Pediatric patients with congenital adrenal hyperplasia have unfavorable changes in their cardiovascular risk profile

Christiaan F. Mooij,¹ Antonius E. van Herwaarden,² Nel Roeleveld,^{1,3} Chris L. de Korte,⁴ Livia Kapusta,^{5,6} Hedi L. Claahsen – van der Grinten¹

1. Division of Pediatric Endocrinology, Department of Pediatrics, Amalia Children's Hospital, Radboud university medical center, Nijmegen, the Netherlands; 2. Department of Laboratory Medicine, Radboud university medical center, Nijmegen, the Netherlands; 3. Department for Health Evidence, Radboud university medical center, Nijmegen, the Netherlands; 4. Medical Ultrasound Imaging Center, Department of Radiology, Radboud university medical center, Nijmegen, the Netherlands; 5. Pediatric Cardiology Unit, Dana-Dwek Children's Hospital, Sourasky Medical Center, Tel Aviv University, Tel Aviv, Israel; 6. Division of Pediatric Cardiology, Amalia Children's Hospital, Radboud university medical center, Nijmegen, the Netherlands.

Disclosure statement: The authors have nothing to disclose

Conclusion

Pediatric CAH patients may already develop an unfavorable CVR profile with an increased BMI with increased fat mass, elevated blood pressure levels, a non-dipping blood pressure profile, and insulin resistance.

Blood pressure levels, percentage of nocturnal dip in blood pressure and HOMA-IR were associated with BMI SDS. Lifestyle interventions to lower BMI in pediatric CAH may play a role in reducing the risk of cardiovascular morbidity in adult life.

Introduction

Congenital adrenal hyperplasia (CAH) is a disorder of adrenal steroidogenesis

Patients with CAH are at risk of developing an unfavorable cardiovascular risk (CVR) profile

Androgen excess and treatment with supraphysiological doses of glucocorticoids may cause unfavorable changes in the CVR profile Elevated BMI, increased fat mass, elevated blood pressure, insulin resistance and an increased intima media thickness (IMT) were described in adult CAH patients

Objective

To evaluate the CVR in a cohort of CAH patients aged 8-16 years

Patients and methods

Cross sectional study in patients with genetically proven CAH, aged 8-16 years (n=27)

Physical examination including anthropomorphic measurements

Blood was withdrawn to evaluate therapy control, glucose, insulin, hsCRP, adiponectin, leptin, tPA, PAI1, and lipid levels

Insulin resistance (IR) was evaluated using the HOMA-IR method

Blood pressure (BP) evaluation by office BP measurement and 24h ambulatory BP measurements (24h ABPM)

Carotid intima media thickness (cIMT) was evaluated by ultrasound

Dual energy X-ray absorptiometry (DXA) scan to evaluate body composition in patients > 12 years

SD scores (SDS) were calculated for BMI, BP levels, fat mass and percentage body fat

Associations between CVR factors and therapy control, treatment or other CVR factors were evaluated using linear regression analyses

Results

Patient characteristics and CVR factors

	Mean (± SD)	Prevalence (%)	SD score
Age (years)	12.2 (2.2)		
Sex	17 boys 10 girls		
Height SDS	-0.04 (1.00)		
Daily hydrocortisone dose mg/m ² BSA	12.2 (2.5)		
Daily fludrociortisone dose ug/m ² BSA (n=24)	98.5 (52.5)		
BMI ¹			0.67 (<i>P</i> =0.012)
Overweight		25.9	
Obesity		14.8	
Fat tissue mass ²			0.94 (<i>P</i> =0.043)
Fat percentage ²			1.59 (<i>P</i> <0.001)
HOMA-IR > 75 th percentile ³		44.4	
Lipid profile	Normal		
cIMT	Normal		
Systolic hypertension (24 h ABMP) ⁴		18.5	
Non-dipping MAP profile ⁵		40.7	
Office systolic blood pressure ⁴			0.83 (<i>P</i> <0.001)
Office diastolic blood pressure 4			0.56 (<i>P</i> <0.001)
Systolic hypertension (office) ⁴		18.5	

24h blood pressure profile

	Mean 24 h BP	Mean daytime BP	Mean sleeping BP
Systolic BP SDS	0.47 ± 1.25	0.23 ± 1.26	$0.51 \pm 1.17 \ (P=0.034)$
Diastolic BP SDS	0.14 ± 0.84	-0.29 ± 0.88	0.58 ± 0.92 (<i>P</i> =0.004)
MAP SDS	$0.37 \pm 0.88 (P=0.043)$	0.00 ± 0.90	0.81 ± 0.96 (<i>P</i> <0.001)

- 1. BMI SDS associated with 17 OHP (r=0.394; P=0.042) and androstenedione (r=0.406; P=0.036) concentrations
 - BMI not associated with hydrocortisone dose
- 2. Fat mass not associated with hydrocortisone dose
- 3. HOMA-IR levels associated with BMI SDS (r=0.500, P=0.008) & daily hydrocortisone dose (r=0.436, P=0.023)
- 4. No association with BMI SDS or treatment
- 5. % dip in MAP associated with BMI SDS (r=-0.489; P=0.01)

Amalia Children's Hospital Radboudumc

Institute for Molecular Life Sciences
Radboudumc









