

Newborn Critical Care Center (NCCC) Clinical Guidelines

Caffeine Therapy for Apnea of Prematurity

INTRODUCTION

Apnea in the premature infant can be caused by decreased central respiratory drive, inability to maintain airway patency, and other causes. The treatment of choice for central apnea, when indicated, is caffeine, and upper airway obstruction leading to apnea may be effectively treated with CPAP. Caffeine is a methylxanthine that acts as a central nervous system stimulant. The effects are mediated by its antagonism of the actions of adenosine at cell surface receptors in the medulla. It increases chemoreceptor sensitivity to CO₂ and the output of the respiratory center in the medulla.

The use of caffeine in the CAP trial (Schmidt et al) was associated with decreased risk of bronchopulmonary dysplasia (at 36 weeks PMA) and cerebral palsy at 2 years.

DRUG INFORMATION

Caffeine Citrate

- *Loading dose:* 20 mg/kg
- *Maintenance dose:* Initial maintenance dose suggested: 5 mg/kg every 24 hours
- *Maintenance dosing range:* 5-10 mg/kg every 24 hours
- *Monitoring:* Clinical response; consider holding dose if HR consistently >180 bpm
- *Adverse Effects:* Tachycardia, restlessness, vomiting, decreased seizure threshold

INDICATIONS TO START CAFFEINE

1. Ensure that there is no other attributable cause of apnea (i.e., infection, seizure, CNS abnormality).
2. < 30 weeks gestation:
 - a. Initiate caffeine on admission regardless of respiratory support, unless there is high likelihood that infant will remain on invasive respiratory support beyond postnatal day 10 due to evidence of non-statistically significant increase in mortality (Amaro, et al).
 - b. If clinical status worsens with significant increase in invasive respiratory support, consider discontinuing caffeine and reloading prior to next extubation attempt.
3. ≥ 30 weeks gestation:
 - a. Administer caffeine if apnea persists after initiating respiratory support (e.g., on CPAP)
4. For all infants, regardless of gestational age or postnatal age, consider caffeine load prior to extubation.

CAFFEINE USE DURING DEXAMETHASONE (DART) THERAPY

1. Caffeine should be initiated at the start of all DART courses to optimize respiratory drive during planned extubation attempts.
2. Continue caffeine for the full 10-day DART course, even if extubation is unsuccessful during the treatment course.

MAINTENANCE DOSING ADJUSTMENTS

In all above gestational age categories:

1. If worsening apnea, consider administering another loading dose of caffeine (10 mg/kg) and increase maintenance dose (up to 10 mg/kg/day) if:
 - a. No improvement in frequency or severity of apnea after initiation of caffeine
 - b. No improvement in frequency or severity of apnea despite escalation of positive pressure support
 - c. Increase in frequency or severity of apnea after prior stabilization
2. Adjust dosing for weight weekly (Mondays) as needed to target desired maintenance dose, rather than allowing infant to “outgrow” the dose.

DISCONTINUING CAFFEINE THERAPY

- Intubation and expected prolonged (> 48 hour) duration of mechanical ventilation
- Suggested end point of therapy is 32-34 weeks post menstrual age
- At the provider’s discretion – former ELBW infants may have symptoms past 34 weeks PMA

APNEA FREE COUNTDOWN

Infants who have been treated with caffeine must complete an apnea free countdown prior to discharge.

- Countdown may be initiated once at least 3 days have passed since the infant’s last dose of caffeine and the patient is no longer on positive pressure support or the infant is 36 weeks PMA, whichever is sooner.
- Patient should demonstrate at least 8 days without apnea prior to discharge. Document this in the chart as day 1 of 8 day apnea free countdown, day 2 of 8 apnea free countdown, etc.

POST OPERATIVE CAFFEINE FOR EXTUBATION

Discuss with Pediatric Surgery/Anesthesia prior to case whether postoperative caffeine to aid extubation is appropriate. In some cases, it may be more appropriate for the patient to return to the unit intubated to recover. If postoperative caffeine is administered, consider observing for a period of time for apnea prior to discharge.

References:

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3. Darnall RA, Kattwinkel J, Nattie C, Robinson M. Margin of safety for discharge after apnea in preterm infants. *Pediatrics*. 1997 Nov; 100 (5):795-801.
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