

A Four Year Survey of Neonatal Narcotic Withdrawal: Evaluation and Treatment

Matityahu Lifshitz MD¹, Vladimir Gavrilov MD¹, Aharon Galil MD² and Daniella Landau MD³

¹Toxicology Unit, ²Zusman Child Developmental Center, and ³Department of Neonatology, Soroka University Medical Center and Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer Sheva, Israel

Key words: neonate, narcotic, withdrawal syndrome, addiction

Abstract

Background: Narcotic abuse has steadily become more prevalent in Israel and may result in an increasing number of children exposed prenatally to narcotics, with a consequent increase in the number of infants born with neonatal abstinence syndrome.

Objective: To report our experience with infants born to narcotic-addicted women between the years 1995 and 1998 at the Soroka University Medical Center.

Methods: The medical records of 24 newborns and their drug-addicted mothers admitted to our Medical Center for parturition were analyzed retrospectively. A diagnosis of NAS was established on the basis of the clinical presentation and anamnesis. The Finnegan Neonatal Abstinence Scoring System was used to assess drug withdrawal. Urine toxicological analysis for narcotics was done only for the year 1998.

Results: Of the 24 newborn infants exposed prenatally to narcotics 23 (96%) developed NAS, and 78% (18 of the 23) had a Finnegan score of 8 or more. These 18 infants were treated pharmacologically (tincture of opium and/or phenobarbital) until the score was reduced to less than 8, after which they received supportive treatment. In one child who became lethargic after the first dose of tincture of opium, the medication was stopped and supportive treatment alone was given. Four of the five neonates with scores of 7 and less were given supportive treatment. One of five infants who had a low Finnegan score at birth nevertheless received pharmacological therapy to prevent further deterioration of his physical state since he was born with severe dyspnea. Ten of the 24 children (42%) were followed for lengths of time ranging from 6 to 22 months after discharge, all of whom showed normal development.

Conclusions: About three-quarters of newborns exhibiting withdrawal syndrome required pharmacological therapy. Previous information on maternal drug abuse is a crucial criterion for early detection and treatment.

IMAJ 2001;3:17-20

It is well recognized that children exposed prenatally to narcotics may become passively addicted and can consequently develop neonatal abstinence syndrome. Various studies have reported that neonatal withdrawal syndrome occurs in 42 to 94% of infants born to drug-addicted mothers [1–3] and that the rate of neonatal morbidity and mortality has increased [4–5]. Since narcotic abuse in Israel is steadily increasing [6–8], it is predicted that this will result in a greater number of NAS victims. This study presents data on the evaluation, treatment and post-discharge follow-up of infants born to narcotic-addicted women between the years 1995 and 1998 at the Soroka University Medical Center.

Material and Methods

The medical records of 24 newborns and their drug-addicted mothers admitted for parturition were analyzed retrospectively. The case histories of the mothers were obtained from social workers and ambulatory clinical departments, or were already available from previous admissions.

Neonates were assessed for drug withdrawal by the Finnegan Neonatal Abstinence Scoring System [9] every 3 hours, starting immediately after birth until the disappearance of the symptoms. The Finnegan scoring system assesses the severity of withdrawal and serves as a guide to therapy. It assigns a specific numeric score of 1 to 5 for 20 symptoms known to occur in intrauterine drug-addicted neonates, the maximum score being 40. The least significant symptoms such as yawning get 1 point, whereas seizures get 5 points. The scoring system assumes that the greater the number of symptoms and the greater their severity, the higher the risks of morbidity and mortality.

In 1998, in addition to drug withdrawal assessment, eight newborns were subjected to urine toxicological analysis for opiates, methadone, cocaine, cannabinoids and benzodiazepines using the homogenous enzyme immunoassay method (DRI, Sunnyvale, CA, USA). Prior to 1998, equipment for this test had not been available in our hospital. At follow-up examinations, child development was assessed according to the Gesell developmental and neurological examination [10].

