Neonatal abstinence syndrome after maternal methadone treatment

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Abstract

Thirty two infants born to mothers taking methadone and 32 matched controls were studied to determine the incidence, timing, and frequency of persistence of withdrawal signs in infants born to maternal methadone users. Twelve (37%) infants received treatment for symptoms of withdrawal. The median length of time from birth to initiation of treatment was 23 hours (range 15-64 hours), the median length of treatment was six days (range 1-22 days). In the first six weeks after birth there was no significant difference in minor withdrawal symptoms and signs, general practitioner or accident and emergency visits between the group who did not receive treatment for withdrawal and the control group.

If immediate treatment for withdrawal is not required major symptoms do not subsequently occur with great frequency. Late withdrawal signs were not seen in this study.

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A newborn infant of a mother who has been dependent on opiates may develop signs of withdrawal from the drug (neonatal abstinence syndrome or NAS). In the United Kingdom signs of NAS have been reported in 70% of infants born to opiate dependent mothers.^{1 2} The incidence may be even higher in the United States where polydrug misuse is often prevalent. The use of methadone replacement treatment, with a view to eventual detoxification in the mother, may be associated with more prolonged and severe withdrawal when compared with street drugs such as heroin or morphine,^{3 4} an effect which may be dose related.⁵ Precipitous late withdrawal symptoms have been reported after the use of maternal methadone owing to the long half life of the drug.⁶

The aim of this study was to determine the incidence, timing, and frequency of persistence of symptoms in infants born to maternal methadone users.

Methods

The study was carried out at Fazakerley Maternity Hospital, Liverpool, between April 1992 and August 1993. Women receiving methadone replacement are followed up at the local drug dependency unit. A midwife attached to the unit coordinates antenatal care and attendance at Fazakerley Hospital. All

women who received methadone replacement and who delivered babies at Fazakerley Maternity Hospital during the study period were included. Informed consent was obtained. All babies were monitored clinically using a drug withdrawal chart which is in routine use in the hospital, and the decision to start treatment for drug withdrawal was made by the medical staff attending the postnatal wards. Oral morphine was used for the treatment of NAS.

During the infant's hospital stay the time of first medication for withdrawal, the length of treatment, and the length of hospital stay were documented. The infant's gestation, birth weight, and feeding status were also documented.

After discharge from hospital, follow up visits were carried out by the same person (LMcI) at 2, 4, and 6 weeks of age. The assessor at two, four, and six weeks of age was not involved in the assessment and management of the infants during their stay in hospital although she knew whether the mothers were acting as controls or were taking methadone. At each visit the mother was asked in a standard way to report any increased vomiting, sneezing, sweating, diarrhoea, restlessness, irritability, crying or pallor. Visits to the general practitioner and hospital admissions were documented and the infants were weighed.

Infants from a control group, matched with index cases for postal district of residence, sex, and week of birth, were visited every two weeks and asked the same questions. None of the mothers of the infants in the control group was known to be taking drugs during pregnancy.

Descriptive statistics were reported and, where appropriate, tests of significance were performed using the Mann Whitney U test. The study had the approval of the hospital ethics committee.

Results

During the study period, 32 infants and 32 controls were recruited. It was not possible to recruit all mothers taking methadone for reasons related to breach of confidentiality. Many drug dependent women had indicated that they did not want anyone other than the midwife who specialises in drug dependency to be aware of their habit unless there were problems with the baby. We were therefore only able to obtain anonymous details of methadone dose and sex, gestation, and birth weight of their infants for these women. However, all mothers that were approached

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Table 1 Details of infants born to known methadone dependent mothers included in the study, those not included, and control infants

	Methadone infants		
	Not included in the study (n=45)	Included in the study (n=32)	Control infants (n=32)
Percentage of males	50	38	44
Median gestation (range)	39 (27–42)	40 (32–42)*	40 (34–42)
No less than 36 weeks' gestation	2	2	1
Median birth weight (kg) (range)	2.86 (0.845–4.48)	2.83 (1.47–4.01)**	3.52 (2.41–4.54)
Breast fed	1	1	11
Median maternal methadone dose (range)	40 (10–80)	35 (5–80)	
No of mothers taking 20 mg or less of methadone (%)	7 (15)	8 (25)	

Significant difference from control infants *p<0.05, **p<0.001.

did consent to take part. There were a total of 77 known methadone dependent mothers delivering during the study period and it is likely that other women whose drug dependency was not known also delivered during this time. The group of infants not recruited was similar to the group studied with respect to sex distribution, birth weight and gestation and methadone dose being taken by the mother (table 1).

