

disrupted TR signaling; thus, the specific mechanism has not been cleared. It has been well known that proper motor coordination is deeply related to long term depression (LTD) of synaptic transmission from parallel fiber (PF) to Purkinje cell (PC) in the cerebellum (Ito, 1989). Therefore, we examined the involvement of TR in synaptic plasticity at PF-PC synapses by using transgenic mice (Mf-1 mice) which express dominant-negative TR specifically in PCs. Since Mf-1 display the impairment of motor coordination and motor learning, a decrease in TR signaling in PCs may alter synaptic plasticity and contribute to motor incoordination. A whole-cell patch clamp recording of Mf-1 PCs revealed the inhibition of LTD but instead the induction of long term potentiation (LTP) of the synaptic transmission at PF-PC synapses. This indicates that the intracellular calcium dynamics may be disrupted in Mf-1 PCs since LTD requires a higher elevation of the intracellular calcium concentration in PCs than LTP does. Indeed, single-PC qPCR showed that the mRNA levels of some important molecules for the intracellular calcium dynamics in PCs (SERCA2, IP₃R, and P/Q-type calcium channel) are downregulated in Mf-1 PCs. This result suggests those genes as possible TR-target genes. Taken together, the present study suggested a novel possible role of TR in synaptic plasticity at PF-PC synapses by regulating the expression of some important genes for LTD occurrence in the cerebellum. This finding could give a new insight into the mechanism of motor deficits in thyroid diseases.

Neuroendocrinology and Pituitary CASE REPORTS IN SECRETORY PITUITARY PATHOLOGIES, THEIR TREATMENTS AND OUTCOMES

Crooke's Cell Adenoma- an Aggressive Form of Cushing's Disease

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SAT-279

Introduction: Cushing's disease is a condition of cortisol overproduction caused by an ACTH-producing tumor. Corticotroph cells surrounding an ACTH-producing tumor usually undergo Crooke's hyaline change, where cytokeratin filaments accumulate in the cytoplasm in response to glucocorticoid excess. These changes are thought to be a mechanism of feedback inhibition and thus facilitate a suppression of ACTH. However, in a subtype of ACTH-secreting tumors known as Crooke's cell adenomas (CCA), the ACTH-producing cells also undergo these hyaline changes. This would be expected to suppress hormone secretion but these cells are still able to release significant amounts of ACTH.

Case presentation: A 32-year-old woman presented to the hospital after an episode of syncope. On head MRI, she was found to have a 2 cm sellar mass with optic chiasm compression. Labs showed low TSH, free FT₄, T₃, FSH, and LH. She was also pre-diabetic with an HgbA1c of 6.2%. Her

baseline cortisol of 20.6 µg/dL did not suppress after 1 mg of dexamethasone. After receiving 4 mg of dexamethasone, her cortisol suppressed to 5.2 µg/dL. She was diagnosed with hypopituitarism except for cortisol and a likely ACTH-producing pituitary macroadenoma. She completed a transsphenoidal pituitary resection and pathology revealed Crooke's hyaline changes with immunohistochemical stains positive for ACTH. The immunostain for the proliferation marker Ki67 showed a relatively low proliferation index. Her course was complicated by diabetes insipidus. She was ultimately discharged on 20 mg hydrocortisone each morning, 10 mg hydrocortisone each afternoon, desmopressin 0.05 µg daily, and levothyroxine 125 µg daily. Two weeks later, the patient was sent to the emergency room by her endocrinologist for hyperglycemia up to 288 mg/dL. She was also found to be newly diabetic with an HgbA1c of 6.5%. A fasting morning cortisol was collected during her admission and showed a cortisol level of <1.0 µg/dL, proving she was cured of Cushing's disease. However, she will need close endocrinology follow up and MRI imaging of her pituitary for this aggressive type of pituitary adenoma.

Discussion: We have come across an interesting case of a young woman who presented for syncope and was found to have a pituitary macroadenoma with pathology consistent with CCA. This type of ACTH-producing tumor is known for aggressive patterns including high rates of recurrence with rates of up to 60% reported in literature, persistent disease after surgery, malignant transformation, and metastases. Despite presentation and symptoms similar to those of other ACTH-producing adenomas, the dangerous pattern of Crooke's cell adenomas necessitate long-term follow-up in affected patients.

Diabetes Mellitus and Glucose Metabolism

DIABETES TECHNOLOGY AND ADVANCES IN CLINICAL TRIALS

Real-World Minimed™ 670G System Use and Glycemic Outcomes of Pediatric and Adult Individuals Living with Type 1 Diabetes (T1D) in the United States

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OR30-01

Introduction: The MiniMed™ 670G system was FDA-approved in 2016 for adults and adolescents ≥14yrs, and in 2018 for children ages 7-13yrs with T1D. Since then, use of the system has grown to over 180,000 people in the U.S. The glycemic control benefits of real-world MiniMed™ 670G system Auto Mode use in the U.S. were assessed. **Methods:** System data (aggregated five-minute instances of sensor glucose [SG]) uploaded from March 2017 to July 2019 by individuals (N=118,737) with T1D and ≥7yrs of age who enabled Auto Mode were analyzed to determine the mean % of overall time spent <54mg/dL/<70mg/dL (TBR); between 70-180mg/dL (TIR); and >180mg/dL/>250mg/dL (TAR). The impact of Auto Mode was further assessed in a sub-group of individuals (N=51,254) with, at least, 7 days