Results

Twenty-two female drug abusers were admitted to the delivery room between 1995 and 1998. Two women delivered twice

NAS = neonatal abstinence syndrome

during this period. The ages of the mothers ranged from 22 to 45 (mean \pm SD 30.5 \pm 5.6 years). Eighteen pregnancies ended in partus spontaneous, 4 women were subjected to cesarean section for maternal reasons, and 2 delivered by vacuum extraction. The addictive drugs included heroin, cocaine, cannabinoids, methadone and benzodiazepines. Twelve women were addicted to two or three drugs. Since there was no previous information available on drug abuse for two women, their addiction to narcotics was estimated clinically on the basis of narcotic abstinence syndrome that developed in the delivery room. Nine mothers had been receiving methadone treatment during their pregnancy.

Of the eight infants born in 1998 who were subjected to urine toxicological analysis, opiates were detected in four, methadone in one, and both opiates and methadone in three infants. Of the 24 births 18 were born at term (gestational age 37–40 weeks) and 6 were born prematurely between 29 and 33 weeks. Birth weight ranged from 1,450 to 4,130 g (mean \pm SD 2,559 \pm 598 g). Five-minute Apgar score for 23 of the newborns was 9 or 10, and 3 for the infant delivered by cesarean section. All except one neonate developed NAS. Twenty-one neonates exhibited withdrawal syndrome on the first day of life, 1 on the second and another on the third. Variety, expression and duration of NAS symptoms differed from one child to another. The most commonly occurring symptoms are presented in Table 1. In some of the neonates withdrawal syndrome attained its greatest significance at 1 or even 3–4 weeks after birth despite pharmacological therapy. The duration of withdrawal symptoms, day of highest expression, and maximal Finnegan scoring are presented in Table 2.

Of the 23 neonates with NAS who had a Finnegan score of 8 or higher, 18 (78%) were treated pharmacologically (tincture of opium and/or phenobarbital) until the score was reduced to less than 8. They were then maintained on supportive therapy. One infant who became lethargic received only a single dose of tincture of opium and he was then given supportive treatment only. Another infant (born to a mother addicted to benzodiazepines), despite a Finnegan score at birth of only 5, was placed on pharmacological therapy (phenobarbital) to prevent further deterioration of his physical state since he had severe dyspnea at birth. Four of the five neonates with a maximal score of 7 or less

received only supportive treatment, which included holding, swaddling, minimal stimulation, demand feeding using a hypercaloric formula (24 cal/oz), intravenous fluids, and replacement electrolytes when required.

For 8 of the 17 neonates receiving pharmacological treatment, tincture of opium proved ineffective and therefore phenobarbital was added. Pharmacological treatment of most of the neonates [11] was begun from the second day of life; 3 were placed on drugs on the first day of life, 3 on the third day of life and 1 on the seventh day of life. A single seizure occurred in 2 of the 23 neonates, which was stopped by the addition of phenobarbital to tincture of opium; this compound also decreased the severity of other withdrawal signs. Thereafter only phenobarbital was administered. The dosage of tincture of opium and phenobarbital depended on withdrawal presentation and weight. The initial dose of diluted (0.4 mg/ml) tincture of opium was 0.3 mg/kg/day administered in 6 doses. According to the severity of the score, the dose was increased by 0.15 mg/kg/day. The maximal dose (0.8 mg/kg/day) was achieved when the Finnegan score was over 17. Once withdrawal signs had been controlled for 3 days, the dose was tapered gradually (10–20% each day) and stopped when dosage constituted 0.2 mg/kg/day. Treatment by phenobarbital was initiated with a loading dose of 20 mg/kg. Maintenance dose was 3.5–5.0 mg/kg/day administered in two doses. Blood levels of phenobarbital were 15–40 ng/ml.

