"Detection of growth promoting peptide doping"

Lena Ekström, Anders Rane (Karolinska Institutet, Sweden)

Project Overview

The administration of recombinant human growth hormone (rhGH) and/or small peptides, i.e. GH releasing factors (GHRF) that stimulate the endogenous production of GH have increased recently as a result of the availability and lack of sensitive tests. Two independent immunoassay methods are currently being employed to detect rhGH doping as well as mass-spectrometric approaches to find GHRFs.

Our research proposal encompasses projects designed to investigate how the use of rhGH and GHRFs affect the traditional markers as well as putative markers such as miRNA. We will conduct a study in healthy male volunteers that will be given rhGH (Somatropin – two different doses) daily for one week. Some participants will be given two doses of sermorelin (Geref), a GHR peptide, for one week. Urine and serum samples will be collected several times prior to the administration in order to study the different markers longitudinally. Moreover, the steroid profile will be monitored in relation to hrGH/GHRP administration in order to see how the biomarkers of the different ABP modules interact. The use of small GH-releasing peptides is difficult to study in controlled settings since small peptides are not available as traditional drugs. Here we will use samples from patients, both men and women, self-reporting doping with peptides (as well as other doping agents) in order to see which peptides can be identified with the different approaches.

Results:

It was found that the GH isoform ratio may detect rhGH intake when 1 and 4IU/day were administered for two weeks to healthy men. Using the biomarker test, none of the participants (n=9) displayed a GH2000 score above the population-based score of 9.98. However, when longitudinally monitored, the GH2000 score and its components IGF-I and P-III-NP, most of the participants showed values outside their individual calculated thresholds (mean four baseline values ±3 SD). Also, the longitudinally testing approach was studied in four individuals in relation to 5 days GHRH(1-44) administration. It was found that monitoring of IGF-I may be useful for identifying also the intake of GHRH. Additionally, it was investigated if rhGH/GHRH administration exert an impact on ABP biomarkers. A minor increase in RET% and OFF-score after rhGH treatment was found, not resulting in any atypical passport findings. The urinary steroid profile, as well as serum concentrations of androgens were not affected by rhGH. Moreover, the validity of putative biomarkers was assessed. It was concluded that miRNAs previously associated with GH supplementary treatment were not affected by the rhGH doses given here. Previous findings that fibronectin 1 may be a promising additive protein for detection of rhGH was confirmed.

Conclusions:

Longitudinally monitoring of IGF-I and P-III-NP in an endocrine module may be a promising method in the future to increase the chances to detect rhGH/GHRH doping in men. The inclusion of additional biomarkers such as fibronectin 1 may increase the effect and/or detection window in some individuals.

Publications:

Lehtihet M, Bhuiyan H, Dalby A, Ericsson M, Ekström L. “Longitudinally monitoring of P-III-NP, IGF-I, and GH-2000 score increases the probability of detecting two weeks' administration of low-dose recombinant growth hormone compared to GH-2000 decision limit and GH isoform test and micro RNA markers.” Drug Test Anal. 2019 Mar;11(3):411-421.

Sieckmann T, Elmongy H, Ericsson M, Bhuiyan H, Lehtihet M, Ekström L. “Longitudinal studies of putative growth hormone (GH) biomarkers and hematological and steroidal parameters in relation to 2 weeks administration of human recombinant GH.” Drug Test Anal. 2020 Mar 1.