IMPROVED EVENING AND NOCTURNAL CORTISOL EXPOSURE TIME PROFILE IN PATIENTS WITH ADRENAL INSUFFICIENCY TREATED WITH DUAL RELEASE HYDROCORTISONE: CORRELATION WITH IMPROVEMENT IN METABOLIC PROFILE

Chiara Simeoli, Rosario Ferrigno, Maria Cristina De Martino, Renata Simona Auricemma, Claudia Pivonello, Mariarosaria Negri, Davide Iacuaniello, Gilda Di Gennaro, Annamaria Colao, Rosario Pivonello

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

BACKGROUND

Conventional glucocorticoid (GC) replacement treatments in multiple doses are unable to mimic physiological cortisol rhythm in adrenal insufficiency (AI) patients. Possible explanations are the supra-physiological maintenance doses and the impaired diurnal serum cortisol exposure-time profile.

Elevated evening levels are associated with alterations in glucose tolerance and insulin sensitivity and visceral obesity.

A new once-daily dual-release hydrocortisone (OD-DR-HC) better reproducing the physiological circadian cortisol profile (Fig. 1), reported a metabolic profile improvement in primary AI patients switched from thrice daily immediate-release HC (TID-DR-HC) to OD-DR-HC.

OBJECTIVES

The aim of this study was to evaluate the serum cortisol profile and its impact on the metabolic outcome in primary (PAI) and secondary (SAI) AI patients treated with cortisone acetate (CA) twice daily (TD) before and 6 months after the switch to OD-DR-HC.

PATIENTS

Eight AI patients, 4 PAI, 4 SAI, 4F, 4M, 20-66 yrs, treated with CA 25-50 mg/day TD (7 am; 4 pm) underwent full sampling for serum cortisol during 24 hrs. All patients were evaluated before and 6 months after the switch to OD-DR-HC (20-40 mg/day; 7 am). 

METHODS

- Serum cortisol samples were collected at 3 hr intervals in 24 hrs
- First sample was collected before treatments
- Consecutive samples were collected at: 7 am; 10 am; 1 pm; 4 pm; 7 pm; 10 pm; 1 am; 4 am; 7 am
- The serum cortisol AUC was evaluated analyzing 6 time slots: (7 am-1 pm), (1-7 pm), (7 pm-1 am), (1-7 am), (7 pm-7 am), (7-7 am)

RESULTS

The total 24hr cortisol profile was reduced by 14.4% providing a higher exposure during the first 6 hrs in the morning and then gradually significant reductions throughout the day and night (Fig. 2).

The decrease in (7 pm-1 am) cortisol AUC was significantly correlated with waist circumference (WC) decrease and insulin sensitivity index (ISI) increase 120° after glucose load (Fig. 3 A, B).

The decrease in (1-7 am) cortisol AUC was significantly correlated with triglycerides and glucose 120° after glucose load levels reduction (Fig. 3 C, D).

CONCLUSIONS

This new OD-DR-HC better mimics the physiological cortisol profile, reducing the late afternoon, evening and nocturnal GC overexposure, mainly related with metabolic alterations, avoiding the second afternoon peak observed during CA TD treatment, suggesting a significant improvement in glucose tolerance, visceral adiposity and lipid profile.

Further studies are needed to confirm and extend these preliminary data on a larger cohort of patients.

References

1. Plat L, et al. Metabolic effects of short-term elevations of plasma cortisol are more pronounced in the evening than in the morning. JCEM (1993)