

# Neonatal and maternal effects of buprenorphine in the treatment of opioid-maintained pregnant women

Christina Inteso, Pharm.D<sup>1,2</sup>; Alicia B. Forinash, Pharm.D., FCCP, BCPS, BCACP<sup>1,2</sup>; Abigail M. Yancey, Pharm.D., BCPS<sup>1,2</sup>; Rebecca Bragg, Pharm.D., BCPS<sup>1,2</sup>; Collin Miller, MSW<sup>3</sup>, Judy Thompson, R.N., CCRC<sup>3</sup>, Jaye Shyken MD<sup>2,3</sup>

<sup>1</sup>St. Louis College of Pharmacy; <sup>2</sup>SSM Health St. Mary's <sup>3</sup>St. Louis University Department of Obstetrics and Gynecology

## Background

- Infants born to women using illicit drugs can experience neonatal abstinence syndrome (NAS)
- NAS is defined as the hyperactivity of the central and autonomic nervous systems
- Clinical presentation depends on duration of opioid use, duration of use prior to delivery, maternal metabolism, and placental metabolism. Symptoms of NAS manifest in the central nervous system (CNS) and gastrointestinal (GI) tract<sup>1</sup>
- The modified Finnegan's Neonatal Abstinence scoring tool to assess for signs and symptoms and severity of NAS. This tool evaluates 21 items in the areas of CNS disturbances, GI disturbances, and metabolic/vasomotor/respiratory disturbances<sup>1</sup>
- Methadone has been the standard of treatment for opioid addiction during pregnancy, but recent studies have shown buprenorphine is effective and decreases NAS<sup>2</sup>
- The Women and Infant Substance abuse Help (WISH) clinic was established in September 2014 as a half-day per week pilot interdisciplinary clinic

## Objective

To determine the neonatal and maternal effects of buprenorphine in opioid-maintained obstetric patients enrolled in the WISH clinic

## Methodology

- This is phase 1 of data collection in a retrospective cohort study
- Inclusion criteria: age  $\geq 14$ , enrolled in WISH clinic prescribed buprenorphine, singleton pregnancy, delivered at a SSM hospital by November 4, 2015
- The chart review included various maternal demographics and infant outcomes
- Primary outcome: infant length of stay (LOS)
- Secondary outcomes: Peak NAS score, time to peak NAS score, total morphine dose, peak morphine dose

## Results

- A total of 22 patients met eligibility criteria and were assessed
- Six infants (27%) were treated for NAS. Four out of six had mothers who smoked tobacco and one was treated for a psychiatric condition
- For the treatment of NAS, morphine was the only medication used
- There were 7 patients who had a positive UDS at delivery. Four opioid (+), one cocaine (+), and one marijuana (+) had infants who experienced NAS
- There was one infant who had a LOS of 97 days and was considered to be an outlier. This data were excluded from the morphine dose, peak NAS score, time to peak NAS score, and length of stay analyses\*

**Table 1: Baseline characteristics of mothers and infants (n=22)**

| Maternal Characteristics                                                                                                                   | Result                                                                                                            |
|--------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------|
| <b>Age:</b> Mean (range)                                                                                                                   | 27.8 years (21-40)                                                                                                |
| <b>Treated for a psychiatric condition</b><br>Yes                                                                                          | 6 (27%)                                                                                                           |
| <b>Tobacco Use</b><br>Yes                                                                                                                  | 19 (86%)                                                                                                          |
| <b>Clinic visits attended:</b> Mean (range)                                                                                                | 8.5 (2-18)                                                                                                        |
| <b>Buprenorphine treatment duration:</b> Mean (range)                                                                                      | 97.3 days (16-273)                                                                                                |
| <b>Urine Drug Screen at delivery</b><br>Negative<br>(+) Opioids<br>(+) Cocaine<br>(+) Barbiturates<br>(+) Benzodiazepines<br>(+) Marijuana | 15 patients (68%)<br>5 patients (23%)<br>1 patient (5%)<br>0 patients (0%)<br>0 patients (0%)<br>4 patients (18%) |
| <b>Gestational age at delivery:</b> Mean (range)                                                                                           | 38 weeks 3 days (34 weeks 6 days-41 weeks 1 day)                                                                  |

**Table 2: Primary and Secondary Outcomes**

| Characteristic                                                                                                                  | Total (n=21)*                                           | Experienced NAS (n=5)*                                |
|---------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------|-------------------------------------------------------|
| <b>Length of Stay</b><br>Total: mean (range)<br>Well-infant nursery: mean (range)<br>Neonatal intensive care unit: mean (range) | 7.71 days (2-22)<br>2.66 days (0-5)<br>5.05 days (0-22) | 16.2 days (11-22)<br>1.2 days (0-2)<br>15 days (0-22) |
| <b>Peak NAS scores:</b> Mean (range)                                                                                            | 9.05 (2-15)                                             | 13 (11-15)                                            |
| <b>Time to peak NAS score:</b> Mean (range)                                                                                     | 46.9 hours (8-118)                                      | 52.4 hours (35-73)                                    |
| <b>Morphine dose</b><br>Total amount required: mean (range)<br>Peak dose: mean (range)                                          | 0.58 mg (0.0-3.42)<br>0.01 mg (0-0.06)                  | 2.46 mg (1.44-3.42)<br>0.056 mg (0.04-0.06)           |

\*One outlier is excluded from results table

## Discussion

- Amongst 22 pregnant women treated with buprenorphine, there were six infants who experienced NAS and were treated
- For infants who experienced NAS, excluding the one outlier, average peak NAS scores were 13.0 and a total of 2.46 mg of morphine was used during the treatment of NAS. Neonatal LOS was 7.71 days on average
- At SSM, infants whose mother was treated with buprenorphine are required to stay a minimum of 4 to 7 days. The minimum LOS requirement changed during the first year of clinic and was at the provider's discretion
- In the MOTHER trial (n=58 infants), 27% were treated for NAS. For the 58 infants, there was a peak NAS score of 11.0 and 1.1 mg total of morphine was used. LOS was 10.0 days<sup>3</sup>
- Treatment of opioid-maintained women with buprenorphine in this clinic showed comparable results to previously published literature
- Compared to previous literature, all buprenorphine-treated patients had fewer infants treated for NAS, a shorter LOS, lower peak NAS scores, and a lower total morphine dose

## Strengths/Limitations

- Strengths
  - Very little data are published on this topic
  - Over one year in duration
- Limitations
  - Minimum required LOS was changed during the study period
  - Small sample size
  - No comparator group to methadone
  - NAS scoring varies depending on hospital unit infant is scored in

## Future Directions

- Methadone data at this institution are being collected and will be compared to buprenorphine data matched by gestational age
- The WISH clinic will be expanding in the near future, so there will be a much larger buprenorphine sample size

## References

1. Hudak ML, Tan RC, The Committee on Drugs and the Committee on Fetus and Newborn. Clinical report: neonatal drug withdrawal [published online ahead of print January 30, 2012]. Pediatrics 2012 [cited 2015 Aug 16];129:e540. Available from: <http://pediatrics.aappublications.org/content/129/2/e540.full.pdf>
2. Jones HE, Kaltenback K, Heil SH, et al. Neonatal Abstinence Syndrome after Methadone or Buprenorphine Exposure (MOTHER Study). N Engl J Med 2010[cited 2015 Aug 16];363:2320-31.