FN+TN)

- Simple linear regression analysis for strength of association between pre and postpartum UDT results
- P-value <0.05 = Statistically significant

Results

Study sample

- 545 deliveries by 503 unique women met inclusion criteria
- 4004 UDTs
- Mean age 28.3, 88.1% White non-Hispanic
- 43% had adequate prenatal care by Kessner index
- 53.5% buprenorphine, 46.5% methadone
- 86% had medical problems, 69% psychiatric diagnosis
- 60% Hep C positive

TABLE 1. Demographic Characteristics of Deliveries to Women with Opioid Use Disorder by Postpartum Toxicology Test Results

Demographic characteristics	Overall (N = 503)	No Postpartum Nonprescribed Substance Use (N = 378)	Any Postpartum Nonprescribed Substance Use (N = 125)	*P*
Age Mean SD	28.3 ± 5.0	28.2 ± 4.9	28.4 ± 5.0	*P* = 0.76
Race/Ethnicity N (%White non-Hispanic)	443 (88.1)	338 (89.4)	105 (84.0)	*P* = 0.11
Insurance N (%)				*P* = 0.81
Public payer	467 (92.8)	350 (92.6)	117 (93.6)	
Private	35 (7.0)	27 (7.1)	8 (6.4)	
Uninsured/Other	1 (0.2)	1 (0.3)	0 (0)	
MOUD at first visit N, (%)				*P* = 0.62
None	10 (2.1)	7 (1.9)	3 (2.4)	
Buprenorphine	262 (56.0)	192 (50.8)	70 (56.0)	
Methadone	196 (42.8)	151 (40.0)	45 (36.0)	
Missing	35	28 (7.4)	7 (5.6)	
MOUD at delivery, N (%)				*P* = 0.20
Buprenorphine	269 (53.5)	196 (51.9)	73 (58.4)	
Methadone	234 (46.5)	182 (48.2)	52 (41.6)	
Medical Problems, N (% any yes)	86 (17.2)	70 (18.6)	16 (12.9)	*P* = 0.14
Psychiatric Diagnosis, N (% any yes)	343 (69.0)	251 (67.3)	92 (74.2)	*P* = 0.15
On any psych medications, N (% any yes)	241 (47.9)	165 (43.7)	76 (60.8)	*P* <0.001
Hep C, N (% positive)	300 (59.8)	217 (57.6)	83 (66.4)	*P* = 0.08
Distance of residence from hospital by address at delivery (km), Mean SD	17.7 ± 18.5	17.4 ± 17.5	18.8 ± 21.3	*P* = 0.44
Kessner prenatal care adequacy index, N (%)				*P* = 0.003
Adequate	216 (43.0)	179 (47.4)	37 (29.8)	
Intermediate	184 (36.7)	129 (34.1)	55 (44.4)	
Inadequate	102 (20.3)	70 (18.5)	32 (25.8)	
Number of postpartum visits, Mean SD	2.3 ± 1.5	2.3 ± 1.4	2.4 ± 1.8	*P* = 0.31

Hep C, hepatitis c; km, kilometer; MOUD, medication for opioid use disorder; N, Number; SD, standard deviation; UDT, urine drug tests.

TABLE 2. Timing and Type of Any Nonprescribed Substance Use on Urine Drug Tests During Pregnancy and Postpartum (Yes/No)

Time Period N (%)	Amphetamine	Barbiturate	Benzodiazepine	Buprenorphine	Cocaine	Methadone	Opiate	Oxycodone	Any Nonprescribed Substance	Total # w/ ≥1 Test/ Period
1st Tri	5 (1.7)	2 (0.7)	24 (8.2)	14 (4.8)	46 (15.6)	8 (2.7)	103 (35.0)	20 (6.8)	133 (45.2)	294
2nd Tri	11(2.4)	5 (1.1)	46 (10.2)	21 (4.6)	59 (13.0)	5 (1.1)	132 (29.1)	32 (7.1)	193 (42.6)	453
3rd Tri	7 (1.3)	7 (1.3)	41 (7.5)	10 (1.8)	63 (11.6)	9 (1.7)	122 (22.4)	30 (5.5)	193 (35.4)	545
90–31 d before delivery	5 (1.0)	6 (1.2)	32 (6.2)	8 (1.5)	55 (10.6)	3 (0.6)	99 (19.0)	22 (4.2)	157 (30.2)	520
30 d before delivery	3 (0.6)	3 (0.6)	21 (4.0)	5 (1.0)	22 (4.2)	6 (1.1)	48 (9.2)	11 (2.1)	92 (17.6)	524
Delivery	3 (0.6)	3 (0.6)	12 (2.5)	1 (0.2)	16 (3.3)	1 (0.2)	38 (7.8)	2 (0.4)	61 (12.5)	487
PP	15 (2.8)	9 (1.7)	34 (6.2)	2 (0.4)	28 (5.1)	5 (0.9)	74 (13.6)	24 (4.4)	135 (24.8)	545

PP, postpartum.

