HOW TO INTERPRET CORTISOL RESPONSES TO ACTH IN PATIENTS WITH NON-CLASSIC CONGENITAL ADRENAL HYPERPLASIA

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INTRODUCTION

Patients with non-classic congenital adrenal hyperplasia (NCCAH) mostly have androgen excess and about a third present subnormal response of cortisol to an acute ACTH stimulation test.

Recent clinical guidelines recommend that all patients with non-classic congenital adrenal hyperplasia (NCCAH) on glucocorticoid therapy (GC) need to be informed about stress doses and suggest the use of GC in the subgroup of patients with low cortisol response during periods of stress even though they are not on GC.

OBJECTIVE

1. To study the cortisol response to ACTH 250 mcg i.v. (Synacthen®, Novartis) in patients with NCCAH.

2. To evaluate the need of GC supplementation in periods of stress in patients with subnormal cortisol response to ACTH

PATIENTS AND METHODS

Descriptive, retrospective study in 46 patients with NCCAH on follow-up in our Pediatric Endocrinology Unit.

- Cortisol levels were evaluated after ACTH test.
- Clinical practice regarding GC usage on these patients was investigated as well as their variation of GC doses under stressing circumstances.

RESULTS

The ACTH test was performed in 44/46 patients with NCCAH. Cortisol response to ACTH was determined in 34 patients. Nine patients (26%) had a cortisol response <18 μg/dl. Eight of these patients were treated with hydrocortisone (Table 1). According to previous clinical guidelines for NCCAH, the patients on substitutive doses of GC did not use GC stress doses and all patients tolerated infection or stress situations well.

Cases	Age at dx (yrs)	17-OHP (0') (ng/ml)	17-OHP (60') (μg/dl)	Cortisol (0') (μg/dl)	Cortisol (60') (μg/dl)	Genotype *(CYP21A2)*	GC
1	10.6	17	>25	13.5	16.1	p.Val282Leu/p.Ile173Asn	**+**
2	5	24.3	>25	9.66	16.05	p.Val282Leu/p.Arg357Trp	**+**
3	4.7	11.89	19	7.7	12	p.Val282Leu/p.Ile173Asn	**+**
4	8.8	14.1	49.9	8.6	11.2	p.Val282Leu/p.Ile173Asn	**+**
5	9.5	37.6	45	13.1	15.03	p.Val282Leu/655G	**+**
6	6.2	5.6	49.9	6.49	11.5	p.Val282Leu/p.Arg357Trp	**-**
7	9	16.9	32.4	14.5	17.1	p.Val282Leu /p.Arg357Trp	**+**
8	6.5	40.8	81.6	7.19	8.57	"Polymorph" c.735GTA/del-conv	**+**
9	7.3	8.2	31.9	12.5	17.8	p.Val282Leu/del-conv exon3-4	**+**

Table 1. Description of patients with cortisol response to ACTH < 18 μg/dl

CONCLUSION

- About one third of our patients with NCCAH presented subnormal cortisol response to ACTH. No correlation was found between 17-OH Progesterone levels and cortisol response.
- Most of the patients with subnormal cortisol response to ACTH presented a *CYP21A2* severe mutation in one allele.
- None of these patients presented signs or symptoms of adrenal crises during periods of stress.
- Nonetheless, the need to increase the dose of GC in patients without significantly suppressed adrenal function require confirmation in a higher number of patients.