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ABSTRACT BOOK

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PD73 - IS THE DEGREE OF URINARY FREE CORTISOL AN EXHAUSTIVE PARAMETER FOR DEFINING CUSHING SYNDROME SEVERITY?

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Background: Cushing syndrome (CS) is characterized by increased morbidity and mortality compared to the general population. However, there are patients who have more aggressive forms than others. To date, there is an arbitrary classification in mild, moderate and severe hypercortisolism, based on the times of exceeding the upper limit of normal (ULN) of urinary free cortisol (UFC).

Aim: To evaluate by a for trend analysis whether the degree of hypercortisolism, defined by the times of exceeding the ULN of UFC levels, is related to the worsening of phenotypic, cardiovascular and metabolic parameters, in a cohort of CS patients.

Materials and methods: We conducted a cross-sectional study on 192 patients with CS, at diagnosis, consecutively presenting at the outpatients' clinic of the Universities of Ancona, Naples and Palermo. Patients were grouped into mild (UFC not exceeding twice the ULN), moderate (2-5 times the ULN) and severe (more than 5 times the ULN) hypercortisolism.

Results: 37 patients (19.3%) had mild, 115 (59.8%) moderate and 40 (20.9%) severe hypercortisolism. A significant trend of increase among the three groups was demonstrated for cortisol at 08.00, 16.00 and 24.00 h levels and cortisol after dexamethasone (all $p < 0.001$). No significant trend of increase was found regarding phenotype [(moon face $p=0.416$, facial plethora $p=0.978$, buffalo hump $p=0.148$, purple striae $p=0.148$, central obesity $p=0.524$)] and comorbidities [(coronary heart disease $p=0.648$, coagulopathy $p=0.180$, peripheral vascular disease $p=0.072$, cerebral vascular disease $p=0.757$, depression $p=0.231$, osteoporosis $p=0.291$, diabetes mellitus $p=0.797$, hypercholesterolemia $p=0.873$, arterial hypertension $p=0.773$ and metabolic syndrome $p=0.540$]).

Conclusions: Our findings show that the degree of hypercortisolism (evaluated by the times of exceeding the ULN of UFC or by serum cortisol levels) does not express the severity of the disease. Indeed, cortisol secretion variability and the exact clinical onset of CS and consequently the duration of disease make it difficult to find adequate parameters to define CS severity and identify aggressiveness at an early stage.

PD78 - HYPERINSULINISM AND POLYCYSTIC OVARY SYNDROME (PCOS): ROLE OF INSULIN CLEARANCE.

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The evidences favour insulin resistance and compensatory hyperinsulinism as the predominant metabolic defects in polycystic ovary syndrome (PCOS). However, hyperinsulinism, as well as being compensatory, can also express a condition of reduced insulin clearance in the kidney, liver and insulin-sensitive tissues. The aim of the present study was to evaluate the differences in insulin action and metabolism between women with PCOS (but normal glucose tolerance) and age- and BMI-matched women with prediabetes (without hyperandrogenism and ovulatory disorders).

Using a cross-sectional study design, 22 PCOS (Rotterdam criteria) and 21 age/BMI-matched women with prediabetes (impaired fasting glucose and/or impaired glucose tolerance), after one month's withdrawal of insulin sensitizers and oral contraceptive pills, were subjected to an Euglycaemic-hyperinsulinaemic clamp and an Oral Glucose tolerance Test. Insulin sensitivity was assessed by the glucose infusion rate during clamp (M-value); insulin secretion by Insulinogenic index, fasting insulin and $AUC_{2h-insulin}$ during OGTT; insulin clearance by the metabolic clearance rate of insulin (MCRI) during clamp; adipose tissue distribution and function by Visceral Adiposity Index (VAI).

Obviously, women with PCOS, compared to women with prediabetes, showed significantly higher levels of fasting insulin ($p < 0.001$) and $AUC_{2h-insulin}$ ($p = 0.011$) and significantly lower levels of fasting glucose ($p < 0.001$) and $AUC_{2h-glucose}$ ($p = 0.008$). Between the two groups, no difference was found regarding insulin-sensitivity (M-value) and glucose-induced insulin secretion (Insulinogenic Index). By contrast, lower levels of MCRI were found in women with PCOS [420 (IQR:227-588) vs. 743 (IQR:597-888) $ml \cdot m^{-2} \cdot min^{-1}$; $p < 0.001$]. Furthermore, in a multiple linear regression analysis, only in the PCOS group there was an independent inverse correlation observed between MCRI and both fasting insulin ($\beta: -0.540$; $p = 0.006$) and $AUC_{2h-insulin}$ ($\beta: -0.858$; $p < 0.001$).

