



eNeonatal Review VOLUME 8, ISSUE 11

Neonatal Abstinence Syndrome

In this Issue...

Neonatal abstinence syndrome (NAS) is a complex, commonly encountered clinical disorder that comprises a range of behavioral and physiologic signs. Affected infants have been exposed to a variety of drugs that, at the cellular level, induce tolerance and dependence, such that when the drug is discontinued, physical signs and symptoms of withdrawal occur. Exposure to these agents may take place either prenatally from maternal use or postnatally from therapeutic indications such as pain relief. Although several classes of drugs may cause NAS, analgesics (specifically, opioids) are the most common. NAS can be difficult to diagnose, quantify, and treat. Recent advances in our understanding of the complex neurochemical mechanisms involved have revealed novel approaches for treatment. Even with the advent of withdrawal scoring systems, treatment algorithms, and new approaches to pharmacologic management of NAS, there is still room for improvement in caring for narcotic-exposed neonates.

In this issue, we review recent literature that addresses the broad range of prenatal illicit drug exposure triggering withdrawal symptoms to help clinicians more effectively implement appropriate treatment strategies.



Program Information

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Length of Activity

- 1 hour Physicians
- 1 contact hour Nurses

Release Date

April 19, 2011

Expiration Date

April 18, 2013

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After participating in this activity, the participant will demonstrate the ability to:

- Identify novel therapies for treating neonatal abstinence syndrome (NAS)
- Discuss the risk factors for and clinical presentations of selective serotonin reuptake inhibitor withdrawal in neonates
- Describe the spectrum of developmental outcomes among children who receive treatment for NAS

IMPORTANT CME/CNE INFORMATION

Program Begins Below

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This activity has been developed for neonatologists, NICU nurses, and respiratory therapists working with neonatal patients. There are no fees for this activity.

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- **Christoph U. Lehmann, MD**, has indicated a financial relationship of honoraria from Mead Johnson and PediatrIX. Dr. Lehmann is also the Editor-In-Chief of *Applied Clinical Informatics Journal*. He serves on the Board of Directors for the American Medical Informatics Association.
- **Anthony Bilenki, MA, RRT, Edward E. Lawson, MD, Lawrence M. Nogee, MD and Mary Terhaar, DNSc, RN** indicated they have no relevant financial relationships with any commercial supporters.

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Guest Faculty Disclosure

Estelle Gauda, MD, and Tamorah Lewis, MD, have disclosed no

relevant financial relationships with commercial entities.

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Unlabeled/Unapproved Uses

The authors have indicated that there will be reference to the unapproved/unlabeled use of clonidine and buprenorphine.



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COMMENTARY

Maternal opiate use is a commonly encountered problem that is usually concentrated in major urban areas in the United States and abroad. The National Pregnancy and Health Survey, conducted from 1992 to 1993, estimated that 5.5% of women delivering live-born infants had used illicit drugs at some time during their pregnancies.¹ In this survey of pregnant women in the United States, as many as one-fourth of those reporting illicit drug use had used heroin or other opioid analgesics within 30 days of the interview.² Infants born to opiate-dependent mothers are at high risk for developing neonatal abstinence syndrome (NAS) after birth, and more than half of all neonates born to methadone-maintained mothers require treatment for the disorder.

Clinical features of NAS include neurologic hyperexcitability, autonomic dysfunction, delayed growth, and abnormal sleep-wake cycling. The current standard of care for opiate-dependent pregnant women is enrollment in opioid maintenance treatment programs, the majority of which are methadone-based. Although a correlation between methadone exposure and severity of NAS has been suggested, methadone dose is not routinely predictive of occurrence or severity of withdrawal.³ Recently, buprenorphine, a semisynthetic opioid, has received approval for use as an alternative to methadone for treating maternal opioid dependency. A randomized, controlled trial showed that neonatal outcomes among infants whose mothers were treated with buprenorphine instead of methadone included significantly reduced length of treatment, decreased length of

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hospital stay, and reduced average dose of morphine required to manage NAS.⁴ Thus, buprenorphine may be an attractive alternative to methadone in the maternal population. Further, buprenorphine is well tolerated in infants and may thus be beneficial for those who require pharmacologic treatment for NAS.

