MATERNAL OBESITY AND GESTATIONAL DIABETES MAY IMPACT CREATINE AVAILABILITY TO THE TERM HUMAN PLACENTA

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Background: Maternal obesity (BMI > 25) and gestational diabetes (GDM) are significant health issues affecting 20% (obesity) and ~15% (GDM) of all pregnancies. Both conditions are known to dysregulate placental metabolism. The creatine kinase circuit is a spatial and temporal ATP buffer within the placenta. Whether this critical pathway is altered by maternal obesity or GDM is unknown. This study examined the mRNA expression of the creatine transporter and synthesising enzymes in placentae of women with pre-existing obesity as well as women who developed GDM.

Method: Term human placenta samples were collected from lean controls (n = 18); obese women without GDM (n = 14); lean (n = 10) and obese (n = 18) women with GDM managed by diet; and lean (n = 20) and obese (n = 14) women with GDM managed with insulin. CDNA was generated and relative mRNA expression of the creatine transporter (SLC6A8) and synthesising enzymes arginine:glycine aminotransferase (AGAT) and guanidinoaceticate methyltransferase (GAMT) was assessed using Fluidigm DNAs and TaqMan chemistry. Data were analysed by Two-Way ANOVA with Sidak’s multiple comparisons.

Results: Compared to lean controls, maternal obesity significantly down-regulated mRNA expression of SLC6A8 (p < 0.01) and AGAT (p < 0.01), the rate-limiting enzyme of creatine synthesis. Insulin treatment of GDM was associated with up-regulation of placental SLC6A8 mRNA (p < 0.001), compared to lean controls. GDM was also associated with up-regulation of GAMT mRNA (p < 0.05), irrespective of maternal BMI or management strategy.

Conclusions: Maternal obesity and GDM may impact creatine availability and placental ATP turnover by the creatine kinase circuit, contributing to the dysregulated placental metabolism observed with maternal obesity and GDM.

EARLY PREDICTION OF DEVELOPMENTAL OUTCOMES AT 3 YEARS FOLLOWING CARDIAC SURGERY

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Background: Infants who have undergone major neonatal cardiac surgery have delays in their neurodevelopmental outcomes at 1 and 3 years of age. The aim of this research was to investigate the ability of 1 year outcomes to predict outcomes at three years following early cardiac surgery.

Method: Cardiac surgical infants who were enrolled in the Development After Infant Surgery (DAISy) study and had complete Bayley Scale of Infant and Toddler Development III (BSID-III) results from the 1 and 3 year assessments were included in the analysis. The outcomes and trajectories of 159 children were classified as below average (< −1 SD), within the average range, or above average (>1 SD). Analysis included group differences, validity and prediction.

Results: The developmental outcomes at three years in all five domains improved between 35% and 58% for those who scored below average at one. Conversely many who performed above average at 1, scored poorer at 3 in all domains (57%-90%). Sensitivity and negative predictive values were high for all domains of the BSID-III, which reflected the changes between 1 and 3. Specificity and negative predictive values varied between domains from very low to high. Maternal education, birth weight, outcome at 1 on the BSID-III and Apgars at 5 was statistically significant predictors.

Conclusions: The bidirectional changes in outcomes for all domains influenced the predictive validity of the BSID-III. Although the predictors were statistically significant, they all remained weak at predicting outcome at 3. This highlights the importance of ongoing follow up. Future research should consider the impact of interventions between assessments.

EARLIER FORTIFICATION FOR LOW BIRTH WEIGHT BABIES – DOES IT MAKE A DIFFERENCE?

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Background: Although milk fortification for low birth weight (LBW) babies is standard practice, commencement criteria varies widely and few studies have evaluated comparative outcomes.

Methods: LBW babies admitted to SCN at the Northern Hospital between October 2014 and June 2016, were randomly assigned to 2 groups (F80, n = 45 ; F160, n = 42), commencing
fortification at total fluid intake achievement of 80 or 160 ml/kg/day (160 being standard protocol). Outcomes measured included weight, protein intake, biochemical markers, feeding intolerance and length of stay (LOS).

Results: Mean birthweight and gestation age were almost identical for F80 and F160 (2028 g vs 2032 g; 34.4 vs 34.2 weeks). F80 fortification commenced 4 days before F160 (2.8 vs 7.0; p < 0.0001) and lasted 3 days longer (15.2 vs 12.2, p < 0.03). Growth velocity was slightly higher for F80 (7.3 vs 7.1 g/kg/day, p > 0.05). On average, F80 babies were discharged 1.25 days earlier (16.96 vs 18.24, p > 0.05). F80 average protein intake during the first week was understandably higher (2.87 vs 2.15 gm/kg/day, p < 0.0001). At 7 days of age, F80 babies achieved better target blood urea levels (>3.2 mmol/l indicating adequate protein metabolism; 70% vs 54%, p < 0.05) and regained birthweight almost 2 days earlier (7.5 vs 9.4, p < 0.01). Feeding intolerance was markedly decreased for F80 (24.4% vs 47.6%, p < 0.03). There were no adverse study outcomes.

