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P053

METABOLIC AND CARDIOVASCULAR PARAMETERS IN ADULT PATIENTS WITH TURNER'S SYNDROME

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Turner's syndrome (TS) is one of the more common genetic disorder, associated with abnormalities of the X chromosome, occurring in about 50 per 100.000 live-born girls, and it is usually associated with reduced adult height, gonadal dysgenesis and infertility. Several studies have also showed that TS is associated with an increased mortality risk from cardiovascular disease, diabetes mellitus and dyslipidemia.
In order to examine the metabolic and cardiovascular profile, in 30 adult patients with TS (age 32.4±1.3 yrs) under hormonal replacement therapy with estrogens, BMI, fasting glucose and insulin, HOMA index, and serum lipids were evaluated and compared with those in a group of age-matched control subjects (CS, age 32.3±1.3 yrs). In TS group, 17β -estradiol (E2), oral glucose tolerance test (OGTT), 24-h ambulatory blood pressure monitoring and intima-media thickness (IMT) on the right and left common carotids arteries were also evaluated.
No difference was found between TS and CS in BMI (23.9±0.9 vs 22.1±0 Kg/m^2) and fasting glucose (77.7±2.3 vs 79.9±1.0 mg/dl), while fasting insulin and HOMA index were higher in TS than in CS (14.0±1.6 vs 9.5±0.4 mcUI/ml and 3.2±0.2 vs 1.9±0.1, respectively; p<0.05); 4 out of 30 TS patients (13.3%) were IGT, while none of them showed glucose levels after OGTT diagnostic for diabetes mellitus. A negative correlation was found between insulin levels, HOMA index or 2h-glucose after OGTT and E2 levels.
No significant differences were found between TS and CS in total cholesterol (199.4±6.6 vs 178.9±3.9 mg/dl), HDL-cholesterol (68.3±3.0 vs 60.7±1.5 mg/dl), and triglycerides (92.8±11.3 vs 93.5±7.3 mg/dl).
Both systolic and diastolic blood pressure was normal in 26 out of 30 TS patients, while in 4 out of 30 TS patients (13.3%) a diagnosis of arterial hypertension was made; IMT was normal in all TS patients.
In conclusion, our results confirm a higher prevalence of insulin resistance in Tuner's syndrome patients, namely in those under inadequate hormonal replacement therapy, suggesting higher risk for cardiovascular disease when compared to controls. Thus, an evaluation of cardiovascular risk factors is mandatory in adult patients with Turner's syndrome and optimal hormonal replacement is recommended.

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HIGH PREVALENCE OF HYPOTHYROIDISM IN PREGNANT WOMEN

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Background: Gestational hypothyroidism occurs in around 2.5% of women and has been associated with adverse neonatal outcomes. The results of many studies showed an increased risk of impaired of some foetal intellectual function for untreated disease.
Objective: To evaluate the prevalence of gestational hypothyroidism in pregnant women and, therefore, to restore euthyroidism as soon as possible to prevent foetal neural damage.
Methods: TSH and fT4 serum levels were measured in 1006 women (mean age: 28.3±5.1 years) at different stages of pregnancy. They were classified into the following 6 groups according to previously published criteria with slight modification: A) TSH >97.5th percentile; B) TSH between the 85th and 97.5th percentile and low fT4 (<2.5th percentile); C) TSH between the 85th and 97.5th percentile and normal fT4; D) normal TSH with low fT4; E) low TSH; F) normal TSH and fT4.
Results: Altogether 92 women had hypothyroidism, 78 in group A (7.7%) and 14 in group B (1.4%). Their TSH and fT4 serum levels were, respectively, 5.6±0.2 - 2.9±0.2 μU/mL and 13±3 -10.3±1 pg/ml. All of them were prescribed LT4 replacement therapy to restore euthyroxinemia. Interestingly, ten women of group A were already taking LT4 for hypothyroidism diagnosed before pregnancy. They had a significantly higher TSH serum levels (13.4±4.6). The women of groups C (88, 8.7%) and D (114, 11.3%) were advised to undergo a second thyroid function and antibody testing.
Conclusions: The results of this study showed a high prevalence of undiagnosed hypothyroidism in the population of pregnant women we studied and a dramatic increase of TSH levels in hypothyroid women under replacement therapy. This suggests that a screening for thyroid deficiency should be warranted during pregnancy and that LT4 replacement therapy should be increased in previously diagnosed hypothyroid women to prevent neurodevelopmental abnormalities in the offspring.

