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High versus low- dose caffeine for apnoea of prematurity: a randomized controlled trial

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Background: The optimum caffeine dose for apnoea of prematurity (AOP) has not been well investigated.

Objective: The main objective of this study is to compare the efficacy and safety of high versus low-dose caffeine citrate on AOP.

Methods: Prospective randomized study was conducted on preterm infants <32 weeks gestation, presented with AOP within the first 10 days of life. We compared high-dose (loading 40 mg/kg/day and maintenance of 20 mg/kg/day) versus low-dose (loading 20 mg/kg/day and maintenance of 10 mg/kg/day) caffeine citrate. The primary outcome was frequency and documented days of apnoea. Secondary outcomes included need for mechanical ventilation in non-ventilated infants; durations of mechanical ventilation, CPAP, and oxygen therapy; extubation failure; length of hospital stay; neonatal mortality; chronic lung disease; necrotizing enterocolitis; intra-ventricular haemorrhage; periventricular leukomalacia; retinopathy of prematurity; and caffeine side effects.

Results: A total of 120 neonates (60 in each group) were enrolled. High, compared to low, dose caffeine was associated with a significant reduction in the frequency of apnoea ($p<0.001$), days of documented apnoea ($p<0.001$), extubation failure ($p<0.05$), and duration of oxygen therapy ($p=0.04$). No significant effect was noted on other secondary outcomes. High- dose caffeine was associated with significant increase in episodes of tachycardia ($p< 0.05$) without a significant impact on physician decision to withhold caffeine.

Conclusion: High-dose caffeine is associated with decreased frequency of apnoea, fewer days of documented apnoea, shorter duration of oxygen therapy, and increased chance of successful extubation without a significant impact on neonatal mortality or morbidity.

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