Conclusion: Commencing fortification for LBW babies at total fluid intake of 80 ml/kg/day, improves nutrition, reduces the duration of post-birth weight loss, reduces feeding intolerance and has potential cost savings in reduced LOS.

IS GENTAMICIN BEING APPROPRIATELY AND EFFECTIVELY ADMINISTERED TO NEOANDES IN THE SPECIAL CARE NURSERY (SCN) AT THE NORTHERN HOSPITAL?

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Background: Gentamicin is an aminoglycoside antibiotic used to treat neonates with presumed or proven bacterial sepsis. Dose and timing in neonates is controversial owing to risks of nephrotoxicity and ototoxicity. A gentamicin trough concentration ≤2 mg/L is associated with minimal toxicity. This retrospective study aims to assess the efficacy of the current 4 mg/kg gentamicin regimen for neonates >32 weeks gestation who had presumed sepsis within the first 7 days of life.

Method: 156 neonates admitted to Special Care Nursery (February 2014 - January 2016) were identified as having had one or more serum gentamicin concentration levels analysed. Trough levels were identified and a chart review was undertaken to investigate comorbidities, patient presentation, gentamicin prescribing patterns and evidence of possible toxicity.

Results: 96% of all neonates had a safe gentamicin trough level ≤2 mg/L. One neonate >37 weeks gestation (0.8%, n = 124), one neonate between 34-36+6 weeks gestation (5.9%, n = 17) and four neonates <34 weeks gestation (26.7%, n = 15; p = 0.0004 when compared to >37 weeks cohort) had trough levels >2 mg/L. Among neonates with elevated trough levels, the current protocol was adhered to in 5 of 6 cases. Gentamicin was either ceased or dosage delayed so that subsequent trough levels were ≤2 mg/L. No ototoxicity was observed on follow up.

Conclusions: A once daily gentamicin regimen of 4 mg/kg has resulted in few toxic trough levels in neonates >34 weeks gestation. However, younger neonates are more prone to elevated trough levels and this requires further evaluation in future gentamicin administration protocols.

OUTCOMES OF VERY PRETERM INFANTS RECEIVING PROSTAGLANDIN (PGE1) FOR DUCT-DEPENDENT CONGENITAL HEART DISEASE.

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Background: Infants with duct-dependent congenital heart disease (DD-CHD) are sometimes born very preterm (<32 weeks gestation). These infants may require prolonged infusions of PGE1 to maintain ductal patency, whilst attaining sufficient weight to undergo cardiac surgery. Literature on the outcomes of this patient group is sparse. The objective was to describe mortality and morbidity of very preterm infants with DD-CHD, treated with PGE1.

Method: A review of medical records of very preterm infants born at the Royal Women's Hospital, Melbourne, between 2006 and 2016 with DD-CHD, treated with PGE1.

Results: 14 infants were identified, with a median (range) gestational age of 30 + 3 weeks (26 + 4 to 31 + 6 weeks’), a median (range) birth weight 1288 g (750 g to 1660 g), 8 (57%) were male. 11 (79%) were diagnosed with DD-CHD antenatally and 12 (86%) received antenatal corticosteroids. 7 (50%) infants had duct-dependent pulmonary circulation, 5 (36%) had duct-dependent systemic circulation and 2 (14%) had transposition of the great arteries. PGE1 was commenced at a median (range) age of 0 days (0 to 12 days), with a median (range) duration of treatment of 23 days (2 to 68 days). 9 (64%) were enterally fed whilst on PGE1. 4 (29%) developed necrotising enterocolitis, with 2 requiring surgery. Mortality at discharge from tertiary centres was 29%, with 1 infant dying prior to and 3 post cardiac surgery.

Conclusions: Very preterm infants with DD-CHD have substantial morbidity and mortality. These findings are important for the treating clinicians, particularly in counselling parents of these high-risk infants.

DOES PLACENTAL TELOMERE LENGTH DIFFER BY MATERNAL REGION OF BIRTH?

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Background: Studies have shown that South Asian women have higher rates of stillbirth, fetal growth restriction (FGR) and operative vaginal birth due to fetal compromise compared to white women and South-East/ East Asian women. Telomere length has been reported to be shorter in placentae from pregnancies complicated with FGR, pre-eclampsia and diabetes. The