clinical features and several endocrinological problems such as hypogonadism, hypothyroidism, Growth hormone (GH) and adrenal deficiency have been described. Since GH-Therapy (GHT) was approved the physical benefits of the treatment have been established in many studies. It is now recommended to start treatment as soon as possible. The aim of this study is to shed light on possible differences in height, carbohydrate and lipid metabolism between children with PWS in whom GHT was initiated either during or after their first year of life. Patients and Methods: This retrospective longitudinal study included 62 children (31 males) with genetically confirmed PWS in whom fasting morning blood samples and auxological parameters were obtained before start of therapy and semi-annually thereafter. The early treatment cohort A consisted of 21 (11 males) infants who were recruited at 0.3–0.99 yrs (mean 0.72 yrs) for GHT. The later treatment cohort B entailed 41 individuals (20 males) in whom GHT was initiated at 1.02–2.54 yrs (mean 1.42 yr). Results: Auxology: Mean length/height-SDS_{PWS} differed significantly throughout the entire observation period between the groups: 1 yr: A: 0.37 (±0.83) *vs* B: 0.05 (±0.56); 5 yrs: A: 0.81 (±0.67) *vs*. B: 0.54 (±0.64); p=0.012). No significant differences were found in BMI, lean body mass or percent body fat. Endocrinological Parameters: Mean IGF-I SDS in group A did not differ significantly from group B and mean IGF-I SDS were mostly below 0 SDS (within normal range) in both groups.Lipid Metabolism: Low-density lipoprotein (LDL) was statistically significantly lower in Group A than in Group B during the entire course of the study (LDL: 1 yr: A: 79 (±20) mg/dl vs. B: 90 (±19) mg/dl; 5 yrs: A: 91(±18) mg/dl vs. 104 (±26) mg/dl; p=0.024).Carbohydrate Metabolism: Significant differences in mean fasting insulin levels and HOMA-IR between the two groups were found (fasting insulin p=0.012; HOMA-IR p=0.006). Significant differences in HbA1c and blood glucose levels were also determined between the two groups (HbA1c: p<0.001; blood glucose: p=0.022). Conclusion:Our analysis shows that early GHT had a statistically significant favorable effect on height-SDS, LDL, HOMA-IR and fasting insulin. The two groups did not significantly differ in BMI-SDS, body composition or IGF-I SDS.

Neuroendocrinology and Pituitary

CASE REPORTS IN SECRETORY PITUITARY PATHOLOGIES, THEIR TREATMENTS AND OUTCOMES

Block and Replace Therapy Successfully Improved Symptoms in Recurrent Cyclic Cushing's Disease

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SAT-271

Background: Cyclic Cushing's disease is rare and treatments have not been established for post-surgical recurrent cases. Here, we report a patient with recurrent cyclic Cushing's disease, whose subjective symptoms improved by administration of metyrapone and hydrocortisone. **Clinical Case:** A 45-year-old woman had exhibited face and peripheral edema, hyperphagia, weight gain, hair loss and limb numbness since September X-10. In May X-9, her ACTH and cortisol levels were high (87.8 pg/mL and 28.8 μg/dL, respectively), and she was referred to our department. A brain MRI revealed a pituitary adenoma of 7mm in diameter. Because blood ACTH and cortisol levels turned normal and typical Cushingoid features were absent at the admission to our department, cyclic Cushing's disease was suspected. Later in September, because subjective symptoms recurred accompanied with blood cortisol level elevation, she was diagnosed as cyclic Cushing's disease with the examinations including inferior petrosal sinus sampling. Transsphenoidal surgery was performed in November, and immunohistology confirmed ACTH-producing pituitary adenoma based on ACTH positivity. After the surgery, endocrine test results were normalized and subjective symptoms were ameliorated. In March X-3, the blood ACTH level increased again; however, no subjective symptoms were observed. From May X, she had experienced limb numbness, hyperphagia and weight gain again. MRI showed no apparent recurrence, but endocrine tests showed the activity of Cushing's disease. Urinary free cortisol (UFC) increased to 300–400 μg/day in a 1-week cycle, indicating the recurrence of cyclic Cushing's disease. Metyrapone treatment was initiated, and the patient was finally discharged after block and replace therapy with metyrapone 2,000 mg/day and hydrocortisone 15 mg/day. After metyrapone treatment, subjective symptoms improved and UFC was normalized. **Conclusion:** Block and replace therapy with metyrapone and hydrocortisone may be effective for recurrent cyclic Cushing's disease, especially in cases with a very short cycle.

