5 PRECONCEPTIONAL FOLATE PREVENTS PRETERM DELIVERY RADEK BUKOWSKI[1], FERGAL D. MALONE[2], FLINT PORTER[3], DAVID A. NYBERG[4], CHRISTINE COMSTOCK[5], GARY HANKINS[1], KEITH EDDLEMAN[6], SUSAN GROSS[7], LORRAINE DUGOFF[8], SABRINA CRAIGO[9], ILAN E. TIMOR-TRITSCH[10], STEPHEN R. CARR[11], HONOR M. WOLFE[12], MARY E. D'ALTON[13], [1]University of Texas Medical Branch, Obstetrics and Gynecology, Galveston, Texas, [2]Royal College of Surgeons in Ireland, Department of Obstetrics and Gynecology, Dublin, Ireland, [3]University of Utah, Salt Lake City, Utah, [4]The Fetal & Women's Center of Arizona, OB/GYN Ultrasound, Scottsdale, Arizona, [5]William Beaumont Hospital, Fetal Imaging Department, Royal Oak, Michigan, [6]Mount Sinai Medical Center, Department of Obstetrics and Gynecology, New York, New York, [7]Montefiore Medical Center/Albert Einstein College of Medicine, OB-Gyn and Women's Health, Bronx, New York, [8]University of Colorado Health Sciences Center, Ob/Gyn, Denver, Colorado, [9]Tufts-New England Medical Center, Obstetrics and Gynecology, Boston, Massachusetts, [10]NYU Medical Center, School of Medicine and Obstetrics & Gynecology, New York, New York, [11]Women and Infants' Hospital / Brown University, Maternal-Fetal Medicine, Providence, Rhode Island, [12]University of North Carolina at Chapel Hill, Department of Obstetrics and Gynecology, Chapel Hill, North Carolina, [13]Columbia University, OB/GYN Maternal-Fetal Medicine, New York, New York

OBJECTIVE: To determine the effect of preconceptional folate supplementation on duration of pregnancy and incidence of preterm delivery.

STUDY DESIGN: In a cohort of 38,033 singleton pregnancies preconceptional folate supplementation was prospectively recorded in the first trimester of pregnancy. Duration of pregnancy was estimated based on ultrasound measurement of crow-rump length between 10 4/7 and 13 6/7 weeks of pregnancy. Natural length of pregnancy was defined as gestational age at delivery in pregnancies uncomplicated by medical or obstetrical complications which may constitute indication for delivery. Pregnancies with those conditions: congenital or chromosomal abnormalities, termination of pregnancy or stillbirth, chronic hypertension, pregnancy induced hypertension, preeclampsia, gestational or pre-gestational diabetes, placental abruption and placenta previa, were censored. The effect of preconceptional folate supplementation on duration of pregnancy was evaluated using survival analysis-Cox regression.

RESULTS: Preconceptional folate supplementation for >= 1 year was associated with a 70% decrease in the incidence of spontaneous preterm delivery between 20 and 28 weeks (HR, 95% CI = 0.22, 0.08-0.62; p=0.004) and 50% decrease in the incidence of spontaneous preterm delivery between 28 and 32 weeks (HR, 95% CI = 0.45, 0.23-0.85; p=0.015). Adjustment for maternal characteristics: age, race, education, marital status and prior preterm birth, did not have a material effect. Preconceptional folate supplementation did not have a significant effect on duration of pregnancy beyond 32 weeks or if supplementation lasted < 1 year. The interaction term between folate supplementation and prior preterm birth was not significant (p=0.6). Proportional hazard assumption was met (p>0.05 for all).

CONCLUSION: Preconceptional folate supplementation is associated with a 50-70% reduction in the incidence of early spontaneous preterm birth. The earlier the preterm birth the stronger the effect. Folate supplementation is equally effective in patient with and without prior preterm birth.

0002-9378/$ - see front matter
doi:10.1016/j.ajog.2007.10.006

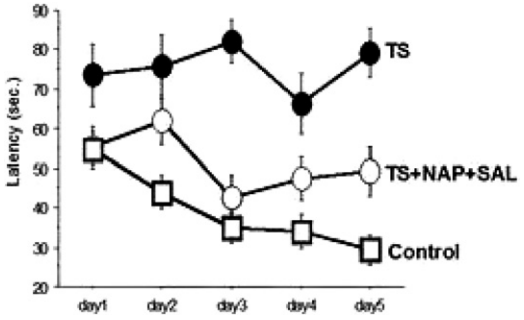
6 PREVENTION OF LEARNING DEFICIT IN A DOWN SYNDROME MOUSE MODEL LAURA TOSO[1], ANDREA JOHNSON[1], STEPHANIE BISSELL[1], ROBIN ROBERSON[1], JOY VINK[2], DANIEL ABEBE[1], CATHERINE SPONG[1], [1]National Institutes of Health (NIH), NICHD&NIAAA, Bethesda, Maryland, [2]Georgetown University, Deapartment of ObGyn, Washington, District of Columbia

