COIN, CAP…..
Treat The Preemie with CPAP!!

KKUH
Riyadh neonatology Club Meeting


SPR 2007
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CAP Study

Caffeine for Apnea of Prematurity

Schmidt et al

Multi-center study (32 centers all over the world)

Primary outcome data presented as a late breaker this year

Neonatal short outcomes are already published in NEJM in 2006

Population	Preterm infants < 1250 gm Enrollment occurred in the 1st 10 days of life
Intervention	Caffeine (20mg/kg loading followed by a maintenance dose of 5-10 mg/kg)
Control	Equivalent volume of normal saline
Outcomes	Primary outcome- Composite of death or Neurosensory impairment at 18 month corrected age Secondary- all important neonatal morbidities

Baseline Characteristics

Table 1. Baseline Characteristics and Status of the Infants at Randomization and Their Mothers.*

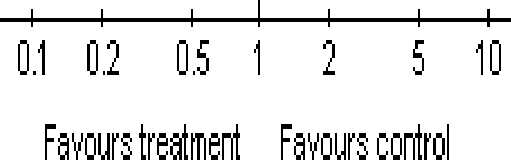
Characteristic	Caffeine Group (N=1006)	Placebo Group (N=1000)
Mothers		
Age — yr	30±6	30±6
Race or ethnic group — no. (%)†		
White	797 (79)	789 (79)
Black	67 (7)	71 (7)
Asian	84 (8)	82 (8)
Other or unknown	58 (6)	58 (6)
Antenatal corticosteroids — no. (%)	890 (88)	873 (87)
Clinical chorioamnionitis — no. (%)	138 (14)	133 (13)
Cesarean section — no. (%)	628 (62)	626 (63)
Infants at birth		
Birth weight — g	964±186	958±181
Gestational age — wk	27±2	27±2
Female sex — no. (%)	508 (50)	470 (47)
Birth weight <10th percentile for gestational age — no. (%)‡	161 (16)	158 (16)
Born at study hospital — no. (%)	903 (90)	890 (89)
Singleton birth — no. (%)	721 (72)	712 (71)
Apgar score at 5 min		
Median	8	8
Interquartile range	7–9	7–9

Neonatal Outcomes
BPD

Review: CAP
Comparison: 01 Caffeine vs. Placebo
Outcome: 01 BPD

Study or sub-category	Caffeine n/N	Control n/N	OR (fixed) 95% CI	Weight %	OR (fixed) 95% CI
CAP	350/1006	447/1000		100.00	0.66 [0.55, 0.79]
Total (95% CI)	1006	1000		100.00	0.66 [0.55, 0.79]

Total events: 350 (Caffeine), 447 (Control)
Test for heterogeneity: not applicable
Test for overall effect: Z = 4.53 (P < 0.00001)



Neonatal Outcomes
NEC

Review: CAP

Comparison: 01 Caffeine vs. Placebo

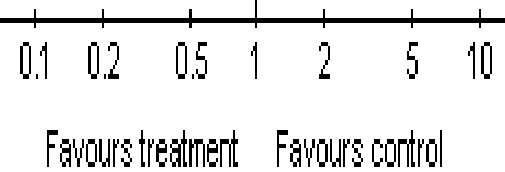
Outcome: 02 NEC

Study or sub-category	caffeine n/N	Control n/N	OR (fixed) 95% CI	Weight %	OR (fixed) 95% CI
CAP	63/1006	67/1000		100.00	0.93 [0.65, 1.33]
Total (95% CI)	1006	1000		100.00	0.93 [0.65, 1.33]

Total events: 63 (caffeine), 67 (Control)

Test for heterogeneity: not applicable

Test for overall effect: Z = 0.40 (P = 0.69)

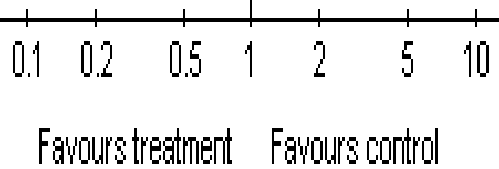


Neonatal Outcomes
Drug Therapy for PDA

Review: CAP
Comparison: 01 Caffeine vs. Placebo
Outcome: 03 Drug therapy for PDA closure

Study or sub-category	Caffeien n/N	Control n/N	OR (fixed) 95% CI	Weight %	OR (fixed) 95% CI
CAP	293/1006	381/1000		100.00	0.67 [0.55, 0.80]
Total (95% CI)	1006	1000		100.00	0.67 [0.55, 0.80]

Total events: 293 (Caffeien), 381 (Control)
Test for heterogeneity: not applicable
Test for overall effect: Z = 4.25 (P < 0.0001)



Neonatal Outcomes
PDA Surgical Closure

Review: CAP

Comparison: 01 Caffeine vs. Placebo

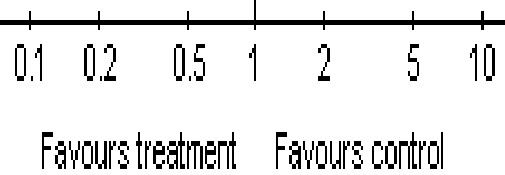
Outcome: 04 PDA Ligation

Study or sub-category	Caffeine n/N	Control n/N	OR (fixed) 95% CI	Weight %	OR (fixed) 95% CI
CAP	45/1006	126/1000		100.00	0.32 [0.23, 0.46]
Total (95% CI)	1006	1000		100.00	0.32 [0.23, 0.46]

Total events: 45 (Caffeine), 126 (Control)

Test for heterogeneity: not applicable

Test for overall effect: Z = 6.25 (P < 0.00001)



