Although in PORD classically the inheritance is generally autosomal recessive, but manifesting heterozygotes are not uncommon[1]. This case also shows the value of Next gen sequencing and the role it can play in DSD

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Cardiovascular Endocrinology

PATHOPHYSIOLOGY OF CARDIOMETABOLIC DISEASE

Role of Linagliptin on CD34+ Endothelial Progenitor Cells and Arterial Stiffness in Renal Function Impaired Type 2 Diabetes Subjects

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SUN-578

Title: Role of Linagliptin on CD34+ Endothelial Progenitor Cells and Arterial Stiffness in renal function impaired Type 2 Diabetes subjects.

Introduction: Endothelial Progenitor cells (EPCs) has been shown to be dysfunctional in both Type 2 Diabetes and Chronic Kidney Disease (CKD) leading to poor regeneration of endothelium and renal tubules. EPCs have been shown to be a robust cardiovascular disease (CVD) risk indicator. DPP4 inhibitor increase endogenous SDF1a which has been shown to increase CD34+ cells migration and thereby improve CVD risk. However, cellular mechanisms of DPP4i mediated improvement of CVD in patients with Type 2 Diabetes with established CKD is not established. **Hypothesis**: Linagliptin, a DPP4 inhibitor when added to insulin, metformin or both may recover endothelial function in a diabetic kidney disease (DKD) population. **Methods**: 31 subjects taking 1–2 grams of metformin and/or Insulin were enrolled in this 12 weeks, double blind, two-arm, randomized placebo matched trial, with 5 mg Linagliptin compared to placebo. Type 2 diabetes subjects (30–70 years old), HbA1c of 6.5–10%, and all stages of CKD were included. CD34+ cell number, migratory function, gene expression along with vascular parameters such as Arterial stiffness, biochemistry, resting energy expenditure and body composition were measured. Data were collected at week 0, 6 and 12. During trial HbA1C was maintained between 7–8% for all subjects. Every subject was used as their own control. A mixed model regression analysis was done with p value <0.05 considered significant. **Results**: A double positive CD34/CD184 cell count had a statistically significant increase ($p<0.02$) as determined by flow cytometry in treatment group though there was no statistically significant increase in CD34+ cell number, or colony formation units. Gene expression analysis on CD34+ cells showed reduced expression of TP53 ($p<0.04$). Arterial stiffness measures such as augmentation Index ($p<0.04$) along with augmentation pressure ($p<0.02$) were significantly reduced in the treatment group. A reduction in LDL: HDL ratio was noted in treatment group ($p<0.04$). No change in renal function was noted during the 12 week period.. We are currently analyzing urinary exosome based data to enquire further into renal function **Conclusions**: In DKD subjects, Linagliptin promotes an increase in CXCR4 expression on CD34+ progenitor cells with a concomitant improvement in arterial stiffness and LDL parameters within 12 weeks of intervention.

Bone and Mineral Metabolism

BONE DISEASE FROM BENCH TO BEDSIDE

Antenatal Oral Iron Supplementation, FGF23 and Bone Metabolism in Kenyan Women and Their Offspring: A Randomised Controlled Trial

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SUN-359

Objectives: FGF23 decreases reabsorption and increases phosphate excretion in the kidney and regulates vitamin D metabolism. Maternal iron deficiency may be implicated in the pathogenesis of hypophosphataemia-driven rickets in offspring through perturbed FGF23 expression. We aimed to determine the effect of antenatal oral iron supplementation on maternal and neonatal markers of bone mineral regulation.

Methods: 470 rural Kenyan women with singleton pregnancies and haemoglobin concentrations ≥90g/L were randomly allocated to daily, supervised supplementation iron (60mg as ferrous fumarate) or placebo from 13–23 weeks gestational age until 1 month postpartum. We analysed maternal and neonatal plasma samples collected at birth, with primary outcomes being concentrations of FGF23 in its intact form (I-FGF23, the phosphate- and vitamin D-regulating hormone) and its C-terminal fragment (C-FGF23).

Results: In mothers and neonates, antenatal iron supplementation reduced C-FGF23 concentration by 62.6% (95%CI: -70.3% to -53.0%) and 15.2% (-28.4% to 0.3%), respectively; increased neonatal I-FGF23 concentration by 21.6% (1.2% to 46.1%); increased maternal hepcidin concentration by 136%, (86% to 200%); and decreased maternal 25-hydroxyvitamin D concentrations by 6.1nmol/L (1.2 to 11.0nmol/L). We found no effect on markers of bone turnover in either mothers or neonates. The magnitude of the

effect of antenatal iron supplementation on concentrations of C-FGF23, I-FGF23 and phosphate, and on estimated glomerular filtration rate (a measure of kidney glomerular function) depended on maternal iron status at baseline
Conclusions: Antenatal iron supplementation may provide health benefits to pregnant women and their offspring beyond increasing iron status. Whether iron supplementation reduces present and future infant risk of rickets remains unclear.

