Neonatal Opioid Withdrawal Syndrome

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KEYWORDS

• Neonatal abstinence syndrome • Neonatal opioid withdrawal
• Perinatal substance abuse • Buprenorphine • Methadone

KEY POINTS

- It is important for all providers to recognize neonatal opioid withdrawal with shifts in maternal prescription opioid use and abuse.
- Current evidence points to a milder withdrawal syndrome with maternal buprenorphine maintenance in comparison with methadone.
- Initial treatment of neonatal opioid withdrawal should be with opioid monotherapy; currently there is no evidence to recommend one regimen over another. Adjunctive therapy, if required, should be with phenobarbital or clonidine.
- The hospital environment should be maximized to promote low stimuli for infants affected by withdrawal, and should include rooming-in and breastfeeding promotion where appropriate.
- At present there is limited evidence on the long-term childhood effects of perinatal opioid exposure, and support is needed for families during early childhood development.

BACKGROUND AND EPIDEMIOLOGY

Neonates who have had in utero exposures from maternal substance abuse can experience central nervous system effects of the drugs, including drug toxicity and withdrawal. Neonatal abstinence syndrome (NAS), initially described in the 1970s, is the term used for the constellation of withdrawal symptoms. The clinical features and treatment of withdrawal from opioids is a specific form of NAS, and has recently been termed neonatal opioid withdrawal syndrome (NOWS). This review focuses primarily on the presentation, diagnosis, and management of NOWS, with emphasis on current evidence for assessment by scoring systems, pharmacologic treatment protocols, and implications for future policy and research.

The authors have nothing to disclose.

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Obstet Gynecol Clin N Am 41 (2014) 317–334
http://dx.doi.org/10.1016/j.ogc.2014.02.010 **obgyn.theclinics.com**
0889-8545/14/$ – see front matter

The rising incidence of maternal opioid use is demonstrated by hospital discharge records revealing a nationwide increase from 1.19 to 5.63 per 1000 births per year from 2000 to 2009.[1] In 2012, an estimated 5.9% of women aged 15 to 44 years were using illicit drugs during pregnancy.[2] Marijuana use is most common, followed by use of prescription opioids and, less commonly, stimulants, heroin, and psychotropic drugs.[3] Unique to the past several years is the rapid increase in prescription opioid abuse,[1,4] which has changed both the number and demographic characteristics of pregnant women using illicit substances, necessitating providers of all geographic and socioeconomic populations to be aware of the management of neonatal opioid withdrawal.

The epidemic abuse of prescription opioids and continued heroin use have increased the rates of NAS from 1.20 per 1000 births in 2000 to 3.39 per 1000 births in 2009, with an estimated 1 newborn per hour born with NAS in the United States in 2009.[1] Health care spending for illicit drug use during pregnancy and related neonatal outcomes has increased from an average of US$39,400 per NAS hospital admission in 2000 to $53,400 in 2009, with 77.6% of these charges attributed to state Medicaid in 2009.[1] The length of stay for NAS averages 16 days and has not significantly changed during this time.[1] According to a recent survey, only about half of neonatal intensive care units (NICUs) in the United States have a written protocol for the diagnosis and management of NAS, which represents an important area for educational improvement.[5]

CLINICAL PRESENTATION AND DIAGNOSIS

Mothers who are abusing opioids may be identified during prenatal care and referred to perinatal substance abuse programs, which will optimally have an affiliated neonatal program. Unfortunately many women with opioid addiction do not obtain prenatal care, and are first seen when they present in labor. Some women, particularly those with addiction to prescription opioids, may be able to obtain a prescription from other physicians or purchase diverted “street drugs” during the pregnancy, and the neonatal exposure will be unsuspected until the withdrawal syndrome develops. Risk factors for maternal drug abuse include poor or no prenatal care, a previously unexplained late fetal demise placental abruption, unexplained intrauterine growth restriction, maternal hypertension, and precipitous labor.[6,7] These factors, clinical suspicion of opioid withdrawal, or a known history of maternal drug abuse or opioid replacement therapy may prompt screening with a maternal or neonatal urine drug screen or meconium toxicology testing. The legal implications of this screening are important to consider before initiation, as several states consider a positive newborn urine drug screen to be evidence of child abuse.[8] The optimal urine sample for neonatal screening is the first urine after birth, as many substances are quickly metabolized and become undetectable.[7] Urine testing can result in false positives, as some prescription medications and over-the-counter products cross-react with testing for drugs of abuse, so that a positive test on the screening procedure requires confirmatory testing by gas chromatography or mass spectrometry.[8] Drugs that are metabolized by the fetal liver and kidneys are concentrated in meconium, which can detect prenatal substance exposure that has occurred months before birth; therefore, meconium testing may be positive when urine testing is negative.[7,8] Analysis of neonatal hair or umbilical cord tissue can also provide a window of screening of weeks to months, but are primarily used only for research purposes at present.[8]

The probability of newborns exposed to maternal chronic opioid use developing withdrawal symptoms that are sufficient to require pharmacologic therapy varies