

## Guidelines for the administration of caffeine for apnea of prematurity

Caffeine is a methylxanthine - a class of medications that have been shown to significantly decrease the rate of clinically-evident apnea in preterm infants.<sup>1</sup> Caffeine is the preferred methylxanthine in the preterm population given its safety profile and relatively wide therapeutic window. In addition to apnea, caffeine administration may decrease need for mechanical ventilation, duration of ventilation, duration of oxygen, and development of chronic lung disease.<sup>1</sup>

### Initiation timing

- Caffeine should be initiated at the time of admission in any preterm infant <32 weeks of gestation

### Dosing

- Upon initiation, a loading dose of 20 mg/dose should be given
- Typical maintenance dosing ranges 5-15 mg/kg/day (our current standard is 10 mg/kg/day)
- Compared to maintenance doses <10 mg/kg/day, higher doses (10-20 mg/kg/day) have been associated with<sup>2-5</sup>:
  - Higher rates of successful extubations
  - Decreased chronic lung disease
  - Fewer apnea events
  - Shorter mechanical ventilation
  - Though higher rates of tachycardia
- There are no clear benefits to routinely obtaining serum caffeine levels, with the possible exception of ruling out caffeine toxicity in an infant with persistent tachycardia

### Discontinuation

- Significant interfacility differences exist with regard to timing of caffeine discontinuation<sup>6</sup>
- AAP guidelines suggest discontinuation of caffeine can be trialed when an infant meets either of the following (whichever comes first)<sup>7</sup>:
  - Has had 5-7 days free of clinically significant apnea/bradycardic off positive pressure ventilation (CPAP, NIMV, SiPap, or mechanical ventilation) OR
  - At 33-34 weeks' post-menstrual age (PMA)
- Continuation beyond 34 weeks' PMA can be considered on a case-by-case basis
  - Common exceptions to discontinuation at 34 weeks may include:
    - Infants on mechanical ventilation nearing a trial of extubation
    - Infants within 1 week after extubation
    - Infants with severe brain injury, CNS malformation, or genetic abnormalities that put them at increased risk for central apnea
  - Later caffeine may decrease intermittent hypoxia<sup>8, 9</sup>, though it is unclear whether these brief subclinical episodes of hypoxia are associated with any long- or short-term outcomes

- Discharge planning must be considered in these cases to avoid delaying discharge solely to “monitor off of caffeine”

### Discharge Timing

- The half-life of caffeine in preterm infants ranges from ~50 to >200 hours depending on the infant and the study<sup>10-12</sup>
- At 36-37 weeks PMA, the half-life decreases to 60-70 hours in most infants<sup>13</sup>
- For any infant born at <28 weeks gestational age, they should be monitored for at least 8-10 days after discontinuing caffeine to ensure that they do not develop clinically significant apnea<sup>14, 15</sup>
  - This should likely be longer in any infant born at <26 weeks (may need as long as 13-14 days)<sup>15</sup>

### References

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