Steroidogenic profiles of males with congenital hypogonadotropic hypogonadism on hCG/rFSH and on testosterone replacement

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INTRODUCTION

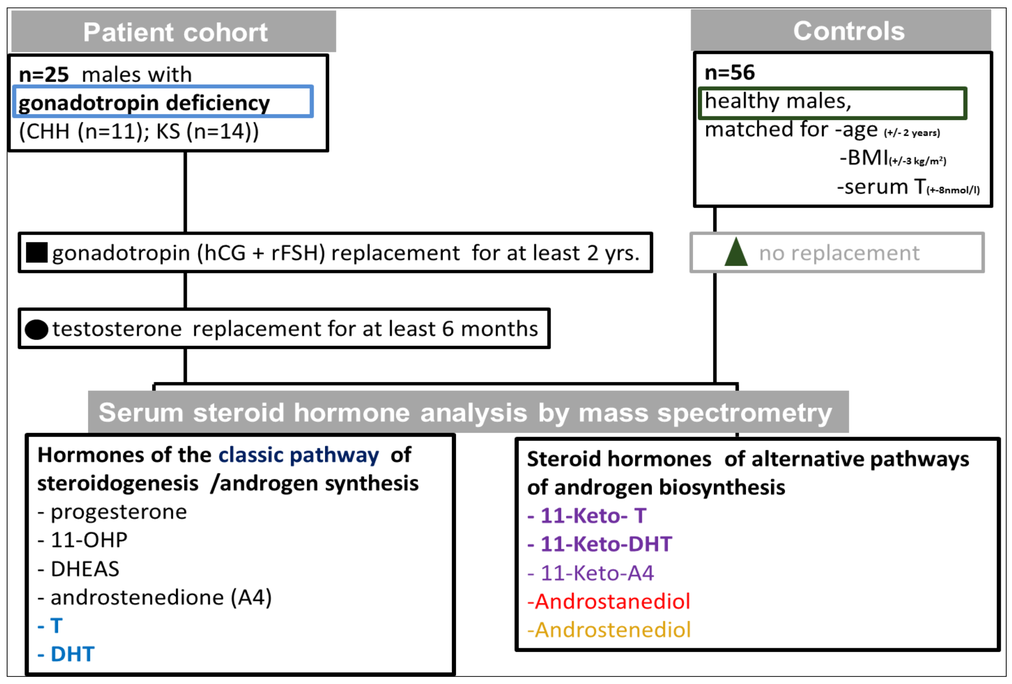
In males with congenital hypogonadotropic hypogonadism (CHH), LH/FSH stimulation of gonads is deficient. Two hormone replacement strategies are employed to induce and maintain virilisation: substitution of testosterone and gonadotropin replacement with hCG/rFSH.

AIMS

We aimed to delineate the role of gonadotropins in pathways of male androgen biosynthesis

PATIENTS AND METHODS

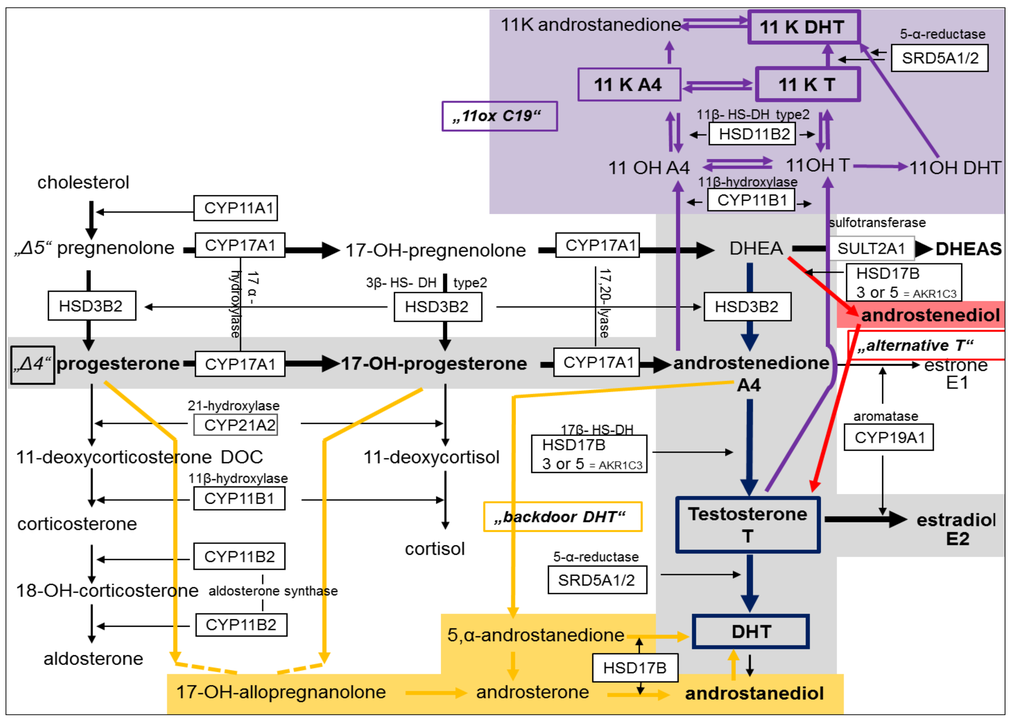
In 25 males with CHH, first undergoing hCG/rFSH treatment and then testosterone replacement, serum steroid hormone profiles (precursors of testosterone and its metabolites) were analyzed, using liquid chromatography-tandem mass spectrometry (LC-MS/MS).
Data were compared to those of healthy controls, matched for age, BMI and serum testosterone (T) concentration.



