

Two newborns of heroin-addicted mothers suffering neonatal withdrawal syndrome

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SUMMARY: Kale-Çekinmez E, Mutlu B, Yapıcıoğlu H, Özlü F, Asker H, Mert K, Narlı N, Satar M. Two newborns of heroin-addicted mothers suffering neonatal withdrawal syndrome. Turk J Pediatr 2012; 54: 421-424.

Neonatal withdrawal syndrome is characterized by non-specific signs and symptoms that occur in infants following *in-utero* drug exposure. The incidence of neonatal withdrawal syndrome is 16-90% in infants of mothers abusing heroin. Clinical signs of withdrawal syndrome usually occur within the first 48-72 hours after birth. Central nervous system and gastrointestinal system symptoms are the main symptoms.

In this case report, two newborns born to the mothers addicted to heroin who suffered neonatal withdrawal syndrome are presented. They were successfully treated with phenobarbital and morphine infusion.

Key words: newborn, withdrawal syndrome, opioid, heroin.

Neonatal withdrawal syndrome (NWS) is a syndrome of drug withdrawal with non-specific signs and symptoms that occur in infants following *in-utero* drug exposure. Some of the drugs and substances that cause withdrawal syndrome are codeine, heroin, methadone, meperidine, morphine, phenobarbital, alcohol, amphetamines, cocaine, clomipramine, imipramine, diazepam, hydroxyzine, and selective serotonin reuptake inhibitors¹.

Heroin (diacetylmorphine, diamorphine) abuse results in a short-term intense euphoria and later a rapid tolerance, and withdrawal symptoms develop. The incidence of NWS in infants of mothers abusing heroin is 16-90%². Clinical signs of withdrawal syndrome usually occur within the first 48-72 hours after birth. Central nervous system and gastrointestinal system symptoms are the main symptoms. Affected infants commonly have irritability, high-pitched cry, tremors, hypertonicity, vomiting, diarrhea, and feeding difficulties³.

In these case reports, we present two newborns born to mothers addicted to heroin who suffered from NWS and were successfully treated with phenobarbital and morphine.

Case Reports

Case 1

This baby girl was born vaginally as the third child of the family, at the 34th week of gestation due to premature contractions. Apgar scores at the 1st and 5th minutes were 8 and 9, respectively. The mother had used intravenous heroin daily since the fourth month of pregnancy. Hepatitis C virus (HCV) serology of the mother was positive. The other children and members of the family were healthy. Her body weight was 2610 g (10-25 percentile), length was 46 cm (25-50 percentile) and head circumference was 32 cm (75-90 percentile). The system examination was normal. Due to the prolonged rupture of membranes and maternal urinary tract infection, intravenous ampicillin and netilmicin treatments were started. Respiratory distress was not observed. On the second day of life, irritability, high-pitched cry, myoclonic jerks, abdominal distention, and vomiting were observed. The Finnegan neonatal abstinence score was 15, and phenobarbital treatment was started as 20 mg/kg loading and 5 mg/kg/d maintenance dose. The withdrawal score fell to 10 in the follow-up, but the patient had convulsion

on the sixth day. With an additional dose of phenobarbital (10 mg/kg), she experienced no further convulsions and withdrawal scores were less than 7 subsequently.

She was given phototherapy due to hyperbilirubinemia. Complete blood count, routine blood biochemical tests, urine analysis, and thyroid function test results were normal. As the mother was still abusing heroin and HCV serology was positive, the baby was fed with formula. The patient was discharged with phenobarbital treatment on the postnatal 10th day; however, she did not admit to the outpatient clinic.

Case 2

This patient was born vaginally as the second child of the family, at the 37th week of gestation. Apgar scores at the 1st and 5th minutes were 6 and 8, respectively. The mother smoked cigarettes and abused heroin before and during the pregnancy. HCV serology of the mother was positive. The father was also addicted to heroin. Her body weight was 1820 g (<10 percentile), length was 41 cm (<10 percentile), and head circumference was 32 cm (<10 percentile). The patient had abdominal distention and irritability on the second day. On the third day she was tachypneic. Chest radiograph showed mild infiltration, and she was given intravenous ampicillin and netilmicin for pneumonia. On the fourth day, she had abdominal distention, irritability, myoclonic jerks, and tremors. Finnegan neonatal abstinence score was calculated as 9, and phenobarbital treatment was started at a dosage of 20 mg/kg loading and 5 mg/kg/d maintenance. Tachypnea resolved gradually in the follow-up, but abdominal distention, irritability, myoclonic jerks, and tremors did not. Intravenous morphine (0.04 mg/kg/dose as 15-minute infusion, 4-hourly) was added to the treatment. The symptoms resolved quickly with the addition of morphine, but three days later she was intubated because of deep apnea during morphine infusion. We considered this as a side effect of the morphine. We continued the treatment with only phenobarbital. She was extubated quickly, but had convulsions on the same day. We thus re-started the morphine treatment, but extended the infusion period to 1 hour instead of 15 minutes. She again

responded quickly to the morphine treatment. On the sixth day, enteral feeding was restarted and increased gradually. Phototherapy was given due to hyperbilirubinemia. Complete blood count, routine blood biochemistry, urine analysis, and thyroid function test results were normal. In the follow-up, the patient's symptoms disappeared, and abstinence scores regressed below seven. The morphine treatment was discontinued on the 24th day after tapering the doses 10% every two-three days. Thereafter, phenobarbital treatment was also tapered gradually and discontinued uneventfully. The patient was discharged on the postnatal 29th day.

