ADRENAL STEROIDOGENESIS IN INAPPROPRIATE HIGH BLOOD PRESSURE

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OBJECTIVES

In the majority of patients with High Blood Pressure (HBP) an extensive diagnostic evaluation is not rewarding and is not cost effective. However in the selected subgroup of patients with Inappropriate High Blood Pressure (IN-HBP) those procedures may be justified and may support therapy selection. The objective of this work was to evaluate adrenal steroidogenesis defects in patients with IN-HBP.

PATIENTS AND METHODS

40 consecutive patients with IN-HBP were studied at the Endocrine outpatient department of a public central hospital after a 15-day anti-hypertensive treatment washout. Adrenal steroidogenesis was explored by the ACTH dynamic test (cosyntropin, 1mg, im). Venous blood samples were collected immediately before and 4 hours (h) after cosyntropin administration. Operative criteria for three possible defects were predefined: 1) 21-hydroxilase defect (21OHD) – serum 17-OH-progesterone (17-OHP) at 4h > 10 ng/mL; 2) 11-hydroxilase defect (11OHD) – serum S compound at 4h > 8 ng/mL; 3) glucocorticoid remediable-aldosteronism (GRA) – serum peak/baseline aldosterone ratio ≥ serum peak/baseline cortisol ratio. Renin was also measured at 0 and 4h. Descriptive statistics and regression analysis were used to explore the results with the program Statistical Package for the Social Sciences (SPSS).

RESULTS

Patients were mainly female (78%) middle aged adults – 38±10 years. Measured steroids were not significantly different between genders and only 17-OHP was slightly and inversely related to age – $r=0.389$, $p<0.05$, $17OHP=3.41-4.27x10^{-2}age$.

Baseline adrenal steroidogenesis was intrinsically related: cortisol was directly related with 17-OHP – $r=0.459$, $p<0.01$ - and S compound - $r=0.546$, $p<0.01$. Similar evidence was found for the renin-angiotensin-aldos-

terone system: renin was directly related to aldosterone, r=0.776, p<0.001. Glucocorticoid and mineralocorticoid production were also directly related, r=0.336, p<0.05 (figure 1).

Results of the cosyntropin test are represented in the table 1.

In 46% of the subjects normal (N) adrenal steroidogeneis as defined was found. 15% and 21% presented evidence of 21OHD or 11OHD defect, respectively. Isolated evidence of GRA (iGRA) was found in 18% of the subjects, although this was extremely common in the presence of other adrenal steroidogenesis defects, namely 40% of those with a 21-hydroxilase defect and 100% of those with a 11-hydroxilase defect. (figure 2). Globally, 46% of the subjects presented evidence of GRA (Figure 3). Accordingly, in subjects with GRA a direct correlation between cortisol and aldosterone – r=0.761, p<0.001 – but no correlation between renin and aldosterone was found. The opposite was verified in subjects without GRA – direct correlation between renin and aldosterone – r=0.902, p<0.001 – and no correlation between cortisol and aldosterone.

	0h	4h
Cortisol (µg/dL)	18.3±8.5 [6-48]	46.0 ±10.4 [23-55]
17OHP (ng/mL)	1.7 ±1.1 [0.3-5.2]	8.1 ±4.4 [2.4-25]
S compound (ng/mL)	2.0 ±1.0 [0.7-5.0]	7.1 ±5.7 [2.0-30.0]
Aldosterone (ng/dL)	16 ±8 [2-41]	39±16 [23-103]
Renin (pg/mL)	10 ±8 [1-43]	9 ±9 [1-51]

CONCLUSIONS

This report presents evidence for a central role of abnormal adrenal steroidogenesis in IN-HBP. The rate of

