The Urinary Steroidome of Treated Children with Classic 21-Hydroxylase Deficiency

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Background

Monitoring treatment of children with classic congenital adrenal hyperplasia (CAH) is difficult and biochemical targets are not well defined. Analysis of urinary steroid hormone metabolites by gas chromatography-mass spectrometry (GC-MS) (urinary steroidomics) is a non-invasive diagnostic means and provides an overview of the whole spectrum of adrenal steroids in a CAH patient, including glucocorticoid, androgen and 17-OHP metabolites in parallel (**Fig. 1**).

Methods

We retrospectively analysed 576 daily urinary steroid hormone metabolite profiles determined by gas chromatography-mass spectrometry of 150 children aged 3.0 to 17.9 years with classic 21-hydroxylase deficiency (21-OHD) on hydrocortisone and fludrocortisone treatment.
Daily urinary excretion of glucocorticoid-, 17α-hydroxyprogesterone (17-OHP)-, and androgen metabolites as well as growth and weight gain were presented.

Figure 1. Schematic overview of steroidogenesis and steroid metabolism in CAH.

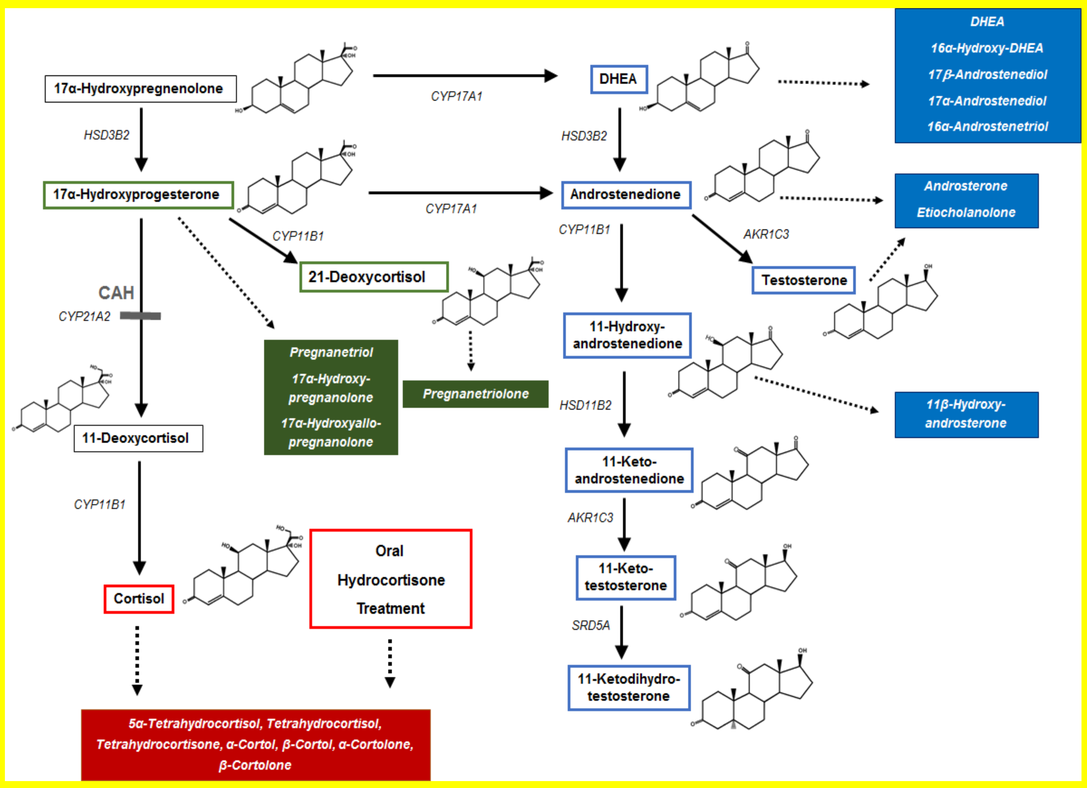
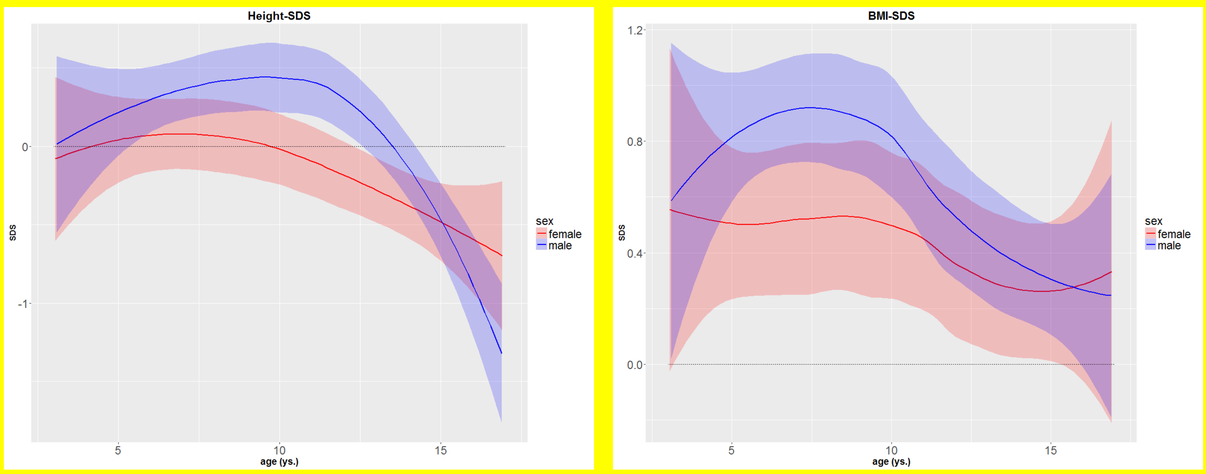


