(PCOS) recommended healthy lifestyle interventions (dietary, exercise, behavioral modification, or combined) as the first-line therapy to mediate favorable metabolic outcomes in PCOS. However, the relationship between lifestyle modifications and reproductive health in PCOS is less clear. Specifically, a favorable dietary composition to facilitate reproductive changes in women with PCOS remains unknown. Further, the longitudinal impacts of lifestyle change programs in women with PCOS is poorly elucidated. We hypothesized that a low glycemic index pulse-based diet containing lentils, beans, split peas, and chickpeas would be more effective than the Therapeutic Lifestyle Changes (TLC) diet at improving insulin sensitivity without an energy-restricted protocol and would improve reproductive health outcomes in women with PCOS after a 16-week intervention. Our objective was to compare the effects of a nutritionally balanced pulse-based diet with the TLC diet on ultrasonographic markers of ovarian morphology, hyperandrogenism, and menstrual irregularity. Women (n=30) randomized to the pulse-based and TLC (n=31) groups completed a 16-week intervention. All women participated in aerobic exercise (minimum 5 days/week; 45 minutes/day) and received health counseling (monthly) about PCOS and the benefits of lifestyle modification. Additionally, we evaluated the effects of the intervention on the reproductive outcomes by longitudinal follow-up of all participants. Follicle numbers per ovary (FNPO, 2-9 mm), ovarian volume (OV), free androgen index (FAI), intermenstrual intervals, and insulin sensitivity (Matsuda index and homeostasis model assessment of insulin resistance [HOMA-IR] were evaluated at baseline, 16-week post-intervention, and 6- and 12-month post-intervention follow up visits. Follicle numbers per ovary (mean change ± SD, -10 ± 15), OV (-2.7 ± 4.8 mL), FAI (-3 ± 2), intermenstrual interval (-13 ± 47 days), and body mass index (BMI, -1.6 ± 4.2 kg/m$^2$) decreased, and Matsuda index (1.1 ± 3.1) increased over time in both groups (All: $P \leq 0.01$), without group-by-time interactions (All: $P \geq 0.27$). Groups maintained reduced OV, FNPO, FAI, and menstrual cycles 6 months post-intervention, despite a propensity for weight regain as evidenced by increased BMI (1.0 ± 4.8 kg/m$^2$; $P < 0.01$). Decreased FNPO, FAI, and HOMA-IR at 16-week tended to revert to baseline levels 12 months post-intervention in both groups (All: $P \leq 0.05$). Both interventions improved ovarian dysmorphology, hyperandrogenism, and menstrual irregularity in women with PCOS. Our observations elucidate the importance of longitudinal surveillance for sustainable adherence to newly adopted healthy lifestyle behaviors and reproductive health in PCOS (ClinicalTrials.gov identifier, NCT01288638).

# Neuroendocrinology and Pituitary

## CASE REPORTS IN UNUSUAL PATHOLOGIES IN THE PITUITARY

### *Lithium Induced Partial Nephrogenic Insipidus: An Unusual Presentation*

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**SUN-283**

Background: Diabetes insipidus (DI) is characterized by hypotonic polyuria and polydipsia. Nephrogenic DI is the result of an inadequate response of the kidneys to arginine vasopressin (AVP), either due to hereditary causes or acquired from various drugs, most commonly lithium. Clinical case: A 30 year old male with past medical history of Hashimoto's thyroiditis, severe mental impairment was admitted to the hospital for abdominal pain. Medical history was difficult to obtain since the patient was nonverbal. His thyroid function tests, electrolytes including sodium, potassium were all normal on admission. During the hospital course, he was made NPO for both an upper and lower GI endoscopy. He notably had a mild increase in sodium level with subsequent improvement after restitution of diet. Two days after the procedure, he was found to be drinking out of the toilet and also attempting to drink from the urine jug. Due to this odd behavior, he had to be put on physical restraints. The day after, he was found to have a serum sodium of 158 mEq/L. Hypotonic saline was started and urine output was notably ranging from 6-10 L/day with a negative balance. Desmopressin (DDAVP) test was done with a resultant urine osmolality of 170, 237, 257 and 264 mOsm/kg after 30, 60, 90 and 180 mins. Subcutaneous DDAVP was started with some improvement of serum sodium and decrease in urine output. Endocrinology service was consulted for the evaluation of hypernatremia and polyuria. Initial review of his medications did not show any potential cause of DI. Further inquiry of his prior medication history revealed that he had taken Lithium for over 10 years and stopped 4 months prior to the admission due to polyuria. After excluding other causes of polyuria, with partial improvement of urine osmolality to a level <300 mOsm/kg and a clinical history of prior Lithium therapy, a diagnosis of partial nephrogenic DI was made. Patient was started on HCTZ and given adequate water intake with subsequent improvement of his serum sodium back to normal. Conclusion: Nephrogenic DI due to Lithium use usually recovers after treatment is stopped but could be persistent for several years after. In our case, the patient compensated for his polyuria with increased water intake. When his water intake was restricted due to physical restraints, polyuria and subsequently hypernatremia became evident. A thorough medication history including past drug use is essential as it can help unravel the offending agent which was Lithium in our case. There needs to be an increased awareness that the effect of Lithium in the kidneys could be persistent even after stopping the drug for up to many years. References: Thompson CJ. Persistent nephrogenic diabetes insipidus following lithium therapy. Scott Med J 1997; 42:16-17.

