(and increased MV isovolumic relaxation time (IVRT) in DHT group compared to C. RSV treatment reversed these changes. In conclusion, RSV improved glucose homeostasis and diastolic dysfunction in the DHT induced rodent model of PCOS and may serve as a novel treatment option targeting the cardiometabolic derangement seen in PCOS. Further studies elucidating the mechanisms underlying the beneficial effects of RSV on cardio-metabolic phenotype in this PCOS rodent model is warranted.

Pediatric Endocrinology

PEDIATRIC SEXUAL DIFFERENTIATION, PUBERTY, AND BONE BIOLOGY

Investigation of Imprinting Defects in MKRN3 and DLK1 in Children with Idiopathic Central Precocious Puberty Through Specific DNA Methylation Analysis

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Background: Loss of imprinting has been implicated in the pathogenesis of several human diseases. Monogenic causes of central precocious puberty (CPP) were identified in families with loss-of-function mutations affecting mainly the coding region of two paternally expressed imprinted genes: Makorin ring finger 3 (*MKRN3*) and Delta-like 1 homolog (*DLK1*). The role of imprinting defects involving these two genes in CPP has not been described so far.

Objective: To investigate the methylation status at primary differentially methylated regions (DMR) of *MKRN3* and *DLK1* in a cohort of children with idiopathic CPP.

Patients and methods: One-hundred and twenty CPP patients (112 sporadic, 8 familial; 115 females, 5 males) were selected for analysis. Leukocyte DNA was obtained from all patients. *MKRN3* and *DLK1* pathogenic allelic variants were first excluded by DNA sequencing analysis. Bisulfite treatment followed by Allele-Specific Methylated Multiplex Real-Time Quantitative PCR was performed with leukocyte DNA, analyzing separately the methylation index (MI) of *MKRN3*:TSS-DMR and *DLK1/MEG3*:IG-DMR for each patient. The MI results were compared with controls with normal pubertal development.

Results: Mean age at puberty onset was 5.8 ±1.9yr for girls and 7.2 ±2.6yr for boys. Hypomethylation at *DLK1/MEG3*:IG-DMR was identified in 3 patients (I, II and III) with sporadic CPP: MI 10%, 16% and 11%, respectively. Interestingly, cases II and III were both girls who had been firstly referred to pediatric endocrinology for presenting precocious menarche; while case I was a boy who had been referred for presenting mild growth retardation, and developed CPP during monitoring. In addition, during follow-up, other clinical findings were noticed: being born small for gestational age, prominent forehead, small hands/feet, overweight/obesity and early onset type 2 diabetes in case III. Additional genetic investigation included SNP array in cases I and II, identifying a maternal uniparental disomy at chromosome 14 (upd(14)mat). Meanwhile, case III had normal genomic microarray and microsatellites analysis, excluding copy number variants and upd(14) mat, and indicating a mechanism of epimutation at *DLK1/MEG3*:IG-DMR. Uniparental disomy and epimutation are molecular mechanisms associated with the imprinting disorder known as Temple syndrome. In the remaining cases, mean MI for *DLK1/MEG3*:IG-DMR was 49±2%. In all cases, mean MI for *MKRN3*:TSS-DMR was 49±6%. There were no significant correlations between age at puberty onset and MI for *MKRN3* (p=0.69) and *DLK1*(p=0.45).

Conclusion: There was no leukocyte DNA methylation defect at *MKRN3* imprinting control region in the idiopathic CPP cohort. *DLK1/MEG3*:IG-DMR hypomethylation was identified in 3 patients with CPP and additional findings of Temple syndrome, indicating that loss of effective imprinting of *DLK1* locus is a mechanism leading to CPP.

Diabetes Mellitus and Glucose Metabolism

CLINICAL AND TRANSLATIONAL STUDIES IN DIABETES

The Prevalence and Clinical Characteristics of Adult Patients Presenting with Sodium-Glucose Co-Transporter-2 Inhibitor Associated Euglycemic Diabetic Ketoacidosis

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The Prevalence and Clinical Characteristics of Adult Patients Presenting with Sodium-Glucose Co-Transporter-2 Inhibitor (SGLT-2i) Associated Euglycemic Diabetic Ketoacidosis

Background: Sodium-Glucose Co-Transporter-2 Inhibitors (SGLT-2i) have been associated with euglycemic diabetic ketoacidosis (EuDKA). The pathophysiology is related to decrease insulin secretion given glucosuria and lower insulin to glucagon ratio, resulting in enhanced lipolysis and ketogenesis at a lower glucose level. SGLT-2i may unmask underlying undiagnosed type-1 diabetes/Latent Autoimmune Diabetes of the Adult (LADA).

Objective: (1)To describe the frequency and clinical characteristics of SGLT-2i associated EuDKA at a Canadian tertiary care centre. (2)To identify the most common underlying diabetes-type associated with EuDKA.

Methods: A chart review identified patients with SGLT-2i-associated EuDKA from June 2015 to May 2019 who presented to a Canadian tertiary care centre. Clinical characteristics include age, gender, diabetes type, SGLT-2i drug prescribed, laboratory results at the time of EuDKA and possible precipitants were reviewed. Pancreatic