The median gestational age and birth weight were lower in the patient group when compared with the control group. Two of the patient group had a gestation of less than 37 weeks (both 32 weeks' gestation) and one control infant had a gestation of less than 37 weeks (34 weeks). More infants in the control group were breast fed than in the patient group (table 1).

Twelve (37%) infants in the patient group received treatment for symptoms of withdrawal. The median length of time from birth to initiation of treatment was 23 hours (range 15–64 hours). The median length of treatment was six days (range one to 22 days). There was no significant difference in the incidence of treatment of symptoms of withdrawal in infants whose mother had reported taking 20 mg or less of methadone (two of eight or 25%) and those whose mothers reported taking more than 20 mg of methadone daily (10 of 24 or 40%). The median length of stay in hospital for the patient group was greater in those infants who received treatment for withdrawal (8.5 days, range 4–25 days) than in those who did not receive treatment (4 days, range 2–9 days) (p<0.001). The median length of stay in the patient group for those infants not treated (4 days, range 2–9 days) was greater than that in the control group (3 days, range 1–7 days) (p<0.05).

The total number of general practitioner visits in the patient group was 35 (median 1, range 0–3) and those for the control group, numbered 29 (median 1, range 0–2). In the patient group eight infants attended the accident and emergency department, two

requiring admission for non-drug related problems. Three infants in the control group attended the accident and emergency department in the first six weeks, none requiring admission. By 2 weeks of age, 22 infants in the patient group had regained their birth weight compared with 28 in the control group, and by 4 weeks of age all infants in both groups had regained their birth weight.

Table 2 shows the incidence of symptoms in the patient group in infants who did not receive treatment for withdrawal and in the control group at 2, 4, and 6 weeks of age. The mean number of symptoms reported per patient was 0.9 at 2 weeks, 0.6 at 4 weeks, and 0.4 at 6 weeks in the patient group, and 1.1, 0.7, and 0.8, respectively, in the control group. There was no significant difference between the patient and control group at 2, 4, and 6 weeks of age in the incidence of each symptom or the mean number of symptoms per patient.

Discussion

This study is, to our knowledge, the first report in the United Kingdom of the short term outcome of infants born to mothers who have been taking methadone. The incidence of NAS requiring treatment was 37%. This is higher than the need for treatment in a group of infants studied in Glasgow whose mothers mainly took intravenous heroin, and lower than another Merseyside study of 26 infants whose mothers mainly smoked heroin.^{1,2} Comparing studies of NAS is difficult. Some of our infants who were not treated probably exhibited minor signs of withdrawal while on the postnatal ward. Furthermore, although using drug withdrawal charts to decide on initiation of treatment improves the objectivity of the assessment of the infant,⁷ reporting withdrawal signs is still open to observer bias.

It is our policy to allow infants of drug dependent mothers to be discharged after 72 hours, after a period of observation on the postnatal wards. This practice is supported by the results of this study, in that all infants

Table 2 Reported symptoms (%) of infants in the patient group not treated for withdrawal (n=20) and a control group (n=32)

Week	Vomiting		Sneezing		Sweating		Diarrhoea		Restlessness		Irritability		Crying		Pallor	
	Patients	Controls	Patients	Controls	Patients	Controls	Patients	Controls	Patients	Controls	Patients	Controls	Patients	Controls	Patients	Controls
2	0	2 (6)	7 (35)	8 (25)	0	4 (12)	2 (10)	2 (6)	3 (15)	6 (19)	2 (10)	5 (16)	1 (5)	5 (16)	2 (10)	2 (6)
4	0	3 (9)	5 (25)	7 (22)	1 (5)	3 (9)	0	3 (9)	2 (10)	5 (16)	2 (10)	2 (6)	0	2 (6)	2 (10)	0
6	1 (5)	3 (9)	2 (10)	1 (3)	0	2 (6)	0	2 (6)	2 (10)	5 (16)	1 (5)	7 (22)	0	4 (12)	2 (10)	1 (3)

requiring treatment for withdrawal symptoms presented within the first 72 hours. We did not observe late NAS, which has been described in infants born to mothers taking methadone.⁶ As this may occur more than two weeks after birth it does not seem justified to keep all infants in hospital for this length of time to detect such a rare event. However, we recommend close community follow up of these infants, either by a hospital liaison or community midwife.

