

ABSTINENCE SYNDROME

Supporting information

Do infants with neonatal abstinence syndrome (NAS) experience better outcomes when their mothers have been treated with morphine rather than methadone?

There is “very little evidence” regarding the comparative benefits of different regimens on outcomes in NAS, as most published studies were conducted prior to the development of modern study design (Theis, 1997).

As slow-release morphine has been shown to be as effective as methadone in maintaining addicts (Etzersdorfer, 1997), it has been hypothesised that it may produce a less severe NAS.

An open, randomised trial in 48 pregnant opiate abusers (Fischer, 1999) compared those maintained on methadone (n = 24) with those given slow-release morphine (n=24). No difference was found in the number of days that NAS was experienced by infants born to either treatment group (mean = 16 and 21 days, respectively). Fewer benzodiazepines ($p < 0.05$) and fewer additional opiates ($p < 0.05$) were consumed by the group maintained on morphine compared with the methadone group.

A later study (Lee, 2000) has also not demonstrated greater efficacy for slow-release morphine.

In the treatment of infants with NAS, a statement from the American Academy of Pediatrics (Anon, 1998) advises that “Drug selection should match the type of agent causing withdrawal. Thus, for opioid withdrawal, tincture of opium is the preferred drug”.

A recent, partially randomised controlled trial in 20 infants (Coyle, 2002) compared diluted tincture of opium (DTO) plus placebo (n = 10) with DTO plus phenobarbitol. Duration of hospital stay was reduced by 48% (79 to 38 days, $p < .001$) in the DTO plus phenobarbitol group.

A single case study in 2 infants (Wijburg, 1991) has described the successful use of morphine to abort epileptic convulsions in NAS.

[A comparative study in 53 neonates born to mothers maintained on methadone \(n=22\), slow-release oral morphine \(n=17\) or buprenorphine \(n=14\) throughout pregnancy \(Ebner, 2007\) found that those receiving morphine needed a significantly shorter period of treatment \(9.9 days vs 17.7 days\).](#)

A Cochrane review on NAS (Osborn, 2005) does not consider morphine vs methadone, but deals with opiates compared to sedatives or non-pharmacological treatments.

Anon. Neonatal drug withdrawal. American Academy of Pediatrics. Committee on Drugs. Pediatrics 1998;101:1079-88

Coyle MG, Ferguson A, Lagasse L, et al. Diluted tincture of opium (DTO) and phenobarbitol versus DTO alone for neonatal opiate withdrawal in term infants. J Pediatr 2002;140:561-4

[Ebner N, Rohrmeister K, Winklbaaur B, et al. Management of neonatal abstinence syndrome in neonates born to opioid maintained women. Drug Alcohol Depend 2007;87:131-8](#)

Etzersdorfer P, Fischer G, Eder H, et al. Comparison of morphine and methadone maintenance in pregnant opiate addicts. NIDA Research Monograph Series, 1997;178:343

Fischer G, Jagsch R, Eder H, et al. Comparison of methadone and slow-release morphine maintenance in pregnant addicts. Addiction 1999;94:231-9

Lee TS. Slow-release morphine was not more effective than methadone in reducing neonatal abstinence syndrome. *West J Med* 2000;172:26

Osborn DA, Cole MJ, Jeffrey HE. Opiate treatment for opiate withdrawal in newborn infants. *The Cochrane Database of Systematic Reviews* 2005, Issue 3. Art. No.: CD002059

Theis JG, Selby P, Ikizler Y, et al. Current management of the neonatal abstinence syndrome: a critical analysis of the evidence. *Biol Neonate* 1997;71:345-56

Wijburg FA, de Kleine MJ, Fleury P, et al. Morphine as an anti-epileptic drug in neonatal abstinence syndrome. *Acta Paediatr Scand* 1991;80:875-7

Evidence Level: III

What are the most appropriate doses for morphine and phenobarbital?

The BNF for Children gives the following recommendations:

Morphine:

NEONATE

initially 40 micrograms/kg every 4 hours until symptoms controlled, increase dose if necessary; reduce frequency gradually over 6–10 days, and stop when 40 micrograms/kg once daily achieved; dose may vary, consult local guidelines

<http://www.bnfc.nhs.uk/bnfc//bnfc/2005/3492.htm>

Phenobarbital:

NEONATE

initially 20 mg/kg *by slow intravenous injection* then 2.5–5 mg/kg once daily either *by slow intravenous injection* or *by mouth*; dose and frequency adjusted according to response

<http://www.bnfc.nhs.uk/bnfc//bnfc/2005/3492.htm>

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