THE TREATMENT WITH "DUAL RELEASE" HYDROCORTISONE (DR-HC) IN CONGENITAL ADRENAL HYPERPLASIA (CAH): SHORT-TERM (6 MONTHS) AND LONG-TERM (12 MONTHS) FOLLOW-UP AFTER THE SWITCH FROM CONVENTIONAL GLUCOCORTICOIDS TO DR-HC

C. Simeoli, M.C. De Martino, D. Iacuaniello, T. Mannarino, A. Cozzolino, M. De Leo, C. Pivonello, M. Negri, C. de Angelis, A. Colao and R. Pivonello

Dipartimento di Medicina Clinica e Chirurgia, Sezione di Endocrinologia, Università Federico II, Naples, Italy.

Background:

Life-long glucocorticoid (GC) treatment is often required in patients with CAH due to 21-hydroxylase deficiency in order to replace their cortisol deficiency and to avoid the ACTH-dependent androgen levels increase. In these patients, the multiple daily doses of conventional GCs required can cause cortisol overexposure, leading to an increased risk of metabolic syndrome (MS), an impaired quality of life and a poor treatment compliance.

Aim:

The current study aimed at investigating the impact of the switch from twice or thrice daily conventional GCs to once daily DR-HC on metabolic and hormonal profile, Quality of Life (QoL), Depression Status (DS) and Treatment Compliance (TC) in a cohort of patients with CAH due to 21-hydroxylase deficiency.

Patients:

Twenty-three CAH pts treated with hydrocortisone (HC) or prednisone (P) for at least 12 months, switched to DR-HC, were evaluated before and after 6-12 months of DR-HC (Tab. 1). The same cohort of pts, stably treated with conventional GCs during the 12 months before the switch was used as control.

TABLE 1
PATIENT CHARACTERISTICS

N° pts	23
F/M	16/7
Age (ys)	20-38
N° pts in HC HC Dose (mg/day)	19 10-40
N° pts in P P Dose (mg/day)	4 6.25-12.5
DR-HC Dose (mg/day)	10-40

Methods:

- Metabolic and hormonal parameters were measured using routine assays and the MS was evaluated according with IDF criteria
- QoL was evaluated using AddiQoL Questionnaire[1]
- DS using Beck Depression Inventory II[2]
- TC using Morisky 8-items medication Adherence Questionnaire[3]

Results: Metabolic profile

At 6 and12 months (M) different metabolic parameters improved: in particular fasting plasma glucose (FG) (6° M p=0.003; 12° M p=NS) (Fig.1); HDL-cholesterol (6° M p=NS; 12° M p<0.001) (Fig.2) and LDL-cholesterol levels (6° M p=NS; 12° M p=0.024) (Fig.3).
A clear diagnosis of MS was performed in one patient at baseline, but this patient displayed no criteria for this diagnosis after 6 and 12 M.
No significant difference was observed between baseline and controls.

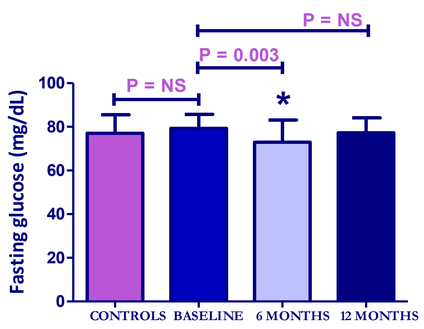

Fig.1 FASTING GLUCOSE

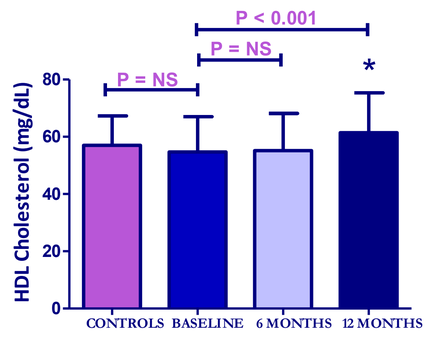

Fig.2 HDL CHOLESTEROL LEVELS

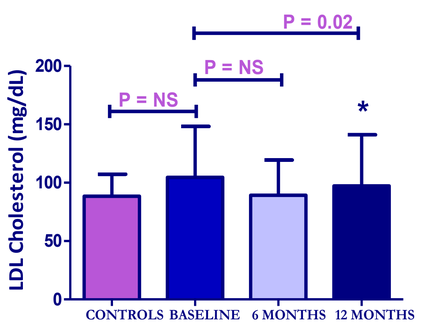

Fig.3 LDL CHOLESTEROL LEVELS

Results: Hormonal profile

No significant change was observed in morning plasma ACTH and UFC. Excluding the 4 pts treated with P at baseline*, a significant increase in morning serum cortisol levels was registered after 6 M (p=0.016), not confirmed after 12 M.
Despite the unchanged fludrocortisone doses, both in the entire cohort (p=0.002) and in Salt Wasting pts** (p=0.005) a significant decrease in renin levels was reported at 6 M, not confirmed at 12 M (Tab. 2).
No significant differences were observed in17-OH progesterone, testosterone, DHEA-S and Δ-4 androstenedione levels both in males and in females (Tab. 3). In particular in females no clinical worsening of symptoms and signs related to hyperandrogenism were reported.
No significant difference was observed between baseline and controls.

