Usefulness of ACTH stimulation in the differential diagnosis of precocious pubarche

Mª Joana Santos[1], Daniela Amaral[2], Catarina Limbert[2], Rosa Pina[2], Lurdes Lopes[2]

1. Endocrinology Department, Hospital de Braga, Braga; 2. Pediatric Endocrinology Unit, Pediatrics Department, Hospital Dona Estefânia, Centro Hospitalar Lisboa Central, Lisboa, Portugal

Introduction: Nonclassical congenital adrenal hyperplasia (NCCAH) is caused by reduced 21-hydroxylase activity, leading to excessive adrenal androgens and premature pubarche (PP); idiopathic PP (IPP) is its main differential diagnosis. The gold standard for the differential diagnosis is ACTH stimulation test (ST). This test also estimates the adrenal cortisol reserve in NCCAH patients.

Objectives: 1. To compare the clinical characteristics and baseline hormonal profile of patients with PP; 2. To determine the importance of ACTH ST in the differential diagnosis between IPP and NCCAH and in the evaluation of the adrenal production of cortisol.

Methods: Cross-sectional study of patients with PP starting after 2 years of age, who underwent ACTH stimulation test, between November 1998-March 2013. The diagnosis of NCCAH was made based on a value of 17-OHP 60' ≥10ng/ml and the diagnosis of IPP was based on a value <10ng/ml. We excluded patients with other signs of precocious puberty (precocious thelarche in girls and testicular volume >4ml in boys). Spearman's correlation and Mann-Whitney U test were used for statistical analysis. We considered a level of significance of 0,05.

Results: 43 patients { **Idiopatic precocious pubarche (IPP): 37 (86%)**; **Non classic congenital adrenal hyperplasia (NCCAH): 6 (14%)**

Clinical characteristics

Variables		IPP	NCCAH	p
Age at 1st visit (years)*		7,4 (2,0); [3,5-9,4]	8,6 (1,6); [7,6-9,4]	0,008
Sex	Feminine	32 (86,5%)	5 (83,3%)	NS
	Masculine	5 (13,5%)	1 (16,7%)	
Age at pubarche (years)*		5,8 (1,9); [2,5-8,9]	6,0 (4,0); [3,0-8,0]	NS
BMI (SD)		1,0±1,0 [-0,7; 3,0]	0,4±1,0 [-1,0; 1,9]	NS
Pubic hair	P2	33 (89,2%)	6 (100%)	NS
	P3	4 (10,8%)	0 (0%)	
Axillary hair	A1	23 (62,2%)	4 (66,7%)	NS
	A2	13 (35,1%)	2 (33,3%)	
	A3	1 (2,7%)	0 (0%)	
Acne		3 (8,1%)	1 (16,7%)	NS
Clitoromegaly		0 (0%)	1 (16,7%)	0,01
Hirsutism		0 (0%)	0 (0%)	NS
Bone age-chronological age*		1,1 (1,4); [-2,8; 4,8]	1,1 (1,9); [-0,58; 1,6]	NS

*Md (interquartile range) [minimum-maximum]

Table I – Clinical characteristics of patients with IPP and NCCAH

Baseline hormonal profile

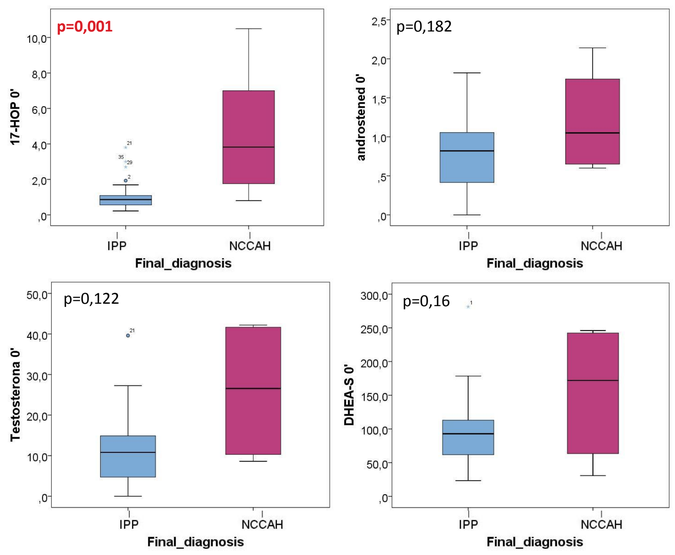


Figure 1 - Basal hormonal profile in both groups

Basal 17-OHP value

- In patients with IPP, the basal 17-OHP value ranged from 0,22 to 3,80ng/ml and in NCCAH patients from 0,80 to 10,50ng/ml.
- Two patients with NCCAH had a basal 17-OHP value < 2,0ng/ml.
- We did not find a threshold value of 17-OHP that clearly distinguished the 2 groups.

