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Pediatrics 2006;117;e1163
DOI: 10.1542/peds.2005-1561

ARTICLE

Effects of Breast Milk on the Severity and Outcome of Neonatal Abstinence Syndrome Among Infants of Drug-Dependent Mothers

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The authors have indicated they have no financial relationships relevant to this article to disclose.

ABSTRACT

OBJECTIVE. The purpose of this research was to assess the effects of breast milk on the severity and outcome of neonatal abstinence syndrome.

METHODS. We conducted a retrospective chart review of 190 drug-dependent mother and infant pairs. Patients were categorized according to the predominant type of milk consumed by the infant on the fifth day of life (breast milk: $n = 85$ or formula: $n = 105$). The Finnegan's scoring system was used to monitor withdrawal, and medication was commenced if there were 2 scores of ≥ 8.

RESULTS. Mean Finnegan scores were significantly lower in the breast milk group during the first 9 days of life even after stratifying for prematurity and exposure to polydrug and methadone. Significantly fewer infants required withdrawal treatment in the breast milk group. The median time to withdrawal occurred considerably later in breast milk group. In a multivariate analysis controlled for exposure to drugs of high risk of neonatal abstinence syndrome, polydrug, and prematurity, breast milk group was associated with lower need for neonatal abstinence syndrome treatment.

CONCLUSIONS. Breast milk intake is associated with reduced neonatal abstinence syndrome severity, delayed onset of neonatal abstinence syndrome, and decreased need for pharmacologic treatment, regardless of the gestation and the type of drug exposure.

www.pediatrics.org/cgi/doi/10.1542/peds.2005-1561

doi:10.1542/peds.2005-1561

Key Words
neonatal abstinence syndrome, breast-milk, drug dependency

Abbreviation
NAS—neonatal abstinence syndrome

Accepted for publication Jan 13, 2006

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MOST ADDICTIVE DRUGS, including methadone, are excreted in variable amounts into breast milk, but the quantity of transferred drug is so low that breastfeeding is considered unlikely to prevent neonatal abstinence syndrome (NAS).[1] Several small studies and clinical observations[2–4] have suggested that breastfeeding may ameliorate the severity of neonatal withdrawal and reduce the length of infant hospitalization. However, there have been no large-scale studies examining the effects of breast milk on the severity of NAS as determined by a quantitative withdrawal scale.

The aim of this study was, thus, to assess the effects of breast milk feeding on the severity of NAS in a population of infants of drug-dependent mothers who were at risk of NAS. We hypothesized that infants fed on breast milk have a reduced frequency and severity of NAS when compared with formula-fed infants.

METHODS

Study Design and Definitions

We conducted a retrospective cohort study of infants of drug-dependant mothers who were admitted to our unit between 1998 and 2004. A total of 190 consecutive charts were reviewed for maternal and infant data.

In our hospital, infants born to drug-dependent mothers are nursed with their mothers in the postnatal wards unless there are medical or social contraindications. All mothers are encouraged to breastfeed or express their milk for bottle or gavage feeding unless there are concurrent contraindications, the most common of which are human immunodeficiency virus positivity ($n = 1$) or maternal intoxication.

For the purpose of this study, the infants were categorized according to the predominant type of milk consumed by the infant on the fifth day of life. Those having >2 feeds per day of formula during the fifth day (because of inadequate breast milk supply or subsequent decision to formula feed) were classified as part of the "formula" group whereas others were classified as part of the "breast milk" group. The fifth day of life was chosen as the cutoff point for feed identification, because by that time, the majority of mothers would have chosen the type of milk feeds with which they were most comfortable. There were a total of 105 infants in the formula group (33 had exclusive formula feeds) and 85 infants (58 breastfed and 27 given expressed breast milk by bottle or gavage tube feeds) in the breast milk group. The median (interquartile range) duration of breastfeeding was 44 (21–90) days.

