MINNESOTA
NEONATAL
PHYSICIANS P.A.

Neonatal Abstinence Syndrome 2.0

I. Admission and Monitoring:

Patients with known or suspected in utero drug exposure will be admitted to level 2 nursery or higher for Finnegan Scoring. Throughout the hospitalization always consider a broad differential diagnosis including but not limited to: sepsis, meningitis, hyperthyroidism, hypoglycemia, asphyxia. Patients need to have inpatient Finnegan scores monitored for a minimum of:

- Four days for a short acting opiate e.g. hydrocodone, oxycodone, heroin
- Five to seven days for opiate with longer half-life e.g. Methadone, Buprenorphine

II. Acute Treatment:

- Patients with scores ≤7 receive non-pharmacologic treatment including gentle handling, ambient noise control, swaddling, and demand feedings.
- Treatment is initiated for a single score >12 or two out of three scores ≥8.
- Infants exposed to short-acting opiates in utero will be treated with morphine.
- Infants exposed to long-acting opiates in utero will be treated with methadone.
- If patient appears over-sedated, decrease next dose by 50%. Do not hold doses unless patient has apnea.

A. Morphine:

1. Starting Dose: 0.05 mg/kg/dose po q three hours or 0.03 mg/kg/dose IV q three hours
2. Escalation:
    I. If Finnegan score >8 but < 12 after two doses, increase dose by 0.025 mg/kg every three hours until scores are < eight.
    II. If Finnegan score >12, increase dose to 0.1 mg/kg/dose po every three hours
3. Maintenance:
    I. Once therapeutic (scores <8), maintain dose for 24-36 hours

B. Methadone:

1. Initial methadone dose based on Finnegan score at time treatment initiated.
2. Maximum methadone dose 0.2 mg/kg/dose
3. Starting Dose:
    a. If Finnegan score ≤12: Methadone 0.05 mg/kg/dose po every six hours.
    b. If Finnegan score >12: Methadone 0.1 mg/kg/dose po every six hours

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4. Escalation:
    a. If Finnegan score >8 but < 12 after two doses, increase dose by 0.025 mg/kg every six hours until scores are < 8.
    b. If Finnegan score > 12, increase dose by 0.05 mg/kg/dose po every 6 hours
5. Maintenance:
    a. Once therapeutic (scores <8), maintain therapeutic dose for 24-36 hours.

III. Weaning:

- Failure to tolerate wean will be defined as two out of three sequential scores ≥8 in the 12 hours prior to the next dose.
- Failure to wean twice in four days will result in addition of phenobarbital as adjutant therapy.
- After 21 days of age, adjust trigger scores by two. In other words, failure to tolerate wean would need scores ≥10.
- During the period of observation after methadone or morphine have been discontinued, prn morphine may be given for two consecutive scores >8.
- It is not expected that outpatient methadone therapy will be required using this protocol. However, if it is required, convert the total daily therapeutic dose at the time and convert to twice daily administration.

A. Morphine

1. Wean by 10% of therapeutic dose every 24 hours as long as Finnegan scores <8.
2. If patient fails wean based on above criteria, return to previous therapeutic dose and delay weaning for a minimum of 24 hours.
3. Based on Children's pharmacy standard morphine concentration of 0.1 mg/0.5 ml, may wean as low as 0.01 mg/kg/dose.
4. After toleration of 8th wean, patient should be at 20% of the original therapeutic dose. After tolerating this dose for 48 hours, discontinue morphine and observe for minimum 48 hours prior to discharge.

B. Methadone

1. Every 24 hours as long as Finnegan score <8, wean by 10% of therapeutic dose.
2. When at 10% of therapeutic dose, DC drug.
3. After stopping methadone, observe for minimum 48 hours prior to discharge.

C. Phenobarbital

1. 10 mg/kg/dose po every eight hours for a total of two doses, then 2.5 mg/kg po every 12 hours

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IV. Discharge Planning:

A. Written Social work/Child Protection Services verification for disposition of infant, i.e. family, foster care.
B. Every patient requiring pharmacologic treatment needs a referral to Early Intervention.
C. Home Health Visit after discharge. Twice/week is optimum.
D. If outpatient medication indicated it must be obtained from a Children's pharmacy. The discharging MD needs to have a conversation with the accepting primary care physician to determine who will manage/prescribe methadone (Primary care physician or Pain & Palliative Care physician). This should be documented in the chart.
E. Methadone script written for a one-week treatment course with no refills.
F. If outpatient phenobarbital required, recommend wean to off within 30 days.
G. Parent/guardian needs to have follow-up appointment scheduled with follow up physician prior to discharge order being written.

V. Rationale:

A. In a subgroup of patients treated for NAS, the treatment process is more complex and monotherapy is not as effective. Early institution of a second medication may minimize inpatient stay.
B. Compared to morphine, methadone has a higher bioavailability, longer half-life, and is metabolized by the P450 cytochrome pathway.
C. Methadone is a synthetic opioid agonist that selectively binds to the mu-receptor exerting morphine-like effects.
D. Morphine is metabolized by glucuronidation in the liver and excreted by the kidney.
E. Opioid receptor affinities are different between morphine and methadone. Morphine is specific to the mu-receptor and is metabolized more rapidly than methadone. Methadone has affinity for a broader range of receptors.
F. Methadone, as opposed to morphine, has NMDA antagonistic effects, which may explain differences in efficacy for withdrawal.

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EXAMPLE

3.0 kg baby exposed to maternal methadone. Finnegan score 15 at 8 hours of age. Started on methadone 0.1 mg/kg/dose = 0.3 mg every 6 hours on first day of life. Scores 3-7 for the next 36 hours so weaning commenced as follows

DAY OF LIFE	DOSE	NAS SCORE	WEANED? Y/N
1	0.3mg	3-7	No
2	0.3	3-7	Yes, by 10%
3	0.27	2-7	Yes, by 10%
4	0.24	3-7	No
5	0.21	2-7, 9	Yes, by 10%
6	0.21	2-6	Yes, by 10%
7	0.18	1-6	Yes, by 10%
8	0.15	2-8	Yes, by 10%
9	0.12	2-6	Yes, by 10%
10	0.09	2-6	Yes, by 10%
11	0.06	2-8, 9, 9	No
12	0.06	1-5	Yes, by 10%
13	0.03	1-5	Med DC'd
14	None	1-7	
15	None	2-4	
Patient DC'd to home			

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