

# Perinatal/Neonatal Case Presentation



## OxyContin and Neonatal Abstinence Syndrome

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Opioids are a commonly abused class of drugs. OxyContin<sup>®</sup> abuse, a long-acting oxycodone derivative, has been increasingly identified as a potent narcotic resulting in drug dependence, overdose and even death. Use during pregnancy may result in withdrawal symptoms in the neonate. However, detection of the drug and its metabolites needs special methods in order to initiate appropriate therapy.

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### INTRODUCTION

Substance abuse during pregnancy results in significant morbidity in the mother, the fetus and the newborn infant. Commonly abused substances during pregnancy include alcohol, nicotine, opioids, cocaine, heroin, barbiturates, and benzodiazepenes. The use of these drugs has been associated with an increased incidence of spontaneous abortion, abruptio placentae, congenital malformations, fetal growth retardation, low birth weight, and infections such as HIV. In utero exposure to opiates is associated with abstinence symptoms (neonatal abstinence syndrome, NAS) that may vary in onset and severity, in as many as 55–94% of the exposed infants.<sup>1,2</sup> The Neonatal Abstinence Scoring System is used for monitoring these symptoms as well as the effects of therapy. The scoring system lists 21 symptoms commonly seen in the neonate. Each symptom is assigned a score based on severity observed over a period of time. A score of 8 or more is an indication for frequent monitoring and for initiating therapy.<sup>1</sup>

Clinical management of infants born to mothers abusing OxyContin (controlled release oxycodone hydrochloride; Purdue Pharmaceuticals, Stamford, CT) during pregnancy is of particular concern because OxyContin and its metabolites are unlikely to be detected by the enzyme immunoassay methods usually used for urine and meconium opiate screens. A more sensitive assay, e.g., gas chromatography (GC) or gas chromatography/mass spectroscopy (GC/MS) may be necessary to detect OxyContin and its metabolites.

Although many opioids have been implicated, we are not aware of any previously published report of NAS following OxyContin use in pregnancy. We present a neonate with withdrawal symptoms following maternal OxyContin use whose initial urine and meconium drug screens were negative.

### CASE REPORT

The patient was a 39 weeks' gestation male infant (birth weight 2864 g (>25th percentile), length 47 cm (<5th percentile), head circumference 33 cm (<5th percentile)), born to a 24-year-old, gravida 3, para 3 woman by spontaneous vaginal delivery at an outlying hospital. She had two previous preterm deliveries. The first was a preterm vaginal delivery at 36 weeks, and the second was a caesarian section at 32 weeks for eclampsia. There was history of barbiturate abuse during the second pregnancy. She had a smoking history of 1 pack per day for 10 years and had been injecting OxyContin (120 to 500 mg/d) intravenously for the past 2 years. Detoxification with methadone was attempted in the second trimester of the present pregnancy, but the mother was noncompliant due to withdrawal symptoms. Pregnancy was further complicated by recurrent urinary tract infections and preterm labor at 36 weeks' gestation that was managed conservatively. She developed seizures in the last trimester that was treated with phenytoin. The mother attempted self-detoxification with methadone obtained illicitly 3 weeks before delivery. At this time, maternal urine drug screen was positive for oxycodone (>3000 ng/ml), oxymorphone (1794 ng/ml), phenothiazine metabolites, methadone (769 ng/ml) and methadone metabolites (2455 ng/ml) and negative for barbiturates, benzodiazepenes, cocaine, cannabinoids, and alcohol. A repeat maternal urine drug screen at delivery was positive for oxycodone, oxymorphone, norpropoxyphene, and phenothiazine derivatives. At birth, the baby was noted to have a shrill cry. Apgar scores were 7 and 10 at 1 and 5 minutes, respectively. The baby initially required oxygen therapy for transient respiratory distress. Serum glucose was in the mid-30s and was treated with D10W orally. The baby was subsequently transferred to the regional medical center at 2 hours of age. At admission, the baby was noticed to be jittery and irritable. On physical examination no dysmorphic features were noted. During the first day, the baby exhibited hypertonia, tachypnea, tachycardia, and an exaggerated startle response. The baby's initial urine and meconium drug screens were negative. However, a subsequent urine GC/MS opiate analysis was positive for oxymorphone (567 ng/ml) but negative for methadone derivatives. Feeds were initiated on day 2 but were not tolerated. Over the next few days, the infant developed

