

# Neonatal abstinence syndrome due to codeine

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## Abstract

**The neonatal abstinence syndrome (NAS) is a potentially life threatening illness associated with significant morbidity especially in the neonatal period. A case of NAS due to codeine prescribed for pain relief during pregnancy is reported.**

**Clinicians should be aware that narcotic derivatives prescribed in late pregnancy can give rise to this type of problem.**

(*Arch Dis Child* 1997;76:F59-F60)

Keywords: codeine; withdrawal; neonatal abstinence syndrome.

The neonatal abstinence syndrome (NAS) is most commonly described in association with narcotic use by pregnant addicts.<sup>1</sup> It is also seen with many other classes of drugs including non-narcotic sedatives, stimulants, antidepressants, anti-epileptics and neuroleptics.<sup>2</sup> More recently, work has focused on symptoms appearing in ventilated neonates after sedation with opiate derivatives.<sup>3</sup> NAS following narcotic use by non-addicted mothers is rare, but there are case reports of symptoms after prescribed oral derivatives during late pregnancy.<sup>2</sup> The association with codeine has been noted in two case reports, the most recent almost 20 years ago.<sup>4,5</sup> We describe a case of NAS that can be clearly ascribed to the regular use of codeine during the last trimester of pregnancy. Moreover, there was no immediate suspicion that the withdrawal symptoms were attributable to codeine, resulting in a delay in diagnosis and treatment.

## Case report

A 25 year old well controlled insulin dependent diabetic was admitted at 34 weeks of gestation after spontaneous rupture of membranes. She had miscarried at 9 weeks and had a healthy girl born at 34 weeks. The present pregnancy had been uneventful before the onset of labour. With good uterine contractions and satisfactory fetal tachygraphic monitoring, labour appeared to be progressing well. However, after 15 hours of labour the cervical os had failed to dilate and with increasing difficulty in controlling maternal blood glucose (hyperglycaemia) the decision was taken to perform a caesarean section.

A boy weighing 2.5 kg (75th centile) was born in good condition with Apgar scores of 9 at 1 minute, 10 at 5 and 10 minutes, and an umbilical cord pH of 7.4. At 2 hours of age he was admitted to the neonatal unit with a blood glucose concentration of 1.2 mmol/l and grunting respirations, and started on a continuous dextrose infusion.

The grunting settled and there were no further low blood glucose recordings in the first 24 hours. Clinical assessment of gestation was consistent with maternal dates. There was no evidence of macrosomia or dysmorphic features. At around 24 hours of age a tremor (jittery) was noticed. As the day progressed the tremor became pronounced. Although alert, the baby was restless and irritable with a strong cry. At 36 hours of age a convulsion was witnessed with movements of the tongue and limbs. Lasting seconds, the convulsion was thought not to warrant anticonvulsant treatment. Other symptoms appearing during this time included intolerance to feeds with large non-bilious gastric aspirates, an occasional apnoea associated with a drop in heart rate and oxygen saturation, intermittent tachypnoea and pyrexia. By 48 hours of age there was widespread hypertonia and loose stools were noted.

The respiratory symptoms settled over the next two days. There were no further convulsions. The baby remained hypertonic, however, with a pronounced tremor and irritability which took over a week to settle. Although loose stools were only recorded on the third day, full nasogastric tube feeds were only possible after five days. Bottle feeding and weight gain were established after a further few weeks before discharge.

Intravenous antibiotics were started at the onset of symptoms and a screen for perinatal infection was subsequently clear. Chest radiography did not show evidence of consolidation or respiratory distress syndrome. Serial head ultrasound scans were unremarkable and electroencephalography (EEG) was not performed. A haematological profile and biochemistry, including serial measurements of plasma calcium and glucose, arterial pH, a urinary metabolic screen, pH, reducing sugars, organic and amino acids were all normal.

With this cluster of symptoms NAS was strongly suspected after 48 hours of observation. The mother's background and pregnancy details were scrutinised. Narcotic analgesia had not been used in labour and there was no evidence to suggest illicit use of drugs. The only medication in pregnancy was an analgesic taken almost constantly during the previous two months for severe headache and lower back pain. The analgesic contained paracetamol and codeine. The estimated dose of codeine was at least 90 mg/day.

## Discussion

The above collection of symptoms and the overall clinical presentation is characteristic of narcotic withdrawal in the newborn.<sup>1-3</sup> The

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Accepted 5 September 1996

absence of some features of NAS can be explained in part by the gestation of the baby, the narcotic involved, and its dosage.<sup>2</sup> The dose of codeine in this case was similar to that reported before.<sup>5</sup> A convulsion early in the illness is unusual in NAS but has been reported with propoxyphene,<sup>6</sup> and the short duration of illness is a feature of NAS with codeine and propoxyphene.<sup>4-6</sup>

Laboratory data helped exclude other possible diagnoses. A low blood glucose recording soon after birth is not unusual in the newborn of a diabetic mother but does not account for the symptoms appearing in this case. Cerebral hypoxic ischaemia is more difficult to rule out. The absence, however, of any perinatal problems, condition at birth, and the timing and nature of the clinical features militates against perinatal hypoxia.

The management of NAS consists of intensive physical support and attention to fluids and nutrition. Drug treatment is helpful for more severe symptoms often based on a scoring system.<sup>1-3</sup> Although chlorpromazine is commonly used, many drugs including narcotic derivatives such as methadone have been useful in the weaning process.<sup>1,2</sup> In the previous cases of codeine withdrawal, codeine itself was effective in reducing symptoms.<sup>4,5</sup> In our case treatment consisted of general supportive measures. Although strongly suspected, a clear diagnosis was not made early enough for drug treatment during the florid part of the illness. Later, the severity of the symptoms appeared not to warrant specific treatment according to a recognised scoring system.<sup>1</sup> It should therefore

be emphasised that urine toxicology should be considered early where NAS is suspected, regardless of whether there is a relevant history.

The consequences of opioid addiction in the mother include premature birth and infants that are small for gestational age. In the newborn period NAS can be a severe illness and later there may be neurodevelopmental delay and behaviour problems.<sup>1,2</sup> Little information exists on the outcome of neonates in this type of case and it cannot be assumed that the course will always be less problematic. Of equal importance is that NAS can occur under conditions that would not normally arouse suspicion before onset of symptoms. With newer over the counter preparations containing larger doses of codeine<sup>7</sup> the above situation may become a more significant problem and needs to be borne in mind by doctors dealing with pregnancy and the newborn.

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*Arch Dis Child Fetal Neonatal Ed* 1997 76: F59-F60

doi: 10.1136/fn.76.1.F59

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