



Renal excretion rates of free cortisol, free cortisone and dehydroepiandrosterone metabolites, but not renal indices of cortisol secretion are associated with urinary volume in healthy children

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Introduction

In experimental studies, a high fluid intake and a corresponding high urine volume have been shown to increase renal excretion rates of urinary free cortisol (UFF) and cortisone (UFE) in adults. Therefore it has been argued that urine volume should be considered as a confounding factor when interpreting data on UFF and UFE.

Aims

- To examine whether 24-h UFF and UFE excretion rates are affected by urine volume in healthy children.
- To examine whether adrenal androgen and its metabolites are also associated with urine volume in healthy children

Subjects and Methods

	Sample 1 (n=200)		Sample 2 (n=200)	
	Pre-Pub	Pub	Pre-Pub	Pub
Subjects	8-9y (m/f) 50/50	12-14y (m/f) 50/50	7-10y (m/f) 50/50	12-15y (m/f) 56/44
Measurements	UFF, UFE, 5 α -THF, THF, THE Specific non-commercial radioimmuno-assays		DHEA; 16 α -hydroxy-DHEA; 3 β ,16 α ,17 β -androstetriol GC-MS	
Assessment	GC3 = THF+THE+5 α -THF: index of glucocorticoid secretion		DHEA&M = DHEA + 16 α -hydroxy-DHEA + 3 β ,16 α ,17 β -androstetriol: index of adrenal androgen secretion	

Pre-Pub, prepubertal group; Pub, pubertal group; THE, tetrahydrocortisone; THF, tetrahydrocortisol; DHEA&M, dehydroepiandrosterone and its 16 α -hydroxylated downstream metabolites

Statistical analysis:

Stepwise multiple regression: models a priori adjusted for the following variables*: sex, weight, height, and total energy intake.

	Explanatory variables	Outcome variables
Model1 (table 2)		
Sample 1	U_volume	UFF, UFE, GC3
Sample 2	U_volume	DHEA&M
Model2 (table 3)		
Only sample1	U_volume GC3	UFF, UFE

Results

Table1 characterization of 200 healthy children and adolescents according to age group[#] (sample 1)

	Pre-pub (8-9 y)	Pub (12-14 y)
n (Male/female)	100 (50/50)	100 (50/50)
Age (y)	8.5 \pm 0.5	13.0 \pm 0.7
Weight (kg)	29.6 \pm 5.7	51.7 \pm 9.6
Height (cm)	133.6 \pm 6.4	162.7 \pm 8.0
Total energy intake (MJ/d)	7.0 \pm 1.5	8.5 \pm 2.0
Urine volume (mL)	657.0 \pm 226.5	932.8 \pm 361.4
Creatinine (mmol/d)	4.9 \pm 1.2	9.0 \pm 2.5
UFF (μ g/d)	12.1 \pm 6.0	15.8 \pm 7.6
UFE (μ g/d)	21.8 \pm 8.9	33.2 \pm 12.3
UFF+UFE (μ g/d)	33.8 \pm 13.5	49.1 \pm 18.7
THF (mg/d)	0.8 \pm 0.3	1.5 \pm 0.55
THE (mg/d)	2.0 \pm 0.8	3.5 \pm 1.3
5 α -THF(mg/d)	1.1 \pm 0.5	2.1 \pm 1.0
GC3 (mg/d)	3.9 \pm 1.3	7.1 \pm 2.6

[#]Values are means \pm SD

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Table 2 Step-wise multiple linear regressions for glucocorticoid and androgen metabolites with urine volume in 24-h urine ^a

Outcome variables	Explanatory variables	Pre-pub			Pub		
		β	R ²	p	β	R ²	p
UFF	a priori adjusted variables*		0.07 ^b			0.18 ^b	
	Urine volume	0.25	0.04	<0.05	0.32	0.06	<0.05
	Model R ²		0.11			0.20	
UFE	a priori adjusted variables*		0.14 ^b			0.07 ^b	
	Urine volume	0.38	0.11	<0.005	0.51	0.24	<0.0001
	Model R ²		0.25			0.31	
DHEA & M	a priori adjusted variables*		0.30 ^b			0.45 ^b	
	Urine volume	0.66	0.05	<0.05	0.60	0.07	<0.005
	Model R ²		0.33			0.52	

^a Urine Volume, UFF, UFE, GC3 and DHEA&M were log₁₀ transformed.

^b sum of the partial R² of a priori adjusted variables.

> Positive associations were observed between 24-h urine volume and UFF, UFE, and DHEA&M, with the highest explained variation for UFE, especially in the pubertal group

> Urine volume was not significant for GC3

Table 3 Step-wise multiple linear regressions for urinary free cortisol and cortisone with GC3 and urine volume in 24-h urine^a

Outcome variables	Explanatory variables	Pre-pub			Pub		
		β	R ²	p	β	R ²	p
UFF	a priori adjusted variables*		0.04 ^b			0.14 ^b	
	GC3	0.30	0.05	<0.05	0.74	0.24	<0.0001
	Urine volume	0.25	0.04	<0.05	0.23	0.03	<0.05
	Model R ²		0.16			0.41	
UFE	a priori adjusted variables*		0.15 ^b			0.06 ^b	
	GC3	0.34	0.07	<0.005	0.73	0.38	<0.0001
	Urine volume	0.38	0.11	<0.005	0.42	0.16	<0.0001
	Model R ²		0.33			0.60	

> After taking glucocorticoid secretion into account, urine volume was still significant, but with a decreased partial R² in the pubertal group. Also the contribution of urine volume to UFF and UFE was similar between the two groups.

> The explained variability of UFF and UFE by GC3 was greater in the pubertal group than in the prepubertal group.

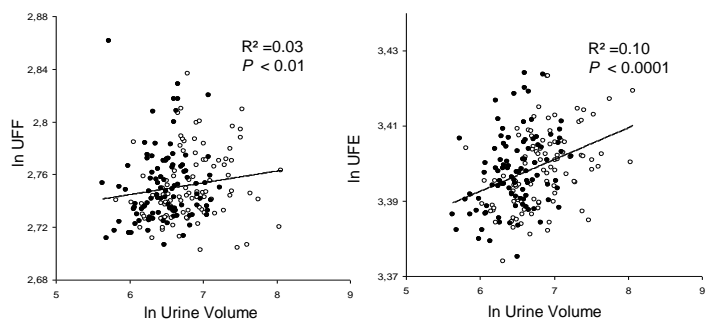


Fig 1 Association of 24-h urine volume with urinary excretion rate of UFF and UFE in healthy children. [n = 200, 100 prepubertal children (•) and 100 pubertal children (◦)]. R² denotes the partial R² from multiple regression analysis for 200 children adjusted for age, sex, weight, height, and total energy intake.

Conclusion

Urinary 24-h excretion rates of UFF, UFE, and DHEA&M, but not glucocorticoid secretion parameters are affected by daily urine volume in healthy free-living children. For a more specific assessment of associations of free glucocorticoids or adrenarche metabolites with (patho)physiologically relevant factors, urine volume has to be considered as a confounder.