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Steroid profiling by liquid chromatography tandem mass spectrometry (LC-MS/MS) in patients with non-secreting adrenocortical adenomas and subclinical hypercortisolism

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Background and aim

Liquid chromatography/tandem mass spectrometry (LC-MS/MS) offers the possibility to perform a precise and simultaneous evaluation of a large panel of steroids. Up to now, no studies have yet investigated the steroid profile and its implications in patients with adrenocortical adenomas and subclinical hypercortisolism (SH). The aim of our study was to analyze the steroid profile in sera from patients with unilateral adrenocortical adenomas.

Methods

Subjects. Ninety-four consecutive Caucasian outpatients with unilateral adrenal adenomas were classified as non-secreting (NS) (n=66) and SH (n=28) by cortisol (F) levels after 1 mg overnight dexamethasone suppression test below and above 1.8 µg/dL (50 nmol/L), respectively. Age- and sex-matched subjects (n=188) drawn from the general population[1,2] were used as controls.

Design. All subjects underwent basal steroid profiling including F, 21-deoxycortisol (21-DF), 11-deoxycortisol (S), 17-hydroxyprogesterone (17-OHP), androstenedione (A), dehydroepiandrosterone (DHEA), testosterone (T), progesterone (P), 11-deoxycorticosterone (DOC), and corticosterone (B) by LC-MS/MS, as detailed elsewhere.[1] Steroid profiling was assayed after 250 µg ACTH stimulation test in a subset of patients (n=56).

Results

Basal steroid profiling. SH patients showed lower levels of DHEA and A than in NS adenomas and controls, in both sexes. T was also lower in SH females (Figures 1 and 2). DHEA and A showed a good accuracy in predicting SH (Figure 3).

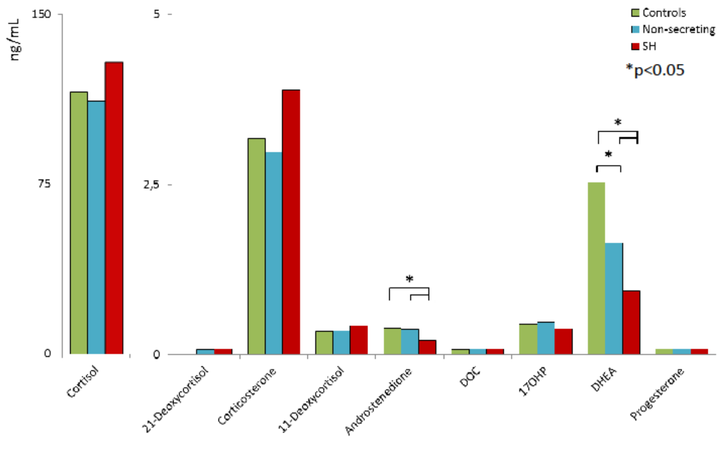

Figure 1. Basal steroid profiling in the whole cohort

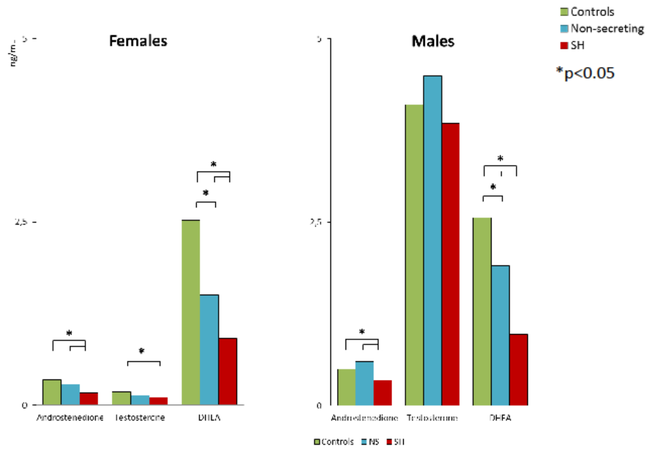

Figure 2. Basal androgens in males and females

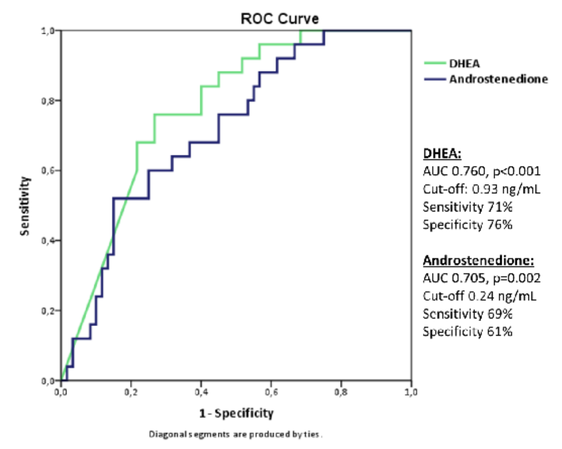

Figure 3. ROC curve for DHEA and A in predicting SH

Clinical correlates. Low DHEA and high F after DST were independently associated with increase in waist circumference. DHEA was not associated with the increase in number of cardiovascular risk factors (CRFs).

