USEFULNESS OF CORTICOTROPIN TEST IN CHILDREN AND ADOLESCENTS WITH CLINICAL HYPERANDROGENISM

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INTRODUCTION

▪CAH is a group of autosomal recessive disorders characterized by impaired cortisol synthesis. The most common form of CAH, accounting for about 95% of cases, is caused by mutations in *CYP21A2*, the gene encoding the adrenal steroid 21-hydroxylase enzyme (P450c21)

- Classic CAH
  - Salt wasting
  - Simple virilizing
  - 1: 9.000 – 1: 12.000 (1: 2273 in greek population)
- Non-Classical CAH
  - 1: 100 – 1: 1000 in caucasians (1: 454 in greek population)

OBJECTIVE

To evaluate the usefulness of ACTH test in diagnosis of cases of

- ➢non-classical congenital adrenal hyperplasia (NCCAH) and
- ➢heterozygosity of CYP21 gene molecular defects

in children and adolescents with clinical hyperandrogenism and basal 17-OHP below 2ng/ml, but higher than the upper normal range for their age.

METHODS

Retrospective study

364 children and adolescents : 70boys , 294girls aged 0.2- 19.5yrs.

332 children (mean age : 7.6 ± 2.1yrs)

- ➢clitoromegaly
- ➢hyperpigmentation of external genitalia,
- ➢advanced bone age,
- ➢early growth of pubic or axillary hair,
- ➢increased axillary body odor,
- ➢acne

32 adolescents (mean age : 14.7 ± 1.8yrs)

- ➢hirsutism,
- ➢intense acne
- ➢and/or abnormal menses

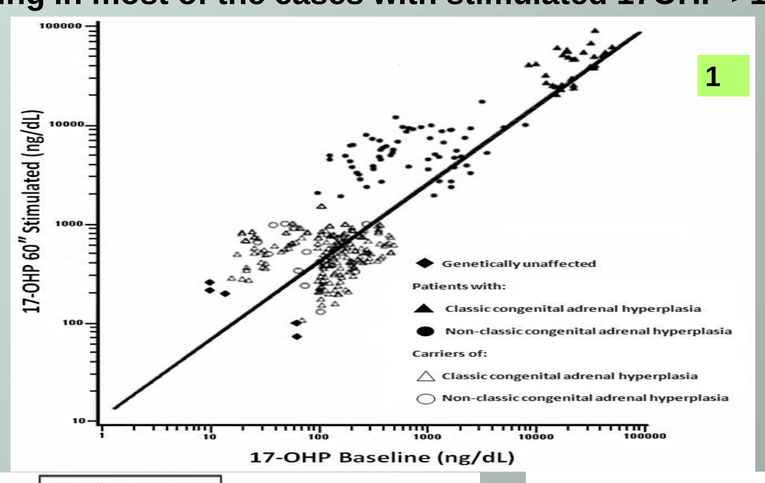
With basal 17OHP levels above the upper normal limit and <2ng/ml

ACTH stimulation test (basal and 60min stimulated 17OHP) with microELISA (DRG Diagnostics

- ➢**NCCAH according to the 17OHP nomogram (1) and 60min stimulated 17OHP >16.6ng/ml (2)**
- ➢**Heterozygosity according to the 17 OHP nomogram (1) and the criterion of the sum of basal and 60min stimulated 17OHP levels >4.9ng/ml (3)**

Genotyping in most of the cases with stimulated 17OHP >10ng/ml

1



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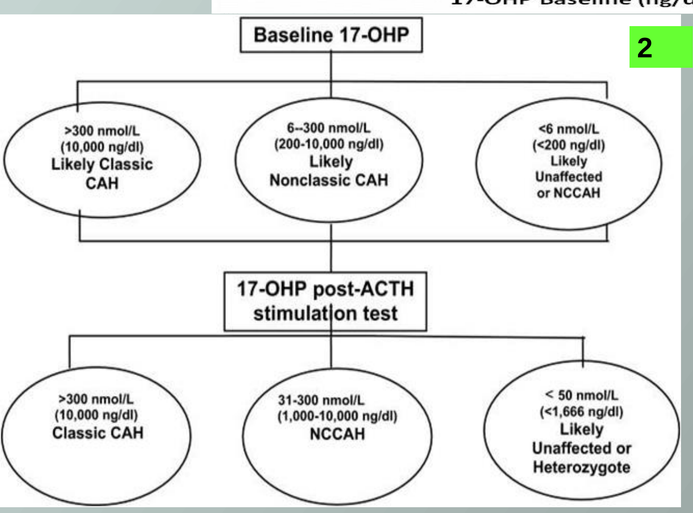

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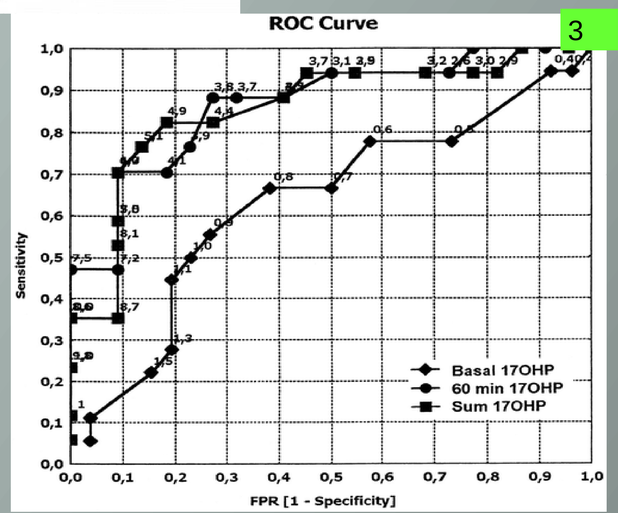


