GENERAL

Abstracts 1-8

Moderators: Laura Riley, MD, President, SMFM; Vincenzo Berghella, MD, Immediate Past President; Wanda Barfield, MD, MPH, FAAP, 2016 Honorary Member

1 Antenatal Late Preterm Steroids (ALPS): a randomized trial to reduce neonatal respiratory morbidity

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OBJECTIVE: Infants born in the late preterm period are more susceptible to adverse neonatal outcome, particularly respiratory morbidity, than those born at term. Our objective was to assess whether administration of betamethasone (BMZ) in pregnancies at risk for late preterm delivery would decrease respiratory and other neonatal morbidities.

STUDY DESIGN: We performed a multicenter, double-blind, randomized controlled trial at 17 tertiary medical centers from 10/2010 to 2/2015. Women with non-anomalous, singleton gestations at high risk for indicated or spontaneous late preterm delivery (34 0/7 to 36 6/7 weeks) were randomized to 12 mg betamethasone intramuscularly or a matching placebo. A second dose was given at 24 hours if the patient was undelivered. The primary outcome was a composite of respiratory morbidity occurring by the first 72 hours of life including continuous positive airway pressure (CPAP) or high flow nasal cannula (HFNC) for ≥2 hours, oxygen (O2) requirement with FiO2 of ≥30% for ≥4 hours, any mechanical ventilation or perinatal death. A more severe respiratory morbidity extending O2 requirement to ≥24 hours and CPAP/HFNC to ≥12 hours was a prespecified secondary endpoint. Charts of all infants admitted to special care were centrally reviewed to verify respiratory outcomes. Our required sample size was 2,800.

RESULTS: 2,831 patients were randomized (1402 placebo, 1429 BMZ). Of those, 60% received 2 doses and 65.2% were <36 weeks. There was a significant reduction in the incidence of the primary outcome in the BMZ group compared with placebo (Table). Severe respiratory morbidity, TTN and surfactant use were also reduced. There were no significant differences in the incidence of chorioamnionitis or neonatal sepsis, but hypoglycemia was more common in the BMZ group.

CONCLUSION: Administration of betamethasone for women at risk for late preterm delivery was associated with decreased serious neonatal respiratory morbidity and the need for surfactant.

	Placebo (n=1400, 49.5%) n (%)	Betamethasone (n=1427, 50.5%) n (%)	RR (95% CI)	*P* val*
Primary outcome	202 (14.4)	165 (11.6)	0.80 (0.66-0.97)	0.023
Severe respiratory morbidity	169 (12.1)	115 (8.1)	0.67 (0.53-0.84)	<0.001
RDS	89 (6.4)	79 (5.5)	0.87 (0.65-1.17)	0.356
TTN	138 (9.9)	95 (6.7)	0.67 (0.53-0.87)	0.002
Surfactant use	43 (3.1)	26 (1.8)	0.59 (0.37-0.96)	0.031
Chorioamnionitis	32 (2.3)	20 (1.4)	0.61 (0.35-1.07)	0.080
Proven Neonatal Sepsis	11 (0.8)	9 (0.6)	0.80 (0.33-1.93)	0.623
Neonatal hypoglycemia (glucose <40 mg/dl)	210 (15.0)	343 (24.0)	1.60 (1.37-1.87)	<0.001
Gestational age at delivery#	36.1 ± 8.2	36.1 ± 7.5		0.517**
Time from initial dose to delivery (hours; median [^Q3, Q1])	30.6 (14.6-111.0)	33.0 (15.2-111.6)		0.565

* Chi-square unless otherwise indicated
**Wilcoxon
^4 patients were lost to follow-up
#Mean (weeks ± SD, days)
^ QxQuartile

2 Effect of treatment of maternal subclinical hypothyroidism or hypothyroxinemia on IQ in offspring

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OBJECTIVE: To determine whether treatment of pregnant women identified with either subclinical hypothyroidism or hypothyroxinemia in the first half of pregnancy improves cognitive function in offspring at five years of age.

STUDY DESIGN: This multicenter study consists of two randomized, double-masked, placebo-controlled trials run in parallel. Women with a singleton gestation presenting for care before 20 weeks' gestation underwent thyroid screening using serum TSH and free T4. Women with a TSH ≥ 4.0 mU/L and a free T4 in the normal range (0.86-1.9 ng/dL) were considered to have subclinical hypothyroidism. Those with a normal TSH (0.08 - 3.99 mU/L) but a free T4 < 0.86 ng/dL were considered to have hypothyroxinemia. Eligible and consenting women were randomized to either levothyroxine replacement or an identical placebo. Maternal thyroid function was assessed monthly and study drug adjusted to attain TSH or free T4 goals. Sham adjustments in placebo were used to maintain blinding. Developmental testing of offspring was performed annually including DAS II at age 3-years and IQ score using WPPSI-III at 5 years of age. If an infant was lost to follow-up after 3 years of age, the DAS II was substituted for the primary outcome. If an infant died prior to 3-year testing they were assigned a score of zero. Sample size estimates for each strata were based on 80% power to detect a 5-point IQ difference between treatment groups.

RESULTS: Between October 2006 and October 2009, 97,226 pregnant women underwent thyroid screening. There were 3,058 women (3.1%) identified with subclinical hypothyroidism, of which 677 (22.1%) were eligible and randomized. There were 2,805 women (2.9%) identified with hypothyroxinemia and 526 (18.8%) were eligible and randomized. The mean gestational age at randomization was 17 weeks. WPPSI-III scores at 5 years of age were obtained in 1,110 (92.3%) of the 1203 offspring, 23 children were lost to follow-up after DAS II testing, and 22 infants died prior to 3-year testing.

CONCLUSION: Treatment of women identified with either subclinical hypothyroidism or hypothyroxinemia during the first half of pregnancy did not result in improved cognitive outcome in offspring at 5 years of age.

Table: Median IQ Scores According to Trial and Treatment Group

Study Group	Placebo	Levothyroxine	P value
Subclinical Hypothyroidism*	N=325 94 [85, 107]	N=323 97 [85, 105]	0.76
Hypothyroxinemia*	N=253 91 [82, 101]	N=254 94 [83,101]	0.30

* Data shown as Median IQ Score [25th %ile, 75th %ile]