Standard treatment of NAS has shifted from sedatives, such as paregoric and phenobarbital, to opioid agonists, such as diluted tincture of opium (DTO), morphine, and methadone. A recent Cochrane review concluded that no one opiate is more effective than another in treating opiate withdrawal syndrome in infants, but when compared with such sedatives as midazolam and phenobarbitone, the use of opiates was associated with a lower risk of treatment failure.⁵ The results of a national survey⁶ reported that opioids are the most common first-line therapy for NAS secondary to narcotic (63% of respondents) or polydrug (52% of respondents) exposure, followed by phenobarbital (32% of respondents). The survey also demonstrated that only 54% of all neonatal intensive care units have a written policy for NAS management, and only 70% of respondents use an abstinence scoring system to direct pharmacologic therapy.

Although opioids have become the drug of choice for treating NAS, the need for slow weaning and prolonged inpatient hospitalization renders alternate treatment options desirable. Two randomized trials that address the efficacy and safety of buprenorphine in neonates have been published.^{7,8}

Another agent, clonidine, was recently shown to be effective in treating NAS, either as an adjunct to other sedative agents or as monotherapy.⁹⁻¹¹ Both buprenorphine and clonidine are promising treatment options for more optimal pharmacologic therapy, based on the cellular mechanisms of NAS. Buprenorphine is a partial μ -opioid receptor agonist that has very strong binding affinity for the μ - and κ -opioid receptors. Clonidine is an α 2-adrenergic receptor agonist, and μ -opioid and α 2-adrenergic receptors are coexpressed on norepinephrine-containing neurons.

Developmental outcomes of infants with NAS are confounded by numerous factors. For example, once inpatient therapy for NAS has been completed, infants of mothers compliant with prenatal treatment programs are often discharged home, while infants of noncompliant or untreated mothers are often placed temporarily into the social services system. Such a combination of social, economic, and other environmental factors makes the interpretation of long-term follow-up difficult. The wealth of data demonstrates that opiate-exposed children perform more poorly on developmental testing compared with their nonexposed peers¹² and are at risk for poor ophthalmologic outcomes.¹³ Although it is not current practice, referral to neurodevelopmental follow-up based on narcotic exposure alone should be considered for optimal developmental outcomes.

Pharmacologic treatment of depression is a common practice, and it is becoming more common for mothers to be treated with antidepressants during pregnancy. As a result, a new type of abstinence syndrome has emerged, known as "neonatal behavioral syndrome."¹⁴ Evidence to date demonstrates that this poor neonatal adaptation following in utero antidepressant (mainly selective serotonin reuptake inhibitor [SSRI] and serotonin norepinephrine reuptake inhibitor [SNRI]) exposure can be treated with close observation and supportive care.¹⁴

Commentary References

1. National Institutes of Health. National Institute on Drug Abuse (NIDA). [Drug use during pregnancy](#). Accessed March 3, 2011.
2. Finkelstein N, Kennedy C, Thomas K, Kearns M. Gender-Specific Substance Abuse Treatment. Alexandria, VA: National Women's Resource Center for the Prevention and Treatment of Alcohol, Tobacco, and Other Drug Abuse and Mental Illness; 1997.
3. Thajam D, Atkinson DE, Sibley CP, Lavender T. [Is neonatal abstinence syndrome related to the amount of opiate used?](#) *J Obstet Gynecol Neonatal Nurs*. 2010;39(5):503-509.
4. Jones HE, Kaltbach K, Heil SH, et al. [Neonatal abstinence syndrome after methadone or buprenorphine exposure](#). *N Engl J Med*. 2010;363(24):2320-2331.
5. Osborn DA, Jeffery HE, Cole MJ. [Opiate treatment for opiate withdrawal in newborn infants](#). *Cochrane Database Syst Rev*. 2010;(10):CD002059.
6. Sarkar S, Donn SM. [Management of neonatal abstinence syndrome in neonatal intensive care units: a national survey](#). *J Perinatol*. 2006; 26(1):15-17.
7. Kraft WK, Gibson E, Dysart K, et al. [Sublingual buprenorphine for treatment of neonatal abstinence syndrome: a randomized trial](#). *Pediatrics*. 2008;122(3):e601-e607.

