Thyroid

HPT-AXIS AND THYROID HORMONE ACTION

Factors Associated with Reduced Thyroid Hormones in Cushing Syndrome Patients Before and After Surgical Cure

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Background: Hypercortisolemia adversely affects thyroid hormone secretion. We previously described the temporal pattern of thyroid function recovery in 23 patients (1). However, the factors leading to suppression and recovery of the hypothalamic-pituitary-thyroid (HPT) axis in Cushing's syndrome (CS) are not fully understood. We performed two separate studies to investigate these factors. Methods: In study 1, we examined patients (pts, n=62) with CS who underwent curative surgery and recorded their serum morning and evening cortisol, ACTH, tumor volume and duration of symptoms and 24-hour urine free cortisol (UFC) at baseline and the morning serum free T4, TSH and T3 at six-month intervals after cure. Data were log-transformed and Pearson correlations were performed. Linear mixed models were used to study factors that predict recovery of thyroid function. In study 2, we examined the diurnal variation of TSH by performing hourly TSH measurement between 3—7 PM and 12—4 AM on a cohort of pts (n=45) before surgery. *Wilcoxon Signed-Rank* method was used for comparisons of mean TSH across time and Pearson correlations were performed on log-transformed data. P values <.05 were considered significant. Results: Study 1: In this larger cohort, we confirmed previous findings of suppressed or low normal fT4 and TSH values with active hypercortisolism, with normalization after cure that reflected changes in the T3:TSH, fT4:TSH and T3:fT4 ratios. There were inverse linear correlations between log10 UFC, serum AM and PM cortisol; and log10 TT3, fT4 and TSH before surgery. Independent negative prognosticators of circulating fT4 recovery included UFC greater than 1000mcg/day (nl: 3.5—45mcg/day), duration of symptoms of less than one year, and ACTH levels greater than 60pg/mL(nl: 5—45pg/mL) Study 2: The nocturnal (12 - 4AM) TSH surge was reduced, so that the difference in day and night TSH values was not statistically significant; this contrasts with the 30—50% nocturnal TSH increase above daytime values seen in healthy subjects. There was an inverse relationship between UFC and nocturnal TSH, daytime TSH and TBG values, but there was no direct relationship between UFC and percent changes in nocturnal TSH values. Conclusions: Our findings suggest that a deficit in TSH stimulation of the thyroid gland may explain the reduction in T3 and T4 levels. There is a dose-response relationship between various measures of hypercortisolemia and both thyroid hormones and the pattern of TSH secretion. Finally, the severity of hypercortisolism correlates with a longer time to recovery of the HPT axis in pts with CS after curative surgery. 1. Shekhar S et al. HPG and HPT Axes in Cushing Syndrome. J Endocr Soc, 3 S1, April May 2019

Neuroendocrinology and Pituitary

NEUROENDOCRINE & PITUITARY PATHOLOGIES

Prevalence of Self-Reported Endocrine Comorbidities in Hypothalamic Hamartoma Patients: Data from the Hope for Hypothalamic Hamartoma Survey

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Background: Hypothalamic hamartoma (HH) are rare, congenital, benign mass lesions in the ventral hypothalamus that can be asymptomatic or associated with gelastic seizures and treatment-resistant epilepsy. Central precocious puberty (CPP) is the main endocrine comorbidity (30-80% of cases). Other endocrine comorbidities have also been described that tends to occur after surgery. However, previous studies reporting its prevalence have shown inconsistent results because of the rarity of the disease, variability of follow-up, and lack of long-term endocrinologic assessment. **Aims:** To evaluate the self-reported prevalence of demographics and endocrine comorbidities in a large cohort of HH patients. **Methods:** Hope for HH is a volunteer-based nonprofit organization founded by parents of children with HH. This international survey was initiated, translated into multiple languages and distributed by mail and electronically to families of children with HH in the Hope for HH database after concerns were raised that there have been multiple ongoing comorbidities (including endocrine) that continues to be under-recognized. **Results:** In total, 257 HH patients (132M/125F, mainly between ages 4-35 years and from the US, Russia, UK, Australia, Canada, Germany and Kazakhstan) participated in the survey. Some patients had a secondary diagnosis of Pallister-Hall (7.0%), Lennox-Gastaut (1.95%), Prader-Willi (0.8%) and West (0.8%) syndromes. The majority of patients (n=163, 63.4%) underwent surgery (MRI-guided stereotactic laser ablation [n=61, 37.4%], endoscopic resection [n=31, 19.0%], transcallosal resection [n=30, 18.4%], stereotactic radiofrequency ablation [n=27, 16.6%], orbitozygomatic resection [n=9, 5.5%]) or gamma knife radiosurgery (n=28, 17.2%). After surgery and/or radiation, ~50% of patients were seizure-free but reported unchanged, poor or very poor quality of life (QoL), with fatigue (56.4%), heat intolerance (46.3%) and adipsia (21.8%) being the more common symptoms. Reported endocrine comorbidities include CPP (42%), hypothalamic obesity (35.0%), abnormal body composition (31.5%), central hypothyroidism (19.8%), osteopenia/osteoporosis with low BMD (12.8%), diabetes insipidus (11.3%), GH deficiency (10.5%), central adrenal insufficiency (10.5%), central hypogonadism (5.1%), and delayed puberty (4.7%), and 26.5% of patients were not seeing an endocrinologist. **Conclusion:** In contrast to previous studies reporting low prevalence, mild and transient endocrine comorbidities in HH patients (2,3), this survey suggests a greater prevalence of other non-CPP endocrine comorbidities with a substantial number of patients reporting unchanged or impaired QoL. Thus, long-term endocrinologic follow-up with the involvement of a