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SUN-632

Vitamin D deficiency during pregnancy may not only impair maternal skeletal preservation and fetal skeletal formation but also influence fetal "imprinting" that may affect chronic disease susceptibility soon after birth as well as later in life.

Vitamin D deficiency has been linked to multiple adverse perinatal outcomes in pregnancy including; pre-eclampsia, gestational diabetes, low birth weight, bacterial vaginosis, pre-term delivery and caesarean section. Aim: to assess 25-hydroxy vitamin D (25OHD) concentrations in women with type 1 diabetes (T1DM) during pregnancy, post-delivery and also foetal (cord blood) 25OHD concentrations and to examine relationships between these. The second aim of the study to examine potential relationships between maternal 25OHD and glycosylated haemoglobin (HbA1c) throughout pregnancy. Materials and methods: This was an observational study of 42 pregnant controls without diabetes and 39 pregnant women with T1DM. Maternal serum 25OHD was measured serially throughout the pregnancy and post-delivery. Cord blood 25OHD was measured at delivery. 25OHD was measured by liquid chromatography tandem mass spectrometry (LC-MS/MS). HbA1c was measured serially throughout the pregnancy. Control and T1DM groups were not significantly different in age or number of previous miscarriages. As expected, the T1DM group exhibited significantly higher HbA1c levels, and also had significantly increased incidence of preeclampsia (2 of 42 cases (4,8%) in control group and 5 of 39 cases in T1DM group (12,8%)) (p= 0,03). Delivery gestational age was significantly lower for babies born to mothers with T1DM (39,6±1,4 weeks in control group and 37,6±2,1 in T1DM group (p= 0,001).

Vitamin D deficiency, defined as 25OHD levels,25 nmol/L, was apparent in both the control and the T1DM groups across the entire pregnancy. Greater than 90% of pregnant women were classified as insufficient at each timepoint, regardless of whether they had T1DM or not. This meant that 10% of this pregnant population were at a sufficient level at some point throughout pregnancy. Similar to maternal vitamin D levels, the neonates had a high incidence of 25OHD deficiency at birth. Also were shown correlations between cord blood and maternal vitamin D. Maternal 25OHD correlated positively with cord 25OHD at all 3 trimesters in the T1DM group. Conclusions: in T1DM pregnancy, low vitamin D levels persist throughout gestation and post-delivery; maternal vitamin D levels exhibit a significant negative relationship with HbA1c levels, supporting a potential role for this vitamin in maintaining glycaemic control; larger studies investigating whether low vitamin D levels are a risk factor for preterm delivery and preeclampsia in women with diabetes are needed.

Diabetes Mellitus and Glucose Metabolism

IMPACTS OF METABOLISM ON CLINICAL CHALLENGES

Immediate Post-Operative Insulin Requirements May Predict Metabolic Outcome After Total Pancreatectomy and Islet Autologous Cell Transplant (TPIAT)

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OR26-04

Immediate Post-Operative Insulin Requirements may Predict Metabolic Outcome after Total Pancreatectomy and Islet Autologous Cell Transplant (TPIAT) **Introduction**: Chronic pancreatitis (CP) is a progressive disease that leads to eventual loss of endocrine and exocrine function. Patients with CP experience abdominal pain, which in some instances can be refractory to medical and endoscopic intervention. Total pancreatectomy and islet auto transplantation (TPIAT) is a treatment option however predicting postoperative metabolic outcomes remains elusive. In this single-center retrospective study, we report pre-TPIAT characteristics, beta cell function indices, islet yield as well as post-TPIAT glucose management data to further understand their relationship.**Methods:**A total of 13 TPIAT subjects were included who underwent beta cell function assessment via intravenous glucose tolerance tests and oral mixed meal tolerance tests. Islet yield, glucose level and insulin requirement for 72 hours postoperatively were collected. In addition, their glucose control and insulin requirements at 3, 6 and 12-month post TPIAT were analyzed.**Results:**The median age was 45 years with median duration of CP for 5 years. The main cause of CP was idiopathic. All 13 subjects had normal baseline fasting glucose levels. Median islet yield was 4882 IEq/kg (interquartile range 3412 to 8987). Median post-operative total insulin requirement on day 3 was 0.43 units/kg. Pre-TPIAT baseline glucose, insulin or c-peptide level did not have a significant correlation with the islet yield. Similarly, there was no correlation between islet yield and insulin requirement at 72-hour post operatively. However, there was an inverse correlation between the absolute islet yield (IEq) and insulin requirement at 6 months and 12 months following post-TPIAT. Further analysis of the relationship between 72-hour post-op insulin requirement and insulin requirement at discharge, 3, 6 and 12 month showed a positive correlation. Despite the new finding of inverse correlation of islet yield with long-term insulin requirement, this study was not able to detect a correlation between the preoperative parameters to postoperative short-term or long-term outcome as noted in other studies.**Conclusion:** The 72-hour postoperative insulin requirement is a helpful

postoperative predictor of patients needing long term insulin management following TPIAT. This observation may identify a high risk group of patients in need of more intensive diabetes education and treatment prior to hospital discharge.

