

Final height data in a cohort of patients with Congenital Adrenal Hyperplasia treated with tailored doses of hydrocortisone

Authors: Pang SWG¹, Rumsby G², Guzzetti C¹, Hindmarsh PC¹, Dattani MT^{1,3}

1. Great Ormond Street Hospital, London
2. Department of Chemical Pathology, UCLH
3. Genetics and Genomic Medicine Programme, UCL GOSH Institute of Child Health, London

Great Ormond Street 
Hospital for Children
NHS Foundation Trust



Background: Patients with congenital adrenal hyperplasia (CAH) are glucocorticoid deficient and require cortisol replacement to maintain homeostasis and prevent adrenal crises. Hydrocortisone is the drug of choice for children and dosing needs to be individualized because of variable cortisol clearance rates. Patients are thus prone to be either over- or under-treated, both of which compromise final height. Performing 24-hour cortisol profiling serially may allow for more accurate titration of hydrocortisone dosage. We believe that this may result in a possible improvement in final height.

Method: Paediatric patients with CAH due to 21-hydroxylase deficiency were retrospectively recruited from a single tertiary centre between 1990 and 2015. We included those patients who had reached their final height and had had at least two serial 24-hour cortisol profiles (2 hourly cortisol and 17OHP measurements) performed, and mean cortisol concentrations were calculated. 08.00 ACTH, plasma renin and androgen concentrations were measured and genetic analysis was performed.

	Final height (SD) (cm)	Mean adult height SDS (SE)	Mid-parental height SDS (SE)	Mean BMI (kg/m ²)	Mean HC dosage (mg/m ² /day) (SD)
Neonatal onset CAH boys	170 +/- 5.0	-0.98 +/- 0.37	0.06 +/- 0.28	26.0 +/- 2.6	13.9 +/- 2.86
Neonatal onset CAH girls	160 +/- 5.2	-0.57 +/- 0.11	0.04 +/- 0.14	24.7 +/- 8.2	14.6 +/- 2.88
Late onset simple virilising boys	168 +/- 6.7	-1.17 +/- 0.42	0.02 +/- 0.15	30.0 +/- 12.6	13.8 +/- 3.20
Late onset simple virilising girls	165 +/- 8.2	0.24 +/- 0.28	0.21 +/- 0.37	25.6 +/- 3.3	10.5 +/- 2.80

Results: We identified 50 children who had attained final height, 34 children (7 M) had neonatal onset CAH whilst 16 (8 M) had late onset simple virilising disease, including 37 white, 4 Afro-Caribbean, 5 asian, 2 middle eastern and 2 mixed children. Genetic analyses revealed that 11 of them harboured homozygous or compound heterozygous mutations of g.999T>A, c.515T>A, p.I172N mutations, three carried mutations including g.1683G>T, c.841G>T, p.V281L, whilst six others had large deletions of the 3'CYP21A1P and 5'CYP21A2 gene. A total of 288 cortisol profiles had been performed between them, with an average number of 5.8 profiles for each patient. Mean cortisol concentrations were calculated and were found to be inversely correlated with 08.00 ACTH concentrations. (R value=-0.28). The final heights of the children were compared to the mean adult height of the population (British 1990 growth reference centiles published by Cole et al) and mid-parental height. The mean hydrocortisone dose prescribed from 3-18 years of age was lower than that previously reported in an ESPE survey¹.

Conclusion: Apart from late onset virilising boys, final height lies within one SDS from mean adult height of the population, and BMI is close to normal range. Mean parental height is similar to the normal population. These results are encouraging compared to previous similar cross sectional studies, and suggest that cortisol profiling may optimise dosing with better control of CAH and improve final height.

References

1. Riepe FG et al. Hormone research. 2002;58(4):196-205.