ESPE 2021
The 59th Annual Meeting Online
22-26 September 2021

HOW DO URINE STEROID METABOLITES OF SPOT SAMPLES CORRELATE WITH 24 HOUR URINE SPECIMENS IN CHILDREN WITH CONGENITAL ADRENAL HYPERPLASIA?

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INTRODUCTION

Monitoring of treatment in children with congenital adrenal hyperplasia (CAH) includes assessment of growth and bone maturation, and measurement of hormone concentrations. Hormone measurement is difficult, because steroid production follows a circadian rhythm and is influenced by short-term stress and steroid drugs. Steroid assessment in urine collected over 24h is most reliable, but for some children this is not feasible. Thus, urine spots might be an alternative. In healthy children, steroid concentrations in 24h and spot urine do not correlate well, but in children with CAH who have a unique urine steroid signature, this could be different.

OBJECTIVE

To investigate whether steroid metabolites in 24h urine collections correlated with those from urine spot samples in children with CAH.

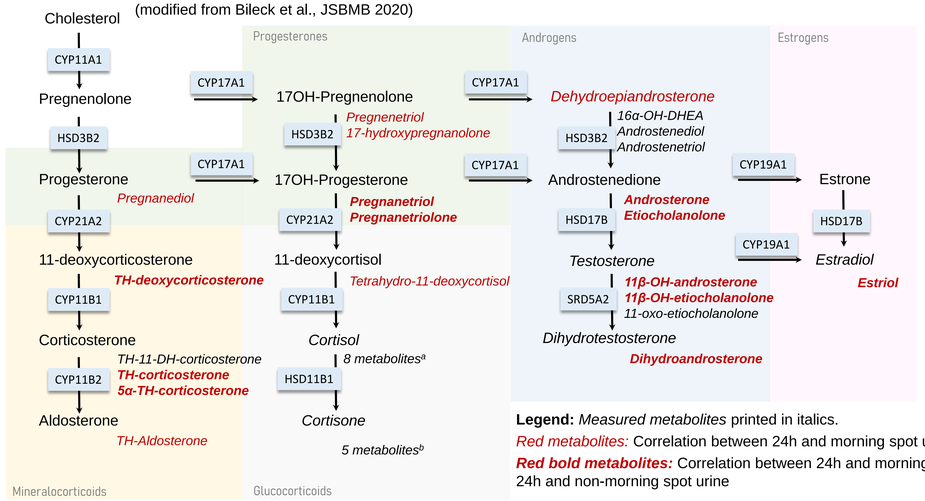
METHOD

- **Study design:** Observational study including data from three European countries (Greece, The Netherlands, Switzerland).
- **Sample:** 40 Children and adolescents with CAH due to 21-hydroxylase deficiency.
- **Collection:** Both 24h urine and urine spots. Urine spots: 20/40 collected in the **morning**; 20/40 later during day (**non-morning**).
- **Biochemical analyses:** 40 steroid metabolites using GC-MS.
- **Statistical analyses:** Correlations between 24h and spot urine metabolites assessed using Kendall's tau-beta. Correlation were considered significant if Kendall's tau >0.45 and p<0.002 to account for multiple testing.

RESULTS

- Strong correlation *between 24h and morning spot* urine for 17 of the 40 measured metabolites and ***between 24h and non-morning spot*** urine for 11/40 metabolites (Figure 1).

Figure 1: Steroid pathway depicting measured metabolites and their correlation between 24h and spot urine
(modified from Bileck et al., JSBMB 2020)



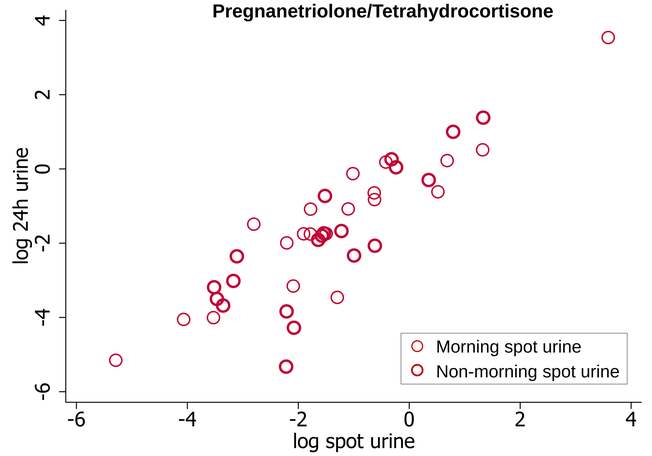
Legend: *Measured metabolites* printed in italics.
Red metabolites: Correlation between 24h and morning spot urine.
Red bold metabolites: Correlation between 24h and morning, and 24h and non-morning spot urine

Abbreviations: CYP, Cytochrome P450 17; DH, Dehydro; DHEA, Dehydroepiandrosterone; HSD, Hydroxysteroid dehydrogenase; OH, Hydroxy; SRD5, Steroid 5α-reductase.

Footnotes: [a]Tetrahydrocortisol, 5α-Tetrahydrocortisol, α-Cortol, β-Cortol, 6β-OH-cortisol, 18-OH-cortisol, 20α-DH-cortisol, 20β-DH-cortisol
[b]TH-cortisone, α-Cortolone, β-Cortolone, 20α-DH-cortisone, 20β-DH-cortisone

- Substrate/Product ratios reflecting 21-hydroxylase activity, e.g. Pregnanetriolone/ Tetrahydrocortisone (Figure 2), correlated strongly between 24h and urine spots.

Figure 2: Correlation of a substrate/product ratio resembling 21-hydroxylase activity between 24h and spot urine



CONCLUSIONS

- Urinary steroid profiling in children with CAH revealed correlations between 24h urine specimens and spot urines.
- Morning spot urine might suffice to recognize the specific pattern of 21-hydroxylase deficiency for management of CAH children (e.g. through marker metabolites Pregnanetriolone, TH-11-deoxy-cortisol or substrate/product ratios).
- In which subgroups of CAH a spot urine can inform about metabolic control of treatment needs to be tested in a larger sample.

ACKNOWLEDGEMENTS

We thank all patients who contributed to our study.

We also thank ESPE for a research unit grant for logistics and laboratory assays and the Swiss National Science Foundation for funding (SNF 320030_197725).

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