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emesis, watery diarrhea, short sleep cycles, mottling, and excoriations on the face and buttocks. The Neonatal Abstinence Scoring system was used for monitoring the infant.<sup>3</sup> The mean score ranged from 10 to 21 during the first week but decreased thereafter. The baby was treated with paregoric (0.2 ml orally every 4 hours) initially for 12 days followed by chloral hydrate (150 mg orally every 6–8 as needed) for 4 days. During this period, no laboratory abnormalities were noted. Formula feedings were well tolerated after beginning treatment. The baby continued to improve and was discharged to foster care on day 16 of life on oral chloral hydrate. This was discontinued on follow-up. The mother underwent counseling and detoxification therapy.

## DISCUSSION

OxyContin, a controlled release oxycodone hydrochloride, is a long-acting synthetic narcotic indicated for postoperative pain control, in cancer patients, and other chronic painful conditions such as osteoarthritis in adults.<sup>4–6</sup> Although its principle therapeutic effect is analgesia, anxiolysis, euphoria, and feelings of relaxation have also been reported. OxyContin effects may be mediated through the opioid receptors in the CNS and spinal cord. Other effects include direct brainstem respiratory depression, cough suppression, smooth muscle dysmotility, meiosis, histamine release, and hypotension. OxyContin is well absorbed orally and has high bioavailability due to low first-pass metabolism. It is metabolized to noroxycodone, oxymorphone, and their glucuronides and primarily excreted through urine. OxyContin has also been detected in breast milk. Although OxyContin has not been found to be teratogenic in experimental animals, it is not recommended for use in pregnancy. Like other opioids, use in pregnancy and during labor may be associated with withdrawal symptoms and respiratory depression in the newborn infant.<sup>7</sup>

Despite polydrug abuse by the mother, we believe that the withdrawal symptoms observed in the baby were due to OxyContin as demonstrated by the presence of oxymorphone in the baby's urine in the GC/MS analysis. The initial urine and meconium drug screens were negative because the screening procedure (EMIT II plus opiate assay, Dade Behring, Cupertino, CA) used in our institution detects oxycodone at levels >5000 ng/ml and oxymorphone at levels >20,000 ng/ml when the opiates cut-off level is set at 300 ng/ml. We specifically requested a GC/MS analysis, which detected oxymorphone in the urine in view of known maternal OxyContin use. The meconium drug screen, however, could not be repeated, as the original sample was not available for analysis by GC/MS. Although methadone use during pregnancy has also been associated with late withdrawal symptoms in the newborn, we did not identify any other drug(s) in the urinary or meconium drug screens in this baby.

In the past few years, OxyContin has become a popular alternative to other street drugs such as heroin.<sup>8,9</sup> OxyContin is available as an oral preparation but is used illicitly by crushing the tablet for inhalation, insufflation, or dissolving in solution for intravenous injection. There has been an increased incidence of OxyContin use

recently, either singly or in conjunction with other drugs, and death has also been reported due to OxyContin overdose.<sup>10</sup>

Although substance abuse among pregnant women is decreasing, there are significant numbers of affected infants born each year.<sup>2</sup> There is, however, very little data on the prevalence of OxyContin use in pregnant women. Methadone maintenance therapy during pregnancy is associated with better maternal and neonatal outcome. Recently buprenorphine has also been used successfully during pregnancy in opioid-dependent women.<sup>11,12</sup>

Purdue Pharmaceuticals, OxyContin's manufacturer, has taken steps to reduce the potential for abuse of this medication including providing physicians with tamper-proof prescription pads, better education for the pharmacists and health care professionals, as well as cooperation with the law enforcement agencies.<sup>13</sup> Recently a task force has also been set up to combat the increasing misuse of OxyContin.<sup>10</sup> In spite of these measures, the abuse of OxyContin and oxycodone products is likely to continue.<sup>9,10,14</sup> It is therefore important to closely monitor the neonate for withdrawal symptoms despite negative screening tests.

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