Investigation about the effects and the detection of finasteride

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Introduction
Finasteride is an inhibitor of 5-alpha reductase and used for the treatment of benign prostatic hypertrophy and androgenetic alopecia. Investigations with finasteride with only one volunteer have shown, that the use of finasteride complicated the detection of the misuse of several anabolic steroids in doping control (1). To confirm this result, excision studies with several volunteers were performed.

Methods
To study the influence of finasteride on the urinary steroid profile and on the metabolism of anabolic androgenic steroids, excision studies with single oral administrations of 5 mg and 1 mg finasteride were performed with 5 volunteers. Urine samples were collected before and till 8 days after the administration and the profiles of endogenous urinary steroids were analyzed by GC/MS according to the screening procedure for anabolic steroids (2).

Results: Influence of finasteride on the steroid profile
It could be shown, that finasteride led to obvious changes of several steroid profile parameters. The excretion of 5-alpha-steroids like androsterone, 5α-androstan-3α,17β-diol, allo-tetrahydrocortisol, 11β-hydroxy-androsterone, and dihydrotestosterone decreased whereas the excretion of the 5β-steroids increased (Fig. 1). These changes could be detected for more than 8 days both with 5 mg and 1 mg finasteride. The ratio testosterone/epitestosterone showed no changes whereas the increase of the excretion of the 5α-allo-steroids showed the same extent for 5 mg and 1 mg finasteride, whereas the increase of the excretion of the 5β-steroids was waste with 1 mg finasteride compared to 5 mg finasteride. The ratio testosteronetestosterone/epitestosterone showed no changes after the application of finasteride and varied within the normal variation.

Results: Detection of finasteride
The main urinary metabolite of finasteride is the carboxy-finasteride (3), see Fig 5). This metabolite can be detected with LC/MS/MS in the screening procedure for diuretics (4). The finasteride metabolite, carboxy-fainasteride, is monitored in the extracted ion chromatograms of on-tenton chromatograms of on-tenton of finasteride. After a single oral application of 5 mg of finasteride the carboxy metabolite could be detected for 90 hours.

Results: Influence of finasteride on the metabolism of norandrosterone
Further excision studies with 5 mg finasteride were performed with 5 volunteers, who administered additionally 20 µg norandrostendione. It could be shown that under the influence of finasteride the excretion of the 5α-steroid norandrosterone, the main metabolite of norandrosterone, is suppressed to 20-40% of values without finasteride, whereas the excretion of the 5β-allo-steroid norrietiocholanolone increased under the influence of finasteride up to 400% of the values without finasteride (fig. 3, 4). Based on these results the ratios of norandrosterone/allo-tetrahydrocortisol changed from values between 1.7-8.4 to values between 0.3-0.7.

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References

Fig. 1: Chromatograms (SIM) of endogenous steroids of a volunteer before and 24 h after the application of 5 mg finasteride (1). 1. androstosterone, 2. androstenedione, 3. 5α-androstane-3α,17β-diol, 4. 5β-androstane-3α,17β-diol

Fig. 2: Relative changes of the ratios androsterone/etiocholanolone in the urine samples of the five volunteers (VP1-VP5) after application of 5 mg finasteride (mean of pretest values = 100%)

Fig. 3: Norandrosterone concentrations of volunteer VP1 after the administration of norandrosterone (20 µg orally) without and with finasteride (5 mg orally)