It has been suggested that maternal methadone dose is related to the incidence and severity of withdrawal.⁵ We detected no difference in the incidence of withdrawal in infants of mothers who were taking a low dose of methadone compared with those taking a higher dose, although the numbers involved were small and concurrent ingestion of other substances could not be excluded. We and others have shown that withdrawal may still occur in infants of mothers taking less than 20 mg of methadone.⁵ These mothers should therefore be counselled accordingly and told that withdrawal symptoms are still possible despite their low dose of methadone.

The length of treatment for withdrawal was variable, with a median of six days, and obviously resulted in an increase in length of hospital stay. The lower gestation and birth weight found in the infants of drug dependent mothers compared with controls is consistent with the findings of previous reports.^{5 8 9} The higher incidence of breast feeding in the control group may reflect lack of motivation on the part of drug dependent mothers to breast feed, or a conscious decision not to breast feed after counselling with regard to possible HIV transmission if the mother previously had taken drugs intravenously.

The greater length of stay for the untreated infants of methadone dependent mothers, compared with controls, is probably a reflection of hospital policy to observe the former for up to 72 hours before discharging them. There was no significant difference between the presence of minor withdrawal symptoms and

signs in the patient group and the control group, and there was no significant increase in attendance at hospital accident and emergency departments or the general practitioner. This indicates that infants born to mothers taking methadone are not perceived as any more difficult babies than 'normal infants'. The incidence of reported symptoms declined over the six weeks in both patient and control groups. The higher incidence of symptoms earlier on in both groups is likely to be due to the stress of coping with a newborn baby at home, the perception of these symptoms decreasing as the mother gets used to the new baby.

Interestingly, some infants in the patient group took up to four weeks to regain their birth weight. This may be a reflection of an increased calorie requirement secondary to withdrawal.⁷ However, none of the infants in the patient group was dehydrated or had any other problems which could be attributed to slowness to regain birth weight.

In summary, it seems that if immediate treatment for withdrawal is not required, clinically relevant symptoms do not subsequently occur with great frequency. Late withdrawal signs were not seen in our study, although community follow up is suggested for the detection of these.

- 1 Alroomi LG, Davidson J, Evans TJ, Galea P, Howat R. Maternal narcotic abuse and the newborn. *Arch Dis Child* 1988; **63**: 81-3.
- 2 Klenka HM. Babies born in a district general hospital to mothers taking heroin. *Br Med J* 1986; **293**: 745-6.
- 3 Herzlinger RA, Kandall SR, Vaughan HG. Neonatal seizures associated with narcotic withdrawal. *J Pediatrics* 1977; **91**: 638-41.
- 4 Zelson C, Lee SJ, Casalino M. Comparative effects of maternal intake of heroin and methadone. *N Engl J Med* 1973; **289**: 1216-20.
- 5 Olofsson M, Buckley W, Andersen GE, Friis-Hansen B. Investigation of 89 children born by drug-dependent mothers. *Acta Paediatr Scand* 1983; **72**: 403-6.
- 6 Challis RE, Scopes JW. Late withdrawal symptoms in babies born to methadone addicts. *Lancet* 1977; **ii**: 1230.
- 7 American Academy of Pediatrics. Committee on drugs. Neonatal drug withdrawal. *Pediatrics* 1983; **72**: 895-902.
- 8 Ostrea EM, Chavez CJ. Perinatal problems (excluding neonatal withdrawal) in maternal drug addiction: A study of 830 cases. *J Pediatrics* 1979; **94**: 292-5.
- 9 Chasnoff IJ, Hatcher R, Burns WJ. Early growth patterns of methadone-addicted infants. *Am J Dis Child* 1980; **134**: 1049-51.