# Pediatric Endocrinology

## UNDERSTANDING AND TREATING PEDIATRIC GROWTH DISORDERS

### *Phase 3 FliGHt Trial: Experience of Switching from Daily Growth Hormone Therapy to Once-Weekly TransCon HGH in Children with Growth Hormone Deficiency*

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**OR10-05**

**Background:** The Phase 3 fliGHt Trial evaluated children with growth hormone deficiency (GHD) of a broad range of baseline demographics and treatment durations who switched from daily growth hormone (hGH; somatropin) therapy to once-weekly TransCon hGH. TransCon hGH is an investigational long-acting prodrug consisting of 3 components: hGH, an inert carrier that protects it, and a linker that temporarily binds the two. When injected into the body, at physiologic pH and temperature, unmodified hGH is gradually released in a predictable manner.

**Methods:** All subjects initiated open-label once-weekly TransCon hGH 0.24 mg hGH/kg/week irrespective of prior daily hGH dose. Subjects 3 to 17 years old must have been treated with daily hGH for 13 to 130 weeks; subjects 6 months to 3 years old may have been treatment-naïve or treated with daily hGH for ≤130 weeks. The primary objective was to assess safety and tolerability over this 26-week trial. Efficacy measures included annualized height velocity (AHV), height standard deviation score (SDS), and insulin-like growth factor 1 (IGF-1) SDS.

**Results:** Of the 146 enrolled subjects, 98.6% completed the trial. Mean age at baseline was 10.6 years (range: 1, 17). The majority (97.9%) were treatment-experienced with a prior daily hGH mean dose of 0.29 mg/kg/week (range: 0.13, 0.49); 3 subjects were treatment-naïve and <3 years old. Just over half the subjects (56.8%) experienced a treatment-emergent adverse event (TEAE), with only 4.1% of subjects experiencing a TEAE considered related to study drug. No TEAE led to discontinuation of study drug. The type and frequency of TEAEs reported were similar to the published adverse event profile of daily hGH therapies. Mean hemoglobin A1c remained 5.2% at baseline and Week 26. No neutralizing antibodies were detected; low-titer anti-hGH binding antibodies were detected in 2.8% of subjects. Growth outcomes were as expected for this treatment-experienced heterogenous population, with a least-squares mean (LSM) AHV of 8.7 cm/year (95% CI: 8.2, 9.2) at Week 26 and LSM height SDS change from baseline to Week 26 of +0.25 (95% CI: 0.21, 0.29). In the age-defined subgroups, mean observed AHV at Week 26 ranged from 8.2 to 16.2 cm/year and mean observed height SDS change from baseline to Week 26 ranged from +0.23 to +0.96. Of note, the linear relationship between average IGF-1 SDS and TransCon hGH doses demonstrated in previous treatment-naïve trials was preserved in this population of treatment-experienced children who had dose titrations.

**Conclusions:** TransCon hGH treatment outcomes, including AHV and height SDS, were as expected across a diversity of ages, disease characteristics, and treatment experiences, reflective of a real-world setting. Dose titrations of TransCon hGH demonstrated a predictable IGF-1 response. Switching to TransCon hGH resulted in a similar adverse event profile to daily hGH therapy.

# Neuroendocrinology and Pituitary

## CASE REPORTS IN CLASSICAL AND UNUSUAL CAUSES OF HYPOPITUITARISM

### *Isolated Hypogonadotropic Hypogonadism in a Male with Sarcoidosis*

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**SAT-237**

Sarcoidosis is a systemic disease of unknown cause that is characterised by the formation of immune granulomas in various organs, mainly the lungs and the lymphatic system. The clinical involvement of the nervous system occurs in 5 to 15% of the cases. Any part of the nervous system can be affected, with the cranial nerves, the hypothalamus and the pituitary gland being the ones most commonly involved. However, hypothalamic-pituitary (HP) manifestations are rare manifestations of sarcoidosis, occurring in <1% of all intrasellar lesions. A 33-year old man was admitted to the emergency room with confusion and cognitive impairment progressively evolving over the past 2 months. The main complains were bilateral headaches, fatigue, adynamia and libido reduction. No visual fields defects were detected. Three months earlier, he had been diagnosed with sarcoidosis with pulmonary and ganglionar involvement, which was confirmed after histopathology analysis of tissue biopsy of the lung and mediastinic lymph nodes. However, the patient remained without any medication. He was admitted to the in-patient department and a brain MRI was performed, which revealed intense infra and supratentorial leptomeningeal enhancement, with involvement of the hypothalamus and optic chiasm. Laboratory evaluation revealed significantly reduced gonadotrophin and testosterone levels (FSH 1.1U/L, LH 0.43U/L, total testosterone 4.5ng/dL), normal prolactin and no other HP hormonal deficits. Clinical diagnosis was consistent with neurosarcoidosis with hypothalamic infiltration resulting in clinical hypogonadotropic hypogonadism. The patient initiated systemic therapy with corticosteroid, showing an overall improvement. After the hospital discharge, he started hormonal reposition with testosterone therapy with additional clinical improvement. Pituitary insufficiency is the presenting form of neurosarcoidosis in only 3 to 9% of the cases. Aside from diabetes insipidus and hyperprolactinemia, hypogonadism represents one of the endocrine disorders more frequently associated with HP involvement. Furthermore, hypothalamic sarcoidosis involvement is usually associated with multiple hypothalamic-pituitary deficits, rather than isolated ones. The case reported herein, illustrates a presumptive case of neurosarcoidosis, conducting to an isolated hypothalamic-pituitary axis deficiency. Although rare, HP involvement