

PROJECT REVIEW

“Influence of LH-RH application on urine and plasma levels of testosterone, LH-RH, LH and steroid profile ”

M. Thevis, W. Schanzer, A. Thomas, H. Geyer, (German Sport University, Germany) **P. Platan** (Ruhr-University, Germany)

The misuse of the peptide hormone LH-RH (Gonadorelin, GnRH, Kryptocur) in elite sports has frequently been reported during the last years, especially in the course of legal statements and confessions of athletes. LH-RH can be administered by means of infusion or facile intranasal application, which influence the endogenous production of the luteinizing hormone (LH) and, via the gonadal axis, an increased release of androgens into circulation is induced.

The present project shall investigate all effects of LH-RH applications by healthy individuals on LH and testosterone in plasma, as well as the steroid profile, LH and LH-RH in urine. The measured parameters shall outline the influence of LH-RH administrations on regularly determined analytes of routine doping controls such as LH and the steroid profile, and further provide information on detection windows for LH-RH in specific doping control procedures.

“Influence of LH-RH application on urine and plasma levels of testosterone, LH-RH, LH and steroid profile”

M. Thevis, W. Schanzer, A. Thomas, H. Geyer, (German Sport University, Germany) **P. Platan** (Ruhr-University, Germany)

Results and Conclusion:

Luteinizing hormone-releasing hormone (LH-RH) is a natural hypothalamic peptide hormone responsible for the stimulation of luteinizing hormone (LH) release from the pituitary. LH in turn stimulates the testosterone production and release from the gonads, regulating plasma testosterone concentrations. Since LH-RH has been available as therapeutic agent in different formulations (i.e. for intranasal and intravenous application), its abuse in sport cannot be excluded and confessing athletes have indicated the misuse of LH-RH during their career. In order to obtain detailed information on the effects and thus measurable parameters to uncover LH-RH abuse, administration studies with intranasal, intravenous, and combined application protocols were conducted with 10 male volunteers, plasma and urine samples were collected and parameters including plasma testosterone, LH, and FSH, as well as urinary LH, LH-RH, and steroid profiles were determined. Established assays (immunological as well as chromatographic-mass spectrometric approaches) as well as new liquid chromatography-high resolution/high accuracy mass spectrometry methods developed in the course of the project were used. LH-RH in bolus and intermittent drug regimen resulted in significant increases of plasma testosterone and LH concentrations. In urine, steroid profiles demonstrated an impact of the LH-RH administrations; however, the effects were not as pronounced as desirable and characterized mainly by increasing androsterone/testosterone and androsterone/epitestosterone ratios towards the end of the study due to suppression effects on testosterone and epitestosterone. The commonly employed testosterone/epitestosterone ratio was found to be insensitive to an LH-RH intervention, even at high therapeutic dosing. Moreover, urinary LH was not substantially affected. In an intra-individual picture, the increase of urinary LH concentrations following an LH-RH application could be correlated; however, LH levels remained within normal reference ranges. Since the steroid profile and urinary LH concentrations did not provide sufficient information allowing to pick up LH-RH misuse, the option to directly detect the peptide hormone in urine was pursued. By means of solid-phase extraction followed by LC-MS/MS, LH-RH was detected in urine specimens after both intranasal and intravenous drug administrations. The detection window was found to be 12-24 h employing state-of-the-art analytical instrumentation available in most doping control laboratories.