P055

ACUTE GNRH-AGONIST ADMINISTRATION DOES NOT INFLUENCE AMH PRODUCTION IN PCOS SUBJECTS

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BACKGROUND: Hyperandrogenism and disrupted folliculogenesis are prominent features of polycystic ovary syndrome (PCOS) and are causatively linked to ovarian dysfunction. In PCOS, increased anti-Müllerian hormone (AMH) serum levels have been related to the severity of the phenotype. However, the regulation of AMH in PCOS remains poorly understood. Therefore, we compared AMH secretory pattern after acute exposure to a GnRH-analogue in women affected by PCOS or by other causes of anovulation and hyperandrogenism, such as functional hypothalamic amenorrhea (FHA) and hyperandrogenaemia of extra-ovarian origin (non-PCOSH).
PATIENTS AND METHODS: 26 PCOS subjects (23.9±4.8 yrs), 9 FHA subjects (26,6±2,6 yrs) and 8 non-PCOSH women (21,2±4,5 yrs) were studied. Testing was performed at early follicular phase, after Liddle test. AMH and ovarian steroid hormones FSH, LH, DHEA-S, 17-OHP, A2, T, DHT, 3-α-DG, E_2, INH B were evaluated at baseline, and over a 20-h and 24-h period after a s.c. injection of Triptorelin (0.1 mg).
RESULTS: Triptorelin induced a significant increase of ovarian steroids in PCOS (OHP nM: 1.6±0.9 to 8.2±4.8; T nM: 1.1±0.3 to 1.4±0.8; E2 pM: 160.6±67 to 1546.0±675), FHA (OHP: 1.5±1.3 to 5.7±3.7; T 0.8±0.2 to 0.8±0.4; E2: 76.6±27.9 to 1453±350) and in non-PCOSH (OHP 0.9±0.6 to 4.6±3.0; T 0.6±0.3 to 0.7±0.4; E2:123.5±36.2 to 1056.0±537). AMH basal levels (pM) were significantly higher in PCOS (43.8±18.9) vs non-PCOSH (21.8±10.5), but significantly lower when compared to FHA (70.1±26). Triptorelin did not induce any effects on AMH serum levels in all groups: AMH peak 44.9±14.8 (PCOS); 78.0±44.5 (FHA); 24.2±12 (non-PCOSH).
CONCLUSIONS: AMH serum levels were increased in PCOS and FHA patients when compared with values observed in women affected by non-ovarian hyperandrogenism, suggesting that extra-ovarian androgens may not be directly involved in the complex AMH regulation network. In contrast with conventional markers of early follicular growth, such as inhibin B and E_2, AMH secretion appears to be independent of gonadotropin acute stimulation in vivo both in PCOS and non-PCOS patients.

P056

EPIGENITIC FINGERPRINT IN ENDOMETRIAL CARCINOGENESIS: THE HYPOTESIS OF AN UTERINE FIELD CANCERIZATION

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Background Transcriptional silencing by CpG island hypermethylation plays a critical role in endometrial carcinogenesis. In a collection of benign , premalignant and malignant endometrial lesions, a methylation profile of a complete gene panel, such steroid receptors (ERα, PR), DNA mismatch repair (hMLH1), tumour-suppressor genes (CDKN2A/P16 and CDH1/E-CADHERIN) and WNT pathway inhibitors (SFRP1, SFRP2, SFRP4, SFRP5) was investigated in order to demonstrate their pathogenetic role in endometrial lesions.
Methods Methylation-specific PCR (MSP) was performed to assess gene inactivation. P53 and steroid receptors expression were evaluated by LSAB/HRP immunohistochemistry.
Results Our results indicate that gene hypermethylation may be an early event in endometrial endometrioid tumorigenesis. Particularly, ERα, PR, hMLH1, CDKN2A/P16, SFRP1, SFRP2 and SFRP5 revealed a promoter methylation status in endometrioid carcinoma, whereas SFRP4 showed demethylation in cancer. P53 immunostaining showed weak-focal protein expression level both in hyperplasic lesions and in endometrioid cancer. Non endometrioid cancers showed very low levels of epigenetic methylations, but strong P53 protein positivity. Fisher exact test revealed a statistically significant association between hMLH1, CDKN2A/P16 and SFRP1 genes methylation and endometrioid carcinomas and between hMLH1 gene methylation and peritumoral endometrium ($p < 0.05$).
Discussion and Conclusions Our data confirm that the methylation profile of the peritumoral endometrium is different from the altered molecular background of benign endometrial polyps and hyperplasias. Therefore, our findings suggest that the methylation of hMLH1, CDKN2A/P16 and SFRP1 may clearly distinguish between benign and malignant lesions. Finally, this study assessed that the employment of an epigenetic fingerprint may improve the current diagnostic tools for a better clinical management of endometrial lesions.