

Neonatal abstinence syndrome in babies of opioid-addicted mothers and follow-up in the neonatal intensive care unit: A single center experience

 Beyza Ozcan

Department of Neonatology, Konya Training and Research Hospital, Konya, Turkey

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Abstract

Aim: Neonatal abstinence syndrome (NAS) is a clinical condition characterized by findings that develop after intrauterine exposure to addictive substances, especially opioids, and is characterized by signs related to the absence of the addictive substance in the postpartum period. Typically, NAS manifests in the first few days of life in the form of hypertonia, autonomic instability, irritability, poor absorption reflex, weight loss and, rarely, seizures. The present study was performed the clinical features of mothers who used addictive substances during pregnancy.

Materials and Methods: Neonates born between September 2016 and December 2019 to opioid-addicted mothers and admitted to the neonatal intensive care unit (NICU) after birth for findings consistent with NAS were included in this study. The patients' files were analyzed retrospectively. Maternal age, drug used/duration of use, smoking/alcohol use, the last time the substance was taken, gestational week of neonates, mode of delivery, birth weight, onset of NAS symptoms, highest Finnegan score, nutritional status, length of hospitalization, treatment duration and NICU follow-up data were recorded.

Results: Nine babies were admitted to the NICU of follow-up for NAS symptoms. All mothers had heroin addiction. The median gestational week of the neonates was 37 (31-40) weeks and median birth weight was 2740(1530-3860) g. Median onset of symptoms was 2(1-4) days and the median Finnegan score of the patients was 10(3-17). Six (66.7%) neonates who did not recover with nonpharmacological treatment received phenobarbital therapy.

Conclusions: For patients with NAS, phenobarbital therapy can be used as the first option when symptoms cannot be controlled by nonpharmacological methods in settings such as Turkey where oral morphine solution is not available. In our study, the symptoms were successfully controlled by phenobarbital therapy. However, more comprehensive studies are needed as there are insufficient data on long-term results.

Keywords: Neonatal abstinence syndrome; opioid addiction during pregnancy; finnegan score system

INTRODUCTION

Illegal drug use during pregnancy is increasing all over the world(1). In our country, where adolescent pregnancies are common, neonatal abstinence syndrome (NAS) and complications related to substance use during breastfeeding are becoming more common with increasing rates of substance addiction in adolescents (2). However, there have been no studies regarding the rate of substance use in pregnant women in our country (2). Opioid use during pregnancy has been shown to be associated with unexplained fetal death, placental insufficiency, intrauterine growth retardation, preeclampsia, premature membrane rupture, premature birth, postpartum hemorrhage, and neonatal morbidity (2,3).

Neonatal abstinence syndrome is a clinical condition that develops after intrauterine exposure to addictive substances, especially opioids, and is characterized by symptoms associated with the absence of the addictive substance in the postpartum period (4,5). It has been reported that system dysfunctions related to withdrawal are seen most frequently in the central nervous system, gastrointestinal system and respiratory system in neonates of mothers with opioid dependence (6). NAS is seen in 55%-94% of neonates exposed to opioids during pregnancy. Withdrawal symptoms occurring in newborns require treatment 30%-80% of cases, and treatment is continued until the withdrawal symptoms disappear completely (7).

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Corresponding Author: Beyza Ozcan, Department of Neonatology, Konya Training and Research Hospital, Konya, Turkey

E-mail: drbeyzaozcan@gmail.com

This study was performed to evaluate the clinical characteristics of neonates exposed to addictive substances during pregnancy.

MATERIALS and METHODS

A retrospective study was conducted in the tertiary NICU of Konya Teaching and Research Hospital, Konya, Turkey, between September 2016 and December 2019. Neonates who were born to opioid-addicted mothers and who were hospitalized for follow-up in the NICU for delivery due to NAS findings were included in the study. This study was approved by the local Ethics Committee. Written informed consent was obtained from the parents before enrollment into the study.

Maternal age, drug used/duration of use, smoking/alcohol use, the last time the substance was taken; gestational week of neonates, mode of delivery, birth weight, onset of NAS symptoms, highest Finnegan score, nutritional status, length of hospitalization, treatment duration and NICU follow-up data were recorded.

According to the opioid-dependent mother-baby follow-up and treatment protocol of our unit, the cases were followed up in an incubator in a calm, quiet, dark room in the NICU and evaluated for NAS symptoms using Finnegan's correlation system (Table 1) at intervals of 4-6 hours. Neurological excitability, gastrointestinal dysfunction, autonomic and respiratory dysregulation levels were evaluated using this scoring system.

