Genetics and Development (including Gene Regulation)

ENDOCRINE DISRUPTING CHEMICALS II

Perfluoroalkyl Substance Exposure Was Negatively Associated With Cortisone Levels in Pregnancy

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Introduction: During pregnancy, maternal cortisol levels are increased threefold by third trimester. The enzyme 11β-hydroxysteroid dehydrogenase (11β-HSD, isoforms 1 and 2) regulates cortisol levels by the conversion between cortisol and cortisone. Perfluoroalkyl substances (PFAS) are persistent chemicals with suspected endocrine disrupting abilities applied in consumer products. PFAS have been reported to inhibit 11β-HSD1 and 11β-HSD2, which could lead to reduced levels of cortisol and cortisone.
Aim: To investigate a possible effect of early pregnancy PFAS exposure on late pregnancy activity of 11β-HSD1 and 11β-HSD2 assessed by cortisol and cortisone levels in urine and blood samples.
Methods: The study is part of the prospective cohort study, Odense Child Cohort (OCC). A total of 1,826 pregnant women had serum (S) concentrations of five PFAS (Perfluorooctanoic acid (PFOA), perfluorooctane sulfonic acid (PFOS), perfluorohexane sulfonic acid (PFHxS), perfluorononanoic acid (PFNA), and perfluorodecanoic acid (PFDA)) measured in first trimester (median gestational week (GW) 11). Diurnal urinary (dU) cortisol and cortisone (n=344), and S-cortisol (n=1,048) were measured in third trimester (median GW 27).
Results: In multiple regression analyses, a two-fold increase in S-PFOS was significantly associated with lower dU-cortisone (β=-9.1%, p<0.05) and higher dU-cortisol/dU-cortisone (dU-C/C) (β=9.3%, p<0.05). The same trend was demonstrated for PFOA, PFHxS, PFNA, and PFDA. In crude models, a doubling in PFOS, PFOA, PFHxS, and PFNA concentrations were associated with a significant increase in S-cortisol, however, these associations became insignificant after adjustment.
Conclusion: Early pregnancy concentrations of maternal S-PFAS were inversely associated with late pregnancy dU-cortisone, indicating reduced activity of 11β-HSD2.

Thyroid

BENIGN THYROID DISEASE AND HEALTH DISPARITIES IN THYROID I

Thyroid Peroxidase Antibody Positivity Predicts Relapse Free Survival Following Anti-Thyroid Drug Treatment for Graves Disease

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Objective: Graves disease is an autoimmune disease characterized by production of autoantibodies directed against the thyroid gland. Thyrotropin-receptor antibodies (TRABs) are clearly pathogenic, but the role of thyroid-peroxidase antibodies (TPOAb) in Graves disease is unknown. *Design:* We retrospectively studied whether TPOAb positivity reduced risk of relapse following anti-thyroid drug treatment in newly diagnosed Graves disease. *Results:* During follow-up of 204 patients with TRAB positive Graves disease, 107 (52%) relapsed following withdrawal of anti-thyroid medication. Mean age was 40.0 years and 82% were female. The average duration of anti-thyroid drug (ATD) treatment was 23.5 months and was not different between patients who relapsed and those with sustained remission. Absence of TPOAb significantly increased risk of Graves relapse (OR 2.21) and displayed a trend towards shorter time to relapse. Male sex and younger age were additional factors significantly associated with increased risk of relapse. *Conclusion:* TPO-antibody positivity significantly improves odds of remission following ATD treatment in newly diagnosed Graves disease.

Thyroid

THYROID NEOPLASIA AND CANCER

Thyroid Nodules > 4cm: High-Risk for Malignancy or Not?

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Background: Thyroid nodules are very common in adults. One percent of men and 5% of women have nodules on exam, and 19-68% of adults have thyroid nodules on ultrasound. Majority (85-90%) of them are benign. Most concerning is the diagnosis of thyroid cancer. These nodules can be stratified into risk groups based on ultrasonographical criteria. There are 5 internationally endorsed sonographic classification systems (ATA, ACR, European Thyroid Association and Korean Society of Thyroid Radiology). After classification, decision to perform FNA biopsy is made based on size of the nodules. Some of the other parameters that have been considered to increase risk of cancer are BMI, TSH level, radiation exposure to the neck before puberty and family history of thyroid cancer. Cytogenetic testing of the FNA specimen may also help determine the need for excision.
Study Design: We retrospectively studied a group of veterans referred for endocrine consultation for thyroid nodules that had undergone FNA based on ACR and ATA ultrasonographical classification (total of 127 nodules). On reviewing these charts over the past 4 years, we noted that approximately 39% (49/127) of the nodules were <2cm, 35% (44/127) were 2-4cm and 26% (34/127) were >4cm in size. We examined patient demographics and characteristics of nodules >4cm, since it is frequently a dilemma whether to clinical monitor these nodules or refer them for surgical excision.
Results: Seventeen percent of patients were females. Majority were between 60-65 years of age, had a BMI 30-35 and TSH of <2. Based on review of ultrasound images and