Table 2. Duration of NAS, day of its highest expression and maximal scoring

Case	Duration of NAS (days)	Day of highest expression	Maximal scoring (Finnegan scoring system)
1	1	1	3
2	28	7	15
3	16	3	14
4	20	9	10
5	9	4	6
6	10	2	8
7	41	5	15
8	8	7	5
9	45	20	3
10	43	11	13
11	43	4	16
12	35	2	15
13	41	3	15
14	28	1	15
15	5	3	6
16	38	26	11
17	47	6	13
18	No signs of NAS		
19	13	3	10
20	34	2	11
21	14	1	18
22	49	12	13
23	34	4	13
24	12	5	10

Table 1. The most common symptoms of neonate withdrawal syndrome*

Symptom	No. of neonates
Excessive high pitched cry	18
Sleeps <1, 2, 3 hours after feeding	22
Hyperactive Moro reflex	16
Mild and moderate to severe tremors	22
Increased muscle tone	17
Sweating	14
Sneezing	12
Respiratory rate >60 per min	15
Excessive sucking	16

* Symptoms are derived from the Finnegan scoring system [9].

The average weekly weight gain (\pm SD) of all 24 infants was 113.7 ± 115.2 g (range 210–242 g). Mean hospitalization (\pm SD) was 32.5 ± 16.5 days (range 5–61 days). Eighteen of the 24 infants (75%) were discharged home to their mothers and 6 (25%) were placed in foster homes. All the infants were referred for developmental follow-up at the Zusman Child Development Center but only 10 (42%) were brought to the appointment. Three children were examined at 6 months of age, 4 at age 12 months, and 3 at 22 months. At the time of examination they all showed normal development.

Discussion

During the past decades there has been an escalating rate of drug abuse in Israel [6–8]. As a response, the Israeli government in 1988 established the National Anti-Drug Authority. This organization coordinates all the drug treatment services in Israel and either directly or indirectly supports most of the country's treatment programs [11]. These services are in many ways similar to those in the United States [12]. Fighting maternal narcotic abuse is a crucial part of these efforts.

Intrauterine exposure to narcotics may result in neonatal intoxication or withdrawal. The onset of narcotic withdrawal syndrome in newborns is usually observed within 24–48 hours after birth [13,14], but can be delayed when the fetus is exposed to barbiturates [15,16] or long-acting benzodiazepines [17]. Neonatal abstinence syndrome is characterized by tremor, irritability, hypertonicity, high pitched cry, vomiting and diarrhea, respiratory distress, sneezing, diaphoresis and fever, poor sucking and on rare occasions convulsions [18,19]. Several scoring systems for evaluating the signs and symptoms of narcotic withdrawal have been proposed, the most well recognized being those by Lipsitz [20], Ostrea [21] and Finnegan et al. [9]. Finnegan's scoring system is the most detailed, with a greater emphasis on symptoms likely to be correlated with morbidity and mortality. Therefore, it has proven the most successful for quantifying the severity of drug withdrawal and for guiding pharmacological therapy. According to Finnegan's criteria, neonates with an abstinence score of 8 or more should receive pharmacotherapy, whereas those with scores of less than 8 should be given supportive therapy only.

Our results showed that 23 of the 24 infants (96%) suffering from intrauterine exposure to drugs developed NAS. The rate of NAS (96%) in our study is higher than in analogous studies (42–94%) [1–3]. It is possible that this high rate is due to the fact that the infants were selected on the basis of previous data on maternal drug abuse. Obviously, all the women in our sample were heavily addicted to drugs and therefore their children were at very high risk to develop NAS. Perhaps, during the study period, other women whose history of drug abuse was unknown delivered babies who were not affected or that withdrawal syndrome had been very mild. A lack of such information could explain our high rate of NAS and should be taken into account when interpreting our results.

