Serum sex hormone binding globulin levels, but not a 4-hour profile of 17-OH progesterone, would be useful in monitoring children with congenital adrenal hyperplasia

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INTRODUCTION

There exists no gold standard for adjustment of treatment in congenital adrenal hyperplasia (CAH). Clinicians try to avoid over- and undertreatment by considering various indicators. Different strategies including a 24-hourly monitoring profile have been suggested to determine the metabolic control (1,2).

AIM

We aimed to investigate the optimal sampling time for 17-OHP and the use of sex hormone binding globulin (SHBG) as a monitoring parameter in salt-wasting CAH due to 21-hydroxylase deficiency.

METHOD

Cross-sectional study, 16 children (9 girls, 7 boys; median age 7 years) with salt-wasting CAH.

First, androstenedione, 17-OHP, cortisol, SHBG, electrolytes, insulin, TSH, free T4 were obtained between 07.00 and 08.00 a.m., prior to morning dose of hydrocortisone and fludrocortisone.

Samples of 17-OHP and cortisol were additionally collected 1, 2, and 4 hours after the morning dose and assayed using high performance LC/MS.

Subjects were divided into good and poor control groups defined according to hyperandrogenic state, considered when

(i) bone age SD score ⩾2,

(ii) annual change in height SD score was ⩾ 0.3

(iii) androstenedione >3.3 ng/mL for girls and >3.1 ng/mL for boys, or

(iv) 17-OHP ≥ 10 ng/mL.

The results are reported as median (interquartile range).

RESULTS

Premedication 17-OHP levels were strongly correlated with 17-OHP levels 1, 2, and 4 hours after the morning dose (rs=0.929, p<0.01; rs=0.943, p<0.01; rs=0.835, p<0.01, respectively).

Clinical features, indicators of hyperandrogenic state, and the ratio of reduction of 17-OHP levels after medication were similar in children with premedication serum 17-OHP levels ≥10 ng/mL (n=9) vs. <10 ng/mL (n=7) while hydrocortisone doses were significantly lower in children with high 17-OHP levels [11 (8) vs 19 (11) mg/m2/day, p=0.017).

Clinical and biochemical features were not different except significantly higher SHBG values [92 (59) mmol/L vs 40 (22), p=0.036] in the growth acceleration group (n=8) and significantly lower daily hydrocortisone doses in children with growth acceleration [7 (7) vs 15 (9) mg/m2/day, p=0.036] and in those with elevated androstenedione levels [9 (6) vs 19 (9) mg/m2/day, p=0.039].

	Premedication 17-OHP, ng/mL		
	<10 Median (IQR)	≥10 Median (IQR)	*p*
Patients (female, male)	7 (3,4)	9 (5,4)	
Age, years	7 (9)	6 (7)	*0.6*
Bone SDS	3 (2)	2(4)	*0.8*
Number of patients with increased bone SDS	6	5	*0.3*
PAH SDS	-0.2 (2)	-0.6 (3)	*0.3*
Annual Δh SDS	0.3 (0.8)	0.5 (0.8)	*0.8*
Number of patients with increased annual Δh SDS	3	5	*1*
17-OHP levels 2-hours after the morning dose	0.3 (1)	14 (88)	*0.001*
17-OHP levels 4-hours after the morning dose	0.4 (1)	18 (98)	*0.007*
Premedication cortisol levels, mcg/dL	0.8 (1)	0.9 (0.5)	*1*
Cortisol levels 2-hours after the morning dose, mcg/dL	37 (34)	12 (10)	*0.01*
Cortisol levels 4-hours after the morning dose, mcg/dL	14 (27)	7 (7)	*0.01*
Delta-4 androstenedione, ng/mL	1 (4)	4 (7)	*0.1*
Number of patients with increased androstenedione	3	6	*0.6*
Hydrocortisone, mg/m2/day	19 (11)	11 (8)	*0.02*

Clinical and laboratory characteristics of patients for 17-hydroxyprogesterone (17-OHP) levels <10 or >10 ng/mL are presented. The results are reported as medain (interquartile ranges) (IQR). Mann-whitney U test and Fisher's exact test were used as appropriate to compare the groups. Abbreviations :SDS: standard deviation score. PAH: predicted adult height. Δh SDS: annual change in height SDS (Final height SDS-Height SDS measured 1-year earlier).

CONCLUSIONS

When over- or undertreatment is suspected, the levels of 17-OHP should not be trusted, it misses the hyperandrogenic state or may falsely suggest unnecessary dose increments.

A 4-hour profile of 17-OHP does not add significant data over early morning premedication 17-OHP levels.

In general, low doses of hydrocortisone should be avoided. SHBG can be considered as an indicator of hyperandrogenemia.

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