PROJECT REVIEW

"Endocrine study on the effects of testosterone gel application in male athletes."

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Testosterone gel is used for the treatment of testosterone deficiency in males. Testosterone is a hormone with strong anabolic effects and, therefore, belonging to the list of prohibited substances in sport. Testosterone misuse is – in most cases – being found by the analysis of steroid profile parameters and values of testosterone metabolites in urinary samples. In the case of testosterone gel application, however, results of preliminary studies done by the Institute of Biochemistry of the German Sport University suggest that this type of testosterone administration may be more difficult to detect.

One possibility to detect the misuse of testosterone gel might be an endocrine test on the integrity of the hypothalamo-pituitary-gonald axis (HPGA) following a routine analysis of the urinary steroid profile. This kind of endocrine testing is routinely used in medical diagnostic investigations including, if indicated, stimulation tests of the HPGA with exogenously injected gonadotropin releasing hormone (GnRH). Under physiological conditions, exogenous GnRH leads to a defined secretion of LH, FSH and, subsequently, testosterone, all of them to be measured in blood samples. In addition, testosterone and its metabolites might also be measured in urine.

In the case of chronic suppression of the HPGA, like after a chronic misuse of testosterone gel in sport, a pathological secretion profile of LH, FSH and testosterone is to be expected. However, there is no data available on the exact profiles of the secretion patterns after different time schedules of testosterone gel application and in dependence of physical exercise in athletes. Therefore, the present study will investigate the effects of different time schedules of testosterone gel applications in physically active people on the stimulatory pattern of LH, FSH and testosterone and its metabolites in blood and urinary samples. Concretely, an endocrine test will be developed and validated for the indirect detection of testosterone gel misuse in sport.

Endocrine Study on the Effects of Testosterone Gel Application in Male Athletes

Results and Conclusions

The misuse of testosterone gel has not been detectable at the beginning of this study. Therefore, the aim of the present study was to investigate the effects of two different time schedules of testosterone gel applications in physically active male athletes on the stimulatory pattern of LH, FSH and testosterone in blood samples, and thereby developing and validating an endocrine test for the indirect detection of testosterone gel misuse in sports. 17 physically active male subjects agreed to participate and were randomly divided into 2 groups. Group 1 (n=8) received 100 mg of testosterone gel per day over a period of 6 weeks in an intermittent manner with 7 days of application being followed by 7 days of wash-out-phases in between (INT). Group 2 (n=9) constantly received 100 mg of testosterone gel (Tgel) per day over the same period of 6 weeks (CON). Total time of application resulted in 3 weeks in INT and 6 weeks in CON. Serum basal concentrations of luteinizing hormone (LH), follicle stimulating hormone (FSH), total testosterone (T), and free testosterone (fT) were determined at 9 a.m. prior to the first Tgel application (W-1), weekly during the 6 week application period (W1 – W6) after each 7-days phase of Tgel application, plus two times after a wash-out period, once after 7 days (W7) and once after 21 days (W10) after the end of Tgel application. Furthermore, we analysed LH, FSH, T and fT 30 min, 75 min, and 120 min after exogenous injection of 100 ug of Gonadotropin Releasing Hormone (GnRH) at each time point of basal hormone measurement.

Main results of the study showed a fast reaction of the pituitary gonadotropins after exogenous Tgel application. We observed a suppression of the spontaneous LH and FSH secretion (basal values) after only one week of Tgel, and a fast restitution in the wash-out weeks during intermittent Tgel and after the last week of Tgel during INT and CON. Doping with testosterone, therefore, indirectly is detectable from repetitive measurements of basal LH and FSH values, if 1st blood sample is taken as soon as possible (within a less than one week period) after finishing doping with testosterone gel, and if concentrations are interpreted individually. Although we found a trend for the expected immediate (e.g. after one week of Tgel) increase in exogenous GnRH-induced LH- and FSH-release, and a following decline according to a reduced gonadotropin biosynthesis, exogenous GnRH-induced LH- and FSH increments were not altered significantly beside a significant delayed reduction in GnRH-induced LH and FSH release after 6 weeks of Tgel, which remained reduced for both hormones even after 1 week of wash-out. The missing significance was mainly due to high inter-individual variability in stimulated LH and FSH secretion. For doping analysis of testosterone gel misuse, the combination of (still) reduced GnRH-induced LH and FSH release and already renormalized LH and FSH basal values after a period of testosterone gel application is another indirect indicator. As total and free testosterone concentrations showed a high inter-individual variability and remained in the normal range in many cases, the simple measurement of their blood values is not sufficient for the detection of testosterone gel doping. Serial measurements of blood concentrations in addition to the values of LH and FSH, however, might help in the interpretation of high-normal values.

Publications

Geyer H, Flenker U, Mareck U, Platen P, Piper T, Schmechel A, Schrader Y, Thevis M, Scha¨nzer W. In Recent Advances in Doping Analysis, vol. 15, Schänzer W, Geyer H, Gotzmann A, Mareck U (eds). Sport & Buch Strauß: Cologne, 2007; 133.

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Piper T, Mareck U, Geyer H, Flenker U, Thevis M, Platen P, Schänzer W: Determination of 13C/12C ratios of endogenous urinary steroids: method validation, reference population and application to doping control purposes. Rapid Commun Mass Spectrom 22: 2161–2175, 2008.