Individualized optimization with 17OHP-saliva profiles leads to changes in hydrocortisone (HC) dosing pattern in children with congenital adrenal hyperplasia (CAH)

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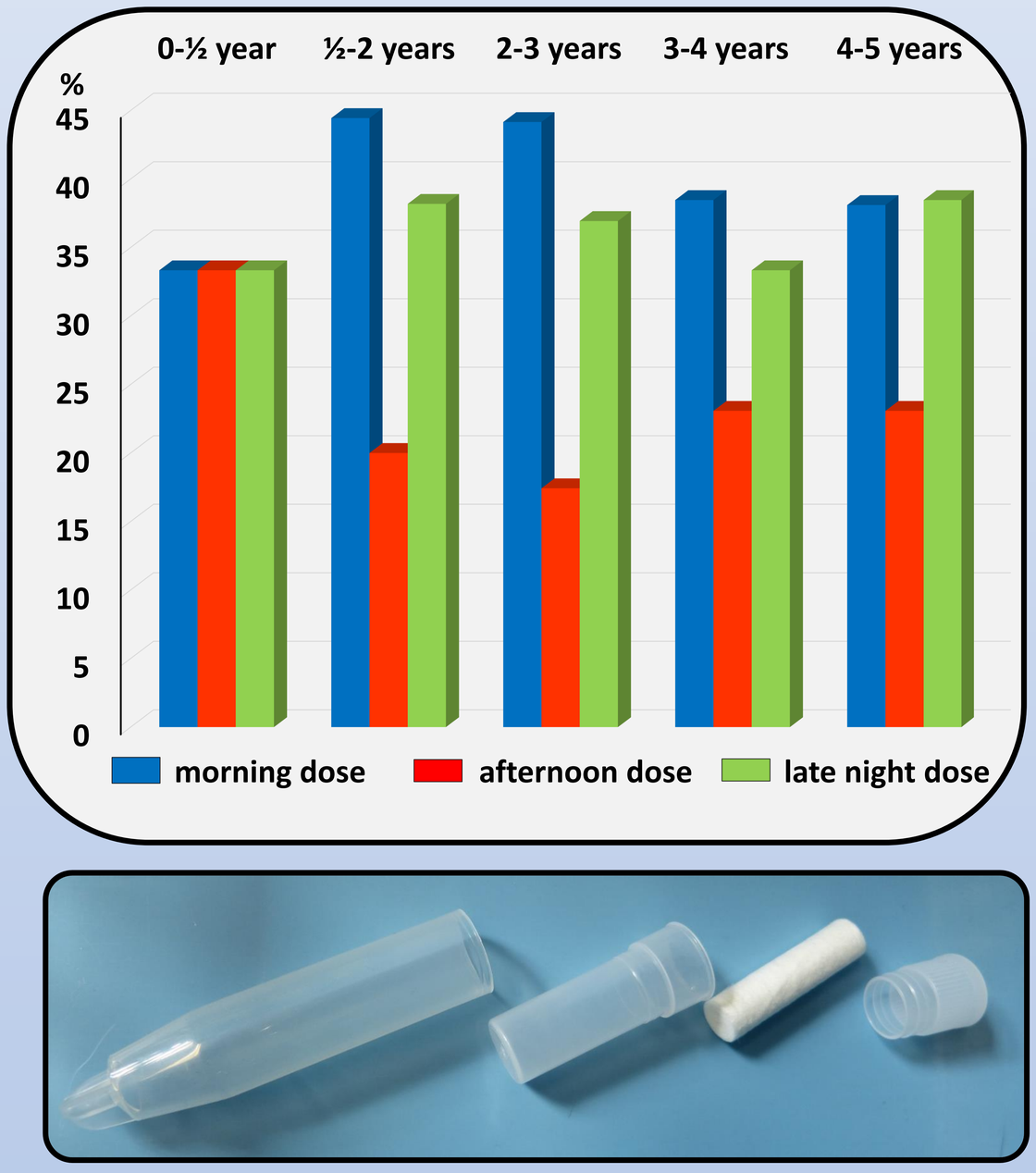
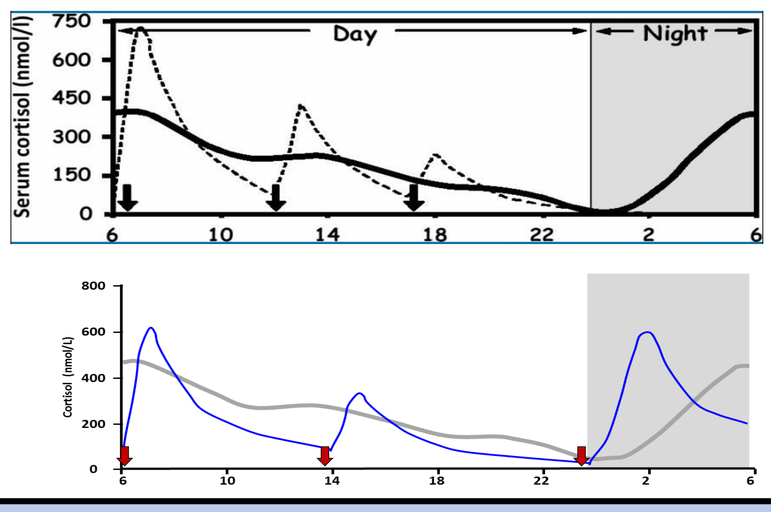
Background: Treatment of CAH in children is compromised by the pharmacokinetic of available hydrocortisone (HC) preparations resulting in un-physiological early morning rise of ACTH and androgens. HC substitution usually follows a fixed dosing scheme (50% - 25% - 25%) monitored by blood sampling. We describe the individualized optimization of HC treatment by 17-OHP saliva profiles and the effects of a high late night dose of hydrocortisone.