Figure 2. Height and weight in treated children with CAH.



Smoothed curves of mean height-SDS (**A**) and BMI-SDS (**B**) are shown for boys (blue) and girls (red).

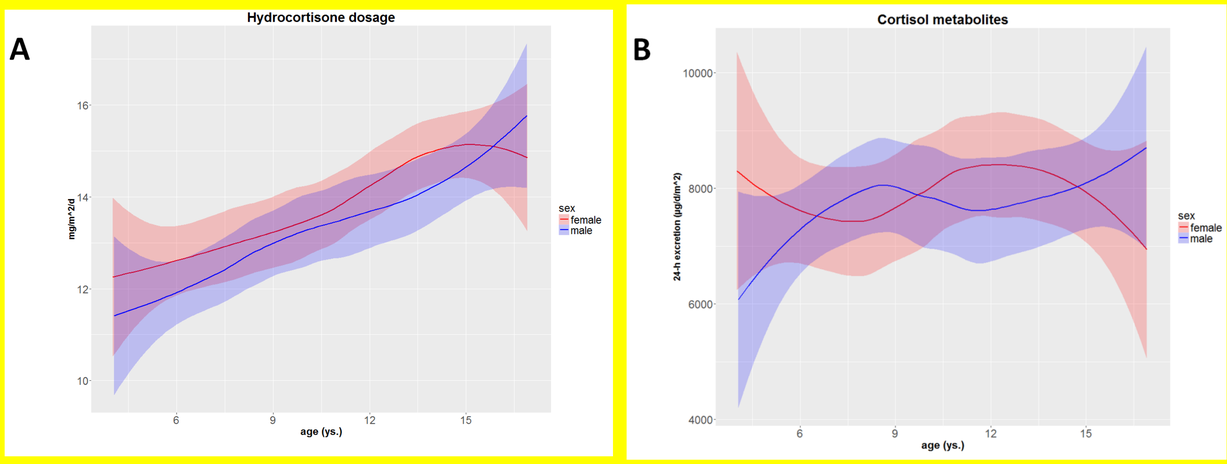
Results

The growth of the children of our cohort indicated that treated children with CAH exhibit a prepubertal overgrowth, while the pubertal growth spurt is diminished (**Fig. 2A**). Treated children with 21-OHD demonstrated increased BMI-SDS values, especially during prepubertal age (**Fig. 2B**). Hydrocortisone dosage increased with age (**Fig. 3A**), whereas BSA-corrected cortisol metabolite excretions were relatively stable and reflected supraphysiological hydrocortisone treatment dosage, which were associated with higher BMI values in children with CAH (**Fig. 3B**). BSA-corrected 17-OHP- and androgen metabolite excretions increased with age. 11β-Hydroxyandrosterone was the dominant urinary adrenal-derived androgen metabolite in CAH children. Adrenarche was blunted in children with CAH under hydrocortisone treatment and androgen metabolites except 11β-hydroxyandrosterone were suppressed. Compared to girls, boys exhibited a somewhat greater increase of androgen metabolite excretions (**Fig. 4**).