8. Kraft WK, Dysart K, Greenspan JS, Gibson E, Kaltenbach K, Ehrlich ME. [Revised dose schema of sublingual buprenorphine in the treatment of the neonatal opioid abstinence syndrome](#). *Addiction*. 2011; 106(3):574-580.
9. Agthe AG, Kim GR, Mathias KB, et al. [Clonidine as an adjunct therapy to opioids for neonatal abstinence syndrome: a randomized, controlled trial](#). *Pediatrics*. 2009;123(5):e849-e856.
10. Hoder EL, Leckman JF, Poulsen J, et al. [Clonidine treatment of neonatal narcotic abstinence syndrome](#). *Psychiatry Res*. 1984;13(3): 243-251.
11. Esmaeili A, Keinhorst AK, Schuster T, Beske F, Schlösser R, Bastanier C. [Treatment of neonatal abstinence syndrome with clonidine and chloral hydrate](#). *Acta Paediatr*. 2010;99(2):209-214.
12. Hunt RW, Tzioumi D, Collins E, Jeffery HE. [Adverse neurodevelopmental outcome of infants exposed to opiate in-utero](#). *Early Hum Dev*. 2008;84(1):29-35.
13. Hamilton R, McGlone L, MacKinnon JR, Russell HC, Bradnam MS, Mactier H. [Ophthalmic, clinical and visual electrophysiological findings in children born to mothers prescribed substitute methadone in pregnancy](#). *Br J Ophthalmol*. 2010;94(6):696-700.
14. Moses-Kolko EL, Bogen D, Perel J, et al. [Neonatal signs after late in utero exposure to serotonin reuptake inhibitors: literature review and implications for clinical applications](#). *JAMA*. 2005;293(19):2372-2383.

SSRI EXPOSURE AND NEONATAL DISCONTINUATION SYNDROME

Oberlander TF, Misri S, Fitzgerald CE, Kostaras X, Rurak D, Riggs W. **Pharmacologic factors associated with transient neonatal symptoms following prenatal psychotropic medication exposure**. *J Clin Psychiatry*. 2004;65(2):230-237.



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In a prospective cohort study, Oberlander and colleagues evaluated 2 cohorts (N=46) of infants exposed to either an SSRI alone (fluoxetine, paroxetine, or sertraline) or an SSRI in combination with clonazepam during pregnancy. The investigators compared these infants with a control cohort of 23 nonexposed neonates. The children were examined by pediatricians for any abnormal symptoms, including jitteriness, tachypnea, hypoglycemia, lethargy, weak/absent cry, desaturations, or other symptoms considered to be of concern by the infant's nurse

Overall, 30% of the exposed infants exhibited symptoms of poor neonatal adaptation, compared with 9% of the control infants. In the SSRI-only group, 25% of exposed neonates exhibited symptoms; in the SSRI-plus-clonazepam group, 39% of exposed neonates exhibited symptoms. Symptoms typically included mild respiratory distress and hypotonia. Developmental outcomes using Bayley scoring at 2 months and 8 months of age did not differ between symptomatic and asymptomatic infants. Maternal drug levels during the third trimester and at birth, as well as infant drug levels from cord blood and serum on day 2 of life, were obtained. When paroxetine was combined with clonazepam, symptomatic infants had significantly higher paroxetine levels compared with similarly exposed asymptomatic infants ($P < .05$). The maternal dose of clonazepam was significantly higher during pregnancy and at delivery among symptomatic infants compared with asymptomatic infants. Many children who were assessed underwent sepsis evaluations, all of which were negative. All symptoms resolved within 48 hours of life, and length of hospital stay did not differ between infants with and without symptoms. Of note, no differences were observed in growth parameters, gestational age at birth, or rate of congenital anomalies between the exposed and nonexposed cohorts.

