Evaluation of long term metabolic effects after prenatal dexamethasone treatment in the context of CAH - the Swedish cohort

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Introduction

Prenatal dexamethasone (DEX) treatment is in many countries offered to the pregnant woman at risk of having a child with classic CAH to reduce virilization in CAH-affected girls. The treatment is effective but may give long lasting effects on somatic and cognitive health.

Objective

To investigate metabolic outcome in children and adults not having CAH and who were exposed to DEX during the first trimester of fetal life.

Methods

DEX treated subjects (n=40, age range 5.1-26.4) as well as control subjects (n=75, age range 4.5-26.6) gave blood after 12 h of fasting to assess renal function, glucose homeostasis and blood lipid profiles. Not normally distributed data were log-transformed before analysis (ANOVA). If a normal distribution could not be achieved through transformation the variable was analyzed using the Mann-Whitney U test.

Results

There were no significant differences between the groups regarding age, weight, height, BMI or birth parameters. There were no significant effects of prenatal DEX treatment on renal function, glucose homeostasis or lipid profile (all p >0.05). However, when analyzing children and adolescence/adult data separately we identified that DEX treated cases (age range 4.4-15.9 y) had higher P-Glucose (**0.000**) and P-Potassium levels (**p= 0.023**). In the older cohort (age range 16-26 y), we found significant differences in P-Cholesterol (p=**0.003**) and P-LDL (p= **0.009**) between DEX treated cases and controls.

[a] F-statistics are calculated on log transformed data. [b] analysed using Mann-Whitney

	Females ≥ 16 years Mean ±SD		Males ≥ 16 years Mean ±SD		[DEX]		[DEX x Sex]	
	DEX (n=11)	C (n=26)	DEX (n=9)	C (n=18)	F	p	F	p
P-Triglycerides [a]	0.87 (0.44)	0.70 (0.32)	0.83 (0.37)	0.76 (0.32)	1.21	0.275	0.13	0.718
P-Cholesterol	4.75 (0.67)	4.26 (0.77)	4.45 (0.85)	3.78 (0.55)	9.79	**0.003**	0.22	0.644
P-HDL [a]	1.67 (0.22)	1.52 (0.35)	1.28 (0.22)	1.30 (0.36)	0.85	0.361	0.96	0.330
P-LDL	2.69 (0.59)	2.41 (0.63)	2.78 (0.89)	2.16 (0.55)	7.35	**0.009**	1.06	0.306
P-LDL/HDL-ratio	1.71 (0.58)	1.67 (0.68)	2.26 (0.90)	1.82 (0.74)	1.54	0.219	1.07	0.304

Conclusions

Prenatal treatment with DEX during the first trimester may affect metabolism later in life. Our results suggest that outcome differs depending on the age of the individual. Long-term effects during late adulthood remain to be investigated since metabolic diseases increase with age. There is therefore a need for a structured follow-up of all DEX treated cases during many decades. The data questions all future use of DEX in the context of CAH.

Table 1. Glucose homeostasis and renal function in the age group < 16 years. Data for the main effect of DEX (DEX) and for the interaction between DEX and Sex (DEXxSex).

	Females <16 y Mean ±SD		Males < 16 y Mean ±SD		[DEX]		[DEX x Sex]	
	DEX (n=7)	C (n= 8)	DEX (n= 12)	C (n = 17)	F	p	F	p
Glucose Homeostasis								
P-Glucose	4.77 (0.21)	4.44 (0.58)	4.95 (0.36)	4.64 (0.40)	**15.07**	**0.000**	1.42	0.241
B-HbA1c	33.0 (2.1)	31.7 (2.0)	32.0 (2.7)	31.4 (2.1)	1.36	0.251	0.22	0.644
S-C-peptide [a]	0.41 (0.13)	0.50 (0.24)	0.50 (0.21)	0.46 (0.21)	0.58	0.450	0.09	0.765
S-Insulin [a]	5.77 (1.56)	7.60 (4.73)	7.18 (5.13)	6.68 (4.03)	0.55	0.462	0.11	0.741
HOMA-Beta [a]	86.6 (20.6)	148.9 (44.3)	101.5 (57.5)	114.7 (51.2)	2.52	0.122	0.03	0.860
HOMA-IR [a]	1.16 (0.33)	1.59 (1.17)	1.71 (1.24)	1.50 (0.90)	3.33	0.077	1.80	0.189
Renal function								
P-Creatinine	41.4 (5.8)	39.6 (7.9)	37.7 (8.2)	37.8 (9.1)	1.59	0.215	1.18	0.284
P-Sodium [b]	139.0 (1.0)	138.5 (1.5)	138.8 (1.1)	138.0 (2.8)		0.464		
P-Potassium [a]	3.91 (0.12)	3.79 (0.18)	3.92 (0.22)	3.81 (0.21)	**5.58**	**0.023**	0.11	0.748
P-Cystatine C	0.717 (0.10)	0.726 (0.90)	0.798 (0.12)	0.771 (0.07)	0.19	0.773	0.31	0.579
U-Albumine	12.0 (3.8)	12.2 (4.4)	12.5 (4.6)	10.8 (4.0)	2.16	0.150	0.21	0.646
U-Creatinine [b]	12.0 (3.8)	12.2 (4.4)	12.5 (4.6)	10.8 (3.9)		0.488		
U-Alb/Crea ratio [b]	1.24 (0.17)	0.72 (0.32)	0.72 (0.47)	1.33 (2.00)		0.353		

[a] F-statistics are calculated on log transformed data. [b] analysed using Mann-Whitney

Table 2. Lipid profile in the age group ≥ 16 years. Data for the main effect of DEX (DEX) and for the interaction between DEX and Sex (DEXxSex).

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