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Contribution of direct measurements of steroids by Liquid chromatography tandem mass spectrometry LC-MS/MS in non-classical adrenal hyperplasia (NCCAH)

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BACKGROUND

To diagnose non classical congenital adrenal hyperplasia (NCCAH) and adrenal insufficiency (AI), current guidelines recommend ACTH test. Cutoffs for 17 hydroxyprogesterone (17OHP) and cortisol are derived from immunoassays values. Thanks to a recently developed and validated mass spectrometry approach (LC-MS/MS) we routinely quantify simultaneously 16 circulating steroids and we are able to speculate on new cut off values and uses.

OBJECTIVE AND HYPOTHESIS

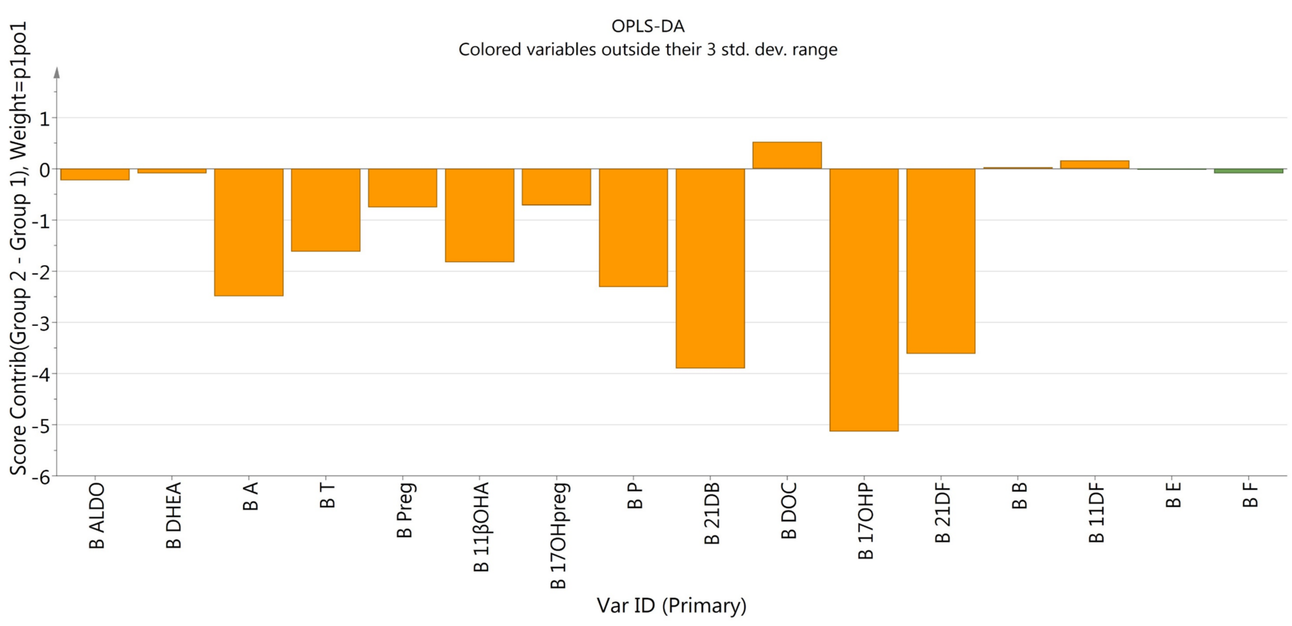
We prospectively analyzed in children addressed to our endocrine unit for premature pubic hair, all steroids assayed by LC-MS/MS, basal and stimulated by ACTH tests. We searched for additional basal variables discriminant enough to the make the diagnosis

PATIENTS AND METHODS:

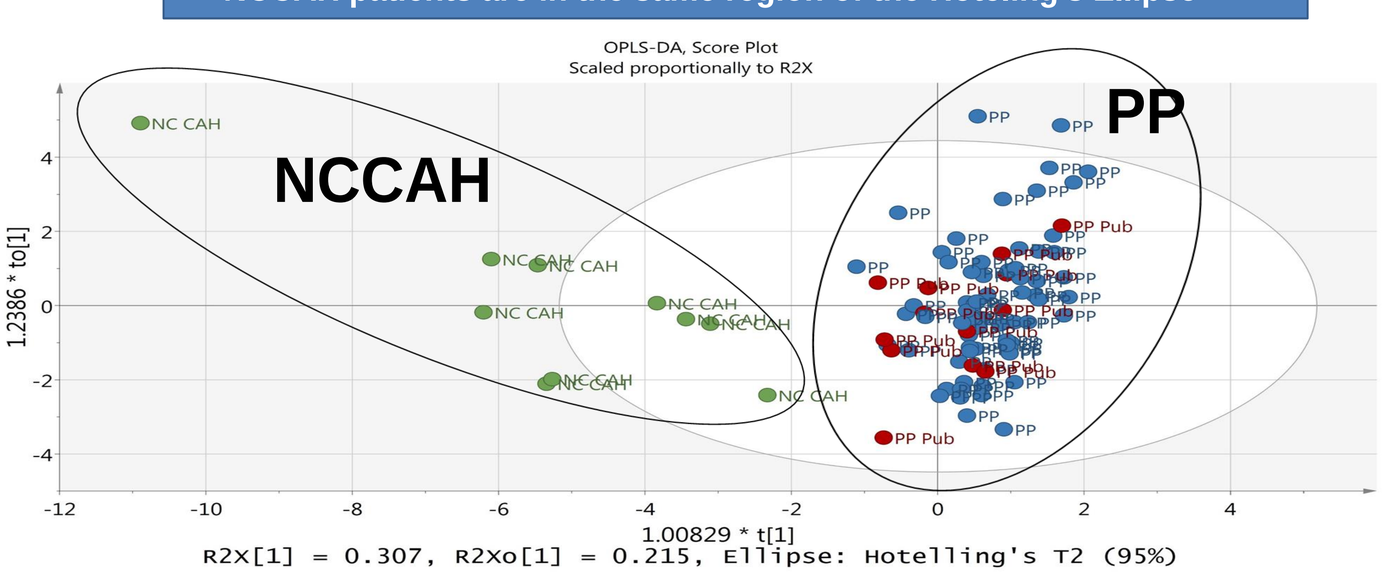
83 patients were referred in our unit in 2017, because of premature pubic hair. Mean age was 7.3 +/- 2.3 yrs, sex ratio was 19 males and 64 females. Patients with stimulated 17 OHP values above 9 ng/ml and their parents gave their consent for molecular testing of CYP21A2 according to our local ethics committee. Hence 69 had a premature pubarche (PP), 9 a NCCAH and 5 male patients were excluded because of central puberty. Bone age was more advanced in the NCCAH group compared to the PP group 2.9 yrs versus 1.3 yrs.

RESULTS:

Contribution of each parameter in the final formula



NCCAH patients are in the same region of the Hoteling's Ellipse



Mean basal 17 OHP ranged from 0.053 to 1.1 ng/ml in PP patients and from 3.62 to 87.94 ng/ml in NCCAH patients ($p<0.0001$). Mean basal 21-Deoxycortisol (21DF) was 0.03 ng/ml in PP patients and 3.42 ng/ml in NCCAH patients ($p<0.0001$).

Basal Testosterone was 0.08 ng/ml in PP patients versus 0.2 ng/ml in NCCAH ($p<0.0001$). Basal Androstenedione was 0.28 ng/ml in PP patients and 0.94 ng/ml in NCCAH patients ($p<0.0001$) and 11 Beta-OH-Androstenedione was 0.57 ng/ml in PP patients versus 2.17 ng/ml in NCCAH patients ($p <0.0001$). ACTH tests revealed 6 AI among the 9 NCCAH patients. Stimulated 17 OHP was 0.27-9.06 ng/ml in the PP group versus 22.73-92.57 ng/ml in NCCAH patients.

Using multivariate data analysis (Partial Least Squares regression (PLS/PLS-DA)), we propose a score with a high contribution of basal levels of 17OHP, 21DF, Testosterone, Androstenedione and 11 Beta-OH-Androstenedione, with a sensitivity/ specificity of 100 % towards the diagnosis of NCCAH.

CONCLUSION:

We propose in addition to the gold standard ACTH test, a new score using different steroids at basal levels to ascertain the diagnosis of NCCAH with an excellent sensitivity.