Pharmacological treatment was given to 78% of the neonates with NAS (18 of 23), whereas 22% (5/23) were given supportive therapy only. Many drugs, including paregoric, tincture of opium, morphine, methadone, diazepam, phenobarbital and clonidine, have been used to treat neonatal drug withdrawal [22]. If pharmacological management is chosen, a drug from the same class as that causing withdrawal is preferable [22]. The most popular drugs are paregoric and phenobarbital [23]. It is well established that infants treated with paregoric for narcotic withdrawal signs have a more physiological sucking pattern, higher nutrient consumption, higher percentage of sucking time, greater sucking pressure exerted at nursing, and more weight gain than infants treated with phenobarbital [24]. It has also been noted that paregoric is more effective than diazepam for prevention of seizures [25]. Furthermore, Finnegan and Ehrlich [26] reported that paregoric is more effective than phenobarbital or diazepam in controlling symptoms of narcotic withdrawal. However, the use of paregoric has declined during recent years because of the known and potential toxic effects of its many ingredients [22]. In addition to morphine, it contains anti-spasmodics (noscapine and papaverine) and such toxic compounds as camphor (a central nervous system stimulant); ethanol (44–46%), a CNS depressant; anise oil, which may cause habituation; and benzoic acid, which is potentially toxic [23]. Therefore, in our patients, administration of tincture of opium was preferred to paregoric. However, phenobarbital was used as an additional drug when therapy with tincture of opium was not sufficiently effective. Phenobarbital has been observed to be more effective in controlling symptoms associated with non-opiate withdrawal [25]. On this basis, it was administered as a single remedy to one neonate whose mother was addicted to benzodiazepines. Theis et al. [23], in their critical analysis of the currently available therapies for NAS, concluded that further studies are still needed to establish satisfactory pharmacological management.

In view of Israel's new health policy of early discharge after delivery (24–48 hours), this study indicates the value of prior knowledge of maternal drug abuse. As we showed, only three neonates received pharmacological treatment on the first day of life because of the overt and considerable presentation of NAS, whereas the other neonates expressed noticeable withdrawal syndrome only later on. Thus, the absence of previous information may result in development of withdrawal syndrome after hospital discharge.

Only 10 children showed up for follow-up examinations and their development was observed for various periods ranging from 6 to 22 months. Obviously, a larger number of observed children and a longer follow-up period of monitoring are necessary for drawing objective conclusions on the development of children prenatally exposed to narcotics.

In conclusion, our study demonstrated that about three-quarters of children exhibiting neonatal abstinence syndrome require pharmacological treatment and that prior information on maternal drug abuse is a crucial factor for successful diagnosis and treatment.

