1 A RANDOMIZED CONTROLLED TRIAL OF MAGNESIUM SULFATE FOR THE PREVENTION OF CEREBRAL PALSY DWIGHT ROUSE[1], [1]NICHD MFMU Network, Bethesda, Maryland

OBJECTIVE: To evaluate whether maternally-administered MgSO4 lowers the risk of cerebral palsy (CP) or death in the offspring of women with anticipated early preterm delivery.

STUDY DESIGN: Randomized, double masked, placebo controlled trial in 20 centers. Non-preeclamptic women with PPROM, advanced preterm labor, or indicated delivery from 24-31 weeks' gestation were randomly allocated to a 6 gm bolus of IV MgSO4 followed by 2 gm/hr, or placebo. The primary study outcome was the composite of moderate or severe CP at the corrected age of 2 years (as diagnosed by centrally trained examiners) or death.

RESULTS: 2241 women were randomized: 87% had PPROM, and 9% twins. Baseline characteristics including gestational age at randomization, risk factor for preterm birth, and proportion of twins were similar in the two study groups--overall, and in those randomized prior to 28 weeks. Follow-up was achieved for 95.6% of children. MgSO4 did not lower the combined rate of moderate to severe CP or death. However, it did significantly lower the rate of moderate to severe CP alone (Table. CP = moderate to severe. Numbers/percentages do not tally because some twin pregnancies experienced both outcomes).

Overall	Magnesium Sulfate (N = 1,041)	Placebo (N = 1,095)	RR (95% CI)
	n (%)		
CP or Death	118 (11.3)	128 (11.7)	0.97 (0.77–1.23)
CP Alone	20 (1.9)	38 (3.5)	0.55 (0.32–0.95)
Death Alone	99 (9.5)	93 (8.5)	1.12 (0.85–1.47)
Randomization < 28 wks	Magnesium Sulfate (N = 442)	Placebo (N = 496)	RR (95% CI)
	n (%)		
CP or Death	89 (20.1)	105 (21.2)	0.95 (0.74–1.22)
CP Alone	12 (2.7)	30 (6.1)	0.45 (0.23–0.87)
Death Alone	78 (17.7)	78 (15.7)	1.12 (0.84–1.49)

CONCLUSION: MgSO4 did not reduce the rate of the primary outcome of moderate to severe cerebral palsy or death, perhaps because death was the predominant component of the outcome. MgSO4 did, however, reduce the rate of moderate to severe cerebral palsy alone--by half.

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2 MULTIPLE COURSES OF ANTENATAL CORTICOSTEROIDS FOR PRETERM BIRTH STUDY KELLIE MURPHY FOR THE MACS COLLABORATIVE GROUP[1], [1]Maternal Infant and Reproductive Health Research Unit, University of Toronto, Maternal Fetal Medicine, Toronto, Ontario, Canada

OBJECTIVE: A single course of antenatal corticosteroids (ACS) is associated with a reduction in respiratory distress syndrome (RDS) and neonatal death. Trials of weekly vs. single courses of ACS suggest benefits (less respiratory morbidity) but also harm (reduced growth in utero). The aim of this trial was to see if multiple courses of ACS, every 14 days, would be associated with benefits in terms of reduced neonatal morbidity and mortality but without the risk of decreased growth in utero.

STUDY DESIGN: 1858 women were randomized to receive multiple courses of antenatal corticosteroids vs. placebo every 14 days until 33 6/7 weeks or delivery which ever came first. The primary outcome was a composite of mortality, severe RDS, intraventricular haemorrhage (grade III or IV), periventricular leukomalacia, bronchopulmonary dysplasia or necrotizing enterocolitis.

RESULTS: Infants born to women who received multiple courses of ACS incurred similar morbidity and mortality (12.9 % vs. 12.5%) as compared to the single course group 1.04 OR (CI 0.77-1.39 p=0.83). Infants born to women who received multiple courses of ACS weighed less (2216 grams vs. 2330 grams, p=0.0026), were not as long (44.5 cm vs. 45.4 cm, p=0.00075) and had a smaller head circumference (31.1 cm vs. 31.7 cm, p=<0.0001) as compared to those who received a single course of therapy.

CONCLUSION: For women who continue to be at high risk of preterm delivery following an initial course of ACS, multiple courses of ACS, every 14 days until 336/7 weeks or delivery which ever comes first, does not offer additional benefits to their infants and appears to be associated with a decrease in birth weight, birth length and head circumference. Therefore multiple courses of ACS, every 14 days, should not be recommended for women who remain undelivered after their initial course of therapy. (ClinicalTrials.gov number, NCT 00187382)

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3 RANDOMIZED CONTROLLED TRIAL OF OMEGA-3 FATTY ACID SUPPLEMENTATION FOR RECURRENT PRETERM BIRTH PREVENTION MARGARET HARPER[1], [1]NICHD MFMU Network, Bethesda, Maryland

OBJECTIVE: Omega-3 fatty acid (Ω3) supplementation and dietary intake have been reported to prolong gestation and decrease preterm birth (PTB). This trial was undertaken to evaluate whether Ω3 supplementation reduces recurrent PTB in women with prior PTB when given along with 17 alpha-hydroxyprogesterone caproate (17-OHPC). Dietary intake of fish was also evaluated.