TABLE 2 HORMONAL PROFILE

	BASELINE	6 MONTHS	12 MONTHS	P 0-6	P 0-12
ACTH (pg/mL)	77.5 ± 146.7	37.2 ± 44.3	44.5 ± 51.6	NS	NS
Urinary free cortisol (µg/24h)	118.2 ± 68.1	175.3 ± 137.7	142.8 ± 80.7	NS	NS
Serum Cortisol (ng/L)					
▪ No. 23 pts	127.9 ± 96.9	193.8 ± 72.3	177.8 ± 49.7	0.002	0.04
▪ No. 19 pts*	148.1 ± 94.7	209.4 ± 69.3	176.8 ± 50.9	0.016	NS
Aldosterone (pg/mL)					
▪ No. 23 pts	124.4 ± 130.9	113 ± 140	110.9 ± 145.5	NS	NS
▪ No. 12 pts**	121.6 ± 169.2	84.8 ± 76	113.1 ± 193.4	NS	NS
Renin (pg/mL)					
▪ No. 23 pts	26.9 ± 32	14.5 ± 19.5	22.4 ± 28.2	0.002	NS
▪ No. 12 pts**	28.6 ± 35.7	15.8 ± 26.1	27.3 ± 37.8	0.005	NS

TABLE 3 ANDROGENS IN FEMALES

	BASELINE	6 MONTHS	12 MONTHS	P 0-6	P 0-12
17OH progesterone (ng/mL)	17.9 ± 36.8	16.4 ± 20.3	16.8 ± 17.1	NS	NS
Testosterone (ng/dL)	40.4 ± 31.7	82.3 ± 101.2	56.7 ± 25.1	NS	NS
DHEA-S (µg/dL)	101.9 ± 105.7	93.6 ± 87.6	146.9 ± 130.8	NS	NS
Δ-4 Androstenedione (ng/mL)	3.1 ± 2.5	3.7 ± 3.1	4.3 ± 1.5	NS	NS

Results: Quality of life and compliance

QoL resulted improved: in particular vitality and working ability ameliorated in 5 pts (22%), general health perception and sleep quality in 4 pts (17%), body pain perception in 9 pts (39 %).
DS improved after 6 (p=0.07) and after 12 M (p=0.04) (Fig.4).
TC significantly improved after 6 (p=0.009) and after 12 M (p<0.001) (Fig.5).

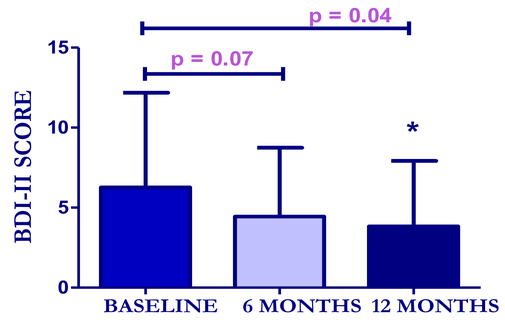

Fig.4 DEPRESSION STATUS

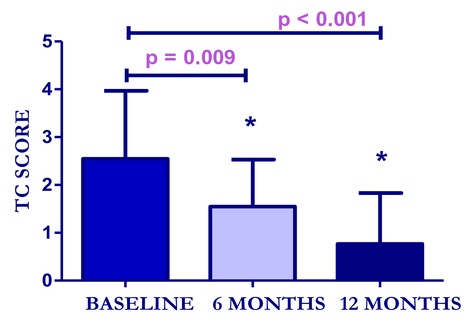

Fig.5 TREATMENT COMPLIANCE

Conclusions:

The switch from conventional GCs to once daily DR-HC in patients with CAH due to 21-hydroxylase deficiency significantly improved metabolic syndrome, depression status and treatment compliance, maintaining an optimal hormone control.

References:

1. Øksnes M. et al. Quality of life in European patients with Addison's disease: validity of the disease-specific questionnaire AddiQol. *JCEM* 2012; 97(2):568-76;
2. Beck AT, et al. Comparison of Beck Depression Inventories -IA and -II in psychiatric outpatients. Journal of Personality Assessment 1996; 67: 588–97;
3. Morisky DE. et al. Concurrent and predictive validity of a self-reported measure of medication adherence. *Med Care* 1986; 24: 67-74.

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CHIARA SIMEOLI
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