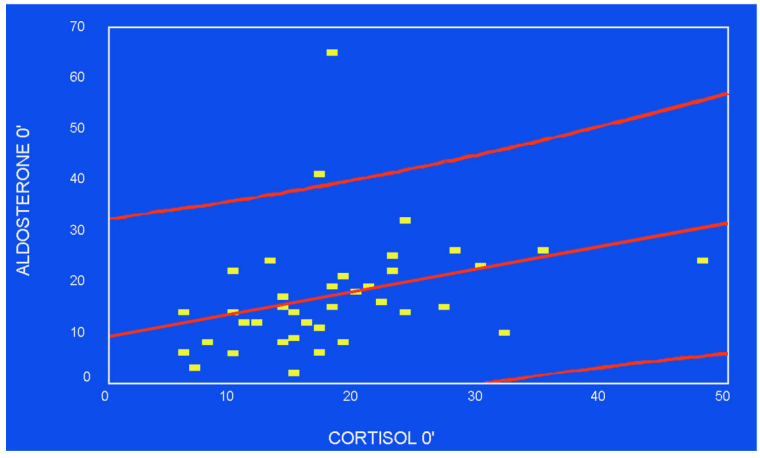

Figure 1

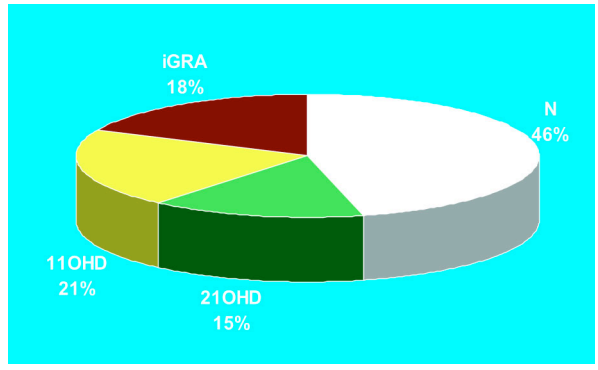

Figure 2

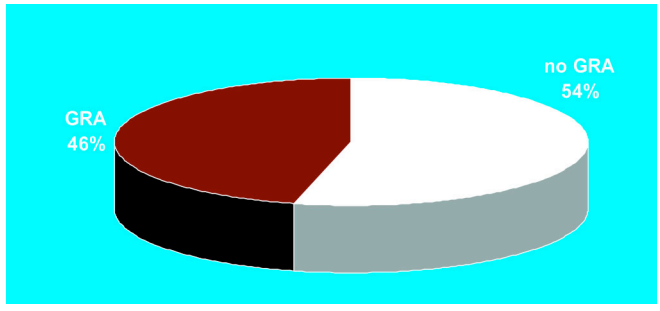

Figure 3

21-OHD – not associated with HBP – is in agreement with the prevalence reported for the general population. However the rate of 11-OHD is much higher than expected supporting a causative role in HBP. Furthermore 46% of the patients presented what conceptually at least, corresponds to GRA. In most instances either 21-OHD or 11-OHD were also present, suggesting that a GRA-like condition may be a subtle index of minor adrenal steroidogensis defects; however in the remaining cases, GRA as defined may be an operative factor by itself. Present results emphasize the usefulness of adrenal steroidogenesis testing in IN-HBP and underline the clinical utility of low dose dexamethasone treatment and/or the use of aldosterone antagonists.

PULSE WAVE VELOCITY (PWV) BEFORE MAJOR VASCULAR EVENTS. STATISTICAL RELEVANT BIOLOGIC FACTORS

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OBJECTIVES

A long period of asymptomatic vascular disease precedes major vascular events. Direct arterial wall examination is not possible in clinical practice. PWV measurement represents a method to indirectly evaluate arterial stiffness/elasticity. Since it is simple and non-invasive, it could easily be used in clinical practice before major vascular events. We measured PWV in common clinical conditions prior to major vascular events and explored relevant biologic factors of PWV.

PATIENTS AND METHODS

135 consecutive subjects were studied: Control (C) [n=30], Obese (Ob) [n=30], Arterial Hypertension (AH) [n=30], Type 2 Diabetes Mellitus (DM2) [n=45]. The Complior device (Servier courtesy) was used to measure PWV in the sitting position, between the left carotid and the left radial artery. The mean of 10 consecutive measurements was used. Blood pressure, heart rate and anthropometrical indexes (height, weight, waist and hip circumferences) were measured simultaneously. Other clinical parameters were obtained from the medical records: a) clinical - age, gender, disease duration; b) epidemiological - smoking and drinking habits; c) common analytical indexes - hematocrit, serum glucose, ionogram, calcium, cholesterol, triglycerides, HDLc; d) endocrine measurements: leptin, HbA1c, insulin, C peptide, ACTH, cortisol, DHEAS, renin, aldosterone. Body Mass Index (BMI), Body Surface Area (BSA), waist-hip ratio (w/h) and insulin/glycemia (I/G) were calculated. The Statistical Package for the Social Sciences (SPSS) program was used to analyse the results: factorial ANOVA with pos-hoc t-student tests and the Bonferroni correction; simple and multiple regression analysis.

RESULTS

Results in the defined groups were as follows (Table 1).

PWV was significantly different across diagnostic groups – $F(3,132)=2.560$, $p<0.05$ – with pos-hoc analysis revealing significantly

	C (N=30)	Ob (N=30)	AH (N=30)	DM2 (N=40)
Gender (M/F)	13/17	3/27	4/26	16/24
Age (years)	39 19	40 13	55 12	58 11
BMI (kg/m2)	23.2 2.9	35.3 8.3	30.0 3.4	29.7 4.6
SBP (mmHg)	128 21	142 14	155 20	153 24
DBP (mmHg)	82 10	93 11	95 13	91 14
HR min^{-1}	70 11	82 13	79 12	86 13
PWV (m/s)	6.9 1.7	7.5 1.4	7.5 1.4	8.1 2.2

Table 1

higher values only in the DM2 group – 8.1±2.2 vs 6.9±1.7m/s, p<0.05 (figure 1). Differences, however, did not persist after correction for gender and age.