OBJECTIVE: Down syndrome (DS) is the most common genetic cause of mental retardation. In DS there is a glial deficit which induces anomalies in neurotrophins, including Activity Dependent Neuroprotective Protein and Activity Dependent Neurotrophic Factor. Previously we have shown that their active fragments NAP+SAL prevented delay in behavioral milestones achievement in the Ts65Dn (Ts) mouse, a DS model. The objective of this study was to test if NAP+SAL prevent the adult DS learning deficit.

STUDY DESIGN: 9-12 month old Ts male mice were treated for 10 consecutive days with either D-NAP+D-SAL or placebo. From treatment day 4 mice were tested for learning on the Morris watermaze for 5 days where latency to find a hidden platform by using visual cues is a measure of learning. Probe tests for long term memory were performed on treatment day 9 and 10 days later (after treatment stopped). Statistics included Bonferroni-Dunn with P<0.05 significant.

RESULTS: 15 Control, 4 Ts and 9 Ts+NAP+SAL were tested. Ts animals did not learn (P<0.001) over the 5-day period vs the control. Ts animals treated with NAP+SAL learned significantly better than the Ts mice (P<0.001, Figure). On treatment day 9 Ts+NAP+SAL retained learning, with results similar to the controls (P>0.05). However, 10 days after therapy, Ts+NAP+SAL did not maintain learning in the probe test.

CONCLUSION: Postnatal treatment with peptides NAP+SAL prevented learning deficit in a model for DS. Possible mechanisms of action include overcoming the glial deficit.



The Morris Watermaze

0002-9378/$ - see front matter
doi:10.1016/j.ajog.2007.10.007

7 PLACENTAL AND RENAL EXPRESSION OF HYPOXIC GENES IN A MOUSE MODEL OF PREECLAMPSIA INDUCED BY OVER-EXPRESSION OF SFLT-1 FANGXIAN LU[1], JULIO MATEUS[1], NIMA GOHARKHAY[1], HUAIZHI YIN[1], ESTHER TAMAYO[1], GARLAND D. ANDERSON[1], MONICA LONGO[1], GEORGE R. SAADE[1], [1]The University of Texas Medical Branch, Obstetrics and Gynecology, Galveston, Texas

OBJECTIVE: sFlt-1 and placental hypoxia have been shown to be implicated in the etiology of preeclampsia. Our objective was to determine the placental and renal expression of selected genes regulated by hypoxia and involved in angiogenesis in a previously characterized rodent model of preeclampsia induced by over-expression of sFlt-1.

STUDY DESIGN: At day 8 of gestation, CD-1 mice were randomly allocated to injection of the adenovirus carrying Flt (1-3) [AdFlt(1-3); 10^9 PFU], adenovirus carrying mFc as virus control (10^9 PFU), or saline (n=4-10/group). At day 18 of gestation, the mice were sacrificed; kidneys and placentas were removed, weighed and snap frozen. mRNA expression of hypoxic-inducible factor-1 α (HIF-1α), transforming growth factor β3 (TGFβ3) and glial cells missing 1 (GCM1) was determined using real-time RT-PCR. One-way ANOVA followed by Newman-Keuls post-hoc test were used for statistical analysis (significance: p<0.05).

RESULTS: The average placental weight in the sFlt-1 group (0.12±0.006 g) was significantly lower compared with the mFc and saline groups (0.19±0.02 g and 0.192±0.019 g, respectively). In placenta from the sFlt-1 group, HIF1α and TGFβ3 gene expression were significantly increased by 3 and 7 folds, respectively, compared with mFc and saline groups (P<0.05). Placental GCM1 gene expression was significantly decreased by 5 folds in the sFlt-1 group compared with the saline and mFc groups. In the kidney, HIF1α expression was significantly increased by 2 folds in the sFlt-1 group compared with the other 2 groups, while no significant differences were seen in the expressions of TGFβ3 and GCM1.

CONCLUSION: Inhibition of angiogenic factors by sFlt-1 results in a hypoxic placenta, which in turn explains the preeclampsia-like condition previously characterized in this animal model. This effect is possibly mediated via the transcription factor HIF-1α and its downstream target molecule, TGFβ3 which lead to altered GCM1 expression. Further investigation of this mechanism may improve our understanding of preeclampsia.

0002-9378/$ - see front matter
doi:10.1016/j.ajog.2007.10.008