

TITLE: THE ROLE OF CAFFEINE IN THE PREVENTION OF POSTOPERATIVE APNEA IN FORMER PREMATURE INFANTS: IF SOME IS GOOD, IS MORE BETTER?

AUTHOR: Leila G. Welborn, M.D., Raafat S. Hannallah, M.D., Robert Fink, M.D., and Jocelyn M. Hicks, Ph.D.

AFFILIATION: Departments of Anesthesiology, Pulmonary Medicine and Laboratory Medicine
Children's Hospital National Medical Center and George Washington University
Washington, D.C. 20010

The use of caffeine as a respiratory stimulant has been shown to be effective in the management of neonatal apnea and postoperative ventilatory dysfunction in former premature infants.^{1,2} In a recent study, the administration of a 5 mg/kg iv caffeine dose resulted in a significant reduction in the severity of postoperative apnea; complete abolition of all types of apnea, however, did not occur possibly because the caffeine blood level achieved was on the lower end of the ideal therapeutic range.² We designed this double blind, randomized, prospective study to examine the effectiveness of a higher dose of iv caffeine in the control of postoperative apnea in ex-premature infants.

Methods: Informed consent and institutional approval for the study were obtained. Former premature infants (< 37 weeks gestational age) undergoing general anesthesia (GA) for minor surgery were studied. All were < 44 weeks conceptual age at the time of surgery. Infants with cardiac, neurologic, endocrine or metabolic diseases and patients already receiving methylxanthines were excluded. All infants received inhaled endotracheal anesthesia with neuromuscular blockade. No barbiturates or narcotics were given. Heart rate and sounds, BP, ECG, temperature, respiration, ET CO₂ and O₂ saturation were monitored. Infants were randomly divided into two groups. Group 1 received iv caffeine 10 mg/kg. The drug was administered slowly immediately following induction so that its peak effect would be evident at the end of surgery. Group 2 received iv saline (controls). The solutions were supplied by the hospital pharmacy. At the completion of surgery, the trachea was extubated in the operating room when the patient was fully awake, and a venous blood sample was drawn to measure caffeine level. The pattern of respiration, heart rate and O₂ saturation were monitored and recorded for at least 12 hrs. postoperatively using a pneumogram with a magnetic tape recorder and Nellcor^(R) N-100 pulse oximeter respectively. The recorded data were analyzed by a pulmonologist for evidence of apnea, periodic breathing, bradycardia and desaturation. Brief apnea was defined as a respiratory pause < 15 secs. Prolonged apnea was a respiratory pause ≥ 15 secs. or < 15 secs. if accompanied by bradycardia. Bradycardia was indicated by heart rate < 100 bpm for at least 5 secs. Periodic breathing (PB) was noted as 3 or more periods of apnea lasting 3-15 secs. separated by < 20 secs. of normal respiration. Desaturation was an O₂ saturation < 95%. The difference in the incidence of apnea and desaturation between the two groups was compared using Fisher's exact test.

Results: 13 premature infants were studied. 7 received caffeine, and 6 received saline. There were no significant differences between the two

groups in gestational or conceptual ages. The incidence of apnea, PB and/or desaturation in the two groups is shown in the table. None of the patients in either group required endotracheal intubation postoperatively. The difference in the incidence of prolonged apnea with bradycardia and desaturation between the two groups is statistically significant (p < 0.005 and < 0.021 respectively).

Age, Incidence of Apnea, Periodic Breathing (PB) & Desaturation

	Group 1 n = 7	Group 2 n = 6	
Gestational age wk. (mean ± SD) (range)	31.0 ± 3.2 26-34	31.7 ± 2.6 28-35	
Conceptual age wk. (mean ± SD) (range)	41.9 ± 2.0 38-44	40.8 ± 1.8 39-44	N.S.
History of pre-op apnea	3(43%)	3(50%)	
Post-op apnea < 15 sec (no bradycardia)	1(14%)	none	
Post-op prolonged apnea with bradycardia	none	5(83%)	p < .005
Post-op PB > 1%	none	none	
Post-op desaturation < 95%	none	4(67%)	p < .021
Post-op caffeine level mg/L (range)	15-19	zero	

Discussion: Both theophylline and caffeine have been extensively used for the therapy of neonatal apnea. Caffeine 5 mg/kg has also been shown to be useful in the control of prolonged postoperative apnea but not brief apnea in premature infants.² The data from this study indicate that caffeine 10 mg/kg is effective in the control of all types of apnea in those infants. The caffeine blood level achieved (15-19 mg/L) with this dose is well within the recommended therapeutic range for this drug. It is still recommended, however, that until a larger sample of patients has been studied, all infants at risk be monitored for apnea and/or bradycardia following GA.

References: (1) Arranda JV, Grondin D et al. Pharmacologic considerations in the therapy of neonatal apnea. *Pedia Clin North Amer* 28:113-133, 1981. (2) Welborn LG, DeSoto H, Hannallah RS et al. The use of caffeine in the prevention of postanesthetic apnea in premature infants. *Anesthesiology* 67:A507, Sept. 1987.