

Clinical Evidence Series

Association Between Serum Caffeine Concentrations, Intermittent Hypoxia and Apnea in Preterm Infants: A Prospective Observational Study



What's different

Combining weekly serum caffeine measurements with continuous pulse oximetry histogram analysis can assess relationship between caffeine exposure, apnea of prematurity (AOP), and intermittent hypoxia (IH) in preterm infants ≤ 30 weeks' gestation.



Interpretation

Lower serum caffeine concentrations were associated with increased apnea during week 3 and greater intermittent hypoxemia burden during weeks 3-5. Histogram-derived SpO_2 data detected these relationships across multiple desaturation thresholds.



Key takeaways

Higher serum caffeine concentrations were associated with fewer intermittent hypoxia episodes across multiple SpO_2 histogram thresholds during weeks 3-5 of life.



Background

- Caffeine citrate is standard therapy for apnea of prematurity (AOP) and intermittent hypoxia (IH)
- Optimal serum caffeine targets and the role of routine therapeutic monitoring remain uncertain
- Intermittent hypoxia is associated with adverse neonatal outcomes including bronchopulmonary dysplasia, retinopathy of prematurity, and neurodevelopmental impairment



Objectives

Evaluate the relationship between serum caffeine concentrations, apnea of prematurity, and intermittent hypoxia in preterm infants ≤ 30 weeks' gestation.



Study design and methods

- Multicenter prospective observational cohort study conducted in two tertiary NICUs in Istanbul, Turkey
- 104 preterm infants ≤ 30 weeks' gestation received standard caffeine therapy with weekly serum caffeine measurements
- Continuous pulse oximetry histograms were used to quantify time spent below three SpO_2 saturation bands: $<80\%$, $80\text{--}85\%$, and $85\text{--}90\%$
- Associations between serum caffeine concentrations, apnea events, and intermittent hypoxia burden were evaluated longitudinally



Results

Gestational age:

Serum caffeine concentrations did not differ significantly between infants born at 23-27 weeks and 28-30 weeks' gestation.

Apnea: During week

3, infants with apnea demonstrated significantly lower serum caffeine concentrations than infants without apnea ($p = 0.016$).

Intermittent hypoxia: Higher serum caffeine concentrations were associated with fewer intermittent hypoxia episodes during weeks 3-5 across all three SpO_2 histogram thresholds. The strongest association occurred during week 4 at the $<80\%$ threshold ($r = -0.451$, $p < 0.001$).