

Maternal methadone dose, methadone meconium concentrations, severity of neonatal abstinence syndrome and other birth outcomes

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AIMS: In utero drug exposure has been associated with a host of negative maternal and fetal outcomes. Currently, the only recommended pharmacotherapy for opiate dependence in pregnant women is methadone, a full μ opioid agonist. It is still a matter of controversy whether maternal methadone dose is correlated to severity and duration of neonatal abstinence syndrome (NAS). Depending upon the severity of the increased startle reflex, tremors, inability to self-quiet, poor-feeding, abnormal sleep patterns, diarrhea, fever and seizures in the infant, pharmacotherapy may be required. The aims of this study were to relate the severity of neonatal withdrawal and other birth outcomes to total and trimester cumulative maternal methadone dose and methadone and metabolite concentrations in meconium.

METHOD: Twelve opiate-addicted pregnant women were enrolled in a methadone replacement program and followed throughout gestation. Tri-weekly urine specimens obtained during study enrollment were analyzed for drugs of abuse by EMIT (Dade Behring, San Jose, CA, US). Newborn meconium specimens were analyzed for methadone, EDDP and EMDP by LC-MS/MS and by GC/MS for opiate and cocaine metabolites. Maternal total and cumulative 1st, 2nd and 3rd trimester methadone dose, birth outcomes and neonatal withdrawal scores were extracted from medical records.

RESULTS: Cumulative (mean \pm SD) maternal methadone doses ranged from 4,190 – 21,270 mg (10,167.1 \pm 4,499.6). Methadone and EDDP concentrations in meconium were 95 -17,268 ng/g (5819.1 \pm 5191.8) and 6,375-80,503 ng/g (37,968.3 \pm 19,312.9), respectively. EMDP was seen in 42% of specimens, but at concentrations less than 27 ng/g. Infant mean birth weight was 2,753.3 g \pm 790.0 (2,025.0 – 4,025.0). All infants displayed neonatal abstinence syndrome (NAS) symptomology with peak scores of 3 to 19 (9 \pm 5) and a duration of 3 to 24 days (8.1 \pm 7.0). Increased birth weight and head circumference were found in infants whose mothers were maintained on higher cumulative methadone doses during the third trimester of gestation. There were no significant relationships between total maternal or cumulative trimester methadone doses, methadone and metabolite meconium concentrations and severity of NAS.

CONCLUSIONS: Maternal total or cumulative trimester methadone dose did not correlate to severity of neonatal withdrawal nor the concentrations of methadone and metabolites in meconium, while a positive significant relationship was observed between third trimester cumulative methadone dose and birth weight and head circumference. Treatment of opiate-addicted pregnant women should include the option of adequate methadone administration to prevent relapse to heroin usage.

KEYWORDS: *Methadone, Meconium neonatal, Abstinence syndrome, In utero outcomes NAS*

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