Table 1. Patient´s clinical characteristics

	NS	SH	P value
Waist circumference, cm	96.1 ± 14.4	99.5 ± 11.1	0.542
Hypertension, n (%)	39 (59.1)	23 (82.1)	0.035
Type 2 diabetes, n (%)	11 (16.7)	7 (25.0)	0.395
Dyslipidemia, n (%)	20 (30.3)	13 (46.4)	0.160
Cardiovascular diseases, n (%)	5 (7.6)	6 (21.4)	0.079
Number of CRFs, mean ± SD	1.9 ± 1.3	2.7 ± 1.1	0.004

Table 2. Multifactorial analysis for increasing waist circumference

	B-coeff	P value
BMI (1 Kg/m2 increase)	1.98	<0.001
F after DST (1 nmol/L increase)	0.14	<0.001
DHEA (1 ng/mL decrease)	-6.63	0.019
A (1 ng/mL decrease)	-	0.379
Age (1 year increase)	-	0.982

Table 3. Multifactorial analysis for increasing number of CRFs

	B-coeff	P value
Age (1 year increase)	0.06	<0.001
F after DST (1 nmol/L increase)	0.01	0.042
DHEA (1 ng/mL decrease)	-	0.816

ACTH stimulation test. SH patients showed enhanced production of F, 21-DF and DOC, and reduced production of DHEA (Figure 4).

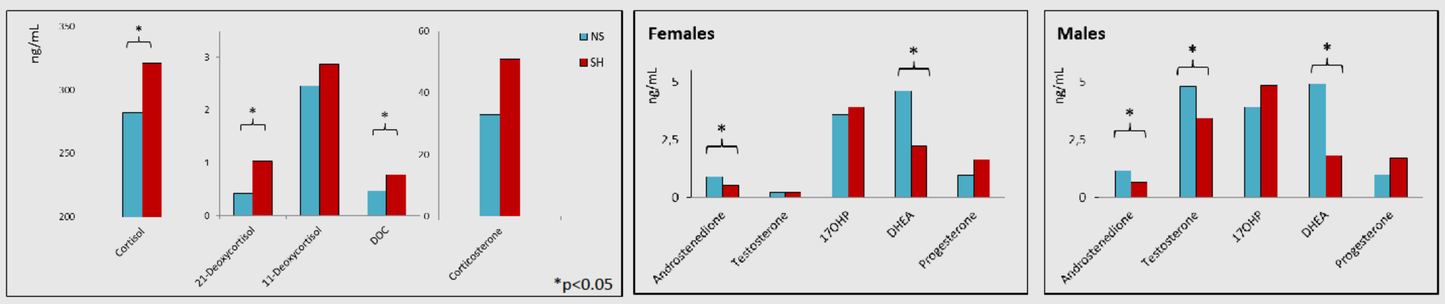

Figure 4. Steroid profiling after 1-24 ACTH in 56 patients with adrenocortical adenomas (NS=39; SH=17)

Conclusion

LC-MS/MS steroid profile performed in sera from patients with adrenocortical adenomas showed impaired secretion of several steroids in SH patients (Figure 5). This fingerprint can help in better characterizing the functional status of these tumors. Further studies are needed to understand the clinical implication of these alterations in SH patients in a prospective long-term setting.

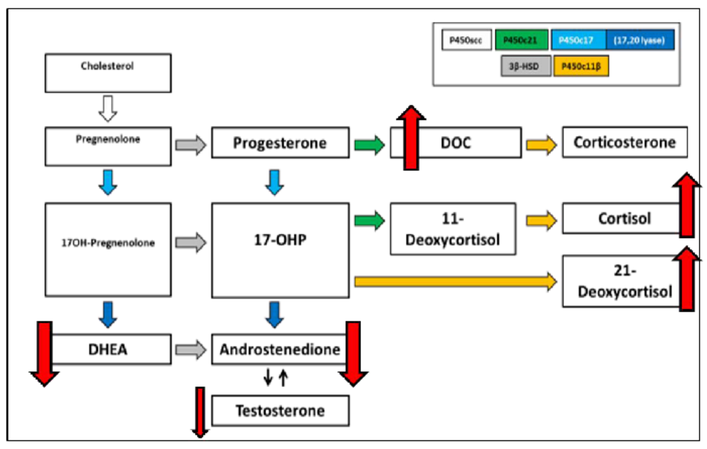

Figure 5. Overview of basal and stimulated steroid secreting pattern in SH patients with unilateral adrenal adenomas

References

1. Fanelli F, Belluomo I, Di Lallo VD, Cuomo G, De Iasio R, Baccini M, et al. Serum steroid profiling by isotopic dilution-liquid chromatography-mass spectrometry: comparison with current immunoassays and reference intervals in healthy adults. Steroids 2011; 76: 244-253.

2. Fanelli F, Di Lallo VD, Belluomo I, De Iasio R, Baccini M, Casadio E, et al. Estimation of reference intervals of five endocannabinoids and endocannabinoid related compounds in human plasma by two dimensional-LC/MS/MS. J Lipid Res 2012; 53: 481-493.

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