The investigators concluded that infants with prenatal exposure to SSRI antidepressants alone or in combination with the benzodiazepine clonazepam have an increased incidence of poor neonatal adaptation, which is particularly true among infants of mothers with high maternal SSRI levels and of those taking high doses of clonazepam in the third trimester. Respiratory distress was the most prominent symptom, and all infants who exhibited this spectrum of symptoms received a heightened level of observation and removal from couplet care. The authors recommended the avoidance of polypharmacy for the treatment of maternal depression and anxiety, whenever possible, indicating that if a benzodiazepine is required, a taper in the third trimester is recommended in an effort to reduce neonatal symptoms. Maternal drug levels during pregnancy and at the time of delivery may help to stratify infants to risk for postnatal symptoms.

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ADVERSE NEURODEVELOPMENTAL OUTCOMES AMONG CHILDREN EXPOSED TO OPIATES IN UTERO

Hunt RW, Tzioumi D, Collins E, Jeffery HE. **Adverse neurodevelopmental outcome of infants exposed to opiate in-utero.** *Early Hum Dev.* 2008;84(1):29-35.



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The authors reviewed the literature and identified a total of 14 studies (from 1966 to 2005), that involved 629 opiate-exposed infants who were followed for developmental progress between 2 months and 10 years of age. All of the studies were case series or case-control in design. The results of the studies were stratified by number of cases (<50 vs. >50 cases) and percentage retention (although no studies were excluded for lack of retention at follow-up). Opiate-exposed infants consistently exhibited evidence of neurodevelopmental impairment, regardless of their age at testing or the tool used to compare these children with unexposed controls.

The authors also conducted their own case-control study, between May 1979 and January 1984, enrolled a total of 133 known opiate-dependent infants (mothers were compliant patients in a methadone program). A total of 103 nonopiate-exposed controls were recruited from the antenatal clinic during the same time period. The mothers were matched for age, height, race, and prior obstetric history. Developmental assessments were conducted in the child's home at the ages of 18 months and 36 months. Of the exposed infants, 56% had received pharmacologic treatment for NAS. Many of the opiate-exposed infants were discharged to foster care; the overall rate of follow-up was 59% at 18 months and 50% at 3 years. Opiate-exposed infants had significantly lower scores on all assessment tools used (the Bayley Scales of Infant Development and Vineland Social Maturity Scale at 18 months; the Stanford-Binet Intelligence Scales, McCarthy Motor Scale, Vineland Social Maturity Scale, and Reynell Expressive Language Scale and Verbal Comprehension Scale at 36 months), except for the Bayley psychomotor developmental index (PDI). Of note, although the PDI was not statistically significant at 18 months, significantly lower scores were reported ($P < .05$) on the McCarthy Motor Scale in opiate-exposed children at 3 years of age. The authors noted that the children for whom they had data were the ones with a home environment conducive to follow-up. They speculated that children who were lost to follow-up more than likely had less stable home environments and predicted that these infants would also have performed less well on the neurodevelopmental assessments. Thus, every effort should be made to follow opiate-exposed children longitudinally for developmental abnormalities, so that in utero effects can be minimized and outcomes can be optimized.

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EFFICACY AND SAFETY OF SUBLINGUAL BUPRENORPHINE FOR THE TREATMENT OF NAS

Kraft WK, Gibson E, Dysart K, et al. **Sublingual buprenorphine for treatment of neonatal abstinence syndrome: a randomized trial.** *Pediatrics.* 2008;122(3):e601-e607.