Diabetes Mellitus and Glucose Metabolism

DIABETES TECHNOLOGY AND ADVANCES IN CLINICAL TRIALS

Mixed Meal Tolerance Test (MMTT) Results from Revita-2, the First Randomized, Sham-Controlled, Double-Blind, Prospective, Multicenter Study of Duodenal Mucosal Resurfacing (DMR) Safety and Efficacy in Patients with Sub-Optimally Controlled Type 2 Diabetes (T2D)

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OR30-07

Background: The duodenum is a key metabolic signaling center and regulator of metabolic homeostasis. Duodenal mucosal hyperplasia is therefore a potential therapeutic target for metabolic diseases related to insulin-resistance. Previous reports demonstrated that DMR, a minimally invasive, endoscopic mucosal ablative procedure, safely improves hepatic and glycemic parameters. Primary endpoints from REVITA-2, the first randomized, sham-controlled, double-blind, prospective, multicenter study of DMR safety and efficacy in patients with T2D, were met and previously reported. Here we further explore mechanisms underlying the beneficial effects of DMR on hepatic and glucose metabolism by analyzing mixed meal tolerance test (MMTT) data from the REVITA-2 study. **Methods:** Eligible patients (HbA1c 7.5–10%, BMI ≥ 24 to ≤ 40 kg/m^2, on stable treatment with ≥1 oral anti-diabetic medication) received DMR or sham procedure (1:1). Exploratory endpoints included median change in fasting plasma glucose (FPG), MMTT glucose area under the curve (AUC) over 2 hours, and change in MMTT C-peptide and glucagon over 2 hours, from baseline to 12 weeks post-DMR. One-sided *P* value based on ANCOVA model on ranks without imputation assessed treatment difference at the 0.05 significance level. The modified intent to treat primary analysis population included randomized patients in whom study procedure was attempted. **Results:** A total of 70 patients (DMR, N = 35; sham, N = 35) were included in the analysis, of which 57% and 54% (DMR, n = 20; sham, n = 19) had baseline FPG ≥ 180 mg/dL. Median MMTT AUC for glucose was significantly reduced post-DMR (-36.38 mg/dL) compared with sham (-4.94 mg/dL; *P* = 0.009), driven by a significant decrease in FPG (DMR, -41.0 mg/dL; sham, -15.0 mg/dL; *P* = 0.003) rather than median MMTT postprandial glucose excursion (DMR, -4.63 mg/dL; sham, 5.34 mg/dL; *P* = 0.209). AUC glucose reductions were more pronounced in patients with baseline FPG ≥ 180 (DMR, -63.03 mg/dL; sham, -20.31 mg/dL; *P* = 0.007) compared with baseline FPG < 180 (DMR, -26.81 mg/dL; sham, 13.81 mg/dL; *P* = 0.271). In patients with baseline FPG ≥ 180, postprandial C-peptide excursion was significantly increased (DMR, 0.41 ng/mL; sham, 0.02 ng/mL; *P* = 0.012) and postprandial glucagon excursion was significantly decreased (DMR, -8.03 pg/mL; sham, 2.13 pg/mL; *P* = 0.027). **Conclusion:** DMR markedly improves glucose responses to a mixed meal challenge, primarily driven by a decrease in FPG, suggesting a primary effect on insulin resistance. Increases in C-peptide and reductions in glucagon levels suggest improvement in beta cell function in addition to improvements in hepatic insulin sensitivity, and ratifies the position of the duodenum as both a culprit endocrine organ and therapeutic target for patients with T2D.

Cardiovascular Endocrinology

PREVALENCE, DIAGNOSIS, AND MECHANISMS OF HYPERALDOSTERONISM

Somatic Transmembrane Domain Mutations of a Cell Adhesion Molecule, CADM1, Cause Primary Aldosteronism by Preventing Gap Junction Communication Between Adrenocortical Cells

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OR34-02

Primary Aldosteronism (PA) is the commonest curable cause of hypertension. Whole exome sequencing (WES) in 2011 and 2013 identified common somatic mutations in genes regulating membrane polarisation in 60–80% of aldosterone-producing adenomas (APA). We undertook WES on 39 consecutive APAs in search of further variants. 1 APA revealed a somatic mutation (Val380Asp) within the single transmembrane domain of *Cell Adhesion Molecule 1* (*CADM1*). An adjacent mutation (Gly379Asp) was discovered on WES from a PA patient in Munich.

Both short and long isoforms (442 & 453 residues) of wild-type (WT) and both mutant *CADM1* genes were cloned into lentivirus vectors and each transduced into adrenocortical (H295R) cells to assess its effect on aldosterone secretion and other parameters. Previous studies in pancreatic islet cells suggested a role of CADM1 in regulating gap junction (GJ) communication. To assess this we microinjected single WT or mutant H295R cells with the GJ permeable dye calceinAM and counted the dye-positive cells after 1 hour. The effect of inhibiting or silencing GJs in H295R cells using peptide gap27 or a Dharmacon smartpool was assessed. H295R cells were also co-transfected with WT or mutant *CADM1* and the GJ protein CX43, tagged with the mApple fluorophore. These were mixed with cells transfected with CX43-Venus, allowing confocal visualisation of GJ formation. Protein modelling was undertaken to determine whether Asp in the intramembranous domain changes angulation of CADM1.

All mutant isoforms had consistently different effects, shown as a range compared to WT. Cells transduced with mutant *CADM1* showed 3-6-fold increase in aldosterone secretion ($p<0.01$) and 10-20-fold increase in *CYP11B2* expression ($p<0.001$) compared to WT. Dye transfer assays showed paucity of dye transfer between neighbouring mutant *CADM1* cells, while calcein passed easily through GJs in WT cells. CX43 inhibition increased aldosterone secretion 2-fold ($p<0.01$), and *CYP11B2* expression 3 to 8-fold (<0.001). Knock-down of GJ proteins increased aldosterone