110 N-ACETYLCYSTEINE PREVENTS PRETERM BIRTH IN AN INTRAUTERINE INFLAMMATORY MODEL OF PRETERM LABOR

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OBJECTIVE: Intrauterine infection is strongly associated with preterm birth particularly at early gestations. Additionally, it is associated with an increased risk of neurologic impairment in survivors. We hypothesized that NAC, a potent anti-inflammatory and antioxidant, would decrease preterm birth and evidence of maternal and fetal inflammation in an infectious model of preterm birth.

STUDY DESIGN: On day 15, timed-pregnant CD-1 mice were given LPS (100 g) or saline via intrauterine injection. They also were randomly assigned to receive either subcutaneous NAC (100 mg/kg) or saline 60 minutes prior to LPS administration. Animals were monitored until delivery. In another set of NAC-treated and untreated animals, LPS or saline was given and the animals were sacrificed at 6 hours and myometrium, placenta, and fetal brain were collected. RT-PCR was performed to determine the expression of IL-6 in these tissues. RT-PCR for expression of TNF- in fetal brain was also performed.

RESULTS: Intrauterine LPS administration is associated with a high rate of preterm delivery within 24 hours compared with controls (79% vs 0%, $p < .005$). NAC treatment significantly reduced preterm delivery [0.45 (95% CI: 0.26-0.83), $p<.008$]. Additionally, LPS administration was associated with an increased expression of IL-6 in myometrium ($p<.03$) and the placenta ($p<.001$). This effect was significantly attenuated with NAC in myometrium ($p<.039$). There was a non-significant increase in IL-6 in the fetal brain and a significant increase in TNF- (<0.01) with LPS adminstration. NAC treatment was associated with a non-significant reduction in TNF- expression.

CONCLUSION: NAC reduces preterm birth in this animal model and may reduce the maternal response in the setting of intrauterine inflammation. Further investigation is warranted to determine whether it can be useful in the prevention of preterm birth.

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111 EFFECT OF PROGESTERONE ON BIOMECHANICAL PROPRIETIES OF CERVIXES FROM RATS EXPOSED TO LPS

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OBJECTIVE: Preterm birth is the leading cause of neonatal morbidity and mortality in the developed country and its prevalence increased in the last years. Administration of progesterone in high risk women may reduce the risk of preterm birth. The aim of this study was to explore the effect of progesterone on the biomechanical properties of cervixes from rats injected with lipopolysaccharides (LPS) to create an inflammatory status.

STUDY DESIGN: Time-pregnant Sprague-Dawley rats were intraperitoneally injected with LPS (500 μg/kg), or an equivalent volume of vehicle, for 3, 6, 12, or 24 hours before laparotomy performed at 22 days of gestational age. Trachelectomy were performed and cervixes were equilibrated in isolated organ baths. This system was used as cervimeter, which stretches the cervical tissues in incremental steps of 0.74 mm at 10-minutes intervals. Biomechanical properties were analyzed in term of maximal amplitude, residual tension and contractions frequency of the cervix. Cervixes were randomly assigned into two groups, with or without progesterone pre-treatment in organ bath (100 μM for 30 min). Statistical analysis included Student's t-test and $p<0.05$ were considered significant.

RESULTS: Mechanical responses from 15 cervixes were analyzed in this new model. The maximal amplitude ($p<0.0001$) and contractions frequency ($p=0.19$) were increased in the LPS group compared to the control group. Our data also showed differences in term of passive tension between cervixes exposed to LPS for 3 and 12 h ($p<0.0001$), the tension being higher in the 3 h group. In the LPS group, we didn't observe any effect of progesterone in term of maximal amplitude ($p=0.56$) and residual tension ($p=0.32$) of the cervix.

CONCLUSION: Our data demonstrate that cervixes, from pregnant rat treated with LPS, display significant differences in their passive and active biomechanical properties. However, acute progesterone treatment didn't modify the mechanical behavior of the cervix.

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112 PRETERM LABOR BIOMARKER DISCOVERY IN SERUM USING PROTEOMIC TECHNOLOGY

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OBJECTIVE: To identify changes in protein expression in normal pregnancy compared to those complicated by preterm labor using 3 proteomic methods in their ability to identify differential protein expression.

