

Data were obtained from nationwide health care registers. Patients were included if they had diagnosis codes for acromegaly and neoplasm of the pituitary gland between Jul 1, 2005 and Dec 31, 2017, and at least one purchase of LA-SSA (lanreotide [LAN] 60, 90, or 120 mg, or octreotide [OCT] 10, 20, or 30 mg). Cox regression models were used for analyses of persistence and switching.

Results

The analysis included 176 pts treated with LA-SSA in 2005-2017. The cohort was subgrouped on year of initiation of LA-SSA (2005-2011, n=90, 51%; 2012-2017, n=86, 49%). In the first period, 36 pts (40%) initiated LAN while 54 pts (60%) initiated OCT while in the later period, 44 pts (51%) initiated LAN and 42 pts (49%) initiated OCT (p=0.17). No patients initiated pasireotide. Patient characteristics were similar between LAN and OCT initiators, but history of pituitary surgery was more common for LAN as compared to OCT (LAN 62%; OCT 46%, p<0.05). Similar results were seen for visual-field defects (LAN 20%, OCT 8%, p<0.05). Median (95%CI) follow-up was not significantly different [LAN 5.3 (3.7; 6.0) yrs.; OCT 6.4 (4.5; 7.6)].

The mean (95%CI) dose interval was not significantly different, 30.5 (28.7; 32.6) days for LAN vs 29.5 (28.5; 30.3) days for OCT. The median (95%CI) duration of 1st-line LA-SSA treatment was 14.4 (10.8; 21.6) months for LAN and 12.0 (7.2; 19.2) months for OCT. Fifty-one pts (64%) discontinued 1st-line LAN while 70 pts (73%) discontinued 1st-line OCT (hazard ratio (HR) LAN vs. OCT 0.80; 95% CI: 0.56-1.15). Due to the use of register data, the reason for therapy change could not be determined. Eight pts (10%) switched LAN to OCT while 29 pts (30%) switched OCT to LAN. Patients initiated on OCT were more likely to switch to LAN than the other way around (HR for switch for 1st-line LAN vs. OCT 0.33; 95% CI 0.15-0.72). Among patients who switched OCT to LAN, 67% of LAN dispensing was 120 mg, 21% 90 mg, and 12% 60 mg. Among patients who switch LAN to OCT, 84% of OCT dispensing was 30 mg, and 16% 20 mg.

Conclusions

There was no significant difference in the number of patients initiated on LAN or OCT despite the later introduction of LAN in Sweden. Patient characteristics were similar but LAN initiators were more likely to have undergone surgery and be diagnosed with visual field defects which could indicate that physicians initiate LAN in patients with more aggressive disease. Extended dose intervals with LAN (dosing every 6-8 w) do not seem to be commonly used in Sweden. In comparison to OCT, patients initiated on LAN were significantly less likely to change LA-SSA therapy.

Thyroid

THYROID DISORDERS CASE REPORTS II

A Case of Congenital Thyroid Hemi-Agenesis- Caution for Complications!

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Introduction: Congenital Thyroid hemi-agenesis is an uncommon clinical entity. We present a case highlighting the importance of awareness of this condition and the need to evaluate and manage co-existing hypothyroidism and risk of malignancy. **Case:** A 20 year old female known to have Hashimoto's thyroiditis (non-adherent to levothyroxine), and hemi-agenesis of left lobe of thyroid gland, presented with right-sided thyroid enlargement. She was clinically euthyroid. Physical exam: enlarged right sided thyroid gland with palpable anterior cervical lymphadenopathy. Left lobe could not be palpated. TFTs were notable for TSH 4.98 uIU/ml (0.358-3.74) and Free T4 0.79 ng/dl (0.76-1.46) consistent with sub-clinical hypothyroidism while Anti TPO antibody was positive at 8332.8 U/mL (0 - 60). CBC negative for leukocytosis. US thyroid: left-sided thyroid agenesis with intact isthmus and enlargement of right lobe of the thyroid 7.7 cm x 1.6 cm x 2.6 cm with 2 sub-centimeter hypoechoic solid nodules and 2 enlarged lymph nodes 1.5 cm and 2.3 cm (not found in US thyroid 2 years ago) Levothyroxine was re-started. ENT evaluation determined that her lymphadenopathy was benign and consistent with Hashimoto's thyroiditis. Subsequent TFTs improved. **Discussion:** Thyroid Gland embryogenesis occurs in the 4th week of fetal life. Subsequent abnormal bilobal differentiation of the thyroid gland is presumed to be the etiology of congenital hemi-agenesis. Its prevalence in several studies is estimated to be between 0.05-0.25%. It is symptomatic pre-dominantly in females and may have familial origin with vast majority of cases having left hemi-agenesis with intact isthmus. It is helpful to know that most symptomatic patients have compensatory hypertrophy of the remnant lobe. It is important to remember that compensatory enlargement of the remnant lobe in the setting of hypothyroidism may be a sign of insufficient endogenous thyroxine production and/or replacement. Although rarely symptomatic, hemi-thyroid remnant may need to be evaluated for co-existing hyperthyroidism, hypothyroidism, carcinoma and multinodular goiter among others, with hypothyroidism thought to be the most common. US thyroid is a useful modality to help guide the evaluation of patients with hemi-agenesis. Awareness of this congenital condition is key in preventing unnecessary evaluations and interventions. Non-resolving lymphadenopathy in Hashimoto's thyroiditis must be evaluated for lymphoma, however, based on studies, no additional risk of malignancy was identified in patients with underlying thyroid hemi-agenesis. **References:** Y.H. Wu, R.O. Wein, B. Carter Thyroid hemiagenesis: a case series and review of the literature *Am J Otolaryngol*, 33 (3) (2012), pp. 299-302

Diabetes Mellitus and Glucose Metabolism

PREGNANCY, LIPIDS, AND CV RISK — IMPACT OF DIABETES ACROSS THE SPECTRUM

Increased Carotid Intima Media Thickness in Pediatric Type 1 Diabetes Is Associated with Disease Duration

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Background & Objective

Patients with type-1-diabetes (T1D) are at risk of long-term micro and macrovascular complications causing significant morbidity and mortality. Overt complications are not common in childhood; however, subclinical impairments in endothelial function, may be found. Better understanding of the timeline for the appearance of diabetic complications and identifying individuals at increased risk is key for developing prevention strategies. We aimed to study endothelial function and its determinants in adolescents with T1D at different time points from diagnosis.