Pediatric Endocrinology

ADVANCES IN PEDIATRIC OBESITY AND CANCER

NF-κB Pathway Is Implicated in Thyroid Embryogenesis

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OR22-01

Background: Congenital hypothyroidism due to thyroid dysgenesis (CHTD) is the most common congenital endocrine disease with a prevalence of 1:4,000 live births. We have suggested a two-hit hypothesis to explain CHTD, combining an inherited or *de novo* variant with a post-zygotic event. This model could explain the sporadicity of the disease (99%), its ethnic predominance and the high discordance rate between monozygotic twins. Despite years of research, more than 95% of cases of CHTD remain unexplained, especially those with thyroid ectopy. This suggests that research on genes and/or pathways not previously associated with thyroid development need to be pursued. Inactivation of the NF-κB pathway can cause deficient anterior pituitary and variable immunodeficiency, or DAVID syndrome. Whether this pathway is also involved in CHTD remains to be established. **Objective:** To evaluate the implication of the NF-κB pathway during thyroid migration. **Methods:** Knock down experiments using morpholinos in a zebrafish model were carried out to investigate the roles of certain genes related to the NF-kB pathway during thyroid development. Rescue experiment was also performed to evaluate the specificity of the morpholino. The first gene to be tested was *IKBKE*, a member of the inhibitor of κB kinase (IKK) family. Thyroid location was assessed by microscopy of live larvae. **Results:** *ikbke* depletion in zebrafish caused defective aortic arch artery formation and abnormal thyroid migration. The thyroid phenotype was partially rescued by injection of human *IKBKE* RNA in *ikbke* morphants. **Conclusion:** *IKBKE* seems important for normal thyroid migration suggesting that the non-canonical NF-kB pathway might be implicated. Further studies targeting other genes in this pathway are ongoing to extend these results.

Reproductive Endocrinology

MALE REPRODUCTIVE HEALTH - FROM HORMONES TO GAMETES

Testosterone Therapy Reduces Inflammatory Activation of Human Monocytes in Hypogonadal Type-2 Diabetic Men as a Potential Mechanism to Improve Atherosclerosis

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SAT-049

Testosterone deficiency is prevalent in men with type 2 diabetes (T2D) and is associated with greatly elevated risk of cardiovascular mortality. Testosterone replacement has beneficial effects on surrogate markers and risk factors of atherosclerosis including inflammation, cholesterol and insulin resistance improving survival in men with T2D. The underlying mechanisms of this action remain poorly understood. Inflammation is a central feature to both T2D and atherosclerosis and is driven by monocyte/macrophages, placing these immune cells at the crossroads of disease pathology. The recruitment of immune cells to atherosclerosis-prone areas of the vasculature is influenced by many factors including the inflammatory status of the circulating monocytes. The present study investigates the influence of testosterone replacement on monocyte inflammatory markers in a randomised double blinded placebo controlled clinical trial. 65 men with poorly controlled diabetes (HbA1c between 53 and 80 mmol/mol) and confirmed hypogonadism via early morning [0800−1200h] total testosterone ≤12 nmol/L or calculated free testosterone ≤255 pmol/L on two occasions ≥1 week apart, with at least two symptoms of hypogonadism were included in the study. Patients were randomly assigned to either placebo or treatment (depot testosterone undecanoate, 6 weekly followed by 3 monthly intramuscular injections) for 6 months. Monocytes were isolated from whole blood collected at baseline, 3 and 6 month visits followed by gene expression of key inflammatory targets IL-1β, IL-6, IL-10, TNFα, ICAM1, TLR2, TLR4, SCARB1 and MCP1 assessed via qPCR. Pro-inflammatory targets TNFα and MCP1 were significantly reduced over time in monocytes from patients treated with testosterone between 3 and 6 months (1.39±0.39 Vs 0.68±0.09, P<0.01; 15.36±7.79 Vs 1.88±0.93, P<0.01 respectively) and TNFα at 6 months compared to the start of the study (1.00±0.00 Vs 0.68±0.09, P<0.001) when normalised to baseline. TNFα expression was also significantly reduced compared to placebo treated patient monocytes at 6 months (0.68±0.09 Vs 3.45±1.50, P<0.01). Other targets were not significantly altered over time or between treatment groups. These findings importantly indicate for the first time that testosterone influences monocyte inflammatory activation in type 2 diabetic men by altering expression of the most potent atherogenic chemokine MCP1 and potent pro-inflammatory cytokine TNFα, as a potential mechanism to protect against atherosclerotic plaque development in hypogonadism.

Adrenal

ADRENAL CASE REPORTS II

Development of Adrenocortical Carcinoma in an Adrenal Nodule After Nine Years of Size Stability on Imaging: A Case for Critical Review of Efficacy of Radiographic Size Criteria

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