Discussion

Maternal drug abuse has increased over the past decades. It was estimated that 5-10% of deliveries in Britain are to women who have abused drugs excluding alcohol¹. The most commonly used substances in pregnancy are cannabis, opiates and cocaine. Heroin used to be the most common opiate abused in pregnancy, but it is now methadone³. There is no reported study about the incidence of drug abuse during pregnancy in our country. These two newborns represent the only patients treated for heroin abstinence in our institution in a 25-year period.

The diagnosis of prenatal opioid exposure is based upon a positive opioid use of the mother. Laboratory tests are less helpful in the diagnosis. Urine tests can give false-positive or false-negative results. Meconium analysis gives information about the second and third trimester, but implementation of the test is difficult. The baby's or the mother's hair analysis reflects the last trimester but is expensive and can be implemented in only a small number of centers^{4,5}. Finnegan and the modified Finnegan scoring systems are widely used in the diagnosis of neonatal abstinence syndrome and for assessing treatment response^{1-4,6}. The Finnegan scoring system is used especially in opiate withdrawal syndrome, but can be a guideline to withdrawal syndromes due to other drugs. Other tools for assessing neonatal abstinence are also available, but they are used less frequently. In our cases, maternal drug abuse stories were apparent, so the diagnoses were made easily, but we could not confirm

the diagnosis with laboratory studies due to lack of capability in our country.

Opioids (morphine, diamorphine, and methadone) activate opiate receptors in the central nervous system, especially in the locus ceruleus, and cause alpha 2-adrenergic hypersensitivity. Their action decreases the activity of adenylate cyclase, resulting in a reduction in cAMP production⁷. Once the opiates are withdrawn, there is loss of the inhibitory effect, and noradrenaline release increases significantly. This also leads to withdrawal symptoms.

Infants born to mothers who are substance abusers are at risk for preterm birth and intrauterine growth restriction. Although the body weights and the head circumferences are not small for gestational age, they are well below those of their peers. One of our patients was small for gestational age. The other patient was not small for gestational age; however, her weight was in the 10-25th percentile.

A large number of infants who are exposed to opiates antenatally become physically addicted and exhibit withdrawal symptoms after birth. Symptoms may appear in minutes, or in 1-2 weeks, but mostly within 2-3 days. Central nervous system and gastrointestinal system symptoms are the leading symptoms respectively⁸. Convulsions, tremor, and hyperirritability are the most frequent findings. The infants are hyperexcitable, cannot sleep for a long time, and have a high-pitched cry. They have excessive sucking^{9,10}. Central nervous system symptoms are followed by gastrointestinal symptoms. Feeding problems like abdominal distention and vomiting are common¹¹. Tachypnea and retractions, fever, frequent yawning, sneezing, nasal stuffiness, sweating, peeling of the skin, increased Moro reflex, and increased muscle tone are some of the other symptoms. Gastrointestinal and central nervous system symptoms were also the leading symptoms in our patients.

About 30-80% of infants exposed to opiates *in utero* require treatment for NWS^{12,13}. The goal of treatment is to provide a normal or near-normal sleep and nutrition. Supportive care like minimal stimulation, swaddling and positioning, and preventing excessive cry with

a pacifier are sufficient in many infants, but if not sufficient or if symptoms are severe, drug therapy should be considered. Increase in irritability, ongoing feeding difficulties and significant weight loss are all indications for drug treatment. A Finnegan score >7 for three consecutive scorings done every 2-4 hours during the first two days may also be regarded as an indication for treatment. However, the Finnegan score should not be followed slavishly and treated as a definitive laboratory value.

The current information suggests that opioids are the most effective treatment in controlling acute problems related to NWS from *in-utero* opioid exposure¹⁴. Methadone and morphine have similar effects at the receptor level, but methadone is more advantageous than morphine. Oral bioavailability of methadone is better and has a longer duration of action. On the other hand, the first-pass metabolism of morphine is more than of others. Methadone might be the treatment of choice, but as we could not provide it in our country we used morphine. The dosage of morphine used in withdrawal syndrome is 0.03 to 0.1 mg/kg, orally, every 3-4 hours. The oral dose is 3-5 five times the intravenous dose. Once the symptoms disappear, the dose is tapered 10-20% every 2-3 days^{3,15}. We closely experienced that morphine was rapidly effective in controlling symptoms in the second patient, in whom we initially tried phenobarbital, but later needed intravenous morphine as the second drug.

Sedative agents such as chloral hydrate, chlorpromazine, diazepam, and phenobarbitone can also be used in the treatment of withdrawal syndrome. Their effects are non-specific. Clonidine is another treatment of choice, and it has an inhibitory effect on the release of noradrenaline³. Side effects of opioid therapy are respiratory depression, nausea and vomiting. The second patient, who had been treated with phenobarbital and morphine, had respiratory depression during morphine infusion, but vomiting and nausea were not observed.

In conclusion, NWS is rare in Turkey; however, in the presence of central nervous system and gastrointestinal system symptoms of unknown origin, NWS should be kept in mind. Phenobarbital and morphine are useful in the management of NWS.

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