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Neonatal abstinence syndrome: Identification and management

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Withdrawal;
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Phenobarbitone

Summary

Neonatal abstinence syndrome (NAS) describes the withdrawal symptoms of infants who are exposed to substance abuse in utero and become physically dependant on them. The most reliable method of confirming the diagnosis is analysis of meconium passed in the first days after birth. Many medications have been used to try and alleviate NAS symptoms, but their efficacy has rarely been tested in randomised or even quasi-randomised trials. The limited data available highlight that phenobarbitone has advantages over supportive care alone or diazepam, but opiates rather than phenobarbitone are the better treatment for the NAS seen in infants of opiate-dependant mothers. Opiate treatment is associated with less treatment failure and a reduced duration of treatment and neonatal unit admission. Appropriately designed trials with long-term outcomes are required to test the effectiveness of both pharmacological and non-pharmacological strategies for NAS, particularly due to maternal polydrug use.

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Practice points

- Analysis of meconium passed in the first days after birth is the most reliable method of diagnosing illicit substance use in utero resulting in NAS
- Opiates are the best treatment for NAS in infants of opiate-dependant mothers

- Infants with NAS can suffer long-term neurodevelopmental and behavioural problems, and thus affected infants require long-term follow-up

Introduction

Substance abuse during pregnancy is common. In the USA, the 1999 and 2000 National Household Survey highlighted that the annual rates of women between 15 and 44 years using illicit drugs was 7.5%; in addition, 30.3% of women

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admitted to smoking and 42.7% to taking alcohol. In 2000, the approximate numbers of births in the USA complicated by the maternal use of illicit drugs, tobacco or alcohol were 134,079, 774,814 and 503,812, respectively. Anonymous screening of consecutive urine samples testing positive for pregnancy in a UK inner city clinic demonstrated that approximately 16% of the women were taking at least cannabis.¹ In the past, heroin was the most commonly abused drug, nowadays women are more likely to take cocaine, methadone, or more than one illicit drug.

Infants exposed to certain drugs in utero can become physically dependant on them and after birth suffer the neonatal abstinence syndrome (NAS). Infants with NAS have multi-system dysfunction with involvement of the central nervous, gastrointestinal and respiratory systems. NAS has been reported to occur in between 55% and 94% of infants exposed to opiates in utero;² other drugs, for example, benzodiazepines and barbiturates, also can cause withdrawal symptoms in the neonate. Between 30% and 80% of babies with NAS will require treatment. If there are no facilities to manage affected babies in the community, NAS can result in a prolonged hospital admission; in one study, the mean duration of neonatal unit stay was 22 days.³ The duration of treatment and hospitalisation is dependant on the type of drugs taken. The combination of diazepam with methadone is associated with a requirement for prolonged treatment. Johnson et al.⁴ observed that the durations of hospital stay and treatment requirement were greatest in infants exposed to methadone with other drugs rather than non-methadone opioids only. The amount of drug taken is also important; the lengths of hospitalisation and treatment requirements correlating with the dosage of maternal methadone.⁵ A prolonged admission may also be required because of feeding difficulties due to an adverse impact of in utero substance abuse on the development of brainstem centres affecting, albeit transiently, the underlying biorhythms of feeding. Other adverse effects of substance abuse during pregnancy include foetal growth retardation and premature delivery. Exposure in the first trimester to substances such as alcohol or cocaine can result in congenital anomalies.

Long-term problems of children exposed to illicit drugs in utero include adverse neurodevelopmental outcomes.⁶ Lower intelligence quotient scores have been reported in children with in utero exposure to cocaine or methadone, speech, perceptual and cognitive disturbances in toddlers who were opiate-exposed and difficulties with expressive language articulation in children of cocaine-abusing mothers. Behavioural problems are also reported in children of mothers who have taken illicit substances in pregnancy. These include lower levels of learning and adapting to new situations, higher sensitivity to their environment resulting in irritability, agitation, aggression, poor social skills, and a lack of imitative play and late emergence of symbolic play.⁶

The large number of infants who suffer from NAS and the associated long-term morbidity mandate that affected infants are accurately identified and their treatment and support optimised. The aim, therefore of this article is to review the relative merits of the methods of diagnosis and treatment and identify to what extent current management can be evidence based.

Diagnosis

Clinical examination

Infants are suspected of having NAS if they exhibit any of the following classical signs: a high-pitched cry, restlessness, hyperreflexia, jitteriness, hypertonia, myoclonic jerks, convulsions, frequent yawning, sneezing, nasal flaring and tachypnoea, excessive sucking or rooting, poor feeding, regurgitation or projectile vomiting, and loose or watery stools. Hyperphagia is a classical feature of NAS and it is usually associated with poor weight gain, however, this may not be the case in all infants.⁷ and excessive weight gain can occur. The timing of onset of the symptoms gives an indication of the maternal drug abuse. Withdrawal from high levels of maternal alcohol can occur within a day or 2 of birth. Heroin has a short half-life and withdrawal also occurs within 48–72 h of birth, whereas methadone withdrawal occurs at 7–14 days. The timing of the onset of withdrawal symptoms, however, can be influenced by the combination and amount of substances abused; for example, the peak of NAS occurred later in methadone exposed infants whose mother smoked more than 20 cigarettes per day rather than 10 or less a day. Infants with signs compatible with NAS are often “scored” using systems such as the Finnegan score or the River score. Such scoring systems are not used to diagnose NAS, but rather to guide to the need for treatment and subsequently dosage alterations. There has been no randomised comparison to determine which score is the most useful. An alternative method of monitoring NAS infants is to use a portable motion detector with a computer memory. In one study, this was shown to be comparable to using a clinical score in the identification of newborns requiring treatment and in determining the severity of withdrawal.⁸ Other abnormalities detected on examination may alert the physician to the diagnosis, but these are rarely specific (Table 1).

Maternal interview

A structured maternal interview has a low sensitivity in detecting cocaine or opiate exposure (65% and 67%, respectively), but is more reliable in identifying cannabis exposure.⁹ In addition, in one study interviews were carried out as early in pregnancy as possible to establish trust and confidence. These were repeated by the same person and despite this structure the false-negative rates for cocaine and opiate use were 55% and 16.7%, respectively. The reliability of maternal interview regarding drug use is adversely affected by many factors, such as the mother’s mistrust of healthcare givers and the fear of the consequences of admitting drug use.

Urine analysis

Urine toxicology screens are easy to perform, but have limitations,¹⁰ in particular related to problems in collecting the urine sample and doing so within a narrow window of time for appropriate analysis. It has been suggested that maternal rather than neonatal urine should be examined, as

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