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Analysis of 17-OH-Progesterone (17OHP) and Androstenedione (A4) Profiles To Rationalise Biochemical Monitoring Of CAH Patients

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Background: There is no consensus on how to monitor biochemical control of CAH as excess ACTH overnight is common on standard therapy. Modified-release hydrocortisone (MRHC) gives potential for improved disease control and the need to understand this impact on disease monitoring.Aim: To define the relationship between 17OHP and A4, in healthy controls and CAH patients. **Methods:** Analysis of 24-hour 2-hourly 17OHP and A4 endocrine profiles in patients randomised to either standard treatment or MRHC (n=122, mean age 36.3 (SD 11.6) years, 78 female, 44 male) and a population of healthy controls (n=20, age 30.0 (12.3), 13 male, 7 female). Markers were regressed, cross correlated and assessed by Bayesian Change Point analysis using *R*. **Results:** Regressing the natural logarithms of 17OHP on A4, Bayesian multiple change point analysis converged on a stable changepoint equivalent to 17OHP of 4.5 nmol/L 149 ng/dl (95%, CI:4.2 to 4.7 nmol/L, Rhat < 1.008). Below the 17OHP change point A4 is proportionally lower than above, with no evidence of difference between sexes or steroid preparation. The relationship between 17OHP and A4 was different for healthy subjects, who for similar levels of A4 have lower levels of 17OHP than CAH patients in nmol/L (ng/dl): A4 of 1 (29) and 10 (286) associated with 17OHP 1.5 (50) and 8.8 (291) in healthy subjects' vs 3.3 (109) and 71.2 (2353) in CAH patients, respectively. There was no consistent rhythm in either marker in healthy patients, shown by an autocorrelation function (ACF) that falls quickly to zero. ACF approaches zero more quickly in CAH patients on MRHC than those on standard therapy who more commonly exhibit a diurnal rhythm with an 0700hrs peak. There was no lag between markers, with cross-correlation function plots symmetrical. **Conclusions:** The relationship between 17OHP and A4 is different in CAH than healthy controls. In CAH, high A4 suggests poor control but a low A4 may still be associated with a raised 17OHP. In CAH patients, 17OHP concentrations within the healthy subject range are associated with A4 below levels seen in healthy subjects. When elevated in CAH patients, A4 and 17OHP rise and fall together with no lag; thus, A4 does not give more information on control over time. On MRHC the biomarkers show a reduced diurnal rhythm; therefore, individual measurements taken in clinic are more likely to reflect the daily average than measurements taken when on standard therapy.

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