Conclusions

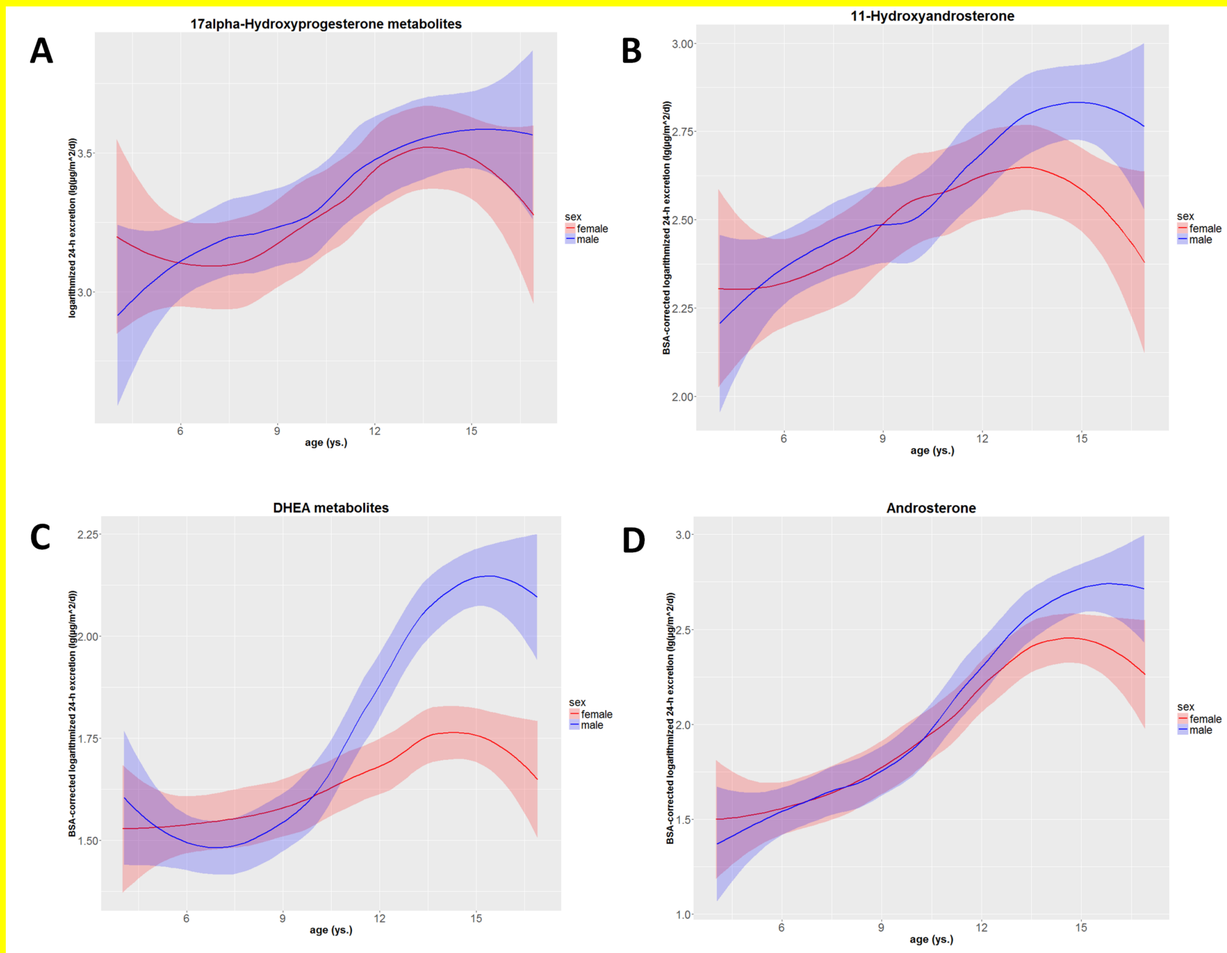
Our data show glucocorticoid, 17-OHP and androgen metabolite excretions of treated children with CAH.
Clinical management of classic CAH has been considered to be a difficult balance between androgen or cortisol excess. However, our data demonstrated that treating children with CAH is a dilemma, because children with CAH are exposed simultaneously to both conditions.
Reference values of daily urinary steroid metabolite excretions of treated children with CAH allow the clinician to adequately classify the individual patient regarding the androgen-, 17-OHP-, and glucocorticoid status in the context of the underlying disorder. Additionally, urinary 21-OHD-specific reference ranges will be important for research studies in children with CAH.

Figure 3. Hydrocortisone dosage and urinary cortisol metabolite excretion in treated children with CAH.



Smoothed curves of mean hydrocortisone dosage (**A**) and daily BSA-corrected ∑ cortisol metabolite excretion (µg/m²/d) are shown for boys (blue) and girls (red). A linear mixed model for CAH children below 10 years revealed significant effects of logarithmized ∑ cortisol metabolite excretion, age and their interactions on BMI-SDS (P = 0.0001 for ∑ cortisol metabolites × age interaction).

Figure 4. Urinary 17α-hydroxyprogesterone and androgen metabolite excretion in treated children with CAH.



Smoothed curves of mean daily logarithmized and BSA-corrected excretion (in lg(µg/m²/d)) of 17-OHP metabolites (**A**), 11β-hydroxyandrosterone (**B**), ∑ DHEA metabolites (**C**) and androsterone (**D**)are shown for boys (blue) and girls (red).

Disclosure: The authors have nothing to disclose.

55ESPE 23--P1

Adrenal

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DOI: 10.3252/pso.eu.55ESPE.2016

Poster presented at: ESPE 2016 PARIS 10-12 SEPTEMBER