

“Doping tests in special situations - low dose testosterone use and in post-conceptual period”

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Project overview:

Our research program encompasses projects designed to investigate how low doses of topical testosterone interfere with the urinary steroid profile and Athletes Biological Passport (ABP). ABP is essential to detect doping with anabolic androgenic steroids, especially with the use of low-dose-testosterone being increasingly used by some athletes.

In addition to genetic variation, there are many other factors that may contribute to the inter- and intra-individual variability in the steroid profile, i.e. concomitant drug use, diseases, menstrual cycle, and pregnancy. The latter two conditions have a marked influence on the metabolism and endocrinology of estrogens, progestagens, and peptide hormones (LH,FSH, hCG). However, very little is known about the natural androgen disposition in these situations. In view of the increasing use of LDD it is important to know the natural profile of androgens in the early post-conceptual phase when women still may not know, or know of the pregnancy. There is a dearth of information how pregnancy influences the androgen profile, but it is likely to confound the test interpretation. We will therefore study the androgen profile in females (no dose administration!) in the post-conceptual phase and first trimester.

It is of great importance that the athletes ABP will be able to compensate for all possible variability in longitudinal steroid profiles. More knowledge is therefore needed about how drug use and pregnancy influence the ABP results and hence the outcome of doping tests.

Results and Conclusions:

The low-dose androgen doping strategy practiced by certain individuals may be difficult to detect, particularly in women during the menstrual cycle and even more so in the early post-conceptual phase because of extensive hormonal changes. Even though doping puts the fetus at danger, highly motivated sports women may disregard this risk. Alternatively, they may be unaware of conception early in pregnancy. It is probable that exogenous androgens will interfere with the hormonal balance in pregnant women. For obvious reasons there is only sparse information on that in the literature.

We have investigated the natural androgen excretion profile in women in different phases of pregnancy, and the potential effect on the testosterone/epitestosterone (T/E) ratio used in doping tests. First,

pregnancy altered the excretion of glucuronide (G) and sulfate (S) conjugated androgen metabolites. Using an LC-MS/MS method we found that both epitestosterone-S (-S = sulfate conjugate) and epitestosterone-G (-G = glucuronic acid conjugate) were significantly increased throughout the trimesters, being normalized post-partum. Importantly, some of the urinary profiles of steroid ratios in the ABP were altered in pregnant women when compared to the same women after delivery, or with non-pregnant women. Two of the ratios were altered during pregnancy; T/E was lower, whereas A/Etio was higher in pregnant women. Prior information about pregnancy would make the interpretation of the test results safer since pregnancy has such an impact on the ABP steroid profile.

The steroid profile was also studied in relation to ethnicity and genetic variation. The results show that pregnant women of Asian origin exert higher urinary concentrations of epitestosterone-G than Caucasians. The genotype – phenotype relation between UGT2B17 deletion polymorphism and T/E ratio was disrupted during pregnancy.

19-Norandrosterone increases in pregnancy and, if above the Decision Limit (DL), analysis of hCG is performed. If the concentration is above 15ng/mL, an IRMS analysis needs to be done in order to confirm if 19-NA is of exogenous origin. In the first trimester 19-NA was below the DL in 55 % of the women. None of the pregnant women reached 15 ng/mL in the first trimester, but 45 % of them were above the DL. The median 19-NA concentrations were increased in the second and third trimester, and in the second and third trimester 56 and 71 %, respectively, of the pregnant women reached the individual DL.

Early pregnancy is a condition that perturbs the hormonal balance and affects the interpretation of common doping tests. Our results are informative about the critical points to be considered in relation to doping tests in fertile female athletes.