Growth hormone is assumed to be widely abused by athletes as a performance-enhancing drug. Although scientific evidence is lacking, that performance enhancement actually is achieved by growth hormone, evidence from confessions of former athletes and confiscation of GH carried by athletes through actions of customs or police officers points toward a widespread abuse. Athletes apparently desire the physiological effects of growth hormone, namely protein anabolism and its lipolytic activity.

Development of a test method to detect growth hormone abuse in sports has been a subject of investigations for more than 10 years by now. Such doping tests are difficult to achieve for growth hormone (hGH) because of the structural identity between recombinant 22 kDa hGH and the major isoform of pituitary derived growth hormone. Also, in contrast to erythropoietin, growth hormone does not have N-linked glycosylation sites and therefore detection strategies analogous to those established for erythropoietin cannot be pursued.

Two different strategic approaches have been developed to detect growth hormone doping in sports: The "marker method" uses GH-mediated changes in concentrations of pharmacodynamic endpoints such as levels of insulin-like growth factor I and collagen-derived cleavage peptides. This approach was initially developed by the consortium GH 2000 under the leadership of Peter Sonksen [5,6]. The advantage of the marker approach lies in the longer half-life of the selected marker as compared to the short half-life of GH in circulation. The markers, however, have an inherent variability between individuals and it was found more specific to combine two markers such as IGF-I and PIIIP as one marker from the IGF-system and one from the collagen system. The power to detect growth hormone application by this method persists longer in males than in females and in individual cases appears feasible in males for up to 2 weeks [4]. For each of the markers, reference ranges need to be established and constant supply of the immunoassay reagents in identical quality has to be assured [1].

The second strategy is based on subtle differences in GH isoform composition depending on the origin of the hGH being either the pituitary or recombinant production. The pituitary secretions a wide variety of GH-isoforms, while injectable recombinant growth hormone represents mostly monomeric 22 kDa hGH. We therefore developed the concept of differential immunoassays whereby every sample is analysed in two different immunoassays, the first of which is preferentially recognizing 22 kDa monomeric hGH, while the second immunoassay uses monoclonal antibodies selected to preferentially recognize other pituitary isoforms of hGH [7]. In keeping with the guidelines issued by the World Anti-Doping-Agency (WADA), independent sets of assays for a screening and a confirmatory kit have been established based on antibodies recognizing different epitopes [2]. By specifically measuring the 20 kDa isoform of hGH it could be demonstrated that pituitary GH-secretion is suppressed after a single injection of recombinant 22 kD GH for more than 24 h [3]. The differential immunoassay approach for the detection of hGH abuse in athletes has been applied during the Olympic Games in Athens 2004 and Torino 2006 with no test declared positive until now. Present efforts aim at making available the necessary reagents to all WADA accredited laboratories.

In conclusion, two different approaches exist to detect GH-abuse in athletes and they may be used complementary in the future, because the detection window for the GH-isoform approach appears limited to 36 h, while the marker method may miss cheats in the early phase after GH application, but has the potential to detect GH abuse for a longer time period.

References