Methods: Retrospective analysis in 20 prepubertal children from birth to 5 years (females n=11, males n=9). HC was applied 8 hourly with 1st dose in the morning (6-8h), 2nd dose in the early afternoon (14-16) and 3rd dose late at night (22-24h). Treatment in newborns started using equal dose distribution. Once saliva production is enhanced by teething usually around 6 month of age the therapy is controlled by timed saliva-17OHP prior to the HC medication. Saliva levels outside of defined target ranges lead to adaptation of the HC dose prior to the sampling point.
17-OHP target range: 5fold concentrations of age specific reference (10fold in the morning)
17-OHP 2x > target range → HC-dose increased
17-OHP 2x < target range → HC-dose lowered
In a sub-cohort of 16 children aged 0-4 years (females n=6, males n=10) participating in a pharmacokinetic (PK) study blood sampling was timed exactly prior to the morning dose of Hydrocortisone.

Results: Newborns (n=15) started with a mean dose of 22,3 mg/sqm/d Hydrocortisone and equal dose. Individualized dose adaptation by saliva-17OHP levels between the age of 6 month and 2 years resulted in significantly lowered afternoon and increased late-night dose (n=20, Hydrocortisone distribution 44,4% - 20% - 38,2%). Similar dose distribution was found at an age of 3-4 years (n=7, 38,5% - 23,1% - 33,3%) and 4-5 years (n=3, 38,1% - 23,1 % - 38,5%).
In the cohort with timed blood-sampling children with the highest late-night dose of Hydrocortisone had significant lower ACTH and higher cortisol levels in the morning prior to the next hydrocortisone dose.





Conclusion: Individualized treatment adaptation by saliva-17OHP-profiles resulted in higher late-night and lower afternoon dose. Adaptation by frequent saliva sampling is able to reduce morning ACTH and androgen levels and thereby able to prevent un-physiologic early morning rise of ACTH and androgens. Further studies to evaluate the consequences of reduced morning ACTH and androgen levels in contrast to the higher cortisol levels at night are needed.

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