

Hydrocortisone (HC) dose in children with congenital adrenal hyperplasia (CAH)

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on behalf of the German / Austrian CAH registry

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Conclusion

- This large, multicentre database provides comprehensive information on prescribed hydrocortisone substitution doses in children with CAH.
- Low absolute doses required in children younger than 6 years of age are difficult to achieve, considering that in the past only a 10 mg tablet formulation is available in Austria and Germany.

Background

Congenital adrenal hyperplasia (CAH) is a heterogeneous genetic (autosomal recessive) disorder affecting one in 5,000 to 15,000 newborns in Europe. CAH leads to insufficient cortisol synthesis and altered hormone profiles depending on the disordered enzyme in the cortisol synthesis. Recommendations for initial and maintenance dose of HC in CAH differ widely between institutions. However, treatment of CAH in young children is complicated by the lack of a suitable low-dose HC preparations.

Objective

The objective of the presented project was the evaluation and discussion of the prescribed hydrocortisone dosages in children with CAH based on a nationwide registry ("deutsches AGS Register (DGKED-QS)" in Germany.

Methods

The German society for paediatric endocrinology and diabetology (DGKED) initiated a registry for patients with classical CAH (German CAH registry (DGKED-QS)). Anonymized data are transferred for central analysis, including a validation step and a benchmarking report, twice yearly. Until March 2018, the DGKED CAH database included 26 737 patient visits from 1567 patients (695 males). 44 centres from Germany and 3 centres from Austria contributed longitudinal data to this registry. Parameters were selected based on current treatment guidelines. A custom-made electronic health record software is used at the participating centres for standardized documentation and anonymous transfer of patient records. Linear regression model were implemented with SAS 9.4.

Results - 1

- Daily hydrocortisone (HC) dose [mg/m² per m² body surface area (BSA)] (mean ± SE) was :
 - 20.02 ± 0.35 for patients birth to 3 months (n=309),
 - 15.10 ± 0.29 for the age-group 4-12 months (n=442),
 - 14.31 ± 0.24 for patients 1-5 years (n=705) and
 - 14.54 ± 0.20 for patients 6-18 years (n=966).

Results - 2

- no significant gender difference regarding dose.
- In patients on fludrocortisone (presumable salt-losing CAH), HC dose was lower in the age-group 0-3 months (19.5 versus 24.4 mg/m², p < 0.05) and in the age-group 1-5 years (14.1 versus 15.1 mg/m²), while in patients older than 6 years a higher HC dose was recorded in patients on fludrocortisone (15.1 versus 13.5 mg/m², p < 0.0001).
- ANOVA regression modelling revealed a significant interaction between age-group and fludrocortisone, as well as between gender and fludrocortisone use (both p < 0.001).