Assessment and Treatment of NAS

Each infant with a history of antenatal drug exposure was monitored by the Finnegan objective scoring system.[5,6] Scoring was started before the first feed and was performed before every feed for the duration of admission. Finnegan scores (total of 6616; mean: 4.0 scores per infant per day) were available for 182 (96%) of the study population. Supportive management (swaddling, frequent feeds if tolerated, and nursing in quiet environments) was applied from birth, and pharmacologic treatment, with receptor-appropriate agents, was commenced if the Finnegan's score exceeded 8 on 2 occasions or was >10 on 1 occasion. Morphine was commenced at a dose of 0.5 mg/kg per day in 4 divided doses for polydrug and opiate-exposed infants and increased or decreased by 10% every 2–3 days to maintain an average Finnegan score of <8. Phenobarbitone (initial 5 mg/kg per day in 2 divided doses) was given to polydrug opiate-exposed infants in addition to morphine if symptoms were not controlled. Phenobarbitone was to be considered as adjunct treatment to allegedly only opiate-exposed infant needing high morphine dosage >0.8 mg/kg per day. Phenobarbitone was also the first-line drug of choice to treat infants withdrawing from nonopiate drugs, for example, sedatives. All of the medications were given orally unless there was severe vomiting or if oral intake was medically contraindicated.

As per the New South Wales Department of Health policy,[7] infants at risk of NAS were advised to remain in hospital for a minimum of 5 days. In our institution, infants were only discharged from hospital (either to a parental or foster home) if their NAS was stabilized (eg, scores averaging <8 for ~2 days, feeding well, and gaining weight) and if there were no adverse social circumstances. There was no ceiling dose of medications for discharge, and the remainder of NAS treatment was completed on an outpatient basis.[8] Toxicology (on either urine or meconium) was performed only on physician orders and was not done routinely.

Statistical Analysis

Statistical analyses were performed using SPSS version 11.5.0 (SPSS Inc, Chicago, IL).[9] The $\chi 2$ test and t test were used where appropriate. The Kaplan-Meier (product-limit) method[10] was used to estimate the number of infants needing treatment with differences compared by the 2-sided log rank test.[11] Multiple logistic regression[12,13] was used to evaluate the factors predictive of requirement for treatment for NAS after controlling for potential confounders. The level of statistical significance for all of the analyses was set at $P < .05$ using 2-tailed comparisons. The significance level was not changed when multiple comparisons were performed.[14]

RESULTS

Maternal Drug Use

Table 1 shows the pattern of illicit drug use obtained by maternal reporting. Sporadic toxicology was performed on the infant urine and meconium. Only 2 infants had urine toxicology screens that were inconsistent with

TABLE 1 **Comparison of Maternal and Socioeconomic Characteristics of the 2 Study Groups**

Characteristic	Breast Milk Group ($n = 85$)	Formula Group ($n = 105$)	*P*
Maternal age, y, mean ± SD	30.4 ± 6.1	29.1 ± 5.6	.126
Aboriginal ethnicity, *n* (%)	7 (8.2)	12 (11.4)	.629
Unemployed mothers, *n* (%)	68 (80.0)	94 (89.5)	.104
No antenatal care, *n* (%)	16 (18.8)	31 (29.5)	.134
Hepatitis C antibodies positive, *n* (%)	52 (61.2)	79 (75.2)	.057
Illicit drugs used, *n* (%)[a]			
Opioid[b]	70 (82.4)	96 (91.4)	.098
Heroin	42 (49.4)	74 (70.5)	.005
Methadone	62 (72.9)	87 (82.8)	.140
Others	9 (10.6)	6 (5.7)	.333
Nonopioid[c]	40 (47.1)	66 (62.9)	.042
Benzodiazepine	15 (17.4)	26 (24.8)	.292
Cocaine	10 (11.8)	17 (16.2)	.509
Amphetamine	6 (7.1)	10 (9.5)	.730
Cannabinoids	21 (24.7)	41 (39.0)	.054
Others	5 (5.9)	4 (3.8)	.745
Polydrugs[d]	33 (38.8)	65 (61.9)	.003
High risk of NAS[e]	65 (76.5)	95 (90.5)	.015
Methadone dose at delivery, mg/day, mean ± SD	68.5 ± 31.3	79.6 ± 40.6	.073
Length of hospitalization, day, mean ± SD	7.7 ± 3.6	7.1 ± 3.7	.231

