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OR03-05

Background: Alterations in circulating amino acids, polyamines and acylcarnitines have been reported in patients with endogenous chronic hypercortisolism. However, lipid metabolites profiling and its interplay with the serum metabolome and degree of hypercortisolism in patients with active Cushing syndrome (CS) has not been previously assessed. **Objective:** To identify new metabolomic biomarkers associated with active CS.
Methodology: Multiple UHPLC-MS platforms were used to analyze the metabolome of serum samples obtained from 25 patients with active endogenous CS and 25 controls subjects matched by propensity score (sex, BMI, T2D, DLP, HBP).
Results: Metabolome of CS patients was deeply disrupted with 122 (27%) of the assessed metabolites significantly altered (p adj. <0.05) out of which 5 bile acids resulted with the highest perturbation (> 2-fold decrease). From the altered metabolites, 3 amino acids (AA), 2 acylcarnitines (ACs), 2 ceramides (CER) and 5 glycerophospholipids showed direction of effect independently associated with 24-h urinary free cortisol (MS) levels. A highly discriminant (AUC 96%) metabolome signature (n=59) characterized by lower levels of AA, ACs, polyunsaturated fatty acids (PUFA) and monoglycerophosphocolines (MGPC) together with increased levels of triacyclglycerols (TG), CER, diacylglycerophosphocholines (DGPC) and cholesteryl esters was identified and cross-validated (R^2Y= 0.92, Q^2Y= 0.68) using PLS-DA VIP scores >1.5. PUFA omega-6, and alanine, aspartate and glutamate metabolism resulted the most impacted canonical pathways (q-stat 19.7, 10.8 (p<0.001). Finally, topological network analysis detected 158 pairwise differential correlations (p <0.005, 10,000-fold permutation) between 141 metabolites due to CS where the acylPC (P-18:1/0:0) resulted a key metabolite in the network (betweenness =0.117 & closeness centrality =0.467).
Conclusion: Active Cushing syndrome leads to a global proatherogenic shift in the circulating ceramides, glycerophospholipids and sphingolipids metabolites which are independently associated to the levels of urinary free cortisol being potential biomarkers of patients' cardiovascular risk.

Reproductive Endocrinology

SEX, GENDER, AND HORMONES

Risk Factors For Low Baseline Bone Mineral Density In Gender Diverse Youth.

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Background
Sex steroids such as testosterone and estrogen are necessary for accumulation of bone mass. Transgender youth treated with gonadotropin releasing hormone analogues (GnRHa) to block natal puberty for gender-affirming care are at risk of low bone mineral density (BMD). Previous studies indicate that transfemale patients assigned male at birth (AMAB) have low BMD at baseline, during and after GnRHa treatment despite cross hormone treatment. Transmales assigned female at birth (AFAB), however, have normal BMD at baseline that decreases upon GnRHa treatment, with normalization upon cross hormone therapy. The reason(s) for the low baseline BMD in transfemales is unclear. We aimed to assess the baseline characteristics of transgender youth at a single multidisciplinary gender clinic prior to medical intervention and determine factors associated with BMD.
Methods
This is a retrospective chart review of patients <19 years old evaluated in the gender clinic. Dual-energy x-ray absorptiometry (DXA) scans were obtained prior to initiation of GnRHa or cross-hormone therapy per Endocrine Society guidelines for the treatment of gender dysphoria. We included patients with DXA scans completed prior to initiation of treatment with GnRHa or cross gender hormones and excluded those with concurrent medical diagnoses that may affect bone density. Data collected were bone mineral density (BMD) Z-scores, anthropometric data, vitamin D and calcium levels, and calcium intake. Multivariable linear regression models were used to assess the impact of vitamin D levels, height Z-score, weight Z-score, and BMI Z-score on subtotal body BMD Z-score, adjusted for sex assigned at birth and age.
Results
Sixty-four patients were included in our analysis. Of these, 73% were AMAB and 27% AFAB. Gender identity was male in 14%, female in 44%, and non-binary in 42%. Average height Z-score was 0.12, weight Z-score 0.27, and BMI Z-score 0.22 (using sex assigned at birth). Subtotal body BMD Z-scores were greater than zero in 11%, between zero and greater than -2 in 59%, and less than or equal to -2 in 30% of tested patients. AMAB patients had lower BMD Z-scores compared to those AFAB (p<0.05 for all Z-scores). There was a positive association with BMI, height, and weight Z-scores and increasing BMD Z-scores after adjusting for sex assigned at birth and age (p<0.05 for all Z-scores). Patients who consumed <2 servings of calcium per day had lower BMD Z-scores (p<0.05 for all Z-scores). Average vitamin D level was 24 ng/ml (+/- 9.5 SD) with no significant association with BMD Z-scores (adjusted for sex assigned at birth).
Conclusions
Patients AMAB and patients with calcium intake of < 2 servings/day are associated with lower baseline BMD in a cohort of adolescents seen in a multidisciplinary gender clinic. Height, weight, and BMI are associated linearly with BMD Z-score, following patterns previously described in other populations.

Reproductive Endocrinology

MALE REPRODUCTIVE HEALTH - FROM HORMONES TO GAMETES

Treatment of Hypogonadal Men with a New Oral Testosterone Undecanoate (TU) Formulation Improves Psychosexual, Well-Being and Body Composition and Bone Density Parameters

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