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Kraft WK, Dysart K, Greenspan JS, Gibson E, Kaltenbach K, Ehrlich ME. **Revised dose schema of sublingual buprenorphine in the treatment of the neonatal opioid abstinence syndrome.** *Addiction.* 2011;106(3):574-580.



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Kraft and colleagues conducted a randomized, open-label, prospective pilot study investigating the safety and efficacy of sublingual buprenorphine in neonates with NAS. A total of 26 infants born to mothers in methadone maintenance who required pharmacologic therapy for NAS were randomized to either sublingual buprenorphine or



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DTO treatment. Sublingual buprenorphine was formulated from the injectable solution and administered in aliquots of <0.5 mL. A pacifier was used to decrease immediate swallowing among the infants.

Sublingual buprenorphine, initiated at 13 µg /kg/day divided into 3 doses and escalated per protocol to a maximum dose of 39 µg /kg/day, was effective as monotherapy in controlling NAS. The mean length of treatment in the DTO group was 32 ± 16 days (mean ± standard deviation), compared with 22 ± 11 days in the buprenorphine group (P=.077). Mean length of hospital stay was 38 ±16 days and 27 ± 11 days, respectively, in the DTO and buprenorphine groups (P=.068). Overall, 3 infants in the buprenorphine arm and 1 infant in the DTO arm received additional phenobarbital because of failure to control NAS symptoms once the maximum protocol dose had been reached. Buprenorphine serum levels were lower than those reported for adults with adequate control of opioid withdrawal symptoms.

In a subsequent randomized, open-label, prospective study designed to determine the optimal dosage of buprenorphine for treating NAS, buprenorphine 15.9 µg /kg/day escalated to a dose of 60 µg /kg/day was compared with oral morphine treatment. Buprenorphine-treated infants had a 40% shorter length of treatment (23 vs. 38 days; P=.01) and a 24% shorter length of hospital stay (32 days vs. 42 days; P=.05), compared with the oral morphine-treated group. Buprenorphine administered at the higher dosages was well tolerated.

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ORAL CLONIDINE USED AS ADJUNCT THERAPY TO OPIOIDS FOR THE TREATMENT OF NAS

Agthe AG, Kim GR, Mathias KB, et al. **Clonidine as an adjunct therapy to opioids for neonatal abstinence syndrome: a randomized, controlled trial.** *Pediatrics*. 2009;123(5):e849-e856.



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This report by Agthe and associates used a blinded, prospective, randomized, placebo-controlled protocol to investigate the efficacy of oral clonidine as adjunct therapy to DTO for treating NAS. In this study, 80 infants were randomized to either oral clonidine plus DTO or placebo plus DTO for treating NAS secondary to in utero opiate exposure (heroin or methadone). The epidural formulation of clonidine 1 µg /kg every 4 hours was administered enterally. Infants at risk for NAS were monitored using modified Finnegan scores (MFSs) and started on treatment if they had consecutive MFSs ≥9. Escalation and de-escalation of DTO were algorithm-driven and based on MFS values. The infants' clonidine dose remained the same throughout treatment course.

The median length of therapy was 27% shorter in the clonidine group than in the placebo group (11 vs. 15 days, respectively; P=.02). The average daily DTO dose/kg was also lower in the clonidine group. Treatment failure occurred in 12.5% of patients in the placebo group vs. none in the clonidine group. Infants exposed to methadone had an average length of therapy that was 3 times that of infants exposed to heroin alone (15 days vs. 5 days, respectively; P=.005). Treatment with clonidine 1 µg /kg every 4 hours was not associated with hypertension, hypotension, bradycardia, or desaturations. This publication reports on the first placebo-controlled trial to show that clonidine, an α2-adrenergic agonist, used as adjunct therapy for treating NAS is narcotic-sparing, shortens the duration of therapy, and prevents treatment failure.

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