Table 1. Modified Finnegan score system	
Symptoms	Score
Central Nervous Symptoms	
High-pitched cry	2
High pitched cry > 2 hours	3
Sleeps less than 1 h after feeding	3
Sleeps less than 2 h after feeding	2
Sleeps less than 3 h after feeding	1
Mild tremors when disturbed	1
Marked tremors when disturbed	2
Increased muscle tone	2
Excoriation of skin	1
Myoclonic jerking in sleep	3
Generalized convulsion	5
Vegetative Symptoms	
Sweating	1
Temperature 37.5 – 38.3 °C	1
Temperature ≥38.4 °C	2
Frequent yawning >3 – 4	1
Mottling	1
Nasal stuffiness	2
Sneezing	1
Respiratory Symptoms	
Tachypnea >60/min	1
Tachypnea >60/min with retraction	2

Gastrointestinal Symptoms	
Francting sucking	1
Poor feeding	2
Regurgitation	2
Projectile vomiting	3
Loose stools	2
Walery stools	3

Oral phenobarbital treatment was initiated in patients with two consecutive scores ≥ 12 or three consecutive scores > 8 . Scoring continued every 3-4 hours after commencement of treatment. In cases in which the score continued as ≥ 12 , the drug dose was increased, and if the score was between 9 and 11, the same dose was continued. In case with the score < 8 we began to reduce the dose and the drug was stopped within about 2 days. Patients who did not show symptoms within 2 days after drug discontinuation were discharged. The babies of mothers who continued to use opioids during pregnancy and refused treatment for addiction were given baby formula.

Descriptive statistical analyses were performed using SPSS V17.0- for Windows (SPSS, Chicago, IL, USA). Categorical data are presented as n (%) and numerical data are presented as median (min-max).

RESULTS

During the study period, a total of nine babies were hospitalized in the NICU for follow-up of NAS symptoms. The median age of the mothers was 23(22-25) years. All mothers had heroin addiction, and 90.9% (8) of the mothers smoke during their pregnancy. Opioid use was delayed to the third month of pregnancy in one (11.1%) mother, until the fourth month of pregnancy in one (11.1%) mother, until the seventh month of pregnancy in one (11.1%) mother and until birth six (66.7%) mothers (Table 2). The characteristics of the cases hospitalized with a diagnosis of NAS are summarized in Table 3.

Table 2. Demographic Features of Mothers	
Maternal age (years)*	23(22-25)
Substance used	Heroin
Smoking (%) (n)	
User	90.9 (8)
Nonuser	9.1 (1)
Alcohol (%) (n)	
User	44.4 (4)
Nonuser	55.6 (5)
Duration of use (%) (n)	
Until birth	66.7 (6)
Until the 3 rd Month of Pregnancy	11.1 (1)
Until the 4 th month of pregnancy	11.1 (1)
Until the 7 th month of pregnancy	11.1 (1)
*Median (minimum–maximum)	

Table 3. Demographic Features of the Patients

Birth weight (g)*	2740 (1530-3860)
Gestational age(week)*	37(31-40)
Fetal Growth restriction (%) (n)**	
SGA	22.2% (2)
AGA	77.3% (7)
Mode of Delivery (%) (n)	
VD	66.6(6)
C/S	33.4 (3)
Gender (%) (n)	
Female	55.5 (5)
Male	44.4 (4)
Onset of NAS symptoms (days)*	2 (1-4)
Highest Finnegan score*	10 (3-17)
Treatment (%) (n)	
pharmacological	66.7% (6)
nonpharmacological	33.3% (3)
Nutrition status(%) (n)	
Breastfeeding	22.2% (2)
Formula	77.8% (7)
Duration of hospital stay (days)	12 (6-44)
*Median (minimum–maximum), VD: Vaginal delivery, C/S: Cesarean delivery, ** SGA: Small for gestational age, AGA: Appropriate for gestational age	

The median gestational week of the cases was 37.0 (31-40) weeks. Two patients were born at <34 gestational weeks. The median birth weight was 2740 g (1530- 3860g), and two (22.2%) neonates had low birth weight for gestational age. None of the nine cases included in the study required resuscitation. The median onset of NAS symptoms was 2(1-4) days, and the highest median Finnegan score was 10(3-17). Phenobarbital treatment was started in six (66.7%) cases. The drug dose was increased in one of the six cases who received treatment. Of the total cases 77.8% were fed with formula and 22.2% were fed with breast milk. The median duration of hospitalization was 12(6-44) days. Two cases with sepsis and premature diagnoses were followed up in the NICU for more than 1 month.

DISCUSSION

The rate of opioid use in pregnancy has been reported to be approximately 5.9%- 55.4% worldwide (8-10). In our country, where adolescent pregnancies are common, NAS has become an important clinical condition with the increasing rates of substance addiction among adolescents. However, there have been no studies of the frequency of substance use in pregnant women in our country (11). Although the use of multiple drugs is not common, accompanied smoking or alcohol use is common (12). In present study, all mothers had heroin addiction and most were also smokers.