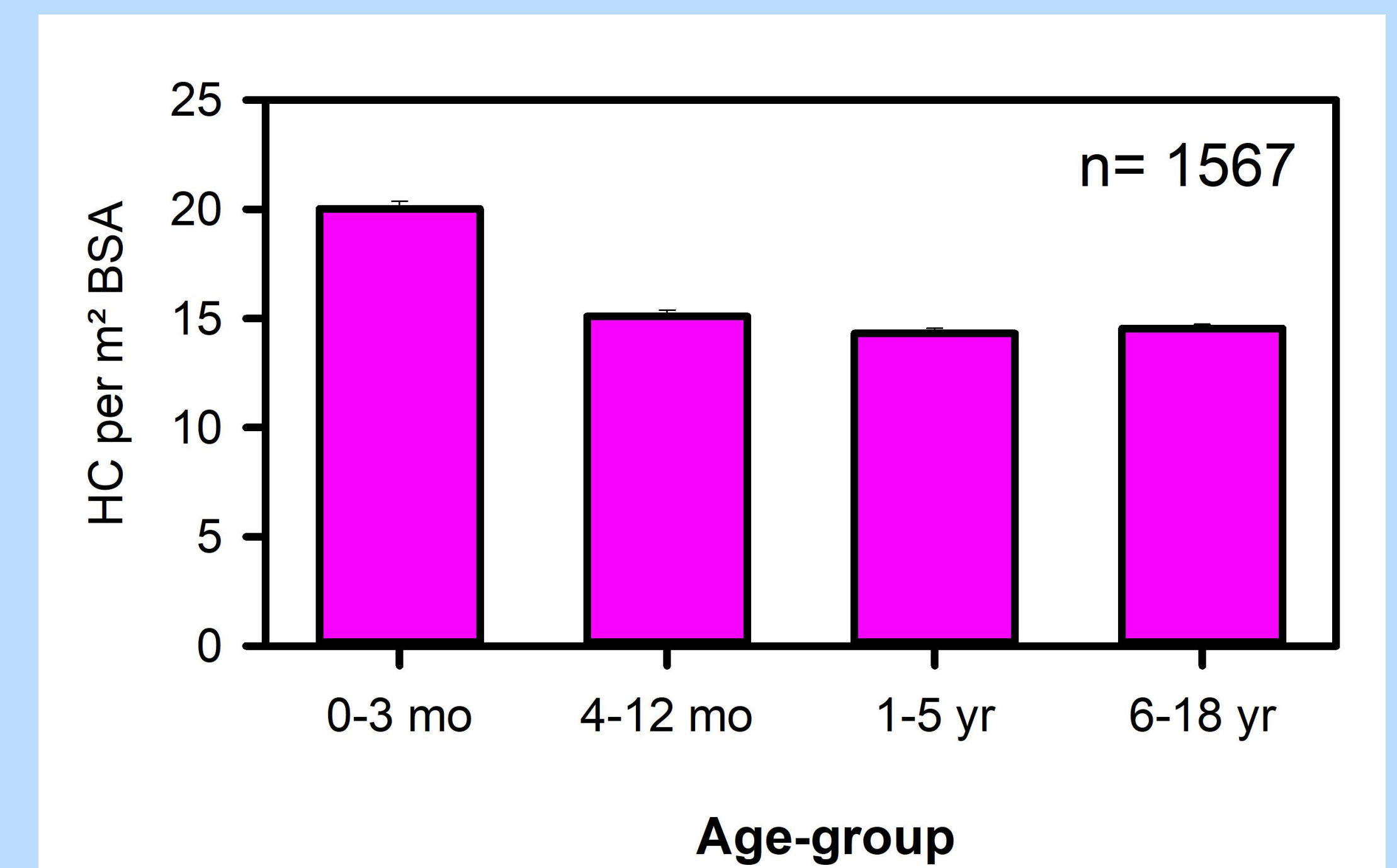


Fig 1: Mean daily HC dosage according to age

- On average, the largest HC dose was administered in the morning. Median absolute doses morning – midday – evening were 2.0 [Q1-Q3: 2.0-2.5] – 1 [1.0-1.4] – 1.0 [1.0-1.5] mg for children < 3 months of age, and 2.5 [2.0-3.0] - 1.1 [1.0-1.8] – 1.3 [1.0-2.0] in the age-group 4-12 months. For children 1-5 years of age, the respective median doses were 4.2 [3.0 - 5.3], 2.3 [1.8 - 2.9] and 2.3 [1.8-2.9] mg.

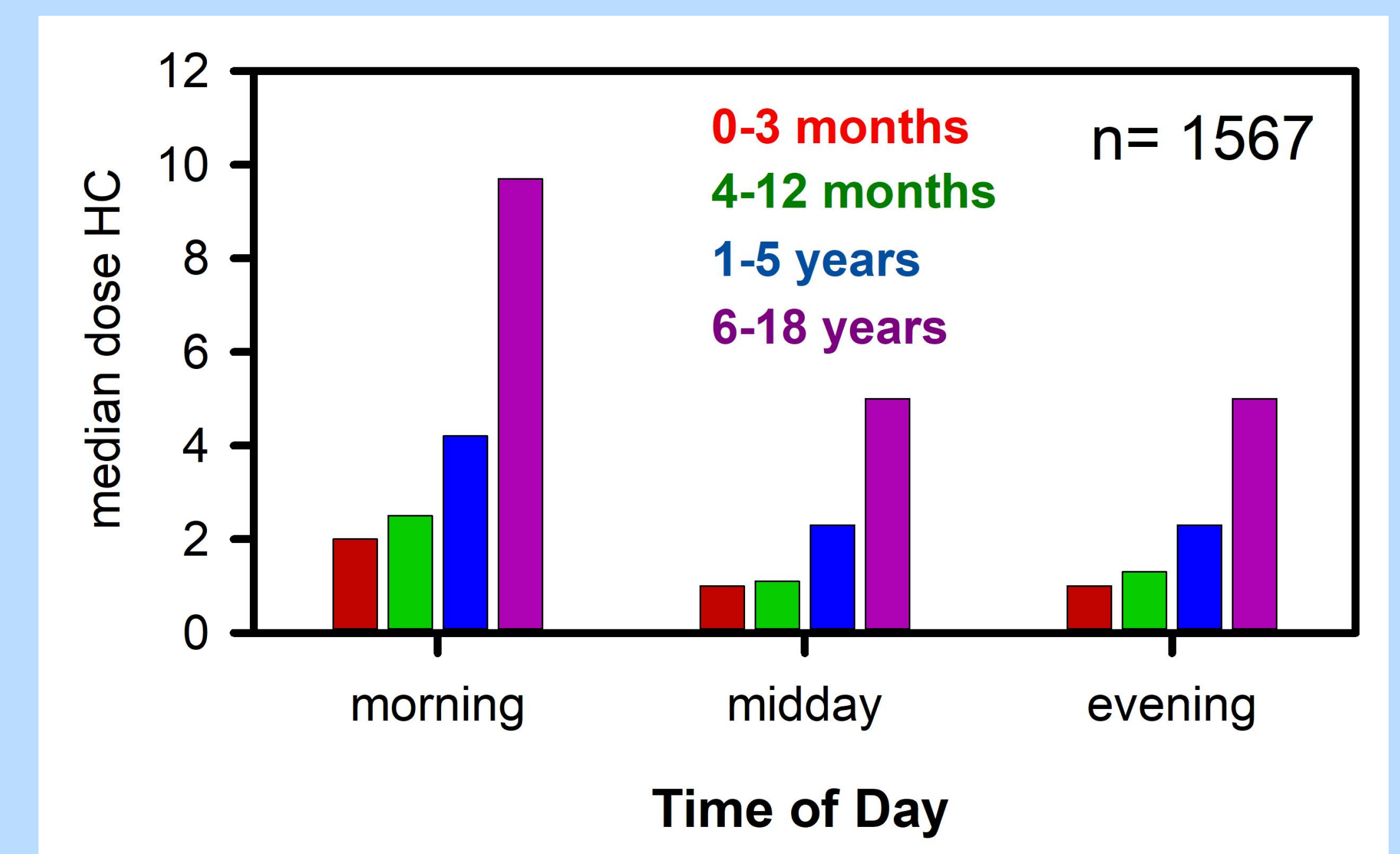


Fig 2: Mean daily HC dosage by age and time of day