PREMATURITY

Abstracts 9 – 17

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9 17-Alpha-hydroxyprogesterone caproate for the prevention of preterm birth in women with prior preterm birth and a short cervical length

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OBJECTIVE: To evaluate 17-alphahydroxy-progesterone caproate (17P) for the prevention of preterm birth (PTB) in women with prior spontaneous PTB (SPTB) and a short cervical length (CL).

STUDY DESIGN: This is a planned secondary analysis of the NICHD-sponsored randomized trial evaluating cerclage for women with singleton gestations, prior SPTB (17-33 6/7 wks), and short CL < 25 mm measured between 16 and 22 6/7 wks. Women were stratified at randomization to the intent to use or not use 17P. Subsequent use of 17P was recorded. The effect of 17P use was analyzed separately for the cerclage and no cerclage groups. The primary outcome was PTB < 35 wks. Secondary outcomes included birth < 7 days from randomization, PTB < 24 and < 37 wks, and perinatal death. Maternal age, race, smoking, drug use, shortest CL and intent to use 17P were considered as possible confounders.

RESULTS: 302 women were randomized and 300 were available for analysis. Of these, 148 were randomized to cerclage and 152 to no cerclage. 17P had no effect on PTB < 35 wks in either the cerclage (p=0.64) or the no cerclage (p=0.51) groups. Shortest CL was a significant variable in both the cerclage and no cerclage multiple logistic regression models. The odds of PTB <24 wks (OR=0.08, p=0.0022) and perinatal death (OR=0.14, p=0.0029) were significantly lower for those with 17P in the no cerclage group. See Tables 1 and 2.

CONCLUSION: 17P in women with a prior SPTB and a short CL < 25 mm at 16-22 6/7 weeks is not associated with PTB < 35 wks. In the absence of cerclage, 17P may reduce previable birth and perinatal mortality.

Table 1. Cerclage group

	17P (n=47)	No 17P (n=101)	Significance
PTB <35 wks - no. (%)	14 (29.8%)	34 (33.7%)	p=0.64
Birth < 7 days from randomization - no. (%)	0 (0.0%)	4 (4.0%)	p=0.31 *
Previable birth < 24 wks - no. (%)	2 (4.3%)	7 (6.9%)	p=0.72 *
Preterm birth < 37 wks - no. (%)	23 (48.9%)	43 (42.6%)	p=0.47
Perinatal death - no. (%)	3 (6.4%)	10 (9.9%)	p=0.76 *

Table 2. No cerclage group

	17P (n=52)	No 17P (n=100)	Significance
PTB <35 wks - no. (%)	20 (38.5%)	44 (44%)	p=0.51
Birth < 7 days from randomization - no. (%)	0 (0.0%)	3 (3.0%)	p=0.55 *
Previable birth < 24 wks - no. (%)	1 (1.9%)	20 (20.0%)	p=0.0022 *
Preterm birth < 37 wks - no. (%)	31 (59.6%)	59 (59.0%)	p=0.94
Perinatal death - no. (%)	2 (3.9%)	23 (23.0%)	P=0.0029 *

*Fisher's exact test

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10 Hap-tag SNPs in genes that regulate the inflammatory response and bacterial vaginosis: evidence of gene-environment interactions associated with spontaneous preterm delivery

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OBJECTIVE: We demonstrated previously that genetic variation within genes that regulate the maternal inflammatory response are associated with an increased risk of spontaneous preterm delivery (SPTD). We sought to determine if an environmental exposure associated with maternal inflammation, bacterial vaginosis (BV), modifies these genetic susceptibilities.

STUDY DESIGN: We conducted a prospective cohort study in which maternal DNA samples were collected from 744 women, and demographics and outcomes data were recorded. Vaginal smears for Gram-staining were obtained from subjects at 26-28 wk gestation. We studied hap-tag SNPs in 5 BioCarta and KEGG pathways in which >3 SNPs were strongly associated (P<0.01) with SPTD at <37 weeks (Illumina GoldenGate 1,536-SNP custom chip panel). Associations between genotype distributions and SPTD were examined using Fisher's exact tests.

RESULTS: In our cohort, 68 women experienced SPTD at <37 wk, while 676 women delivered at term (9.1% SPTD rate). 306 women had asymptomatic BV (Nugent score ≥7) at 26-28 wk, and BV was not associated with an increased risk of SPTD (P=0.30). 20 hap-tag SNPs were associated with an increased risk of SPTD (P<0.05) in the BV+ group. For 9 SNPs in 3 genes (FLT1, PRKCA, and IL6), the OR of SPTD ranged from 2.0-7.0 among BV+ women who were carriers of the rare allele, and the OR for SPTD were 2.0-5.0 times greater among BV+ women than among BV- women (P<0.05 for test of homogeneity between ORs).

CONCLUSION: These results demonstrate that the risk of SPTD associated with hap-tag SNPs in genes that regulate the maternal inflammatory response is modified by environmental exposures such as BV. Additional studies to identify functional SNPs within these hap-tag regions and potential mechanisms by which gene-environment interactions cause SPTD are warranted.

Odds Ratios of SPTD for the minor allele in 3 hap-tag SNPs, stratified by BV status

SNP	Gene	OR Overall	OR BV (−)	OR BV (+)
rs17686640	PRKCA	2.5 (1.0, 6.2)	2.0 (0.2, 17.0)	7.0 (1.8, 26.4)
rs1990503	PRKCA	2.0 (1.3, 3.2)	0.8 (0.3, 2.6)	4.0 (1.7, 9.0)
rs1800795	IL6	1.6 (1.1, 2.5)	1.2 (0.6, 2.7)	3.0 (1.4, 6.2)

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