Opioid exposure during pregnancy is associated with unexplained intrauterine growth retardation, fetal death and neonatal morbidity, including placental insufficiency, and premature rupture of membranes (2,3). Among these complications, only one of our patients had intrauterine growth retardation. In addition, only two patients were born before 34 gestational weeks. The possibility of developing NAS was found to be lower in preterm babies, with an immature central nervous system and shortened exposure time due to the short gestational period compared to term babies. In addition, diagnosis is difficult in premature babies due to the difficulty in recognizing clinical symptoms (7). Recognition of NAS symptoms in preterm babies included in the study allowing the provision of appropriate treatment were attributed to good maternal history and communication with the obstetrics team.

Neonatal abstinence syndrome occurs in 21%-94% of neonates exposed to intrauterine opioids(13). It has been reported that the onset time of the findings changes according to the dose of the substance used, half-life, permeability of the placenta, exposure time during pregnancy and the time between birth and the last dose (13). When substance use is discontinued in early pregnancy, the likelihood of the emergence of NAS symptoms is negligible. The probability of NAS is low if more than one week has passed between birth and the last use of the substance (14). In present study, in accordance with the literature, severe NAS symptoms developed in babies of mothers who continued to use opioids until delivery, while no findings were observed in patients whose exposure was discontinued in the early period of pregnancy. In fact, among the patients included in our study, NAS symptoms were not observed in patients whose mothers stopped substance use in the third, fourth and seventh months of pregnancy. Findings of opioid use occur between the first 24 hours and 5 days after birth. Therefore, babies of mothers with a history of substance addiction should be followed up in the NICU for at least 5 days for signs of NAS (14).

The treatment decision is made according to various scoring systems, primarily the modified Finnegan scoring system (15). The first treatment option in NAS is non-pharmacological treatment. Patients should be followed-up in a quiet and dimly light environment and Finnegan scoring should be performed every 3-4 hours. When the Finnegan score is > 8 (twice consecutively) or ≥12, pharmacological treatment should be started (14). Studies have shown that 50%-80% of patients diagnosed with NAS require pharmacological treatment (13). The duration of hospital stay for patients given pharmacological treatment was approximately 23 days (13). In our study, the need for treatment and duration of hospital stay were similar to those reported in the literature.

In the American Academy of Pediatrics and Cochrane analyses, the first-line pharmacological treatment in newborn neonates exposed to opioids was oral morphine solution, methadone or buprenorphine. Phenobarbital,

clonidine, and chlorpromazine are used in second-line treatment for babies who do not respond to first-line drugs (16-17). It has been reported that phenobarbital treatment is not suitable for use alone, and its use is more appropriate in combination with oral morphine solution (17). However Nayeri et al. (18), compared morphine sulfate and phenobarbital treatment, and found no difference in terms of treatment duration, hospital stay or additional treatment requirement. Ozdemiroglu et al. presented a preterm case followed-up with phenobarbital treatment (19). Phenobarbital treatment was given to the patients because suitable doses of oral morphine solution and methadone for the neonates are not available in our country. The symptoms of the treated neonates were controlled successfully. With the changes in NAS management over the past 10 years, there is increasing emphasis on non-pharmacological treatment (20). However, there is a need for well-designed prospective studies of the effectiveness of non-pharmacological treatments in cases of NAS.

Neonates are exposed to opioids, albeit at low levels, because they pass into the milk from the mother through systemic circulation and are taken orally by the baby and digested in the intestine (11). The decision to feed neonates with breast milk depends on the mother's discontinuation of substance use in the early period of pregnancy, treatment for addiction, and the presence or absence of medical contraindications for breastfeeding (11). Similarly, in our study, neonates of mothers who did not have a history of opioid use during the last 3 months of their pregnancy were fed by their mothers. Recent studies have shown that optimal breastfeeding after birth is acceptable to increase the effectiveness of non-pharmacological treatment and thus the need for pharmacological treatment is reduced (21). Favara et al. reported that breastfeeding by mothers who received medical treatment decreased the symptoms of NAS (22). We fed neonates whose mothers had received treatment for their addiction with their mother's milk and there were no symptoms of NAS.

CONCLUSION

For patients who develop NAS, phenobarbital can be used as the first choice of treatment when oral morphine solution is not available, as in Turkey, and when the symptoms cannot be controlled by non-pharmacological methods. However, insufficient data are available regarding the long-term results, further comprehensive studies are needed. It is very important to identify, treat and follow up pregnant women who use drugs, and inform these women and their partners about pregnancy and health problems. Therefore, drug-addicted pregnant women and neonates should be followed up with a multidisciplinary approach by a psychiatrist, public health specialist and neonatologist or pediatrician, as well as the obstetrician.

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