Continental Ballroom 1-9, Hilton San Francisco

1 A RANDOMIZED CONTROLLED TRIAL OF 17-HYDROXYPROGESTERONE CAPROATE (17-OHPC) FOR THE PREVENTION OF PRETERM BIRTH IN TWINS

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OBJECTIVE: 17-OHPC has been shown to reduce the rate of recurrent preterm birth in singleton gestation. This study was undertaken to evaluate whether 17-OHPC would reduce the rate of preterm birth in twin gestation.

STUDY DESIGN: We performed a randomized, double masked, placebo controlled trial in 14 centers. Healthy women with twin gestation and uniformly established gestational age were allocated to either weekly 250 mg intramuscular injections of 17-OHPC, or matching placebo, starting at 16-20 weeks and ending at 35 weeks' gestation. The primary study outcome was delivery prior to 35 weeks. Power was 90% to detect a 1/3 reduction in the primary outcome rate.

RESULTS: Six hundred sixty one women were randomized. Baseline demographic data were similar in the two study groups including gestational age at randomization, maternal age, race, BMI, parity, prior preterm birth, smoking, marital status, chorionicity as diagnosed by ultrasound, and conception method. Six women (<1%) were lost to follow-up. Primary and selected secondary outcomes are provided in the Table.

Outcomes	17-OHPC	Placebo	RR (95% CI)
	n =325	n =330	
Delivery <35 weeks			
Overall	135 (42%)	123 (37%)	1.1 (0.9, 1.3)
By indication			
Spontaneous	101/324 (31%)	86/330 (26%)	1.2 (0.9, 1.5)
Indicated	33/324 (10%)	37/330 (11%)	0.9 (0.6, 1.4)
By chorionicity			
Mono	29/56 (52%)	26/53 (49%)	1.1 (0.7, 1.5)
Di	104/267 (39%)	95/273 (35%)	1.1 (0.9, 1.4)
By conception method			
ART	48/122 (39%)	38/108 (35%)	1.1 (0.8, 1.6)
Spontaneous	87/203 (43%)	85/222 (38%)	1.1 (0.9, 1.4)
Delivery <32weeks	54 (17%)	46 (14 %)	1.2 (0.8, 1.7)

CONCLUSION: Treatment with 17-OHPC did not reduce the rate of preterm birth in women with twins.

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2 LONG TERM FOLLOW-UP OF INFANTS RECEIVING SINGLE VS REPEAT COURSES OF ANTENATAL CORTICOSTEROIDS (ACS) FROM THE MFMU RCT

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OBJECTIVE: In the RCT, repeat courses of ACS improved specific neonatal respiratory outcomes but reduced birth weight and increased IUGR, especially in infants that received 4 or more courses. Here we report the 2 year follow up evaluation.

STUDY DESIGN: Woman between 24 and 32 weeks gestation remaining pregnant 7 days after an initial course of ACS were randomized to weekly courses of betamethasone or a placebo. Between 22 and 36 months corrected age a physical examination and Bayley MDI and PDI were performed by trained examiners using standardized criteria.

RESULTS: From the 495 women randomized (581 surviving infants), 484 infants (83.3%) had physical exams and 465 (80.0%) had Bayley exams. There were no differences in gestational age at delivery, latency period or frequency of twins. At follow-up (Table), there were no differences in anthropometric measurements or Bayley results. However, more in the repeat group had cerebral palsy (RR 5.68: 95%: CI 0.69, 46.7). 5 of the 6 infants with CP in the repeat group received ≥4 courses and 5 were beyond 33 weeks at delivery. The mean GA at birth of the infants with CP in the repeat group was 35 wks.

Infants with physical exam *	N*	Weight kg	HC cm	Bayley PDI	Bayley MDI	CP n	CP % (of pregs)	CP ≥4courses %	CP + Death ≥4courses %
Placebo	236	13.7	49.1	93.8	86.4	1	0.5	0.8	1.4
Repeat	248	13.5	49.0	95.8	86.2	6	2.9	3.6	5.6

CONCLUSION: At 2 years there was no difference in weight, head circumference, or Bayley scores between infants exposed to single vs. repeat courses of ACS. Although not statistically significant, the rate of CP in infants exposed to multiple courses is concerning. We suggest that exposure to repeat courses of ACS should be limited.

