

“Extension of the Athlete Biological Passport: Inclusion of the isotope mass spectrometric data”

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Project overview:

The detection of the exogenous administration of synthetic androgens (the so called “pseudo-endogenous” steroids) having the same chemical structure of the compounds produced endogenously (i.e testosterone, 5 α -dihydrotestosterone or androstenedione) is primarily based on the alterations of the urinary endogenous steroid profiles.

A Bayesian approach and adaptive model has been adopted by WADA for the management of the steroid profiles and all the parameters obtained by the Accredited Laboratories will be collected starting 1st January 2014 in a global database integrated in the Athletes Biological Passport (ABP), permitting to establish the individual reference ranges of every athlete.

The detection capacity of the steroid profile can be improved by the inclusion of the urinary hydroxylated androgen metabolites excreted in lower amounts but whose diagnostic values become more significant after the administration of endogenous steroids. The additional inclusion of the isotope ratio mass spectrometric (IRMS) data has demonstrated to improve the statistical discrimination between basal samples and samples obtained after controlled administration of testosterone.

Finally, the use of IRMS is a very powerful tool for the detection of pseudoendogenous steroids if the starting material for their synthesis has a ¹³C composition different from the endogenously produced molecule. The detection of formulations able to circumvent their detection by IRMS already occurred since the criteria are based on population data and not on athlete's previous data.

The main goal of this project is to establish the long term variability of the IRMS delta values of both target (TC) and endogenous reference compounds (ERC), and of the steroid profile parameters including hydroxylated androgens metabolites in order to improve the evaluation of the longitudinal profiles. This should permit to enlarge the detection capacity and to potentially detect the abuse of preparations of pseudoendogenous steroids with delta values in the endogenous region.

Results and Conclusions:

There is a definite need of finding more efficient ways to detect the exogenous administration of pseudoendogenous steroids. Although the implementation of the ABP has been a clear step forward, there is still a gap between our capacity to suspect and to confirm the abuse of these substances. The use of more specific markers of the urinary steroid profile like some hydroxylated steroids has been investigated, although their implementation is not easy and would require big efforts to harmonize their detection and quantification as was done for the current markers of the ABP. The potential inclusion of the IRMS data in the ABP as a direct evidence of doping by pseudoendogenous steroids has been evaluated. As for the ABP markers, instead of comparing the obtained data with reference population ranges (present approach as a confirmation strategy), we suggest to incorporate these data to the ABP and to evaluate the values to the reference data produced by every single athlete.

To reach this goal, the first step was to investigate the stability of the IRMS data in both healthy volunteers and athletes.

The variability of the IRMS data in a short, medium and long term period in 8 males and 6 females volunteers when compared to data of athletes submitted to investigations by the respective NADO due to atypical steroid profiles, showed that the variability of the individuals' absolute delta values of the parameters studied are at least one half lower than the population ones and much lower than the markers of the steroid module of the ABP. The data obtained from real samples of athletes showing atypical steroid profiles, show a variability comparable to the non-athletes volunteers, demonstrating that sports practice and the use dietary supplements do not influence the delta values of the endogenously produce steroids. These IRMS values depend mainly on the individuals' diet and metabolism.

This would allow defining individual reference ranges much narrow than the currently applied ones. This would permit (1) to extend the detection window of the pseudoendogenous administration and (2) to potentially detect the use of steroids from pharmaceutical preparations showing delta values close to the endogenous values.

The results of the present project, suggest that the IRMS data obtained with the procedures already in place in the WADA accredited Laboratories, can be used in a more performing way. If the data instead of being only used during the confirmation evaluation of an atypical steroid profile would be evaluated longitudinally, the information obtained would permit to enlarge the detection window of pseudoendogenous steroids abuse and the potential detection of pharmaceutical preparations showing delta values in the endogenous region. We are not proposing the implementation of a new method but the better exploitation of the data already obtained. By doing so, the gap between the ability of detecting suspicious steroid profiles and the capacity of confirming them by IRMS will be drastically reduced.