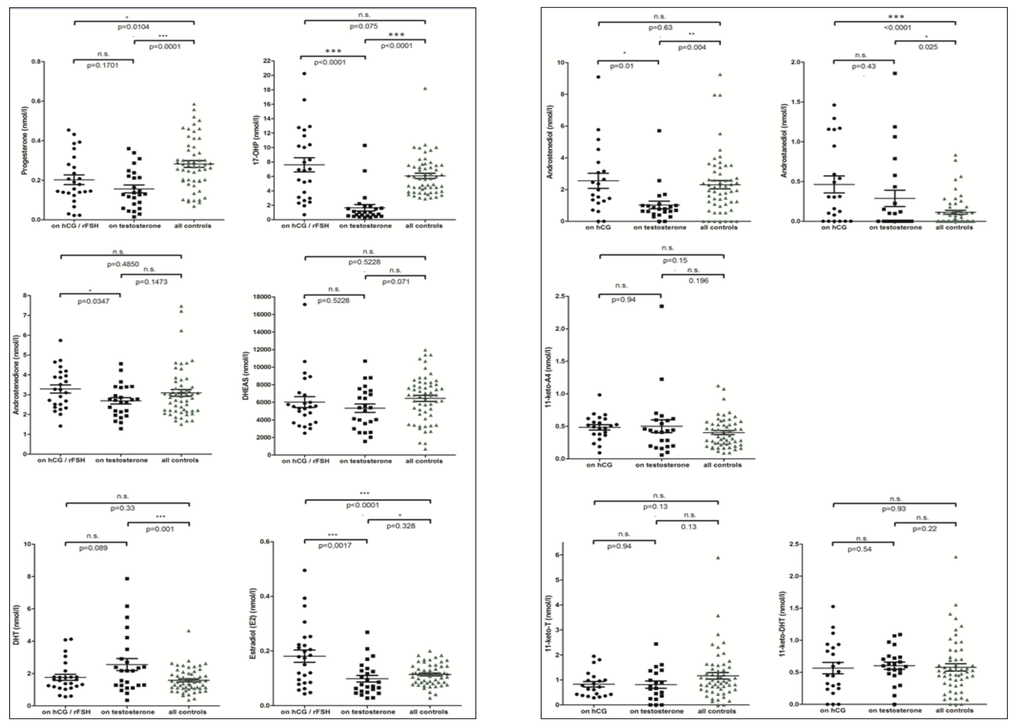
RESULTS

Combined treatment of CHH males with hCG and rFSH resulted in steroid hormone profiles similar to those of healthy men, but this was not the case, while a regimen based on exogenous testosterone was used:

While CHH patients were **on T substitution**, decreased serum concentrations of some members of the **classical Δ4 pathway** of androgen biosynthesis (progesterone (p=0.0104), 17-OH-progesterone (17 OHP) (p<0.0001)) and of the **alternative T pathway** steroid androstenediol (p=0.004)) were observed, compared to controls.
The marker steroid of the **backdoor DHT** pathway androstanediol (p=0.025), was slightly increased.
Some Δ4 pathway steroids (androstenedione, (A4)), the **testosterone metabolites** DHT and 17-ß estradiol (E2), the **Δ5 pathway** steroid dehydroepiandrosterone sulfate (DHEAS) and all measured **11-oxygenated C19 androgens** (11-keto-testosterone (11 K T), 11-keto-dihydro-testosterone (11 K DHT) and 11-keto-androstenedione (11 K A4)) were comparable to those of controls.



By contrast, **on hCG/rFSH replacement**, steroid profiles resembled those of healthy male controls, regarding the **Δ 4 pathway** of androgen biosynthesis (17-OHP, A4) and the metabolite DHT, the marker steroid of the **alternative T pathway** androstenediol, the **Δ5 pathway** steroid DHEAS and all aforementioned **11-oxygenated C19 androgens** (11 K A4, 11 K T, 11 K DHT).
Serum progesterone (**Δ 4 pathway)** was slightly decreased (p=0.0104);
the **testosterone metabolite** E2 and the **backdoor DHT pathway** steroid androstanediol were increased (both p<0.0001).



CONCLUSIONS

In males with CHH, a replacement with hCG/rFSH mimics physiologic steroid hormone profiles better than a substitution with testosterone.
Gonadotropins induce Δ4 classic pathway steroid production and co-activate the alternative pathway of T biosynthesis.
The backdoor pathway of DHT, synthesis of DHEAS and of 11-oxygenated C19 steroids are activated independently of gonadotropins.
The documented differences in replacement strategies may impact on long term male health.

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