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3 PERI-OPERATIVE PROGNOSTIC FACTORS IN TWIN-TO-TWIN TRANSFUSION SYNDROME TREATED BY FETOSCOPIC LASER OCCLUSION OF CHORIONIC PLATE ANASTOMOSES

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OBJECTIVE: To describe peri-operative prognostic factors of survival without impairment in twin-to-twin transfusion syndrome (TTTS) treated by fetoscopic laser occlusion of chorionic plate anastomoses.

STUDY DESIGN: Monochorionic pregnancies complicated with severe TTTS and treated by fetoscopic laser surgery were reviewed between 1999 and 2005. Peri-operative factors studied included maternal characteristics, severity of the fetal syndrome and characteristics of surgical procedures and were collected prospectively but analysed retrospectively. Primary outcome was survival >28 days of at least one twin without severe impairment. Univariate and multivariate analyses using logistic regression were conducted.

RESULTS: 10 of a total of 323 cases were lost to follow-up and excluded from analysis. Median gestational age at diagnosis (25th, 75th percentile) was 21 (19, 23) weeks of gestation. Distribution across Quintero stages was: 17.4%, 40.2%, 37.3% and 5.1% for stages 1, 2, 3 and 4 respectively. Overall survival rate of at least one twin without severe impairment was 65%. Significant factors found in univariate analysis were donor and recipient estimated weight at diagnosis ($p=0.02$, OR = 1.77 [1.07-2.96] and $p=0.001$, OR = 2.12 [1.27-3.59] respectively), discordant growth ($p=0.04$, OR = 1.66 [1.01-2.77]), number (≥4 vessels) and proportion (≥60% of all coagulations) of selective coagulations (($p=0.01$, OR = 1.81 [1.11-2.99]) and ($p=0.02$, OR = 1.77 [1.08-2.92]) respectively) as well as amniotic fluid volume ≥1 litre drained ($p=0.001$, OR = 2.18 [1.26-3.79]). Multivariate analysis showed that only the recipient's estimated weight at diagnosis and selective coagulations ≥4 during the procedure were significantly predictive of survival ($p=0.002$, OR = 2.20 [1.34-3.63] and $p=0.001$, OR = 1.89 [1.17-3.07] respectively).

CONCLUSION: In severe TTTS treated by fetoscopic laser occlusion of chorionic plate anastomoses, peri-operative prognosis is based upon estimated fetal weight at diagnosis and selectivity of the procedure.

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4 COMPREHENSIVE PROTEOMIC ANALYSIS OF HUMAN CERVICAL-VAGINAL FLUID AND IDENTIFICATION OF NOVEL BIOMARKERS FOR PREDICTION OF SPONTANEOUS PRETERM BIRTH

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OBJECTIVE: To characterize the cervical-vaginal proteome in pregnancy and to identify novel protein biomarkers for positive prediction of spontaneous preterm birth (SPTB).

STUDY DESIGN: CVF samples were collected prospectively from 2005-2006 at Oregon Health & Science University from women in preterm labor (PTL) <37 weeks and gestational age matched asymptomatic controls. All subjects had IAI excluded by placental histopathology and/or amniocentesis. CVF samples were analyzed using fluorescence two-dimensional differential in-gel electrophoresis (2D-DIGE), multidimensional liquid chromatography tandem mass spectrometry (2D-LC-MS/MS) and label-free quantification (spectral counting). Pair-wise comparison was performed using χ^2 goodness-of-fit tests. Significance for each protein was determined after adjusting for multiple comparisons via the false-discovery rate (FDR) method. Western blots for specific targets were used to confirm differential expression.

RESULTS: Of 60 subjects, 23 (54%) had SPTB < 37 weeks, 15 had PTL but delivered at term, 22 were asymptomatic controls. Comprehensive proteomic analysis of CVF revealed 206 unique proteins. Major functional categories in the CVF proteome were metabolism (33%) and immune response-related (22%) proteins. Label-free quantification identified 23 proteins in CVF, which exhibited significant differences in pair-wise comparisons and 16 proteins in progressive comparisons from asymptomatic to PTL to SPTB groups. Potential biomarkers included calcium modulators (Calgranulins, annexins, S100 calcium-binding protein A7), acute phase reactants (α-1-antitrypsin, α-1-acid glycoprotein, serotransferrin, haptoglobin) extracellular matrix proteins (fibronectin, epidermal fatty acid binding protein), and abundant proteins in amniotic fluid (IGFBP1 and vitamin D binding protein).

CONCLUSION: This dataset provides a foundation for evaluation of CVF protein biomarkers in pregnancy. Further characterization and quantification of SPTB markers in a larger cohort could provide the basis for non-invasive prediction of preterm birth.

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