Diabetes Mellitus and Glucose Metabolism

DIABETES COMPLICATIONS II

Effect of High Salt Diet on Kidney Weight in Neonatal Streptozotocin Induced Noninsulin Dependent Diabetic Rats

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MON-692

Diabetic kidney hypertrophy may contribute to the development of diabetic kidney disease. Hyperglycemia is recognized as a cause for the kidney endangerment. Salt may accelerate progression of kidney disease in diabetes. To further study the effect of high salt intake on kidney disease we used neonatal streptozotocin induced Noninsulin Dependent Diabetic (NIDD) rats fed ad libitum with regular Purina chow and 2% salt Purina chow. Rats in 5 groups were sacrificed at 6 weeks. Each group had 5–7 rats of diabetics on 2% salt and on regular chow and controls on 2% salt and on regular chow. Blood glucose in diabetics on salt ranged between 185±19–576±20 and in diabetics on regular chow 184±20–458±78 mg/dl. Controls on 2% salt 105±8.6–133±10.3 and controls on regular chow 110±8.9 - 130±3.11. Kidney weights in diabetics on salt was 1.85±0.09–2.0±0.06 gr, diabetics on regular chow 1.6±0.04 - 1.56±0.06 controls on salt 1.19±0.03–1.32±0.05 and controls on regular chow 1.23±0.03. Blood glucose in diabetics on salt and on regular chow was higher than in controls $p<0.05$ but did not differ between the diabetic groups. Kidney weight was increased in both diabetic groups compared with controls $p<0.05$ and was increased in diabetics on salt compared with diabetics on regular chow $p<0.05$ at all glucose levels. Controls on salt and on regular chow had similar kidney weights. Also kidney weight relative to body weight was higher in diabetics than in controls $p<0.05$ and was higher in diabetics on salt compared to diabetics on regular chow $p<0.05$, but there was no difference between controls on salt and controls on regular diet. Kidney % of water was similar in all four groups but protein to kidney DNA ratio was higher in the diabetic groups $p<0.05$ confirming the kidney hypertrophy. Insulin sensitivity measured in controls was not different between groups when glucose transport, glucose oxidation and lipogenesis were measured in fat cells showing no effect of salt on insulin sensitivity. We suggest that high salt intake is an additional risk factor for increased kidney weight in NIDDM that is additive to that of the prevailing glycemia.

Bone and Mineral Metabolism

BONE AND MINERAL CASE REPORTS I

Severe Symptomatic Hypocalcemia Related to Cinacalcet Administration Introduction

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SAT-355

Background: Cinacalcet, a class of drug used to treat secondary hyperparathyroidism due to end-stage renal disease, is also indicated for the treatment of hypercalcemia in patients with parathyroid carcinoma. This drug acts as a calcimimetic agent by allosteric activation of the calcium-sensing receptor that is expressed in various tissues. Common side effects of cinacalcet include nausea, vomiting, diarrhea and weakness. Although mild hypocalcemia is a common side effect, severe hypocalcemia is rare.
Case Presentation: A 61-year-old man was evaluated for treatment of type I diabetes mellitus. He reported several months of progressive fatigue, muscle weakness, and paresthesia of his hands and feet. He was prescribed cinacalcet for a parathyroid disorder since 2014 and his previous physician increased the dose of cinacalcet about 2 months ago from 60mg daily to 120mg daily. Since that time his paresthesias have been more severe. Physical examination: normal vital signs, Chvostek's and Trousseau's signs were positive. Rest of the examination was normal. Laboratory: corrected serum calcium (Ca) of 6.7 mg/dL (ref 8.6–10.0), down from 7.6 mg/dL 2 months earlier. Additional laboratory: Ionized Ca 3.4 mg/dL (ref 4.5–5.6), PTH 68 pg/mL (ref 15–65), 25-OH vitamin D 37 ng/mL (ref 29–100), phosphorus 4.9 mg/dL (ref 2.5–4.5) and calculated GFR 97 mL/min. Cinacalcet was stopped. The patient was treated with calcium intravenously in the ICU resulting in normal serum calcium levels after 36 hours of treatment and complete resolution of symptoms. He was discharged on oral calcitriol and calcium supplementation, which was discontinued within 1 week of discharge.
Discussion:
In vast majority of cases hypocalcemia associated with cinacalcet therapy are mild and self-limited. Generally hypocalcemia develops within 16 weeks of starting therapy and resolves spontaneously within 2 weeks. This case is unusual in that the hypocalcemia occurred years after starting therapy and the patient experienced severe symptoms, undiagnosed for a prolonged period of time and required admission for close monitoring. Additionally, this patient was without the most common risk factor for cinacalcet-associated hypocalcemia which was secondary hyperparathyroidism, and he had normal renal function. The marked decrease in serum Ca levels may be related to his low baseline serum Ca levels and due to the recent increase in cinacalcet dose. However this has not always verified based on retrospective studies. Interestingly the cinacalcet dose was increased in up to 14% of patients with severe hypocalcemia (<7.5 mg/dL) and even in this population severe symptomatic hypocalcemia symptoms were rare. In conclusion, clinicians should closely monitor patients on calcimimetic drugs for hypocalcemic symptoms although mild asymptomatic hypocalcemia may resolve without intervention.