RESULTS

7 cases (1,92%) (6girls and one boy) were detected with NCCAH

- ➢Six of them among the group of prepubertal children (1.8%), and
- ➢a girl aged 18.5 years among the adolescents (3%)

They all had 17-OHP 0' <2ng/ml
17-OHP 60' >16.7ng/ml

In 5/7 of them genotyping confirmed the diagnosis. The two subjects in whom molecular confirmation was not available, had 60min 17OHP stimulated value 50.4ng/ml and 33.8ng/ml respectively

112 cases (30.8%) of possible heterozygosity

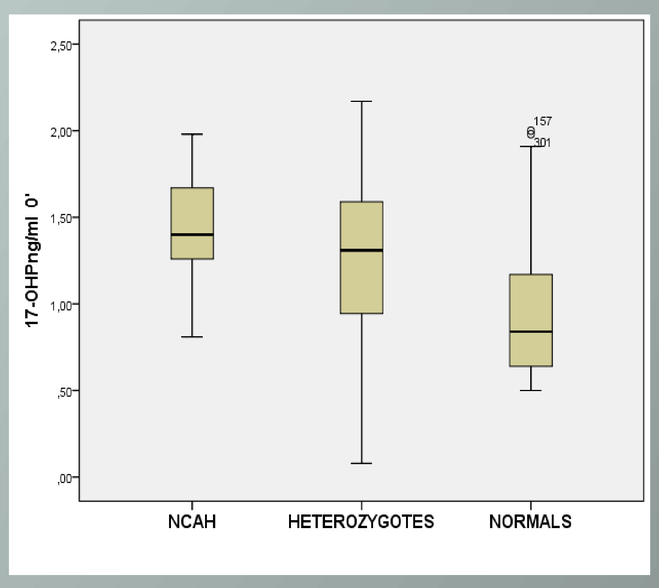
104 (31.9%) prepubertal

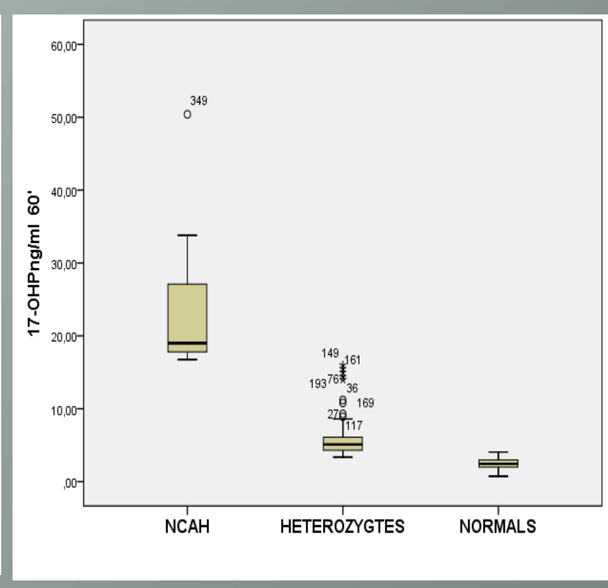
8 (25%) pubertal.

In 56/112 confirmed by genotyping

	Unaffected (n=245) Mean (SD)	Heterozygotes (n=112) Mean (SD)	NCCAH (n=7) Mean (SD)	P
17-OHPng/ml 0'	0.93 (0.34) a vs b**,p=0.000	1.28 (0.45) b vs c, p=0.37	1.93 (0.38) a vs c **, p=0.002	*P= 0.000
17-OHPng/ml 60'	2.5 (0.69) a vs b**,p=0.000	5.74 (2.47) b vs c**,p=0.000	25.13 (12.6) a vs c **, p=0.000	*P=0.000

a =unaffected, b=heterozygotes, c= NCCAH
* = Kruskall-Wallis , ** = Mann-Whitney





CONCLUSIONS

In a population of 364 children and adolescents with clinical hyperandrogenism the use of the basal 17OHP value of 2ng/ml as a threshold for performing ACTH test would miss the diagnosis in approximately 2% of our patients

Taking into account that the percentage of NCCAH patients in Greek children with premature adrenarche has been reported to be 8.3% (4), the number of missed cases is not negligible.

The frequency of possible heterozygosity as evaluated from the ACTH test was 31% in this group of chilldren and adolescents with signs of hyperandrogenism. As genetic confirmation was not available in all subjects, a certain degree of overlapping between heterozygotes and "unaffected" is aknowledged

The clinical significance of detecting heterozygosity among children and adolescents with signs of clinical hyperandrogenism is not clear

However, the significance of detecting heterozygosity by the ACTH test -even as a strong possibility- for genetic counselling, is very obvious, taking into account the high prevalence of heterozygosity in Greek population (25%) (4)

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Adrenal

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