Methods

Forty adolescents 11-20 years of age with T1D followed at our pediatric diabetes clinic and 18 healthy control subjects were included. Two groups of patients were recruited based on time from T1D diagnosis; 20 individuals were diagnosed 2-4 months prior to the study visit and 20 at least 7 years prior to the visit. Investigations included: i) medical and demographic data ii) anthropometrics iii) fasting blood samples iv) EndoPAT testing of endothelial function and heart rate variability (Itamar Medical Ltd., Israel) v) Carotid intima media thickness (CIMT).

Results

Mean age differed slightly between groups being 14.1±2.0 years in individuals with recent-onset T1D, 16.2±2.5 in those with prolonged T1D, and 14.8±2.3 in the control group (p=0.02). There were no significant differences in pubertal stage or in BMI z-score between groups. Thirty-three (57%) females participated. No patient suffered from diabetic complications. Mean CIMT was significantly higher in individuals with prolonged T1D (0.49±0.07mm) compared to control subjects (0.43±0.05mm; p=0.013) and did not differ significantly between patients with recent-onset T1D (0.45±0.07mm) and controls. This difference remained significant when age and sex were included in the model. EndoPAT measures of endothelial function and heart rate variability did not differ significantly between groups. Mean HbA1c at the time of the visit differed between groups (6.7%±0.7, 9.6%±1.8, 5.4%±0.3, p<0.001). However, the average of HbA1c reflecting the 6-7 months prior to the visit did not differ significantly between subjects with recent onset T1D (9.8%±1.3) and those with prolonged T1D (9.5%±1.7). LDL was higher in subjects with prolonged T1D (114±28mg/dl) compared to either controls (93±26mg/dl) or recent onset T1D (88±19mg/dl), p=0.002. Diastolic blood pressure was higher in subjects with prolonged T1D (70±6mmHg) than in controls (61±6, p=0.007).

Conclusions

Our results demonstrate disease duration to be an important factor in the development of subclinical arterial damage in the pediatric age group. Early in the course of T1D, CIMT results were similar in patients and control subjects, suggesting an important window for prevention. Larger studies could shed light on the precise timeline of endothelial impairment.

Adrenal

TRANSLATIONAL STUDIES ON ADRENOCORTICAL FUNCTION IN HEALTH AND DISEASE

Metformin Inhibits Activation of the Melanocortin Receptor 2 and 3 in Vitro, a Possible Mechanism for Its Anti-Androgenic and Weight Balancing Effects in Vivo

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OR19-07

Metformin is recommended as one of the first-line drugs for the treatment of type 2 diabetes and the metabolic syndrome. In addition to its insulin sensitizing effects, it has been shown to attenuate androgen excess in women with polycystic ovary syndrome (PCOS) or congenital adrenal hyperplasia (CAH), as well as to ameliorate obesity. The mechanisms of metformin action seem manifold. Preclinical studies suggest that it inhibits the cellular stress response at the level of the mitochondrial OXPHOS system and through AMPK dependent and independent mechanisms. Recent studies have shown that metformin decreases ACTH secretion from pituitary and reduces ACTH-stimulated adrenal secretion. In this study we investigated the effect of metformin through its specific melanocortin receptor 2 (MC2R) on signaling targeting adrenal steroidogenesis. To assess this effect, we used mouse adrenal OS3 cells, which do not express the MC2R. Cells were transfected with the human melanocortin receptor 2 and stimulated by ACTH. Downstream cyclic AMP production was then assessed by a co-transfected cAMP-responsive vector producing luciferase that was measured by a dual luciferase assay. The amount of luciferase produced in this assay corresponds to the amount of receptor activation with varying amount of ACTH. The effect of metformin was then tested in this system. We found a significant inhibition of ACTH induced MC2R activation and signaling with 10 mM metformin. The ACTH concentration response curve (CRC) was half-log shifted indicating antagonism. This effect was dose dependent with an IC₅₀ of 4.2 mM. Metformin did not affect cell viability and basal cAMP level under used conditions. We also tested the effect of metformin on homologous receptors (MCRs). No significant effect was found on MC1R and MC4R activity. However, a 2-log shift in ACTH EC₅₀ was observed with MC3R. In conclusion, metformin seems to act on MC2R and MC3R signaling directly. The role of MC2R for steroidogenesis is well established. MC3R is involved in energy balance and seems to act as a rheostat when the metabolism is challenged. Our study may explain how metformin attenuates the excess response to ACTH and helps in weight loss and improving androgen excess in PCOS and CAH.

Pediatric Endocrinology

PEDIATRIC SEXUAL DIFFERENTIATION, PUBERTY, AND BONE BIOLOGY

High Throughput Genetic Analysis Revealed Novel Genomic Loci and Candidate Genes Involved in Central Precocious Puberty Associated with Complex Phenotypes

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