A prospective study of children 0-8 years with congenital adrenal hyperplasia and adrenal insufficiency on treatment with hydrocortisone granules monitored by 17-OHP saliva sampling

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INTRODUCTION

Children with **congenital adrenal hyperplasia (CAH)** and **adrenal insufficiency (AI) require hydrocortisone replacement** from birth, and continuous monitoring of therapy during growth is necessary. **A licensed paediatric formulation that allows accurate dosing down to 0.5mg is now available**.

AIM

To investigate **safety and efficacy** of **hydrocortisone (HC) granules** in capsules for opening **in 0-8 year old children** with CAH and AI monitored through 17-OHP saliva profiles.

METHOD

- **17 children with classic CAH (9 male)**
- **1 child with hypopituitarism (male)**

Age at study entry:

- cohort 1 (2-<6 years): n=9
- cohort 2 (1 month-2 years): n=6
- cohort 3 (<28 days): n=3

Study visits included

- physical examination, measurement **of weight, length, blood pressure**.

Monitoring of HC-therapy

- daily 17-OHP-saliva profile every three months.
- **HC doses were adapted according** to the predose **17-OHP salivary profiles**. If the value for 17-OHP was out of range, the dose 8 hours before that sample time point was adjusted.

RESULTS

Children were treated with **HC granules three times daily every eight hours**. Median duration of treatment (range) was 795 (1-872) days with **150 follow-up visits**. Six children withdrew early. Hydrocortisone dose was adjusted at 40/150 visits (in 32 based on 17-OHP saliva profiles and 8 based on blood sampling). In CAH, saliva sampling started at about 6 months of age. **Hydrocortisone doses** used at different time points **varied from 0.5mg to 10mg**. Height and weight showed no trends for accelerated or reduced growth. **No adrenal crisis** was observed despite 193 treatment-emergent adverse events, which were mainly common childhood illnesses.

Average dose and dose distribution of hydrocortisone (morning – afternoon – nighttime dose) across visits according to the age of the children

	Average dose distribution	Mean HC dose	Proportion of administrations containing 0.5 mg granule dose
Children aged 0-3 month	33,3 – 33,3 – 33,3 %	1.5 – 1.5 – 1.5 mg	0 – 0 – 0 %*
Children aged 4 month – <2 years	46 – 22 – 32 %	2.3 – 1.1 – 1.6 mg	0 – 7 – 10 %
Children aged 2-<4 years	40.6 – 18.7 – 40.6 %	2.6 – 1.2 – 2.6 mg	41 – 18 – 23 %
Children aged 4- 8,4 years	36 – 14 – 50 %	3.2 – 1.3 – 4.6 mg	18 – 43 – 15 %

* half of the patients were treated with a hydrocortisone dose of 2-2-2 mg and half of the patients with 1-1-1 mg resulting in a mean dose of 1.5-1.5-1.5 dose.

Daily dose of hydrocortisone and fludrocortisone at the beginning and end of study in different age groups, median (range), and number

	Cohort 1	Cohort 2	Cohort 3	Overall
First Visit				
HC dose (mg/m^2)				
Median (range)	11.9 (7.20-15.5)	9.9 (8.6-12.2)	12.0 (11.1-29.5)	11.4 (7.2-29.5)
N	9	4	3	16
FC dose ($\mu g/m^2/day$)				
Median (range)	102 (62-159)	146 (124-180)	492 (369-900)	127 (62-900)
N	9	4	3	16
Last Visit				
HC dose (mg/m^2)				
Median (range)	10.2 (7.0-14.4)	9.8 (8.9-13.1)	8.6 (8.2-13.7)	9.7 (7.0-14.4)
N	4	4	3	11
FC dose ($\mu g/m^2/day$)				
Median (range)	61 (45-77)	70 (65-94)	213 (92-216)	72 (45-216)
N	4	4	3	11

CONCLUSIONS

This first prospective study of glucocorticoid treatment in children with AI demonstrates that an **individualised therapy** consisting of a 3-monthly 17-OHP saliva profile and an accurate dosing from birth with hydrocortisone granules in capsules for opening **results in hydrocortisone doses at the lower end of the recommended dose range** and **normal growth without** occurrence of an **adrenal crisis.**

REFERENCES

Neumann U, et al. A Prospective Study of Children Aged 0-8 Years with CAH and Adrenal Insufficiency Treated with Hydrocortisone Granules. J Clin Endocrinol Metab. 2021;106(3):e1433-e1440.

CONFLICTS OF INTEREST

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