Our study suggests that in women with PCOS there is peripheral insulin sensitivity similar to that found in other disorders characterized by insulin resistance, such as prediabetes. What characterizes PCOS is hyperinsulinism, which is simplistically defined "compensatory"; actually, this is related to a decreased insulin clearance whose specific causes and dynamics have yet to be studied.

PP015 - RELATIONSHIP BETWEEN GONADAL HOMEOSTASIS AND METABOLIC PARAMETERS IN A POPULATION OF HOSPITALIZED DIABETIC MALES.

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INTRODUCTION: The 2011 update of AACE reported that a biochemical assessment of hypophysis-testis axis in male patients with type 2 Diabetes Mellitus (T2DM) has to be performed. It is well known that low testosterone is commonly associated with adipose tissue dysfunction in T2DM and metabolic syndrome.

AIM: To investigate in a cross-sectional study gonadal function in T2DM patients with poor metabolic control.

METHODS: We performed a physical and hormonal assessment of the gonadal state in a population of 70 T2DM males (mean age 54.81 ±14.22) hospitalized from emergency areas for dehydration, hyponatremia and hyperglycemic state. Patients were divided into tertiles of serum total testosterone (TT) levels (tertile I: TT < 2.62 ng/ml; tertile II: TT 2.62-5.13 ng/ml; tertile III: TT > 5.13 ng/ml). Data were analyzed by ANOVA and χ^2 for trend.

RESULTS: The study showed that the levels of TT are inversely correlated with older age (p=0,041), disease duration (p=0.012), waist circumference (WC) (p=0.003), BMI (p<0.001), triglycerides (p=0.03), hsCRP (p<0.001), fibrinogen (p<0.001) and visceral adiposity index (VAI) (p=0.023). A direct correlation was found with HDL-cholesterol (p<0.001). No significant correlations were found among TT levels and HbA1c, GOT/GPT, gonadotropin, estradiol and testis volume.

CONCLUSIONS: Our data show no correlation between gonadal function and glycemic control, while by contrast TT levels decrease when disease duration increases. The overlap in estradiol levels between the TT-tertiles suggests no role for adipose aromatase activity leading to the hypothesis that there exists a direct effect of adipocytokines on gonadal function. Moreover, the atherogenic lipid profile, inflammation markers and visceral adipose tissue are intimately associated with lower TT. In this light low testosterone concentration in men can be considered as a marker of cardiovascular risk in T2DM male patients.

PP104 - INSULIN SECRETION AND SENSITIVITY DURING PASIREOTIDE TREATMENT IN PATIENTS WITH RECURRENT CUSHING DISEASE: A CASE SERIES

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Background: Pasireotide is currently recommended in patients with persistent or recurrent Cushing disease (CD) after surgery and has demonstrated long-term effectiveness for the biochemical control and clinical improvement of patients with CD. However, it is associated to high frequency of hyperglycaemic adverse events.

Aim, materials and methods: In a prospective study, we evaluated the effects of pasireotide on glucose metabolism and insulin secretion and sensitivity in a group of five patients with CD recurrence. Anthropometric, metabolic and hormonal parameters were evaluated at baseline, after 6 and 12 months. We also studied M value during euglycemic hyperinsulinemic clamp, HbA1c and AUC_{2hc}-peptide during meal mixed test.

Results: Significant differences were observed between HbA1c baseline and at 6 months [median (IQR): 6 (5.35-6.65) vs. 6.4 (5.7-7.05) %; p= 0.042], HbA1c baseline and at 12 months [6 (5.35-6.65) vs. 6.7 (5.75-7.15) %; p= 0.043]. A significant decrease was observed between baseline BMI and at 6 months [40.8 (28.6-51.7) vs. 35.4 (26.5-44.7) kg/m²; p=0.042], and baseline BMI and at 12 months [40.8 (28.6-51.7) vs. 31 (23.8-42.7) kg/m²; p=0.043]. A significant decrease of waist circumference (WC) was observed comparing baseline and 6 months [119 (101.5-131.5) vs. 114 (94.5-124) cm; p=0.042] and baseline and 12 months [119 (101.5-131.5) vs. 112 (93.5-121.5) cm; p=0.043]. No significant differences were observed about AUC_{cpeptide} and M value. One out of five patients did not experience hyperglycaemia, while four out of five who were diabetic, experienced a worsening of glycaemic levels, managed by addition of GLP-1 analogues to the antidiabetic treatment.