TABLE 3. Any Prenatal Nonprescribed Substance Use as a Predictor of Nonprescribed Postpartum Use Using Urine Drug Tests

	90–30 d Before Delivery			30 d Before Delivery			At Delivery		
Post-Partum	≥ 1 Positive UDT 90–31 d Before Delivery	Negative UDT 90-31 d Before Delivery	Total	≥ 1 Positive UDT 30d before delivery	Negative UDT 30d before delivery	Total	≥ 1 Positive UDT at Delivery	Negative UDT at Delivery	Total
≥ 1 Positive UDT Post- Partum	57	72	129	33	93	126	34	93	127
Negative UDT Post- Partum	100	291	391	59	339	398	27	333	360
Total	157	363	520	92	432	524	61	426	487
Sensitivity		44.2%			26.2%			26.8%	
Specificity		74.4%			78.5%			92.5%	
Pos Predictive Value		36.3%			35.9%			55.74%	
Neg Predictive Value		80.2%			85.2%			78.2%	
Chi-Squared Test		$P = 0.033$			$P = 0.006$			$P < 0.001$	

D, days; UDT, urine drug test.

Table 2: Any Prenatal Non-Prescribed Substance Use as a Predictor of Non-Prescribed Postpartum Use using Urine Drug Tests

	1st trimester			2nd trimester			3rd trimester		
Post-Partum	**≥ 1 Positive UDT in 1st tri**	**Negative UDT in 1st tri**	**Total**	**≥ 1 Positive UDT in 2nd tri**	**Negative UDT in 2nd tri**	**Total**	**≥ 1 Positive UDT in 3rd tri**	**Negative UDT in 3rd tri**	**Total**
≥ 1 Positive UDT Post-Partum	42	21	63	62	46	108	65	128	193
Negative UDT Post- Partum	91	141	232	131	216	347	70	282	352
Total	133	162	295	193	262	455	135	410	545
Sensitivity	67%			57%			34%		
Specificity	61%			62%			80%		
Pos Predictive Value	32%			32%			48%		
Neg Predictive Value	87%			82%			69%		
McNemar's Test	P<0.001			P<0.001			P<0.001		

UDT, urine drug test; tri, trimester

TABLE 4. Multivariable Model Using GEE)* Looking at Factors Predictive of Any Nonprescribed Substance Use Postpartum

Parameter	Estimate	Standard Error	aOR†	95% CI	
Positive Delivery UDT	1.31	0.36	3.72	1.84	7.51
Positive 30 d to Delivery hospitalization UDT	0.34	0.34	1.40	0.73	2.72
Positive 90–31 d before delivery	0.52	0.28	1.68	0.98	2.90
White non-Hispanic vs non-White race/ethnicity	−0.47	0.34	0.62	0.32	1.20
Public insurance vs private/other	0.11	0.49	1.11	0.43	2.89
Methadone vs Buprenorphine treatment at delivery	0.67	0.25	1.96	1.20	3.22
Any psychiatric diagnosis	0.27	0.27	1.30	0.77	2.21
Hepatitis C	−0.038	0.014	0.97	0.94	0.99
Adequate vs Intermediate/ Inadequate Prenatal care	0.46	0.26	1.59	0.95	2.64

*GEE was used to account for clustering of deliveries by the same women across the study period. A binary outcome was used (0 = no nonprescribed substances on toxicology testing within six months of delivery, 1 = evidence of nonprescribed substances on toxicology testing within 6 months of delivery).

†Model was adjusted for all covariates listed.

CI, confidence interval; GGE, generalized estimating equations; OR, odds ratio; UDT, urine drug test; d, days.

Supplementary Table 3: Simple Model using Generalized Estimating Equations (GEE) Looking at Factors Predictive of Any Non-Prescribed Substance Use Post-Partum

Parameter	Estimate	Standard Error	OR	95% CI	
Non-Prescribed 90-30d before delivery UDT	0.6972	0.2162	2.3022	1.5069	3.5172
Non-Prescribed 30d before delivery UDT	0.6708	0.2501	2.0375	1.2480	3.3264
Non-Prescribed delivery UDT	0.8184	0.2867	4.5079	2.5702	7.9066
Non-Prescribed 1st trimester UDT	0.7612	0.2982	3.1883	1.7771	5.7200
Non-Prescribed 2nd trimester UDT	0.6898	0.2238	2.2234	1.4338	3.4478
Non-Prescribed 3rd trimester UDT	0.6725	0.2063	2.046	1.3704	3.0772

OR, odds ratio; CI, confidence interval; UDT, urine drug test; d, days

*GEE was used to account for clustering of deliveries by the same women across the study period. A binary outcome was used (0=no non-prescribed substances on toxicology testing within six months of delivery, 1=evidence of non-prescribed substances on toxicology testing within six months of delivery)

Discussion

- Non prescribed substance use declined throughout pregnancy with lowest rate at delivery, and increased post partum
- Non prescribed use at delivery (but not between 90 and 31 or between 30 days and delivery) was statistically associated with ongoing post partum use
- PPV and sensitivity of prenatal UDT results to predict post partum use was significantly lower than NPV
- Presence of mood disorders, type of OAT, adequacy of prenatal care and other unmeasured variables are contributory factors
- Shared decision-making process at the time of delivery should guide decisions around breastfeeding in pregnant women with OUD
- Conclusion: Limited clinical correlation between prenatal non prescribed substance use and post partum use; prenatal UDTs alone are insufficient to support or advise against breastfeeding. Non prescribed use at delivery had strong association with postpartum use.

Limitations

LIMITATIONS:

- 489 of 1034 deliveries were excluded based on inclusion criteria
- Equal weight given to 1 vs 10 positive UDTs
- Included any test within 6 months post partum
- Generalizability to other SUDs
- Limitations of UDTs
- Residual confounding

QUESTIONS:

- Prospect/RCTs are needed to assess value of UDTs to guide breastfeeding
- Qualitative studies to explore maternal views, barriers, facilitators, wellbeing

Our Discussion

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