

NAS Pharmacologic Treatment Protocol: Dosing Guidelines

Morphine

Morphine is indicated when the average of three scores is ≥ 8 according to the Modified Finnegan Scoring System or when the average of two scores or the score for two consecutive intervals is ≥ 12 .

If the scores remain ≥ 8 for 3 consecutive scores or ≥ 12 on 2 occasions, the morphine dose is increased to the next range ie by 0.16 mg/kg/day. If 0.80 mg/kg/day fails to control signs of withdrawal, morphine may be increased to 0.96 to 1.0 mg/kg/day. Clonidine (see below) should be considered at this point.

Weaning

Weaning is initiated when scores are <8 for 24 to 48 hours and ordinarily occurs by 10% of the total daily dose with each wean occurring no more frequently than every 48 hours to 72 hours. When the total daily dose is <0.2 mg/kg/day, consideration may be given to weaning every 24 hours at the discretion of the physician.

An alternate approach used by some centres is to wean by 0.05mg/kg/day every 48 to 96 hours as tolerated.

In both approaches, morphine is discontinued when scores are stable for 48 to 72 hours on a dose of 0.05 to 0.1 mg/kg/day.

Dosing guidelines

Score	Oral Morphine Dose
8-10	0.32 mg/kg/day divided q4-6h
11-13	0.48 mg/kg/day divided q4-6h
14-16	0.64 mg/kg/day divided q4-6h
17+	0.80 mg/kg/day divided q4-6h

Phenobarbital

Phenobarbital may be used in combination with morphine in infants exposed to polydrug abuse (sedatives, alcohol or barbiturates in addition to opiates).

Phenobarbital 10 mg/kg is given every 12 hours for 3 doses, then 5 mg/kg/day is continued as a maintenance dose. The doses of morphine used in combination with phenobarbital are lower than those given when morphine is used alone:

Dosing guidelines

Score	Oral Morphine Dose in combination with Phenobarbital
8-10	0.16 mg/kg/day divided q4-6h
11-13	0.32 mg/kg/day divided q4-6h
14-16	0.48 mg/kg/day divided q4-6h
17 or >	0.62 mg/kg/day divided q4-6h

Clonidine

Clonidine has been explored as a possible therapeutic option in combination with morphine. There is Level 1 evidence from one small randomized controlled trial demonstrating that clonidine in addition to standard opioid therapy reduces the duration of pharmacotherapy for neonatal abstinence¹. Therefore clonidine may be considered as an adjunct to morphine when high doses (see above) fail to control withdrawal symptoms.

Some studies gradually increased doses over 1 to 2 days to begin therapy, and tapered doses by 0.25 mcg/kg every 6 hours to discontinue (or by 25% of the total daily dose every other day).

Dosing guidelines*

- 0.5 -1 mcg/kg, given orally every 4-6 hours
- Much higher doses (0.5 to 3 mcg/kg/h) have been used as a continuous infusion²

*Adequate clinical trials to establish an efficacious and safe dose still are required

¹ Agthe AG, et al., Clonidine as an adjunct therapy to opioids for neonatal abstinence syndrome: A randomized, controlled trial. *Pediatrics*, 2009; 123:e849-56

² Esmaeili A Keinhorst AK, Schuster T, Schlosser R, Bastanier C. Treatment of neonatal abstinence syndrome with clonidine and chloral hydrate. *Acta Paediatrica* (2009) Oct, 1-6 (on line)