[a] Patients may be counted in >1 group.
[b] Opioid includes heroin and methadone and others like codeine, pethidine, and so forth.
[c] Nonopioid includes benzodiazepine, cocaine, amphetamine, cannabinoids, and others like tryptanol, valium, and so forth.
[d] Polydrug use includes use of ≥2 illicit drugs from different classes.
[e] High risk of NAS includes those exposed to heroin, methadone, and/or benzodiazepine.

their mother's histories (in both instances, cocaine was identified in their urine), although maternal reporting is known to underestimate true drug use.[15] The majority of mothers were opiate dependent, and, of these, the majority were maintained on methadone treatment (Table 1). Methadone doses were not significantly different between the 2 groups, but polydrug use was significantly more common among mothers of formula infants (61.9% vs 38.8%, respectively; $P = 0.003$).

As shown in Table 1, mothers of formula-fed infants were more likely to be from a socially disadvantaged situation. They were more likely to be of aboriginal ethnicity, younger, and unemployed. These mothers had also had fewer antenatal visits than mothers of breast-milk fed infants.

Infants' Characteristics and Outcome

There were more premature infants in the formula group, but, otherwise, growth parameters were comparable between the 2 groups (Table 2). Significantly more formula infants were classified as children-at-risk, with the rate of fostering being ~3 times the breast milk group. The mean duration of hospitalization was ~5 days longer in the formula group than the breast milk group.

The mean Finnegan scores for the first 9 days of life were considerably lower in breast milk infants (Fig 1). The Finnegan scores for the formula group were consistently higher in the subgroups of premature infants and those exposed to polydrug, methadone, opioid, or maternal methadone dose >80 mg/kg per day (Fig 2).

TABLE 2 **Comparison of Infants' Characteristics and Outcome of the 2 Study Groups**

Characteristic	Breast Milk Group ($n = 85$)	Formula Group ($n = 105$)	*P*
Gestational age, wk, mean ± SD	37.9 ± 3.0	37.4 ± 3.0	.246
Gestation <37 wk, *n* (%)	14 (16.5)	32 (30.5)	.041
Birth weight percentile, mean ± SD	38.1 ± 29.5	39.5 ± 30.6	.750
Small for gestation (<10th percentile), *n* (%)	12 (14.1)	11 (10.5)	.595
Male gender, *n* (%)	52 (61.2)	52 (49.5)	.152
Child at risk, *n* (%)	27 (31.8)	72 (68.6)	<.001
Foster care, *n* (%)	8 (9.4)	31 (29.5)	.001
Required treatment for NAS, *n* (%)	45 (52.9)	83 (79.0)	<.001
Required 2 medications to control NAS, *n* (%)	6 (7.0)	18 (17.1)	.065
Maximum dose of morphine mg/kg per day, mean ± SD	0.57 ± 0.22	0.59 ± 0.22	.526
Duration of treatment, day, mean ± SD	85.4 ± 71.7	108.2 ± 81.8	.185
Length of hospitalization, day, mean ± SD	14.7 ± 14.9	19.1 ± 15.0	.049

