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Background

At present, treatment of „classic” congenital adrenal hyperplasia (21-hydroxylase-deficiency, 21OHD) consists of

- ✓ glucocorticoid and
- ✓ mineralocorticoid

replacement. However, androgen excess and its negative metabolic impact are often difficult to control without accepting glucocorticoid overtreatment, especially in adolescence. In healthy subjects oral contraceptives (containing ethinylestradiol) increase cortisol binding capacity and free cortisol, while prolonging half-life of unbound cortisol and reducing its clearance. Intake of combined contraceptives (ethinyl-estradiol/progestin) in healthy women leads to decreased androgen levels by inhibition of ovarian and adrenal androgen synthesis and by an increase of sex hormone binding globulin (SHBG).

Therefore we aimed to investigate the effect of contraceptives in female adolescents with 21OHD on androgen levels in a pilot study.

Methods

In a retrospective chart analysis laboratory data of female adolescents with confirmed 21OHD under glucocorticoid and mineralocorticoid treatment were reviewed before and after introducing an oral or transdermal contraceptive. The following laboratory parameters (serum) could be assessed basally and 3-6 months after introduction of the contraceptives:

- ✓ 17-OH-progesterone (17OPH)
- ✓ androstenedione
- ✓ DHEA
- ✓ DHEA-S
- ✓ free testosterone

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Age at start (years)	16.4	14.2	14.8	17.2	14.8
Hydrocortisone (mg)	5 - 0 - 0	10 - 0 - 0	5 - 0 - 0	5 - 0 - 0	7.5 - 7.5 - 10
Prednisone (mg)	2.5 - 0 - 2.5	2.5 - 0 - 5	2.5 - 0 - 2.5	2.5 - 0 - 2.5	-
Estrogen in contraceptive (mg)	EE2 0.03	EE2 0.035	EE2 0.6 (patch)	E2-valerat 1-3 (cyclic)	EE2 0.03
Progestin in contraceptive	Levonorgestrel	Cyproterone-acetat	Norelgestromin (patch)	Dienogest	Desogestrel

Table 1: Population of female patients with classic 21OHD, their glucocorticoid therapy and the respective contraceptives.

Results

So far, five adolescents with available data sets could be identified in our center. Mean age was 15.5 years. Four patients took hydrocortisone, prednisolone and fludrocortisone as their long-term medication, one patient hydrocortisone and fludrocortisone. Table 1 gives an overview of the population including details of glucocorticoid medication and the contraceptives. Figures A-D show the serum parameters before and after introduction of the contraceptive. Two patients were able to reduce their hydrocortisone dose after the introduction of a contraceptive.

