Prolonged administration of opioids and/or benzodiazepines may induce drug tolerance and physiological dependency. Abrupt discontinuation or (too rapid) weaning of these drugs may result in iatrogenically acquired withdrawal syndrome (IWS). Infants prescribed opioids via continuous infusion for as little as 5 days can develop opioid tolerance or dependence. Cumulative dose and duration of administration of opioids are highly predictive in the occurrence of such complications and therefore rational prescribing and weaning is recommended.

Withdrawal Assessment

Signs of withdrawal may not be immediate and may take up to 48 hours to manifest. Narcotic withdrawal can be objectively assessed using the NAS observation chart and should be used in conjunction with this protocol. Refer to Neonatal Abstinence Syndrome (NAS) guideline, Pharmacological Treatment.

Initiate NAS chart assessments in all neonates perceived at risk e.g. received intravenous opioid for 5 days or more, or in neonates exhibiting potential symptoms following weaning or cessation. Score every 4 hours if scores < 8, score every 2 hours if scores > 8. Severe symptoms (total score > 8 on 3 consecutive occasions or > 12 on two occasions) should be reported to the medical staff for further management.

Management of Iatrogenic NAS

Category 1: Narcotics Administered for Less than 5 Days
Reduce rate as clinically indicated and tolerated (i.e. reduce infusion rate by half every 4-6 hours). Initiate NAS observation chart only if withdrawal symptoms are observed. Score every 4 hours and initiate treatment as indicated by scores.

Category 2: Narcotics Administered for 5 to 14 Days
Reduce rate by 20% every 24 hours. Initiate withdrawal observation chart for all infants in this category. Score every 4 hours and initiate treatment if indicated by the scores. Monitor for signs of withdrawal for at least 48 hours post cessation of medication.

If withdrawal symptoms are identified (score > 8 for 3 scores) reduce the rate of weaning to 10% per 24-48 hours. If symptoms persist with scores >8 revert to previous prescribed dose and delay weaning for 24 hours and reassess rate and frequency of weaning to be undertaken.

Category 3: Narcotics Administered for Greater than 14 Days
Consider a prescribed slower rate of wean due to increased risk of adverse effect. e.g. reduction by 10% every 24-48 hours. Initiate NAS observation chart as specified
above and remain alert for potential symptoms to be assessed and treated without delay and weaning protocol revised.

**Therapeutic Agents**

Intravenous fentanyl and morphine are the most frequently used analgesic agents in the NICU that underlie opiate IWS. Equivalent opioid calculators may be used for dose conversion between formulations and preparations, however are to be used with caution of significant interpatient variability in bioavailability and metabolism of agents. A recommended approach is to calculate the total dose received in 24 hours prior to conversion to another agent or route of delivery.

<table>
<thead>
<tr>
<th>Neonatal Opioid Dosage Conversion (conversion via TOTAL DAILY DOSE)</th>
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<tbody>
<tr>
<td>IV Therapy</td>
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<tr>
<td>IV Morphine</td>
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<tr>
<td>100 microg IV Morphine = 10 microg IV Fentanyl</td>
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</tbody>
</table>

e.g. A 24-hour total dose of IV morphine equals 1mg, oral morphine equivalent will be 2mg. (daily oral dose is twice the daily IV dose)

IV fentanyl continuous infusion at 1 microgram/kg/hr in a 3kg patient

= 24 microgram/kg/day = 72 micrograms in 24 hours.

1 microgram of fentanyl is equivalent to 10 micrograms of IV morphine

Equivalent IV morphine 24 hour dose = 720 micrograms of IV morphine

Convert to oral morphine (Oral dose is twice the dose of IV morphine)

= 1440 micrograms of oral morphine in 24 hours

= 240 micrograms PO q6 hourly.

**Clonidine**

Clonidine is a centrally acting α2-adrenergic receptor agonist that inhibits sympathetic activity, and may significantly reduce the symptoms of opiate withdrawal with minimal adverse effects when used either as adjunctive therapy or monotherapy. Clonidine has been shown to reduce the overall duration of pharmacotherapy in NAS treatment. Clonidine may be administered via intravenous infusion or orally and the dosage is in micrograms per kg, refer to Neonatal Medication Protocol: Clonidine.
References


Related WNHS policies, procedures and guidelines

Neonatology Clinical Guideline - Neonatal Abstinence Syndrome (NAS)

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