of SG data for both Auto Mode turned ON and turned OFF. The % of TIR, TBR and TAR, and the associated glucose management indicator (GMI) were evaluated for the overall OFF (2,524,570 days) and ON (6,308,806 days) periods, and across different age groups. **Results:** System data TIR was 71.3%; TBR was 0.4% and 1.9%, respectively; and TAR was 26.8% and 6.2%, respectively. User-wise data of Auto Mode OFF versus ON showed a mean of 70.3% of the time spent in Auto Mode, that TIR increased from 60.9% to 69.9%; and that both TBR and TAR decreased. For those 7-13yrs (N=1,417), TIR increased from 48.7% to 61.5%; TBR increased from 0.5% to 0.6% and from 2.0% to 2.2%, respectively; and TAR decreased from 49.3% to 36.3% and from 20.5% to 13.0%, respectively. For those 14-21yrs (N=4,194), TIR increased from 51.0% to 61.5%; TBR decreased from 0.7% to 0.6% and from 2.3% to 2.0%, respectively; and TAR decreased from 46.7% to 36.5% and from 18.5% to 12.5%, respectively. For those ≥ 22 yrs (N=45,643), TIR increased from 62.2% to 70.9%; TBR decreased from 0.7% to 0.5% and from 2.6% to 1.9%, respectively; and TAR decreased from 35.2% to 27.3% and from 9.9% to 6.3%, respectively. The mean GMI decreased by 0.23% (overall), 0.48% (7-13yrs), 0.35% (14-21yrs), and 0.22% (≥ 22 yrs), respectively, with Auto Mode ON versus OFF. **Discussion:** In over 6 million days of real-world MiniMed™ 670G system Auto Mode use in the U.S., TIR of a large pediatric and adult population with T1D improved by 9% compared to when Auto Mode was OFF, which was comparable to or exceeded the TIR observed in the smaller pivotal trials. These results further support outcomes of the pivotal trials and increased glycaemic control with system use.

Pediatric Endocrinology

SEXUAL AND GENDER DEVELOPMENT IN THE PEDIATRIC POPULATION

Blockers and Bones: Loss of Absolute Bone Mineral Density Is Common in Trans- and Gender-Diverse Adolescents Treated with GnRHa.

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OR15-01

Background: The expected pubertal accrual of bone mineral density (BMD) may be disrupted in trans and gender diverse (TGD) adolescents who undergo pubertal suppression with Gonadotropin Releasing Hormone agonists (GnRHa)¹. The extent of this effect remains unclear and is confounded by varying methods used to assess BMD¹.

While BMD Z-scores in GnRHa-treated TGD adolescents may be expected to decline relative to pubertal peers, this measure provides no information on actual changes in BMD. Annualised, percent change in BMD (%BMD velocity, %BMDV) provides a standardised measure of accrual or loss, but has not been reported in this context.

Aims: (1) To evaluate bone accrual or loss using %BMDV in a cohort of GnRHa-treated TGD adolescents; **(2)** to explore associations between baseline characteristics (BMD Z score, Vitamin D status and Tanner Stage) and %BMDV.

Methods. Retrospective 10yr audit at tertiary pediatric gender service. Bone densitometry data were collected at baseline and 12-24monthly during GnRHa. Areal BMD values and Z-scores for lumbar spine (LS) and total hip (TH) were obtained. %BMDV between baseline and final scan was calculated for LS and TH. Population data for %BMDV before and during puberty were derived from the BMD in Childhood Study². Results are reported as mean (\pm SD) or mean difference (MD; 95% confidence interval).

Results. Data from 28 patients (20 transfemale; 8 transmale) who commenced GnRHa at 13.3 (± 2.0) yrs and were observed over 23.2 (± 11.5) mo were included. Mean (\pm SD) %aBMDV during GnRHa therapy was -0.66 (± 4.54) %/yr for TH and +1.91 (± 4.23) %/yr for LS, both substantially lower than %aBMDV in pre-pubertal population controls ($\sim +3-4\%$ /year). 53% of GnRHa-treated youth exhibited negative %aBMDV, indicating bone loss, at TH and/or LS. %aBMDV was lower in (i) Vitamin D deficient youth, with MD at TH (-6.07; -9.00, -3.13); and LS (-4.93; -9.56, -0.30) relative to Vitamin D sufficient peers and (ii) youth who were Tanner stage 4+ at baseline, with MD at TH (-4.1; -7.7, -0.44) and LS (-3.6; -7.2, 0.01) relative to Tanner stage 2-3 peers. Height-adjusted Z scores declined from baseline with GnRHa treatment in >95% of patients and were not predictive of %aBMDV.

Conclusion. GnRHa-treated TGD adolescents in this cohort exhibited lower BMD accrual rates than pre-pubertal population controls. Over half of our cohort lost BMD, which is a significant concern in adolescence. Vitamin D deficiency and more advanced pubertal stage at GnRHa initiation were associated with greater bone loss during treatment. These data highlight the need to monitor and optimise bone health in GnRHa-treated TGD young people. We recommend routine annual densitometry and %BMDV evaluation regardless of baseline Z-scores as well as routine screening and treatment of vitamin D deficiency while on GnRHa.

References.

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Cardiovascular Endocrinology

ENDOCRINE HYPERTENSION AND ALDOSTERONE EXCESS

Changes in Albuminuria Precede Dietary Sodium-Dependent Changes in BP During Aging - a Longitudinal Study

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SAT-550

Background: Hypertension (HT) is a well-established independent risk factor for adverse cardiovascular and renal (CVR) outcomes and a high salt (HS) diet is the main cause