Body Weight Difference

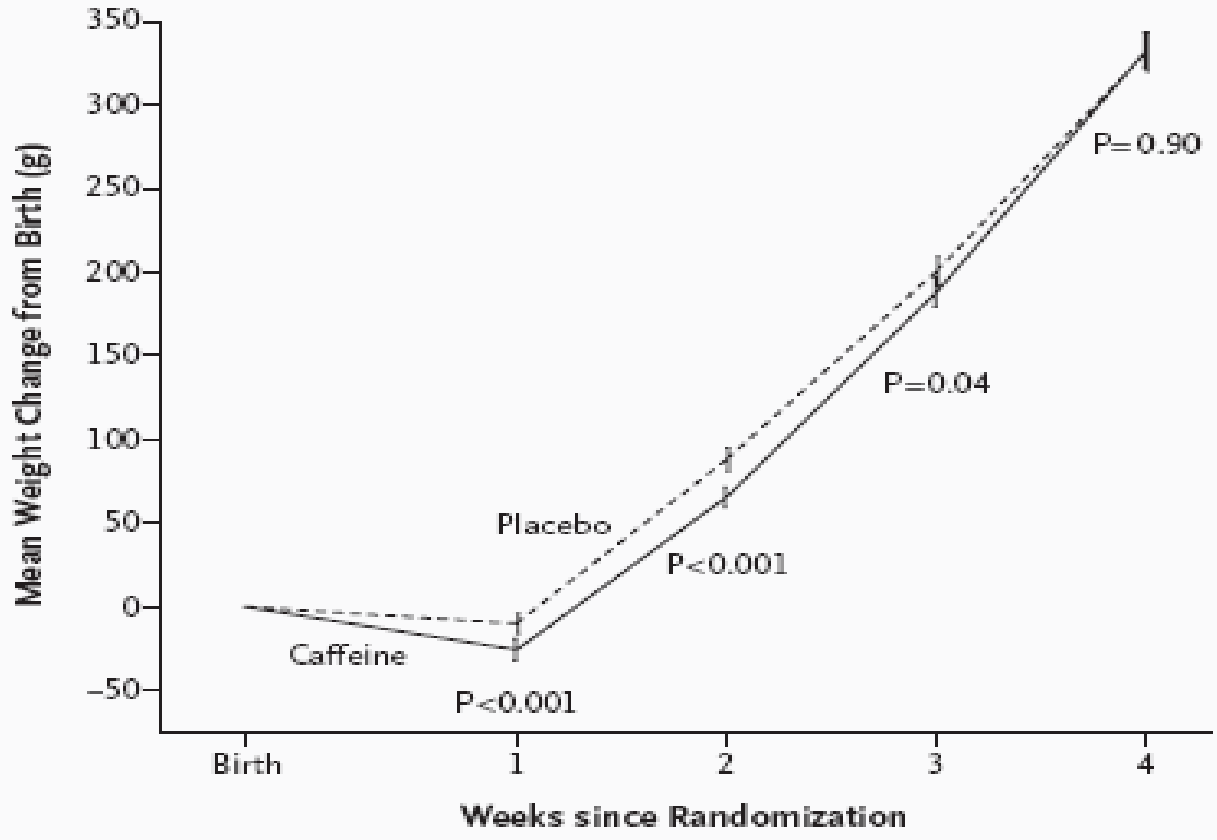


Figure 2. Mean Change in Body Weight during the First Four Weeks after Random Assignment to Caffeine or Placebo.

The mean difference in weight gain was −16 g after one week (95 percent confidence interval, −25 to −7), −23 g after two weeks (95 percent confidence interval, −32 to −13), and −13 g after three weeks (95 percent confidence interval, −25 to −0.4).

Long term Outcomes

93% follow-up rate at 18-21 months corrected age

Outcome	Caffeine	Placebo	OR (95% CI)
Death or Neurosensory impairment	40%	46%	0.77 (0.63,0.93) P=0.006
Cerebral palsy	4.4%	7.3%	0.58 (0.39,0.87) P= 0.009
Cognitive delay	34%	38%	0.8 (0.65, 0.98) P=0.03
Deafness	No Difference		
Blindness	No Difference		

COIN Study

Nasal CPAP or Ventilation for Very Preterm Infants at Birth. A Randomised Controlled Trial

Morley et al

Multicenter international study- 17 centers

Recruitment 1999-2006

Population	Preterm infants 25- 28^{+6} Enrollment occurred immediately after delivery if breathing at 5 minutes and needing respiratory support
Intervention	Immediate nasal CPAP at 8 cm H2O Given initially with nasopharyngeal tube via NeoPuff Then transferred into bi-nasal cannula in the NICU No Surfactant
Control	Mechanical Ventilation with Surfactant
Outcomes	Primary outcome: Death or oxygen requirement at 36 wks CGA

COIN Study

Criteria for intubation in the CPAP group:

Pco2 >60
Fio2 >60%
Apnea

610 infants enrolled
33% between 25-26 weeks
Mean bwt 940 g (215)
94% received antenatal steroids
67% delivered by CS

COIN Study

Outcome	CPAP	Ventilation	OR (95% CI)
Death or O2 treatment (28 days)	0.63 (0.46 to 0.87) p=0.006)		
Death or O2 treatment (36 weeks)	0.80 (0.58 to 1.12) p=0.21		
Surfactant use was halved			
50% of the CPAP group managed with no need for endotracheal intubation			
Pneumothorax	9%	3%	p<0.003
Mortality	No Difference		
No Difference in other neonatal morbidities (trends to better outcomes in the CPAP group)			