

Buprenorphine and Methadone Backdated Investigation of Neonatal Outcomes (BAMBINO)

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INTRODUCTION

- A devastating result of the opioid crisis has been the >50% increase in opioid-dependence among pregnant women from 1998 to 2011 in the U.S.¹
- Neonatal abstinence syndrome (NAS) is the expected withdrawal suffered by neonates born to mothers who are exposed to opioids during pregnancy.
- Methadone has long been the traditional treatment of choice for medication assisted treatment (MAT) of opioid dependent mothers; however, recent literature suggests buprenorphine may serve as a alternative to methadone resulting in a shorter withdrawal period and lower intensity withdrawal symptoms.²⁻⁴
- Women with polysubstance use disorders and use of psychotropic medications have been historically excluded from studies comparing methadone and buprenorphine.²⁻⁴

OBJECTIVES

- Primary outcome:** Length of hospital stay (hrs) of neonates born to mothers receiving methadone versus buprenorphine
- Secondary outcomes:** Peak Finnegan score, peak morphine and clonidine dose (mg), and total morphine and clonidine dose (mg)

METHODS

Design: Retrospective cross sectional via chart review

Inclusion Criteria:

- Neonates - gestational age ≥ 33 weeks, born at TMC between Jan. 2015 to Mar. 2019 and admitted to neonate intensive care unit (NICU) for NAS
- Mothers - history of drug/alcohol abuse and documented record of current MAT therapy

Data Analysis:

- Demographic Characteristics: T-test and Chi-Squared analysis
- Primary/Secondary Outcomes: Multiple linear regression adjusted for mother's age and polysubstance use, and infant's gestational age, birth weight, delivery type, and comorbidities.
- The a priori level was set to 0.05.

RESULTS

Table 1: Baseline characteristics of study population*

Characteristic	Methadone (N=98)	Buprenorphine (N=21)	P-value
Mothers			
Age (yr)	28.3 \pm 4.7	29.5 \pm 5.6	0.26
Race			
White	81%	90%	<.0001
Other/Unknown	19%	10%	
Ethnicity			
Hispanic	30%	48%	0.1390
Non-Hispanic	59%	52%	
Unknown	11%	0%	
Height (cm)	162.6 \pm 8.09	164.7 \pm 6.99	0.49
Weight (kg)	77.7 \pm 15.0	79.14 \pm 15.9	0.70
Neonates			
Age (wk)	38.1 \pm 1.9	38.2 \pm 2.1	0.48
Head circumference (cm)	33.1 \pm 3.6	33.5 \pm 1.6	0.0005
Baby length (cm)	52.4 \pm 50.6	49.1 \pm 2.6	0.0001
Baby weight (g)	2890.7 \pm 526.9	2978.3 \pm 489.7	0.74
Comorbid Sum [†]	0.34 \pm 0.6	0.24 \pm 0.44	0.22

* Plus-minus values are means \pm SD
[†] Comorbid Sum: Sum of additional comorbidities neonate diagnosed with at birth including; sepsis, necrotizing enterocolitis, hypoxic ischemic encephalopathy, neonatal hypoglycemia, respiratory distress syndrome, patent ductus arteriosus, retinopathy of prematurity, inability to nipple feed/feeding difficulty, unsafe home situation, gastroesophageal reflux, abdominal wall defect, major surgical intervention, meningitis, major congenital abnormalities.

Table 2: Adjusted Hospital length of stay (primary outcome)

MAT	Mean LOS (hours)	Parameter Estimate (SE)	P-value
Buprenorphine (N=21)	408.4	-275.36 (92.9)	0.0037
Methadone (N=98)	714.3		

Table 3: Peak withdrawal scores and medication use (secondary outcomes)*

Secondary Outcome	MAT	Mean	Parameter Estimate (SE)	P-value
Peak Finnegan Score	Buprenorphine (N= 20)	12.3 \pm 4.79	-2.27 (0.95)	0.018
	Methadone (N= 89)	14.31 \pm 3.58		
Total Morphine (mg/kg)	Buprenorphine (N= 14)	5.72 \pm 1.40	-12.6 (12.19)	0.30
	Methadone (N= 84)	24.55 \pm 5.04		
Peak Morphine (mg/kg/day)	Buprenorphine (N= 14)	0.56 \pm 0.33	-0.45 (0.27)	0.11
	Methadone (N= 84)	1.04 \pm 0.98		
Total Clonidine (mcg/kg)	Buprenorphine (N= 9)	112.2 \pm 28.12	-93.79 (48.02)	0.058
	Methadone (N= 38)	212.6 \pm 20.95		
Peak Clonidine (mcg/kg/day)	Buprenorphine (N= 9)	8.55 \pm 1.60	-0.083 (1.58)	0.96
	Methadone (N= 38)	8.76 \pm 0.61		

* Plus-minus values are means \pm SD

CONCLUSIONS

- Buprenorphine was associated with a shorter length of stay (approximately 300 hours) compared to methadone for neonates born to mothers on MAT after adjusting for mother's age and polysubstance use, and infant's gestational age, birth weight, delivery type, and comorbidities.
- Peak Finnegan scores (a measure of withdrawal severity) were lower among infants born to mothers on buprenorphine compared to methadone.
- No difference in total morphine score and peak morphine or total and peak clonidine were observed between the two groups.
- Results of this study have added to the literature on MAT and neonatal abstinence syndrome by controlling for mothers on concurrent psychotropic and illicit substances.

LIMITATIONS

- Did not account for changes in practice (i.e. prescribing practices changed to include clonidine as a treatment adjunct)
- Cross sectional design does not allow for causal inference
- Did not control for MAT adherence during the entire course of the pregnancy

FUTURE DIRECTIONS

- Further exploration of neonatal short term and long term outcomes
- Survey of mothers' preference in MAT

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DISCLOSURE

- The authors have no conflict of interest to disclose. For any questions, please contact Mon-Yee Fung at