Conclusions: Pasireotide treatment causes a mild increase of glycaemic levels, without an apparent impairment of insulin secretion and sensitivity. However, the sample of analysed patients is small and further studies on larger samples are required in order to confirm the observed results and eventually clarify the pathophysiological mechanisms of the hyperglycaemic effect.

PP206 - PTC REFRACTORY TO RADIOIODINE: A CROSS-SECTIONAL STUDY

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Background: Some patients affected by Papillary Thyroid Cancer (PTC) in postoperative phases are undergoing radioiodine treatment, which is commonly used for thyroid cancer follow-up. A small but not negligible percentage of differentiated thyroid cancers become refractory to radioiodine treatment either because they lose the ability to take up iodine over time or because, despite persistent uptake capacity, the effect of radioiodine is lost in terms of tumor burden reduction. Our study evaluated the prevalence of refractory cases and possible predictors at diagnosis.

Methods: We performed a cross-sectional study on 286/385 patients who received radioiodine therapy (74.3%). At present 273 patients (95.5%) proved to be disease-free and 13 (4.5%) showed radioiodine-refractory disease.

Results: In univariate analysis, the refractory patients had a higher prevalence of peri-thyroid tissue invasion [30.8 vs. 11 %; OR 3.58 (IC95%: 1.04-12.35) p=0.043], lymph node metastasis [53.8 vs. 16.8; OR 5.75 (IC95% 1.85-17.92); p=0.003], distant metastasis [23.1 vs. 2.9 %; OR 9.9 (IC95% 2.27-43.03) p=0.002]. No other significant association was found with gender, age, thyroid autoimmunity, iodine deficiency, family history of cancer, histological types, and tumor size.

Conclusion: The definition of predictor factors for PTC radioiodine-refractory could be used to select those patients suited to starting innovative therapies able to improve radioiodine sensitivity. Our data suggest the importance of the co-presence of the three factors, peri-thyroid tissue invasion, lymph node metastasis and distant metastasis, as predictors of radioiodine-refractory disease.

PP210 - THE CLINICAL ACTIVITY SCORE IN MANAGEMENT OF GRAVES' OPHTHALMOPATHY: CORRELATION WITH ORBITAL MR IMAGING.

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Graves ophthalmopathy (GO) is a common extrathyroid disorder of Graves disease (GD) and it is unanimously considered clinically relevant to identify the acute inflammation phase at an early stage of disease.

Our aim was to investigate the correlation between GO ocular parameters obtained by MRI with contrast administration and the well-known clinical indicators of GO and to examine the relationships between the clinical course of hyperthyroidism and GO severity.

From June 2013 until November 2014, 28 consecutive patients (9 men and 19 women; mean age 48.42 years), with a diagnosis of GO were enrolled. All patients were subjected to MR on the same day as the clinical evaluation. MR examination was performed with a 1.5T scanner (3mm thin slices, FSE T2w and T1w sequences with and w/o fat saturation; pre- and post-Gd T1w sequences were obtained). Endocrine evaluation considered serum parameters (TSH, FT3, FT4, TRAb), thyroid ultrasound and medical records collection (disease duration, remission phases, smoking, therapy). Ophthalmological evaluation considered proptosis (by Hertel Exophthalmometry), ocular pressure, soft tissue signs to calculate the clinical activities score (CAS) according to EUGOGO consensus statements. All patients were divided into two groups according to their ophthalmopathy severity: 13 with mild (46.4%) and 15 with moderate to severe GO (53.6%). No cases of sight-threatening GO were included. 14/15 patients with moderate/severe disease had a activity GO (CAS \geq 3). No difference was found for gender, age, smoking, duration of disease, serum thyroid parameters and thyroid ultrasounds between the two groups. Moderate to severe GO patients showed a significant increase in all the ocular parameters evaluated by MRI [proptosis, cross sectional area and transverse diameters of the ocular extrinsic muscles (inferior, superior, medial and lateral rectus muscles; all $p < 0.05$).

CAS confirms an optimal indicator of GO severity and activity, as demonstrated by its correlation with a greater volume of extrinsic muscles and inflammation MRI documented. MRI may be considered the technique of choice for orbital imaging because of its lack of ionizing radiation, its fine delineation of detail.