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

Clemens Kamrath, Lisa Wettstaedt, Michaela F. Hartmann, Claudia Boettcher and Stefan A. Wudy

Justus-Liebig-University, Centre of Child and Adolescent Medicine, Division of Pediatric Endocrinology and Diabetology, Steroid Research & Mass Spectrometry Unit, Giessen, Germany

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.

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 supraphysiologic 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 boys, girls 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 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.

Disclosure: The authors have nothing to disclose.