

Basal levels of 17-hydroxyprogesterone can distinguish isolated precocious pubarche from non-classical congenital adrenal hyperplasia in children: a prospective observational study

Anna Grandone¹, Pierluigi Marzuillo^{1*}, Caterina Luongo¹, Roberto Toraldo¹, Michela Mariani¹, Emanuele Miraglia del Giudice¹

¹Department of Woman, Child, General and Specialized Surgery, Università degli Studi della Campania “Luigi Vanvitelli”, Naples, Italy

Background

Basal levels of androgens, in particular 17-OHprogesterone (17OHP), are widely debated as predictors of non-classical congenital adrenal hyperplasia (NCCAH) among patients with precocious pubarche (PP). So many authors suggested the execution of ACTH stimulation test in all children with PP. The aim of our study was to identify clinical and biochemical predictors of NCCAH in children with PP.

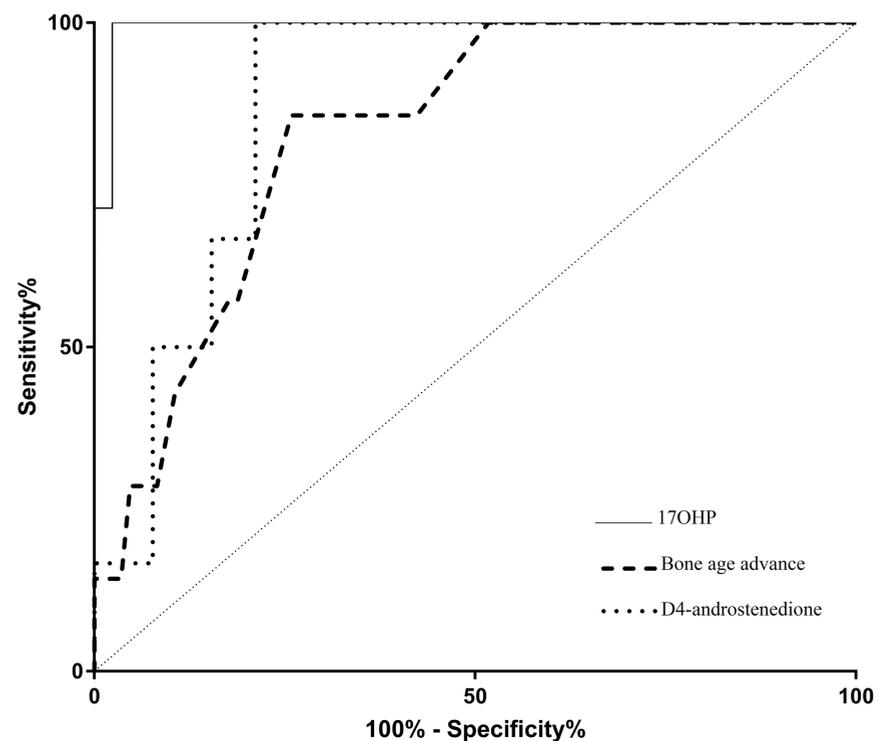
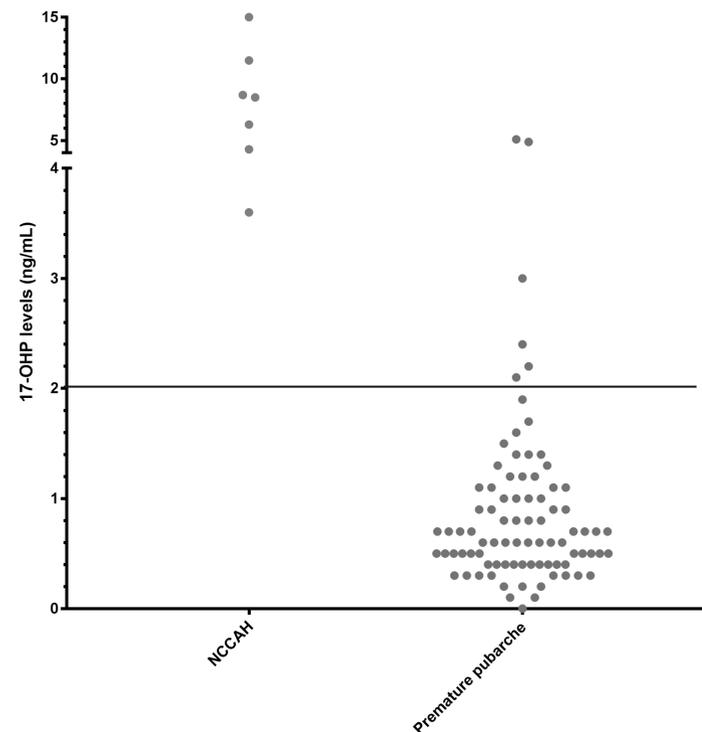
Methods

We conducted a prospective study of 92 patients with PP undergoing an ACTH stimulation test. We tested the association of basal clinical and biochemical factors with NCCAH diagnosis. Patients were suspected to have NCCAH if their stimulated 17-OHP plasma levels were ≥ 10 ng/ml and then genotyped to confirm the diagnosis.

Results

Seven (7.6%) patients resulted having NCCAH. The best basal biochemical predictor for NCCAH was 17OHP level >2 ng/ml. In fact a basal 17OHP level >2 ng/ml had 100% (95%CI, 59.04–100) sensitivity, and 93% (95%CI, 85.3–97.37) specificity. The area under the ROC curve for 17OHP was 0.99 (95% CI, 0.98–1.007).

Variables	NCCAH	Premature pubarche	p
n	7	85	
Clinical			
Sex male n (%)	2 (28.5%)	11 (13%)	0.3
Age at pubic hair onset	6.3 \pm 1	6.4 \pm 1.1	0.5
Age at first examination	7.2 \pm 1.1	7.5 \pm 1.2	0.5
Bone age minus chronological age, years	3.7 \pm 0.7	1.9 \pm 1.2	0.002
BMI z-score	1.26 (1.25-1.5)	1.02 (-0.1-1.7)	0.5
Height SDS	1.4 (1.6-2.7)	1.2 (0.1-1.8)	0.2
Biochemical			
Basal 17-OHP ng/ml	8.5 (4.3-11.5)	0.9 (0.4-1.1)	0.0002
Peak 17-OHP ng/ml	26.0 (20-32)	2.6 (2.1-3.4)	p<0.0001
Basal cortisol mcg/dl	6.9 (4.4-10.2)	9.9 (5.7-10.5)	0.42
Peak cortisol mcg/dl	18.4 (17.8-23.1)	30.1 (26.8-34.4)	0.002
DHEAS micrg/ml	0.95(0.8-3.1)	0.7(0.4-1.1)	0.2
Delta4A ng/ml	1.4 (1.1-2.3)	0.9 (0.7-1.1)	0.003
Testosterone ng/dl	15.5 (3.8-25)	7.5(4.5-15)	0.4



Conclusion

We suggest a selection strategy based on basal level of 17OHP, with a cut-off that can be different depending on the assay used, to decide in which patients with PP is necessary to perform an ACTH test. This approach, in our opinion, is cheaper and less distressing for children and their families, sparing several unnecessary ACTH tests.

No conflict of interest to declare