PREMATURITY

Abstracts 9-19

9 Randomized controlled trial of n-acetylcysteine to prevent adverse neonatal outcome in pregnancies with intra-amniotic infection/inflammation

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OBJECTIVE: Compelling animal data suggests restoration of maternal-fetal oxidative balance by N-acetylcysteine (NAC) may reduce risk of adverse neonatal outcome in pregnancies complicated by intra-uterine infection/inflammation. We aimed to evaluate if maternal administration of NAC lowers risk of morbidity or death in infants of women with intra- amniotic infection (IAI).

STUDY DESIGN: In a randomized, placebo-controlled, double-blind trial we assigned women from 23-33 weeks' gestation with an indication for delivery in the context of IAI to receive NAC or placebo. IAI was diagnosed in all cases by trans- abdominal clinically indicated amniocentesis. NAC was administered intravenously (IV) 150 mg/kg loading dose (1 h), followed by 50 mg/kg IV continuous infusion rate for 4 h, and followed by 100 mg/kg IV continuous infusion rate until delivery. The primary outcome was a composite of mortality and severe short-term neonatal morbidities at discharge from NICU. Maternal and umbilical cord plasma levels of NAC, endogenous free thiols (cysteine [CYS], cysteine-glycine [CYS-GLY], glutathione [GSH]) were analyzed by HPLC. Cytokines were quantified by multiplex immunoassay.

RESULTS: A total of 68 women pregnant with singletons were randomized. Demographics and clinical characteristics of the groups were similar (Table). Bolus administration was achieved in 98% of women with 42% of women completing the 4 h dose. The rate of the primary outcome was significantly different between the NAC (12%) and placebo (32%) groups: RR: 0.31 (95% CI 0.11-0.85), p=.023, with the highest protection achieved for broncho-pulmonary dysplasia (BPD), RR: 0.09 (95% CI 0.01-0.07), p=.019], independent of gestational age or sex. In both maternal and fetal compartments, the achieved concentration of NAC significantly correlated to CYS (r=0.92, p<.001) and CYS-GLY (0.63, p=.005). NAC did not impact on the fetal cytokine profile or red blood cells GSH.

CONCLUSION: Fetal exposure to NAC prior to an impending preterm birth in the context of IAI significantly reduced the rate of the primary composite neonatal outcome, with the highest protection against BPD. Protective mechanism of NAC may involve increase in anti-oxidative pool of endogenous thiols. Intrapartum NAC infusion is practically feasible, safe and does not increase frequency of neonatal sepsis.

Variables	NAC n=34	Placebo n=34	p value
Characteristics			
GA at delivery, *weeks* *	27.3 [23.9-30.5]	27.4 [25.4-30.50]	0.878
PPROM †	23 (68)	19 (56)	0.454
Duration of infusion, *h* *	5.2 [2.9-11.1]	3.7 [2.9-11.1]	0.087
Infusion volume, *mL* *	344 [266-475]	300 [243-363]	0.158
Birth weight, *g* *	1095 [815-1605]	995 [808-1553]	0.922
Cesarean delivery †	11 (32)	12 (35)	1.000
Newborn male sex †	15 (44)	16 (47)	1.000
Apgar at 1 min *	8 [5-8]	7 [3-8]	0.089
Apgar at 5 min *	9 [8-9]	8 [6-9]	0.014
Outcomes			
Primary outcome †‡	**4 (12)**	**13 (38)**	**0.023**
BPD †	1 (3)	11 (32)	0.001
Sepsis, early onset †	1 (3)	2 (6)	1.000
Sepsis, late onset †	8 (24)	10 (30)	0.590
Newborn deaths †	2 (6)	6 (18)	0.259

* Data presented as median [interquartile range] and analyzed by Mann- Whitney test
† Data presented as n (%) and analyzed by Fisher's exact test
‡ Composite of IVH gr.2-4, NEC gr.2-4, ROP gr.2-4, BPD and death

10 Stress, local immune responses, and spontaneous preterm birth risk in a majority African American cohort

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OBJECTIVE: The role of host immunity and maternal psychosocial stress in the pathogenesis of spontaneous preterm birth (sPTB) remains unclear. Antimicrobial proteins in the cervicovaginal CV) space, such as beta-defensins (βD), modulate immune responses to bacteria. While stress is known to induce immunological changes, no study has examined the interplay between stress and the CV immune response in association with sPTB.

STUDY DESIGN: From the *Motherhood & Microbiome* cohort (n=2000), we performed a nested case-control study of 519 pregnant women (110 sPTB and 409 term). Stress and CV-βD were measured at 16-20 weeks' gestation. Stress was dichotomized at 30 on Cohen's Perceived Stress Scale (PSS-14). We measured CV-βD with ELISA and dichotomized at the median. We compared sPTB rates with Chi-Square tests and modeled adjusted associations of stress and CV-βD with odds of sPTB with logistic regression.

RESULTS: In the dataset, 73% were African American, 64% were overweight or obese, 31% were married, 51% had Medicaid insurance, and 20% had a PSS-14 score >30. Median CV-βD levels were 17,098 pg/mL, IQR: 64,559. The cohort sPTB rate was 6%, but 21% in the analytic dataset. sPTB rates were 28% and 19% with high and low stress, respectively, and 24% and 18% with low and high CV-βD levels, respectively. Women with both low stress and high βD had the lowest sPTB rate (17%) and women with both high stress and low βD had the highest rate of sPTB (38%) (Fig 1). In adjusted models, high stress and low βD were each associated with increased odds of sPTB (aOR 1.8 (1.1- 3.0) and 1.6 (1.001-2.5), respectively),