"Evaluation of the Athlete Steroidal Passport – Confounding Factors and Sport Specific Features in Swedish and Norwegian Athletes"

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Project Overview

The steroidal module of the Athlete Biological Passport has now been in use for 24 months. The biomarkers used are testosterone, four of its metabolites and epitestosterone. Using these, five steroid ratios are calculated and monitored in the adaptive model. An atypical passport finding will be generated if any of these ratios are outside the individual reference limits, and it is the task of the Athlete Passport Management Unit to evaluate whether further confirmation (i.e. IRMS or follow up testing) is needed. With the exception of the extensively studied T/E ratio, the impact of doping or other confounding factors on the other biomarkers needs further investigation. The largest confounders of the steroid biomarkers are genetic factors, bacterial contamination, alcohol and certain non-prohibited drugs. These confounders are well known and the adaptive model compensates for these, or, in the case of alcohol and bacterial contamination, this is reported by the laboratory. However, it is evident after two years of monitoring steroid ratios in the biological passport that there is still large unexplained variation in the ratios. The origin and extent of this variation in actual doping test results and longitudinal profiles in athletes have not been investigated to date.

This will be a retrospective study analyzing the variation in steroid profiles (single samples) for > 6000 urine samples, as well as longitudinal profiles (passports) in athletes with >10 samples in their steroidal passport (n ≈ 200), from the beginning of 2014 to date. In order to improve the future interpretation of steroid profiles, we will study the behavior of the biomarkers in e.g. different types of sport, in/out of competition samples, seasonal variations, in athletes using non-prohibited drugs as well as in reported AAFs for prohibited drugs (anabolic agents and/or hormones and metabolic modulators).

Results and Conclusions:

The steroid module of the Athlete Biological Passport has now been in use for about four years. Its usefulness has been proven when detecting doping with endogenous steroids, e.g. testosterone, especially in individuals with naturally low T/E ratios due to the UGT2B17 deletion polymorphism, with an increased number of positive IRMS analyses in samples with T/E < 4.0. However, the steroid profiles are complicated to interpret and there is still much variation in the five ratios that is difficult to explain. A large systematic study of natural variation and confounders of the steroid ratios and concentrations is needed in order to provide the scientists evaluating the passport with sharper tools, not only to select the profiles suspicious of doping, but also to be able to reject and not spend unnecessary time and

resources on profiles showing atypical results due to natural causes. The ultimate goal is to be able to proceed with a passport case, where the steroidal passport is the only evidence of doping.

In this study, we used over 11 000 steroid profiles from Swedish and Norwegian athletes to determine both the inter- and intra-individual variations of all steroids and ratios in the steroidal passport. Furthermore, we investigated if these variations could be associated with factors such as gender, age, type of sport, collection time of day and time of year as well as if the sample was taken in competition or out of competition.

We show that there are factors reported in today's doping tests that significantly affect the steroid profiles. There were large interindividual variation in the steroid profiles and only part of this variation, up to 16 %, could be explained by the factors studied. The factors with the largest influence on the steroid profile was what type of sport classification the athlete belonged to and if the urine was collected In or Out of Competition. For women all steroids showed higher levels when collected IC than OOC except for 5βAdiol. T/E, A/Etio and 5αAdiol/5βAdiol show higher levels in competition whereas A/T and 5αAdiol/E are lower. For men all ratios but A/T were affected but to a lesser extent. There were also significant differences based on what time of day and time of year the urine sample was collected.

If these significant changes are relevant when longitudinally monitoring athletes in the steroidal module of the ABP, must be further evaluated.