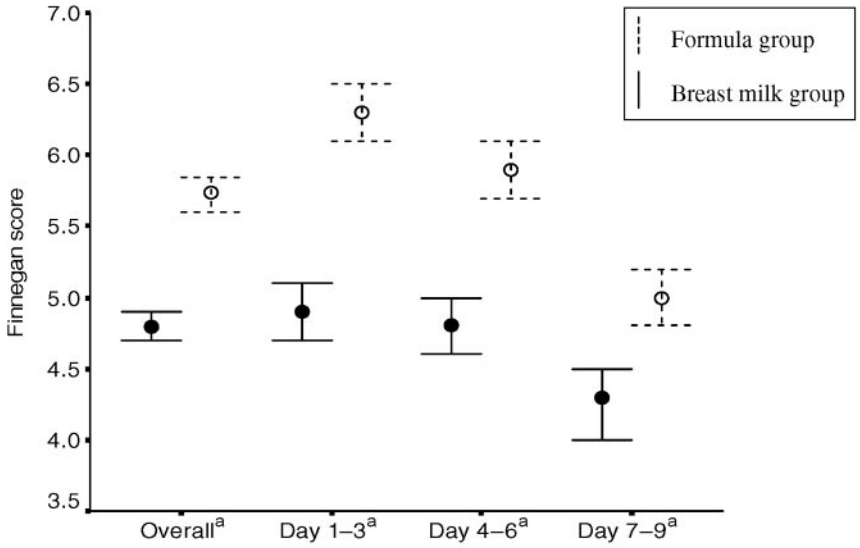

FIGURE 1
Comparison of severity of NAS between the 2 study groups during the first 9 days of life. [a] Mean, 95% confidence interval, $P < .05$.

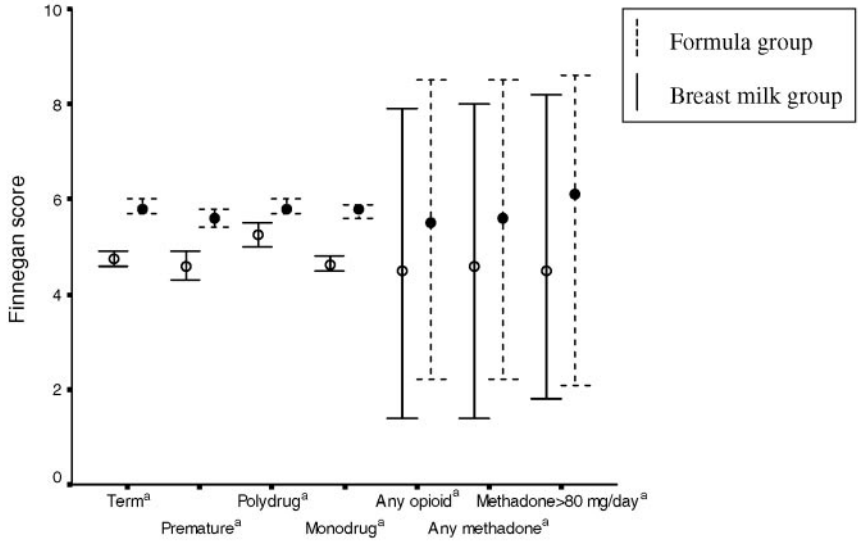

FIGURE 2
Stratification of the severity of NAS between the 2 study groups for selected categories. [a] Mean, 95% confidence interval, $P < .05$.

Within the breast milk group, there was no difference in Finnegan scores between breastfed infants and those given breast milk by bottle or gavage tube (data not shown).

The median time to withdrawal occurred considerably later in breast milk infants in comparison to the formula group (10 vs 3 days; $P < .001$; Fig 3). Breast milk infants were less likely to require pharmacologic treatment for withdrawal (52.9% vs 79.0%, respectively $P < .001$). In addition, the maximum amount of morphine was considerably lower in the breast milk group. Six (7.0%) infants from the breast milk group and 18 (17.1%) from the formula group required phenobarbitone in addition to the morphine to control NAS. Overall treatment duration was ~20 days less in the breast milk group (Table 2).

In a multivariate analysis examining the factors predictive of requirement for treatment for NAS and after controlling for polydrug use, high risk of NAS (defined as those exposed to heroin, methadone, and/or benzodiazepine), and prematurity, breast milk was found to be independently associated with a decreased need for pharmacologic NAS treatment (Table 3).

DISCUSSION

Until recently, the American Academy of Pediatrics recommended allowing breastfeeding for mothers on ≤20 mg of methadone a day.[16–18] This dose restriction for methadone was revised in 2001, and methadone is now deemed compatible with breastfeeding.[19] Artificially lowering a pregnant woman's methadone dose in an attempt to prevent NAS may increase the woman's craving, because it is well established that a woman's volume of distribution increases during pregnancy and that the

