



The Treatment of Neonatal Abstinence Syndrome with Fentanyl in a Premature Infant

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Abstract

Neonatal abstinence syndrome (NAS) is a clinical condition in which infants born to mothers with substance addictions (heroin, cannabis, opiates, etc.) exhibit withdrawal symptoms and physical addiction as they have been exposed to the substances prenatally and are lacking the substance postnatally. Most often emerges with the central nervous system and autonomous nervous system findings in NAS. Seizures have been reported rarely and require emergency treatment. We report the patient who born to a mother addicted to heroin who suffered NAS and was successfully treated with fentanyl infusion as far as we know, is the first in the literature.

Keywords: Addiction; fentanyl; neonatal abstinence syndrome.

Neonatal abstinence syndrome (NAS) is a condition of drug (codeine, heroin, etc.) abstinence that emerges with non-specific signs and symptoms in infants that have been exposed to drugs in-utero.^[1] Heroin abuse causes short-term intense euphoria, then tolerance and withdrawal symptoms develop rapidly, which has been reported in infants 16–90%. The clinical signs of withdrawal symptoms generally emerge within 48–72 h after birth.^[1,2]

Central nervous system (CNS) and autonomous nervous system dysfunctions together with gastrointestinal system dysfunction symptoms are the primary findings. Affected infants usually present with jitteriness, lethargy, loud crying, tremor, increased muscle tonus, vomiting, diarrhea,

and feeding difficulties. Sometimes, infants suffering from NAS present with seizures (2–11%) because of sodium channel upregulation which decreases the seizure threshold.^[3,4]

The case is here presented of a newborn infant who developed NAS secondary to maternal heroin use and was successfully treated with fentanyl.

Case Report

Infant girl was delivered by cesarean section at 30 weeks as the first pregnancy of a 26-year-old mother. Immediately the infant was delivered, 2 min of resuscitation were applied as she was not crying, there was cyanosis, bradycardia, and respiratory problems. The APGAR score was 6 at

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1 min and 7 at 5 min. In the physical examination applied at 72 h postnatally, loud shrill crying, unstimulated tremor, tachypnea, retractions, yawning, reduced desire to suckle, a short sleeping duration after breastfeeding, hypertonicity, and myoclonic spasms were determined.

From the anamnesis, it was learned that the mother had a drug addiction, smoking and had not been followed up regularly during pregnancy. Complete blood count, C-reactive protein, transcranial ultrasound, glucose, calcium, and other electrolyte levels were normal. The infant had a modified Finnegan score of 14 and together with the clinical and laboratory findings, NAS was considered. For follow-up and treatment planning, the modified Finnegan score was evaluated again at 3–4 h. For the finding of NAS, such as tremor, increased muscle tonus, and high-pitched crying was observed, so morphine treatment was started at 0.025 mg/kg at 4-h intervals.

After 8 h of follow-up, convulsion appeared, phenobarbital treatment (20 mg/kg loading dose and 5 mg/kg/day routine dose) was administered. On the amplitude examined on EEG, epileptiform discharges occurred. As the patient continued to have focal seizures in the right-side upper and lower extremities and myoclonic convulsions, a single dose of midazolam 0.1 mg/kg were administered intravenously. The seizures continued and at 12 h the Finnegan score was 13, so fentanyl was administered as an intravenous infusion at the dose of 1.5 mcg/kg/hr. At 2 h after the fentanyl administration, the seizures did not recur. With the decrease in Finnegan scores to 10 after 2 h and to 0 after a further 12 h, the morphine dose was reduced. After 48 h, the fentanyl infusion was terminated and with no recurrence of the complaints, the patient was discharged on postnatal day 15.

Discussion

NAS is a significant healthcare problem with increasing frequency and importance with greater levels of awareness in recent years. It is differentiated from other neonatal problems with different findings and treatment options. In the UK, it is estimated that 5–10% of births are to mothers with narcotic abuse, not including alcohol. NAS prevalence showed an increase from 7/1000 in 2004 to 27/1000 in 2013.^[1,5]

In the diagnosis of NAS, the most important step is the maternal history of drug use. The modified Finnegan scoring system is the most widely used measurement for the evaluation of NAS and of treatment follow-up. The Finnegan scoring method for assessment of acute opioid withdrawal in newborn infants is based on nursing observations, with

each sign and symptom assigned a numerical scale (scores: 0–7 mild, 8–11 abstinence, 12–15 severe abstinence syndrome). Drug treatment is usually given for Finnegan abstinence scores, which made at intervals of 3–4 h of ≥ 8 (for an average of three scores) or for two scores > 12 .^[2,6,7] In our case, the mother had an evident history of drug addiction and the Finnegan score was extremely high.