We explored relevant biologic factors of PWV, consecutively considering epidemiological; clinical and anthropometrical; common analytical indexes; and endocrine factors. Male subjects had higher PWV – 8.4±2.4 vs 7.3±1.5m/s, p<0.05 (figure 2). Univariate analysis revealed only a mi-

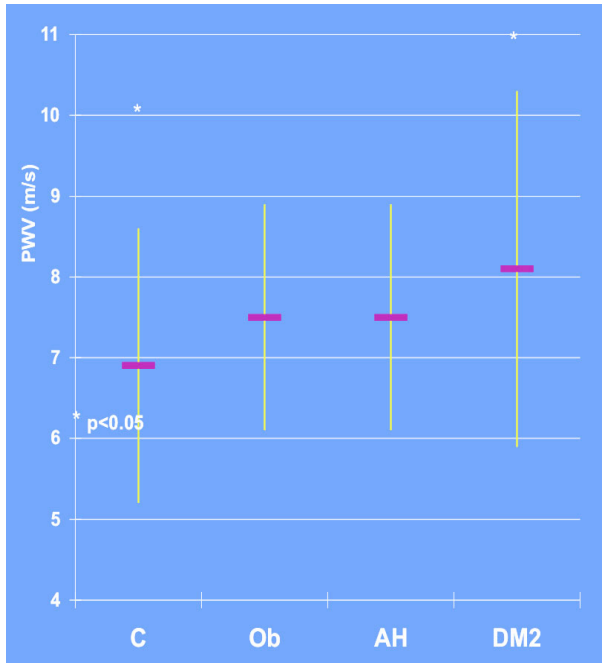

Figure 1

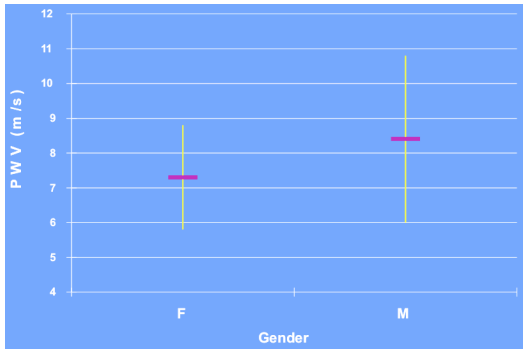

Figure 2

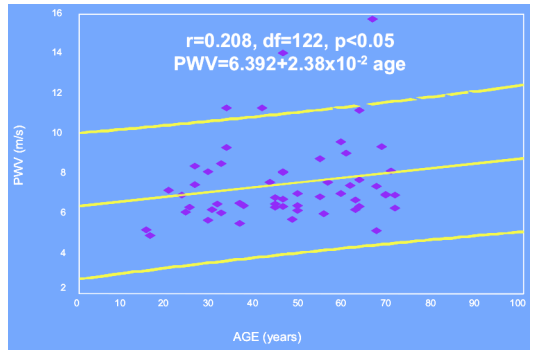

Figure 3

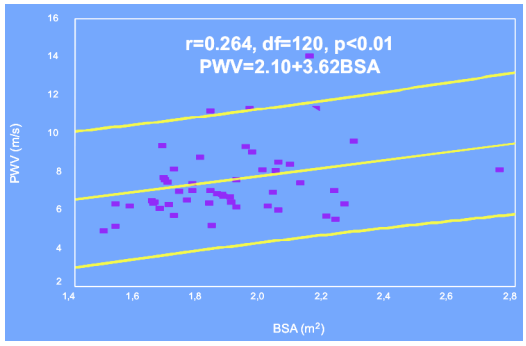

Figure 4

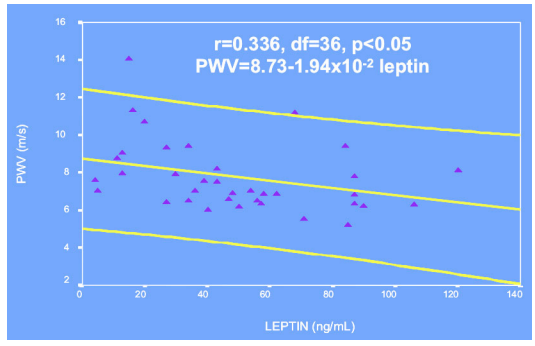

Figure 5

nor significant influence of Age – r=+0.208 (figure 3); BSA – r=+0.264 (figure 4); Systolic Blood Pressure (SBP) – r=+0.148; Hematocrit – r=+0.324; serum glycemia – r=+0.187; serum cholesterol – r=-0.162; ACTH – r=+0.231; leptin – r=-0.336 (figure 5) - $p<0.05$ in all cases. None of these factors remained significant after correction for gender and age except for BSA and leptin.

CONCLUSIONS

Using multivariate analysis the best predictive models used either: a) gender, age and BSA – $r^2=0.12$; b) serum insulin, ACTH and leptin – $r^2=0.20$.

PWV changes across diagnostic groups, but differences disappear after correction for age and gender. PWV is an independent measure of the arterial wall compliance that is independent of acute hemodynamic indexes or of common metabolic parameters and is also not related to disease duration. Besides gender and age only BSA and leptin presented a slightly albeit significant influence on PWV. These relations were independent of heart rate, suggesting that obesity per se contributes to increase arterial rigidity. Leptin may have some direct or indirect vascular effects.