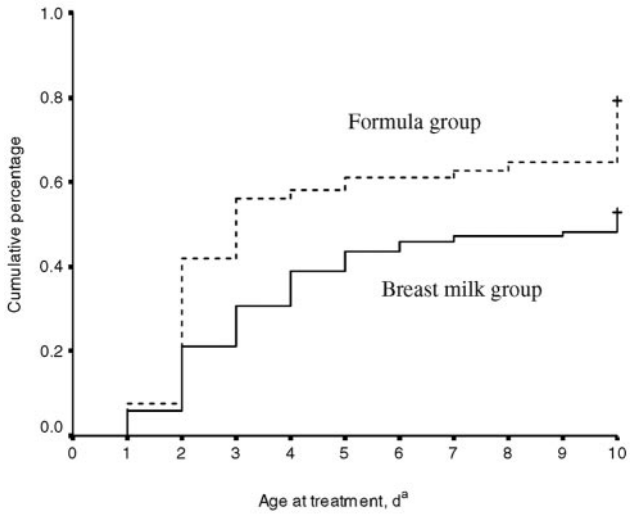

FIGURE 3
Age at which treatment started for the NAS in the 2 study groups. [a] $P < .05$.

maintenance dose of methadone during the last trimester of pregnancy may become considerably higher than her prepregnancy requirements.[20–22] In our institution, methadone doses are dictated by the needs of the individual woman, and the highest methadone dose in a breastfeeding mother was 150 mg per day.

Our study is the first large-scale study to demonstrate that breast milk significantly ameliorates the severity of NAS. In particular, infants who were fed predominantly on breast milk had significantly reduced mean NAS scores, delayed onset of withdrawal, a decreased need for medication, and shorter hospitalization than formula-fed infants. These results concur with those of previous smaller publications[2,3] and also agree with the opinion of Begg et al[1] that breast milk is unlikely to completely prevent NAS, although Malpas and Darlow[4] described 2 cases of abrupt onset of NAS in methadone-exposed infants after unexpected cessation of breastfeeding.

Breastfeeding itself has been shown to be beneficial in soothing agitated infants,[23] and to discount the possibility that effects noted were because of breastfeeding and not because of breast milk, we compared infants fed breast milk by bottle or by gavage tubes to those who exclusively breastfed and found no difference between the 2. Most studies have been performed on methadone, because it is the easiest drug to quantify, and it seems that the minute quantities of passively transferred drug are sufficient to decrease the intensity and severity of NAS (McCarthy and Posey estimated that the mean daily methadone ingestion in a breastfed newborn was ~0.05 mg/day).[24]

Naturally, the influence of unidentified drugs on our results cannot be discounted, because our institution relies heavily on voluntary maternal disclosure as the primary indicator of drug use. For a period, however, neonatal urine and meconium toxicology was performed on almost every patient (at the discretion of the attending clinician), and this demonstrated that only 2 of 195 infants had screens that contradicted their maternal history. Both of these mothers were from the formula group but neither of their infants withdrew sufficiently to require pharmacologic treatment. Breast milk-fed, polydrug-exposed infants, whereas having worse scores than infants exposed to single in utero drugs, had considerably lower mean Finnegan scores during the entire 9 days than formula-fed infants.

The Finnegan's scoring system was used to monitor withdrawal in this study despite being only validated for opiate withdrawal, because no reliable system has been found for assessing nonopiate effects, such as from cocaine, cannabinoids, and amphetamines. Until such a tool is available, we appreciate the limitations placed on a study like ours, but we must emphasize that the majority of infants in this study were exposed to opiates and only a few to stimulants such as cocaine and amphetamines.

The higher numbers of premature infants in the formula group may have either reflected poorer antenatal care or merely be an indication of the consequences of prematurity, that is, premature infants are often formula fed because their mothers have difficulty in providing sufficient milk. Doberczak et al[25] showed that premature infants had less severe withdrawal than term infants (the type of milk ingested by the infants in this study was not disclosed) because of their developmental immaturity and reduced total drug exposure during the intrauterine period. Hence, because of the increased numbers of premature infants in the formula group, one would have expected lower Finnegan scores, but the converse was found in our study. We found that infants of women on higher methadone doses (>80 mg per day) had slightly higher scores than those on lower doses but, again, the observation held, namely that infants fed on breast milk had lower scores than formula-fed infants regardless of maternal methadone dose.