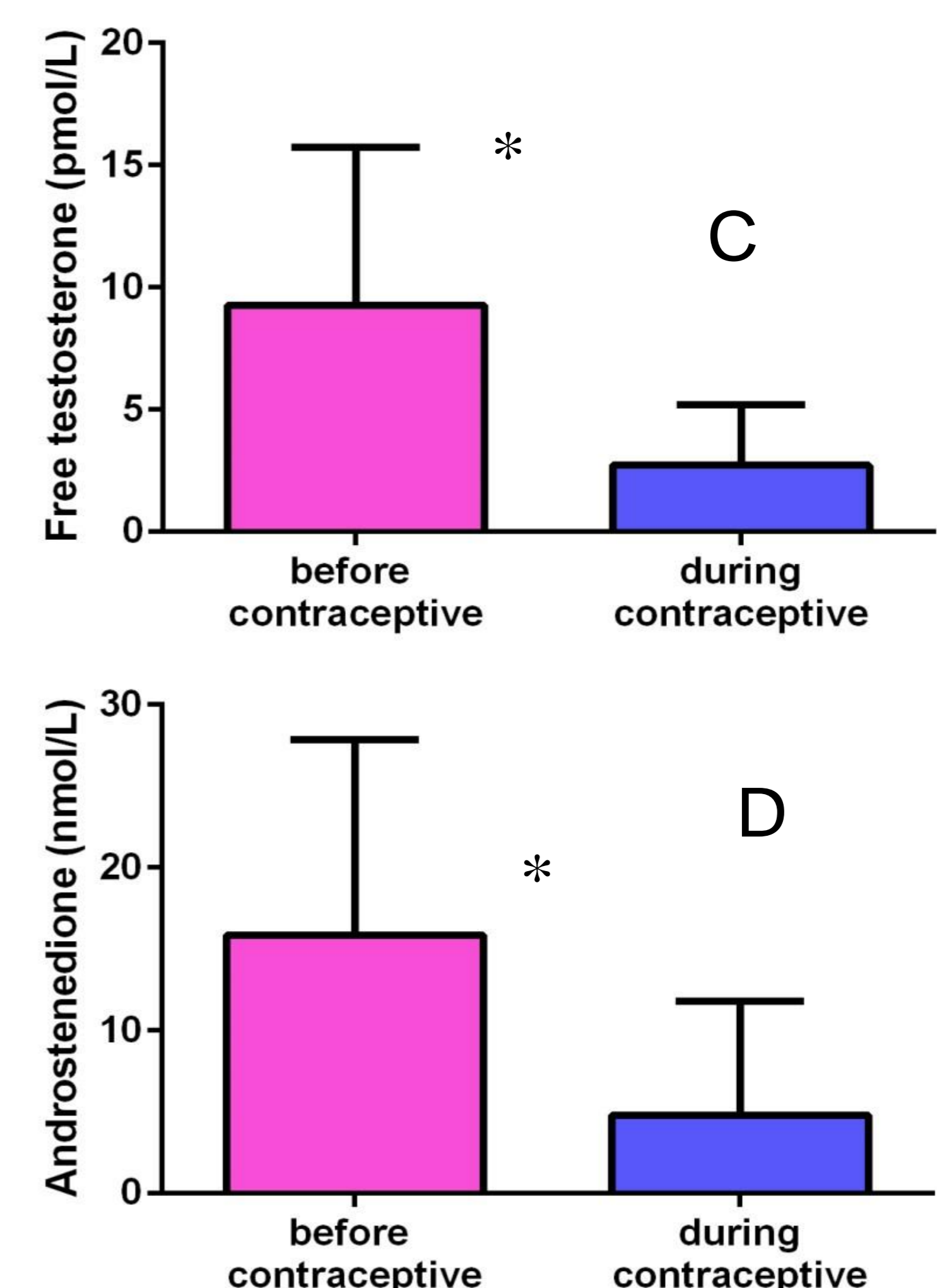


Figure C, D: Free Testosterone (C) and Androstenedione (D) before and after introduction of contraceptives. * $p < 0.05$;

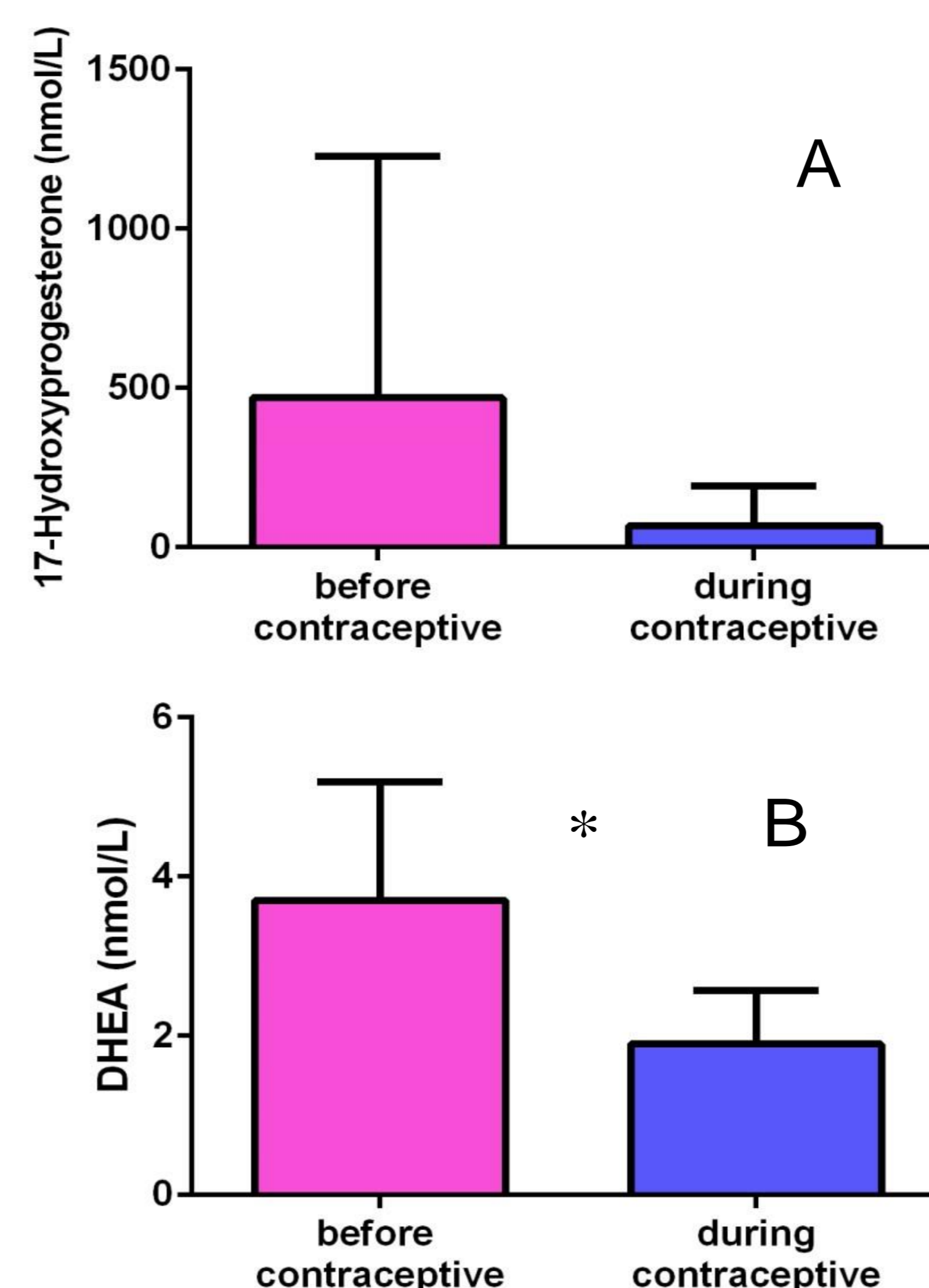


Figure A, B: 17OHP (A) and DHEA (B) before and after introduction of contraceptives. * $p < 0.05$;

Conclusion

In this pilot study in five young females with classic CAH due to 21OHD, we saw a significant reduction in serum androgens after introduction of contraceptives. We therefore plan to confirm this promising result in a larger multicenter cohort study with a prospective design looking at clinical and biochemical parameters under use of contraceptives. Steroids will be measured from serum and urine by mass spectrometric methods and hydrocortisone needs calculated. Markers of metabolic syndrome will also be assessed.