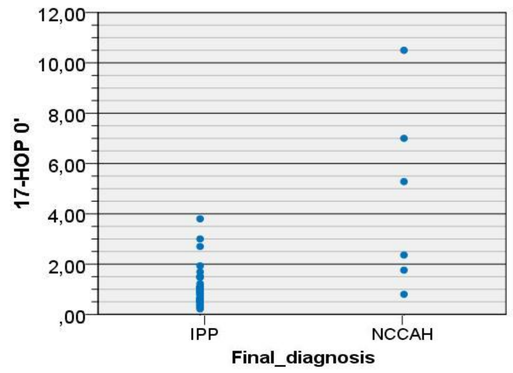
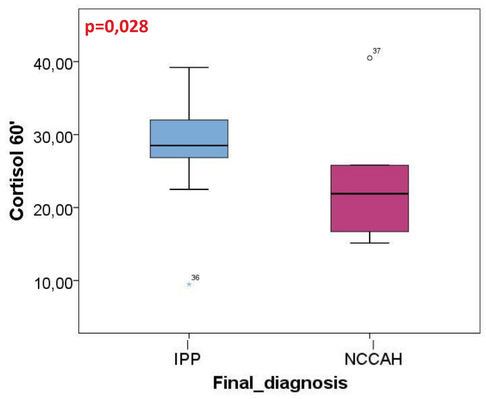


Figure 2 - Basal 17-OHP in both groups (ng/ml)

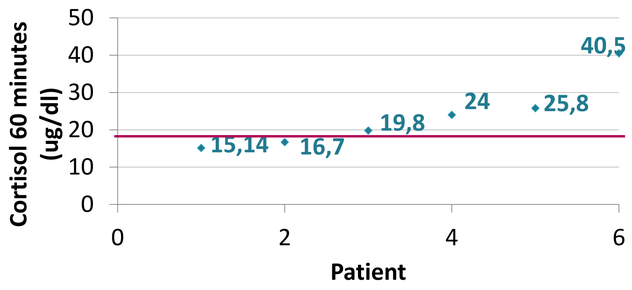
Adrenal production of cortisol



After ACTH stimulation test, NCCAH patients had a significantly lower secretion of cortisol than IPP patients.

Cortisol levels at 60 minutes:
- NCCAH:23,66±9,21ug/dl [15,14-40,50]
- IPP: 29,28±5,37ug/dl [9,49-39,2])

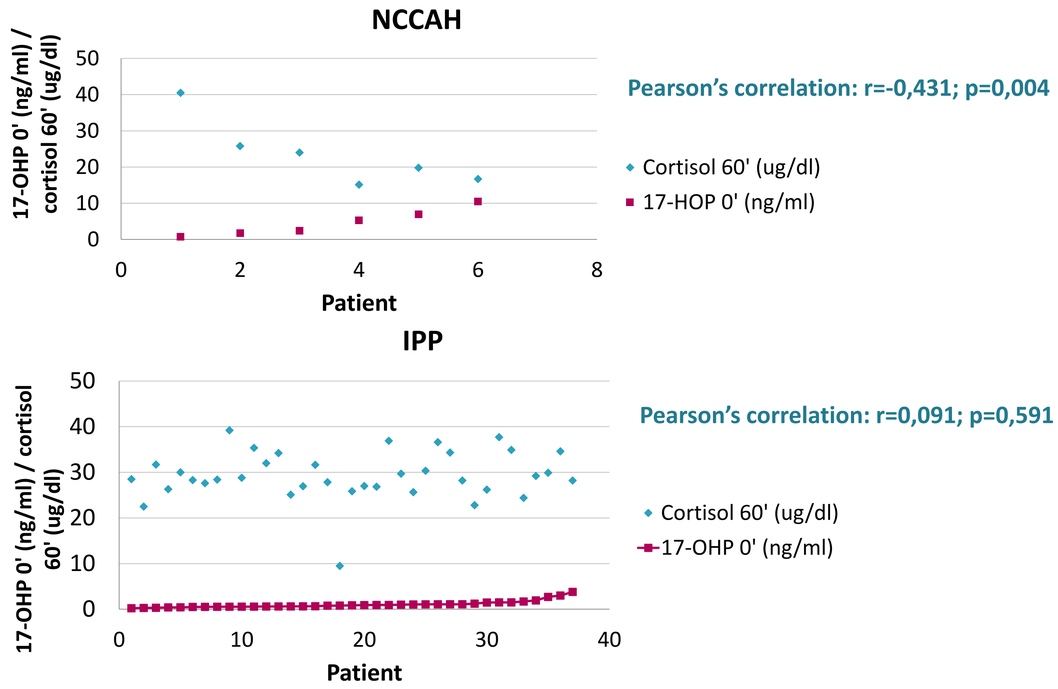
Figure 3 - Cortisol levels after ACTH stimulation test in both groups



Two (33,3%) patients with NCCAH had a suboptimal cortisol response after stimulation.

Figure 4 - Cortisol levels after ACTH stimulation test in NCCAH patients

Basal 17-OHP and stimulated cortisol



We found a significant negative correlation between basal 17-OHP and stimulated cortisol levels in patients with NCCAH. In this group, patients with the highest basal 17-OHP presented the lowest cortisol level at 60 minutes, due to reduced 21-α-hidroxilase activity.

Figure 5 - Basal 17-OHP and stimulated cortisol levels in both groups

Conclusion: The ST was useful to distinguish between patients with NCCAH and IPP, for no basal 17-OHP level could allow for a definitive differential diagnosis in the individual patient. In some NCCAH cases, it also showed inappropriate cortisol secretion under stress, contributing to the therapeutic decision.

Bibliography:

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