Reprint from

RECENT ADVANCES IN DOPING ANALYSIS (5)

W. Schänzer
H. Geyer
A. Gotzmann
U. Mareck-Engelke
(Editors)

Sport und Buch Strauß, Köln, 1998

A.T. KICMAN, S.B. COUTTS, D.J. HANDELSMAN, F.C.W. WU, D. A. COWAN:

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In: W. Schänzer, H. Geyer, A. Gotzmann, U. Mareck-Engelke (eds.) Recent advances in doping analysis (5). Sport und Buch Strauß, Köln, (1998) 49

ADRENAL GLAND CONTRIBUTION TO URINARY EPITESTOSTERONE IN MEN

AT Kicman, SB Coutts, DJ Handelsman, FCW Wu & DA Cowan
Drug Control Centre, King's College London

ABSTRACT

Investigating the origins of epitestosterone (EpiT) and how stress may effect the urinary output of this steroid can help to further evaluate the specificity of the T/EpiT drug test. Differences in GC-MS data, generated by the analysis of urine collected from men and women, suggests that a large proportion of epitestosterone produced is of testicular origin. The adrenal gland contribution is not known but it is generally assumed to be much smaller. Wilson and Lipsett (1966) showed that the production rate of total EpiT (free, glucuronide and sulphate) was increased by an average of 29 % with ACTH stimulation.

The aim of our current study was to investigate the amount of urinary EpiT derived from adrenal origin in men. To achieve our aim, we compared the urinary excretion rate of EpiT in six healthy men (eugonadal group) to that of six adult male patients with primary or secondary hypogonadism (hypogonadal group). After collection of basal samples, each volunteer received an i.m. injection of depot tetracosactrin (Synacthen depot; 1 mg) at 8 a.m. on day 0 and day 1. Blood samples were collected at 0 h, 1.5 h and 8 h on day 0 and day 1 and also at 24 h following injection on day 1. 24 h urine sample samples were collected on days -2, -1, 0 and 1. Plasma concentrations of T, EpiT and cortisol were determined by immunoassay and urinary T and EpiT by GC-MS after glucuronide hydrolysis.

The mean concentration of plasma T in the eugonadal group decreased by approximately 50 % of the mean basal value (18 nmol/L) following tetracosactrin stimulation; the mean urinary T decreased to 64 % of basal. In the hypogonadal group the mean plasma T concentration at basal was 2 nmol/L, remaining unchanged after stimulation and likewise no significant changes were observed in the urine. There was a significant difference in plasma EpiT basal concentrations between the two groups, smaller concentrations being observed in the hypogonadal group (1.3 v 0.7 nmol/L). With stimulation, plasma EpiT did not change significantly in the eugonadal group but small increases were observed in the hypogonadal group. After stimulation, the 24 h urinary EpiT excretion rate remained unchanged in the eugonadals. For individuals in the hypogonadal group, urinary excretion of EpiT increased between 270 to 2500 %; mean basal rate of the group was 4 μg/day, which increased to 25 μg/day after stimulation.

The urinary excretion rate of EpiT is much smaller in hypogonadal men than in eugonadals, indicating that the testis directly or indirectly contributes to >90 % of the urinary EpiT in healthy men. After tetracosactrin stimulation there were large increases in the urinary excretion rate of EpiT in the hypogonadal group whereas there was no significant change in the eugonadal group. Plasma and urinary T decreased in the eugonadals which corresponds with evidence in the literature reporting that testosterone levels decrease in men receiving glucocorticoid therapy. This raises the possibility that tetracosactrin stimulation causes an increase in adrenal production of EpiT or a peripheral precursor in the eugonadals but there is a corresponding decrease in testicular production due to the raised plasma cortisol. In hypogonadals this 'adjustment' is not possible, thus explaining the enormous rises in their urinary EpiT excretion rate.