STUDY DESIGN: In this randomized, double-masked, placebo controlled, multicenter trial, women with prior spontaneous (s)PTB and a singleton gestation were assigned to take either an Ω3 supplement (1200 mg eicosapentaenoic acid and 800 mg docosahexaenoic acid) or matching placebo (PL) daily from 16-22 through 37 wks' gestation. All participants received weekly 17 OHPC (250mg) IM. A validated food frequency questionnaire was used to assess dietary intake of fish at baseline.

RESULTS: Of the 852 women randomized, none were lost to follow up and all completed the food frequency questionnaire. (Table) The relative risk of PTB < 37 wks for Ω3 vs placebo was 0.91 (0.77-1.07), and when stratified by fish intake, 0.92 (0.78-1.08). However, women reporting ≥ 1 fish meal per month had significantly decreased PTB, odds ratio adjusted for baseline risk factors and treatment group: 0.62 (0.45- 0.86).

CONCLUSION: Among women with prior sPTB receiving 17-OHPC, omega-3 supplementation did not reduce the rate of PTB. We observed an association between dietary intake of fish and reduced PTB.

	Ω3	PL	p Ω3 vs PL	Fish ≥ 1 meal/month	Fish < 1 meal/month	p Fish Intake
N	434	418		599	253	
PTB <37w	37.8%	41.6%	0.25	35.9%	48.6%	0.0005
sPTB <37w	29.0%	31.8%	0.38	27.2%	37.9%	0.002
PTB <35 w	18.9%	19.9%	0.72	17.2%	24.5%	0.014

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4 PROPHYLACTIC MATERNAL N-ACETYLCYSTEINE (NAC) SUPPRESSES FETAL, THOUGH NOT MATERNAL, IL-6 INFLAMMATORY RESPONSE TO LIPOPOLYSACCHARIDE (LPS) RON BELOOSESKY[1], ZEEV WEINER[1], NIZAR KHATIV[1], RACHEL MANDEL[1], DAVE A. GAYLE[2], NIR MARAVI[1], MICHAEL ROSS[2], JOSEPH ITSKOVITZ-ELDOR[1], [1]Rambam Medical Center, Dept. of Ob/Gyn, Haifa, Israel, [2]Harbor-UCLA Med. Ctr. (LABioMed), Dept. of Ob/Gyn, Torrance, California

OBJECTIVE: Maternal and fetal infections and inflammation have been implicated in the genesis of cerebral palsy and chronic lung disease. High newborn blood proinflammatory cytokines are a marker of fetal inflammatory response syndrome (FIRS), which is associated with acute and long term morbidity. Studies have suggested that changing the redox balance by enhancing the activity or availability of antioxidants may prevent cytokine-induced tissue damage. We sought to determine whether prophylactic administration of NAC, a known antioxidant, can blunt fetal inflammatory responses to maternal LPS-induced inflammation.

STUDY DESIGN: Pregnant Sprague Dawley rats (n=28) at 20 days gestation were studied. Maternal rats received intraperitoneal injections of saline (Sal) or N-acetylcysteine (NAC) (300 mg/kg) at time 0, followed by LPS (500 μg/kg) at time 30 min, (Sal-LPS, NAC-LPS). At 6 h after the first injection, rats were sacrificed and IL-6 levels in the fetal and maternal serum were determined by ELISA. Independent effects of NAC (Sal-NAC) and saline (Sal-Sal) were also determined.

RESULTS: In response to maternal LPS, maternal and fetal serum IL-6 markedly increased compared to control (maternal 46±3 to 4358±973 pg/ml; fetal 41±4 to 2560±866 pg/ml). NAC given prior to maternal LPS did not change maternal (2692±1458 pg/ml) but significantly reduced the fetal (378±92 pg/ml; p<0.05) proinflammatory IL-6 response. NAC alone (Sal-NAC) did not alter basal maternal or fetal IL-6 levels.

CONCLUSION: Maternal NAC inhibits fetal, though not maternal, IL-6 responses to maternal LPS. These results suggest that NAC administered prophylactically to pregnancies with maternal infection may protect the fetus from adverse inflammatory sequelae, while permitting an appropriate maternal inflammatory response.

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