Premature infants with NAS, the risk of opioid withdrawal symptoms is lower than in full-term infants. Possible reasons for this have been shown to be the immature development of the CNS in premature infants, a shorter period of intrauterine exposure to the substance, a small amount of fat tissue for storage of the substance, and the difficulty of evaluating withdrawal symptoms in premature infants compared to full-term infants.^[8,9] In this respect, it is significant that our case was premature.

Unlike other seizures in newborns, in the convulsions seen in NAS, involuntary eye movements and arm-leg tremors are rare. In general, more exaggerated movements and myoclonic spasms are noticeable in the arms and legs. In addition, abnormal EEG findings are seen in 30% of infants diagnosed with NAS.^[1,3] In our case, focal seizures and myoclonic spasms were observed in the right upper and lower extremities in addition to EEG abnormalities.

The existing information indicates the most effective treatment to control the acute problems related to NAS from in-utero exposure to opioids. The potency of fentanyl is much stronger than morphine and because of this property was selected for the current case as symptoms were severe and no response was obtained to morphine. The morphine dose used in withdrawal syndrome is 0.03–0.1 mg/kg orally every 3–4 h.^[1,9,10] As the Finnegan score was high in our case, treatment was started with morphine and because of convulsions in the follow-up, phenobarbital and midazolam treatment was then started. As the convulsions continued despite this treatment, fentanyl was administered as an intravenous infusion. The symptoms recovered. The Finnegan score decreased to 10 after 2 h and to 0 after 12 h so the morphine and phenobarbital doses were reduced respectively. After 48 h the fentanyl infusion was terminated. Treatment of neonatal withdrawal syndrome the first approach is to reduce environmental stimuli as much as possible. However, despite all the pharmacological first choice of treatment is opioid derivatives (morphine if necessary and methadone).^[11] Fentanyl is an opiate such as morphine. However, due to the difficulty in providing oral morphine in Turkey and the stronger effect of fentanyl; fentanyl infusion may be used in the presence of severe withdrawal

symptoms resistant to oral morphine and phenobarbital at the highest appropriate dose range.

Conclusion

This case report presents for the 1st time in literature that fentanyl can be successfully used to treat a premature infant with NAS when symptoms did not recover with morphine and phenobarbital.

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References

- Raffaelli G, Cavallaro G, Allegaert K, Wildschut ED, Fumagalli M, Agosti M, et al. Neonatal abstinence syndrome: Update on diagnostic and therapeutic strategies. *Pharmacotherapy* 2017;37:814–23. [\[CrossRef\]](#)
- Regan J, Chambers F, Gorman W, MacSullivan R. Neonatal abstinence syndrome due to prolonged administration of fentanyl in pregnancy. *BJOG*. 2000;107:570–2. [\[CrossRef\]](#)
- Kennare R, Heard A, Chan A. Substance use during pregnancy: Risk factors and obstetric and perinatal outcomes in South Australia. *Aust N Z J Obstet Gynaecol* 2005;45:220–5. [\[CrossRef\]](#)
- Stover MW, Davis JM. Opioids in pregnancy and neonatal abstinence syndrome. *Semin Perinatol* 2015;39:561–5. [\[CrossRef\]](#)
- Hudak ML, Tan RC. Neonatal drug withdrawal. *Pediatrics* 2012;129:540–60. [\[CrossRef\]](#)
- Behnke M, Smith VC. Prenatal Substance Abuse: Short- and long-term effects on the exposed fetus. *Pediatrics* 2013;131:1009–24. [\[CrossRef\]](#)
- Abdel-Latif ME, Pinner J, Clews S, Cooke F, Lui K, Oei J. Effects of breast milk on the severity and outcome of neonatal abstinence syndrome among infants of drug-dependent mothers. *Pediatrics* 2006;117:1163–9. [\[CrossRef\]](#)
- Lozano J, García-Algar O, Vall O, de la Torre R, Scaravelli G, Pichini S. Biological matrices for the evaluation of in utero exposure to drugs of abuse. *Ther Drug Monit* 2007;29:711–34. [\[CrossRef\]](#)
- Jansson LM, Velez M. Neonatal abstinence syndrome. *Curr Opin Pediatr* 2012;24:252–8. [\[CrossRef\]](#)
- Bio LL, Siu A, Poon CY. Update on the pharmacologic management of neonatal abstinence syndrome. *J Perinatol* 2011;31:692–701. [\[CrossRef\]](#)
- Bozkaya D, Öktem A, Yurdakök M. Eroin kullanan anne ve neonatal yoksunluk sendromu. *Çocuk Sağlığı Hastalık Derg* 2016;59:72–5.