Only 1 mother was actively discouraged from breastfeeding: she was HIV-positive, and infant transmission of HIV has been shown to be increased with breastfeeding.[26,27] The method of feeding in other cases was entirely dependent on maternal choice, and all of the other women were encouraged to breastfeed (as is our routine practice) unless intoxication was to such a degree that smothering during a breastfeed was a risk. In those cases, the mothers would be requested to express and discard the milk before and after a feed after the last known occasion of drug use.

Our results showed that breastfeeding mothers were more likely to have comprehensive antenatal care, were less likely to admit to polydrug use, and were less likely to be notified as an at-risk parent to child welfare services. They might, thus, have been more capable of

TABLE 3 **Multiple Logistic-Regression Model for Features Predictive of Requirement for Pharmacologic Treatment for NAS Among Infants of Drug-Dependent Mothers**

Factor	β Coefficient (SE)	Odds Ratio (95% Confidence Interval)	*P*
Predominantly fed breast milk	−1.032 (0.353)	0.356 (0.178–0.711)	.003
Exposure to polydrug[a]	0.724 (0.354)	2.063 (1.031–4.128)	.041
High risk of NAS[b]	0.077 (0.425)	1.080 (0.469–2.486)	.856
Prematurity	−0.432 (0.518)	0.356 (0.178–0.711)	.003
Constant	0.724 (0.354)	—	—

[a] Polydrug use includes ≥2 illicit drugs from different classes.
[b] High risk of NAS includes those exposed to heroin, methadone, and/or benzodiazepine.

calming and soothing a fractious NAS infant and thereby reducing the infant's withdrawal scores. It may be said that breastfeeding requires dedication and commitment and, thus, would be chosen as the accepted form of infant feeding by women who are already socially well adjusted and aware of the beneficial effects of breast milk.[28,29] Nevertheless, successful encouragement of breastfeeding, whether during the prenatal or postnatal period, has also been shown to enhance parental bonding, promote attachment, and significantly reduce the rate of child removal.[30]

The mothers in our service are advised to continue exclusive breastfeeding for at least a few months or ideally, for a year. They are made cognizant of the possibilities of acute but mild withdrawal should an abrupt reduction or cessation of breastfeeding or breast milk supply occur for any reason. However, should a mother in our service choose to stop breastfeeding and the infant was at risk of withdrawal, we recommend that she wean gradually with alternate breast and bottle feeds over at least a week. Unfortunately, we were not able to study the effects of the duration of breastfeeding or the effect of weaning on the severity of withdrawal in the infant, because formal Finnegan's scoring is not continued after leaving the hospital.

It was surprising that a difference was found in the length of hospitalization between the breast milk and formula group. As per guidelines recommended by the Department of Health in the state of New South Wales, infants exposed to in utero methadone were encouraged to remain in the hospital for ≥7 days, and differences in the length of hospitalization may have been diluted by this policy. The majority of infants, however, were discharged while they were still on withdrawal treatment, and the bulk of this treatment was weaned at our outpatient clinic. If breastfed infants did not withdraw sufficiently to require medications for ≥7 days after birth, they were discharged from the hospital and followed up weekly for ≥4 weeks (depending on the social and medical situation) at the outpatient clinic.

Because our service relies heavily on outpatient weaning of withdrawal medications, it is obviously important for us to be confident that the mothers or carers of the infants were reliable in drug administration. We have never had recourse to conduct routine postdischarge toxicology on the infants treated with morphine or phenobarbitone, and we have found that the converse was more likely, that the mothers or carers were often quite anxious that the infant kept to the dosing schedules recommended for the withdrawal regime.

Our results have important clinical and policy implications. The study has demonstrated that substantial breast milk intake significantly reduces the severity of NAS. This is achieved by delaying the onset of NAS and by decreasing the need for pharmacologic treatment, regardless of the gestation of the infant or of the type of drug exposure. Therefore, in conclusion, unless there are definitive medical contraindications to breastfeeding, we suggest that women of all infants at risk of NAS be encouraged to breastfeed.

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