



Association of maternal opioid use, fetal exposure and short-term adverse neonatal outcomes

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Background

- The effect of chronic fetal opioid exposure on adverse neonatal outcomes remains unknown, including ways to predict who is at risk for opioid withdrawal syndrome (NOWS) and long-term neurocognitive sequelae.
- Meconium opioid levels (MOLs) have been described as a method to detect illicit maternal opioid use; however, it remains unclear whether MOLs correlate with adverse neonatal outcomes.

Goals of this study

- Feasibility of quantifying known fetal opioid exposure using MOLs.
- Association between maternal opioid exposure with MOLs.
- Interaction between opioid exposure, MOLs and short-term adverse neonatal outcomes.

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Subjects = 15 mothers with chronic opioid exposure (> 2 weeks of prescribed opioid use during pregnancy)

- Buprenorphine, codeine, fentanyl, hydrocodone, hydromorphone, methadone, morphine, oxycodone, oxymorphone

Methods = Meconium collected at birth

- Opioid concentrations measured using ultra-performance LC-MS/MS.
- **Primary outcome: adverse neonatal outcome** - composite outcome with ≥ 2 criteria:
Neonatal resuscitation; NICU admission (> 1 day), IV morphine use; Finnegan score (> 7); LOS > 5 days

Analysis = effect of chronic maternal opioid use on fetal exposure and neonatal outcomes

- 2-group comparison between cases with neonatal adverse outcome versus no adverse outcome examining
 - 1) High maternal opioid use (defined as MME ≥ 90) vs low use (MME < 90)
 - 2) Total MOLs

Results

- Oxycodone was the most used opioid (N=7).
- High maternal opioid use (MME ≥ 90) occurred in 7/15 cases (of which 4 were on methadone or buprenorphine).
- Prescribed maternal opioids (and their metabolites) expected to be found in the meconium were found in all samples, except for 1 outlier with high levels of unprescribed codeine, morphine, fentanyl.
- Adverse neonatal outcomes occurred in 5/15 cases (33%).
- Proportion of high opioid use (MME ≥ 90) did not differ between neonates with and without adverse outcome.
- MOLs were significantly higher in cases with neonatal adverse outcome compared to cases without.

Table. Two-group analysis evaluating chronic maternal opioid use, total meconium opioid levels and neonatal outcomes

	No adverse neonatal outcome N = 7	Adverse neonatal outcome N = 4	P-value	AUC (95% CI)
MME ≥ 90 (count (%))	2 (28.6%)	2 (50.0%)	0.576 (Fisher test)	--
Total MOL (mean (1 SD); ng/g)	61.6 (56.9)	2731.5 (4246.4)	<0.001 (Mann-Whitney U test)	0.93 (0.76, 1.00)

N= 11 (4 patients on methadone or buprenorphine not included)

MME = morphine milligram equivalent

MOL = meconium opioid level; total MOL was calculated using potency and concentrations (ng/g)

Total MOL calculated using potency conversion factor (codeine 0.15; hydrocodone 1; hydromorphone 4; morphine 1; oxycodone 1.5; oxymorphone 3)

AUC = area under the receiver operating characteristic curve (≥ 0.90; excellent discrimination)

Key Points

- High total MOL correlated with neonatal adverse outcome (e.g. NICU admission & prolonged hospital stay).
- Rapid real-time quantification of chronic fetal opioid exposure is feasible in meconium samples - within hours of sample collection.
- The ability to determine meconium opioid concentrations at birth offers new avenues for the clinical prediction of neonates at risk for NOWS and further research exploring the impact of fetal opioid exposure on short term outcomes and long-term neurobehavioral development.