STUDY DESIGN: Serum was collected from 25 women: nonpregnant (n=5) and pregnant at 24-40 wks (n=20) who had preterm labor resulting in preterm delivery (PLPTD, n=5), preterm labor with term delivery (PLTD, n=5), term labor resulting in delivery (TLTD, n=5) or at term with contractions (n=5). Undepleted sera was used for SELDI, performed on IMAC30, H50, CM10 and NP20 surfaces and immunodepleted serum for MALDI and 2D electrophoresis (2DE).

RESULTS: SELDI identified significantly different peaks ($p<0.05$, Mann Whitney Rank Sum) between PLPTD vs TLTD and PLPTD vs PLTD using 4 surfaces. In PLPTD vs PLTD, a peak at 7783.2 m/z was significantly upregulated ($p<0.001$) and another at 3164 m/z downregulated ($p<0.05$, Mann Whitney Rank Sum) on three surfaces tested. Analysis of 2DE data identified protein 5364 to be significantly different ($p<0.05$, ANOVA & post-hoc Tukey's HSD) between PLPTD and TLTD. In PLPTD, six proteins showed a trend towards decrease and one towards an increase vs PLTD. MALDI showed the most striking difference at 55,000 m/z, between PLPTD and TLTD. Peak intensity differences were also observed in PLPTD vs PLTD.

CONCLUSION: SELDI identified significant differences in several proteins. Two proteins (7783.2 m/z and 3164 m/z) fulfill the criteria of putative biomarkers being found on 3 out of 4 surfaces tested and with AUC of 1 and 0 respectively. Identification of these two biomarkers may aid in identifying women with preterm labor who will deliver preterm. MALDI provided a qualitative assessment of the differences, while SELDI and 2DE provided quantitative and statistically relevant comparisons of differences observed. Protein expression profiles differed in sera of preterm or term women regardless of proteomic methodology used.

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113 NEONATAL AND DEVELOPMENTAL OUTCOMES IN CHILDREN BORN IN THE LATE PRETERM PERIOD VERSUS TERM

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OBJECTIVE: Neonatal outcomes are poorer for late preterm (LP) (34′0 to 36′6 wks) compared with term infants. The brain undergoes significant maturation during the LP period, suggesting long term neuro-developmental outcomes may be affected. We evaluated differences in morbidity at birth and indicators of potential developmental delay for infants born at 34, 35, or 36 completed weeks, compared with infants born at ≥39 weeks, using the Ages and Stages Questionnaire (ASQ), a screening tool validated against the Bayley and McCarthy Scales that identifies children needing further evaluation.

STUDY DESIGN: LP children of participants in a randomized placebo-controlled trial of 17 OHPC to prevent recurrent preterm delivery were compared with 39' week children from the same study; congenital malformations were excluded. Follow-up occured at a subset of the participating centers. If a child scored <2 SD below population-derived means on 1 or more of 5 domains, the ASQ was considered abnormal. ASQ and height/weight percentiles were evaluated between groups. Composite neonatal morbidities (respiratory distress syndrome, necrotizing enterocolitis, intraventricular hemorrhage, hyperbilirubinemia, sepsis, ventilator support, or death) were also evaluated.

RESULTS: 287 neonates were included; 145 were followed up at a median age of 48 months (range 32-64). Neonatal morbidity decreased with increasing gestational age ($p<0.0001$). There were no differences in ASQ performance. Height/weight percentiles were also similar. Adjusting for treatment group and race yielded similar results.

CONCLUSION: Despite increased neonatal morbidity, ASQ scores and height/weight are similar between children born in the LP period and those born at 39' weeks. While reassuring, this finding warrants validation with a larger sample size and diagnostic testing.

Table 1

	ASQ Abnormal	Morbidity
34 WKS	3/15 (20.0%)	10/30 (33.3%)
35 WKS	2/14 (14.3%)	4/38 (10.5%)
36 WKS	8/35 (22.9%)	5/62 (8.1%)
39+ WKS	22/81 (27.2%)	3/157 (1.9%)
Total	35/145 (24.1%)	22/287 (7.7%)
P-value	0.8160	<0.0001

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