References

1. Alroomi LG, Davidson J, Evans TJ, Galea P, Howat R. Maternal narcotic abuse and the newborn. *Arch Dis Child* 1988;63:8–13.
2. Klenka HM. Babies born in a district general hospital to mothers taking heroin. *Br Med J* 1986;293:745–6.
3. Harper RG, Solish GI, Purow HM, Sang M, Panepinto WC. The effect of a methadone treatment program upon pregnant heroin addicts and their newborn infants. *Pediatrics* 1974;54:300–5.
4. Zelson C, Rubio E, Wassermann E. Neonatal narcotic addiction: 10-year observation. *Pediatrics* 1971;48:178–89.
5. Fricker HS, Segal S. Narcotic addiction, pregnancy and the newborn. *Am J Dis Child* 1978;132:360–6.
6. Barnea Z, Gil G, Rahav G, Rosenblum J, Teichman M. Drug and alcohol use among the residents of the State of Israel: epidemiological study. Tel Aviv, 1990: Pori and the Anti-Drug Authority.
7. Barnea Z, Teichman M, Rahav G. Substance abuse and abuse among deviant and non-deviant adolescents in Israel. *J Drug Educ* 1993;23:222–36.
8. Ben-Yehuda N. Extent of drug use in Israel, a static phenomenon or one that is spreading? A sociological hypothesis. *Delinquency and Social Deviance* 1989;19:75–86.
9. Finnegan LP, Kron RE, Connaughton JF Jr, Emich JP. A scoring system for evaluation and treatment of the neonatal abstinence syndrome: a new clinical and research tool. In: Morselli PL, Garattini S, Serini F, eds. *Basic and Therapeutic Aspects of Perinatal Pharmacology*. New York: Raven Press, 1975:139–53.
10. Knobloch H, Stevens F, Malone AF. *Manual of developmental diagnoses. The administration and interpretation of the revised Gesell and Amatruda. Developmental and neurologic examination*. Cambridge, London: Harper Row, 1980.
11. Barnea Z, Teichman M. Alcohol and drug abuse in Israel in the twenty-first century: implications for social work education. *Int Soc Work* 1993;36:357–72.
12. O'Brien CP. Drug abuse treatment. NIDA Capsules (CAP27). Rockville MD: National Institute on Drug Abuse, 1988.
13. Zelson C, Lee SJ, Casalino M. Neonatal narcotic addiction. Comparative effects of maternal intake of heroin and methadone. *N Engl J Med* 1973;289:1216–20.
14. Desmond M, Wilson GS. Neonatal abstinence syndrome. Recognition and diagnosis. *Addict Dis* 1975;2:113–21.
15. Desmond M, Schwanecke R, Wilson G, Yasunaga S, Burgdorff I. Maternal barbiturate utilisation and neonatal withdrawal symptomatology. *J Paediatr* 1972;80:190–7.
16. Blinick G, Wallach R, Jerez E, Ackermann G. Drug addiction in pregnancy and in the neonate. *Am J Obstet Gynecol* 1976;125:135–42.
17. Sutton LR, Hinderliter SA. Diazepam abuse in pregnant women on methadone maintenance. Implication for the neonate. *Clin Pediatr* 1990;29:108–11.
18. Harper RG, Solish G, Feingold E, Gerstein-Woolf NB, Sokal MM. Maternal ingested methadone, body fluid methadone, and the neonatal withdrawal syndrome. *Am J Obstet Gynecol* 1977;129:417–24.
19. Finnegan LP, Kaltenbach K. Neonatal abstinence syndrome. In: Hoekelman RA, Friedman SB, Nelson NM, Seidel HM, eds. *Primary Pediatric Care*. 2nd ed. St Louis: Mosby Year Book, 1992:1367–78.
20. Lipsitz PJ. A proposed narcotic withdrawal score for use with newborn infants. A pragmatic evaluation of its efficacy. *Clin Pediatr* 1975;14:592–4.
21. Ostrea EM. Infants of drug-dependent mothers. In: Burg FD, Ingelfinger JR, Wald ER, eds. *Current Pediatric Therapy*. Vol 14. Philadelphia: WB Saunders, 1993:800–1.
22. American Academy of Pediatrics. Committee on Drugs. Neonatal drug withdrawal. *Pediatrics* 1998;101:1079–88.
23. Theis JGW, Selby P, Ikizler Y, Koren G. Current management of the neonatal abstinence syndrome: a critical analysis of the evidence. *Biol Neonate* 1997;71:345–56.
24. Kron RE, Litt M, Eng D, Phoenix MD, Finnegan LP. Neonatal narcotic abstinence: effects of pharmacotherapeutic agents and maternal drug usage on nutritive sucking behavior. *J Pediatr* 1976;88:637–41.
25. Herzlinger RA, Kandall SR, Vaughan HG. Neonatal seizures associated with narcotic withdrawal. *J Pediatr* 1971;91:638–41.
26. Finnegan LP, Ehrlich S. Maternal drug abuse during pregnancy and pharmacotherapy for neonatal abstinence syndrome (NAS) [Abstract]. *Pediatr Res* 1987;21:234A.

Correspondence: Dr. M. Lifshitz, Toxicology Unit, Soroka University Medical Hospital, P.O. Box 151, Beer Sheva 84101, Israel. Phone/Fax: (972-7) 648-0187, email: matyl@bgumail.bgu.ac.il.