11 Outcomes of children at two years after multiple courses of antenatal corticosteroids for threatened preterm birth: the multiple antenatal corticosteroids study (MACS)

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OBJECTIVE: A single course of antenatal corticosteroids (ACS) is associated with a reduction in respiratory distress syndrome and neonatal death. Our placebo controlled trial of multiple courses of ACS, every 14 days, found no benefit. Infants exposed to multiple courses of ACS weighed less and had smaller head circumferences. (Lancet 2008; 372: 2143-51). The secondary outcome of this study was to determine if there was a difference in the risk of death or neurological impairment at 18-24 months of age.

STUDY DESIGN: 1858 women were randomized to receive multiple courses of ACS vs. placebo, every 14 days, until 33 6/7 weeks or delivery whichever came first. The primary outcome was a neonatal composite outcome. The secondary outcome was death or neurodevelopmental impairment defined as cerebral palsy or abnormal cognitive development. Abnormal cognitive development was defined as a score of < 70 on the Bayley Scale of Infant Development-II or comparable neurocognitive assessment or a delayed mental developmental age in the absence of a standardized assessment. Biometry was also assessed.

RESULTS: Of the original 2305 infants/foetuses, a total of 2104 (91.3%) were assessed at 18-24 months of age. The risk of death or neurodevelopmental impairment was similar between groups (148 [13.8%] ACS vs. 142 [13.7%] placebo group; OR 1.001; 95% CI 0.75-1.31, p=0.95). Toddlers exposed to multiple courses of ACS weighed less than those exposed to placebo (11.94g ACS vs. 12.14g placebo; risk difference −0.2; 95% CI −0.38,-0.006; p=0.04).

CONCLUSION: Administration of multiple courses of ACS, every 14 days, did not lead to a difference in death or neurologic impairment at 18-24 months of age. However, children exposed to multiple courses of ACS weighed less. Longer term follow-up studies are required (ClinicalTrials.gov number, NCT 00187382).

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12 Pharmacological actions of progesterone (P4) or 17-alpha-hydroxyprogesterone caproate (17P) to inhibit cervical ripening or prevent term delivery depend upon the route of administration and effects on the myometrium

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OBJECTIVE: Recent clinical reports indicate that progestins, P4 or 17P applied vaginally or parenterally, might be useful to treat recurrent preterm labor. Our objectives were to evaluate the cervix throughout pregnancy and estimate the effects of P4 (vaginal application and injection), 17P and the P4 antagonist RU-486 on cervical ripening and delivery in pregnant rats.

STUDY DESIGN: The cervices of timed-pregnant rats (normal delivery on day 22) were followed with LIF (collagen light-induced fluroescence). Daily treatments consisted of: (1) P4 (4mg s.c.) (2) P4 (2mg to 15 mg, vaginally bid) (3) 17P (10 mg s.c) or (4) vehicle (n=6 for each group) from day 13 of pregnancy until delivery. Some rats were also treated with a single injection of RU-486 (3 mg s.c.) on day 16 .Cervical ripening was assessed every second day in vivo by LIF using a collascope instrument by placing the probe on the cervix. Statistics were assessed by ANOVA and the Student's t-test ($P<.05$).

RESULTS: LIF is significantly higher in the P4-injection group and in the 17P treated group (until day 19 only for the 17P) compared with vehicle controls. There is no significant difference between the vaginal P4 group and vehicle controls at any time in gestation. Only injection of P4 delays delivery. LIF is significantly lower in the RU-486 treated rats during preterm delivery compared to controls.

CONCLUSION: The cervix progressively softens during pregnancy and reverts to a rigid state postpartum. Parenteral treatment with P4 delays and reduces softening and completely blocks delivery. Vaginal P4, even at very high dose, has no effect on cervical softening or delivery. Injections of 17P also delays and reduces cervical softening until term but it does not inhibit delivery. Parenteral P4 treatment may be the preferred treatment to prevent preterm cervical ripening and prevent delivery as it also inhibits uterine contractility.

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13 Development of a noninvasive test for intraamniotic infection using proteomic analysis of cervicovaginal fluid in women with preterm labor

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OBJECTIVE: To develop a noninvasive test for intraamniotic infection (IAI) in women with preterm labor, intact membranes (PTL-I).

STUDY DESIGN: Among 105 cases of PTL-I before 37 wks, IAI was defined by amniocentesis results: positive amniotic fluid culture and/or 16S ribosomal DNA PCR (16S-rDNA), a highly sensitive & specific test for presence of eubacteria, *Mycoplasma,* and *Ureaplasma sp.* Immunoassays were used to quantitate proteins in cervicovaginal fluid (CVF). Candidate CVF proteins were entered individually and in combination into logistic regression models.

RESULTS: IAI was present in 13% (14/105), 11 by both 16S-rDNA & culture, 3 by 16S-rDNA alone. From 75 candidate CVF proteins associated with IAI, 5 were included in a final model: 1 plasma protein, 2 cytokine/chemokines, 1 cell adhesion protein, 1 peroxidase. Final model had area under ROC 0.983. A dichotomous classification rule based on these 5 proteins had sensitivity 93%, specificity 93%, PPV 72%, NPV 99% for prediction of IAI, and screen positive rate 19%. Test performance was not impaired by blood in the CVF specimen (present in 12 cases without IAI, none with IAI.)