Unaltered ratio of circulating levels of growth hormone/GH isoforms in adults with Prader-Willi syndrome after GHRH plus arginine administration.

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Human growth hormone (GH) is a heterogeneous protein hormone consisting of several isoforms, the most abundant being 22 kDa- and 20 kDa-GH. The availability of analytical methods to measure these GH isoforms might represent a valuable diagnostic tool to investigate GH hyposecretory states, including Prader-Willi syndrome (PWS), one of the most common causes of syndromic obesity. The aim of the present study was to measure circulating levels of 22 kDa- and 20 kDa-GH in PWS adults (n=14; M/F: 5/9; genotype DEL15/UPD15: 12/2; age: 19.0±3.7 years; BMI: 29.9±8.7 kg/m^2) after combined GH releasing hormone (GHRH) plus arginine (ARG) administration. The results were analysed subdividing the study population in obese vs. nonobese (6/8) and GH deficient vs. nonGH deficient (GHD) (6/8) subjects, according to appropriate BMI-related diagnostic cut-off limits of GH peak response to the provocative test. Circulating levels of 22 kDa-GH were measured by a chemiluminescent method based on a detection monoclonal antibody targeting an epitope in the loop connecting helix 1 and 2 of GH, which is missing in 20 kDa-GH; the 20 kDa-GH was measured using a time resolved fluorescence assay based on two monoclonal antibodies with no cross-reactivity to 22-kDa GH.

GHRH plus ARG significantly stimulated the secretions of 22 kDa- and 20 kDa-GH in nonobese (at 30, 45, 60 and 90 min and at 45, 60, 90 and 120 min vs. 0 min, $p<0.05$,with GH peaks of 15.8±10.3 ng/ml and 2.7±1.2 ng/ml, respectively) and in nonGHD PWS (at 30, 45 and 60 min and at 45, 60 and 90 min vs 0 min, $p<0.05$, with GH peaks of 12.5±9.0 ng/ml and 2.0±1.8 ng/ml, respectively). No significant GHRH plus ARG-induced changes in 22 kDa- and 20 kDa-GH were observed in obese or GHD PWS patients, the only exception being the increase of 22 kDa-GH ($p<0.05$) 60 min after the stimulus administration in GHD group (with GH peaks of 6.9±4.7 ng/ml and 0.8±0.6 ng/ml in obese subjects and 8.5±6.0 ng/ml and 1.2±1.0 ng/ml in GHD subjects for 22 kDa- and 20 kDa-GH, respectively). The GH responses for both isoforms were significantly higher in nonobese than in obese PWS patients (at 45 and 60 min for 22 kDa-GH and at 45, 60, 90 and 120 min for 20 kDa-GH, $p<0.05$), while no differences were detected between GHD vs. nonGHD groups. As previously reported in healthy subjects, the ratios of circulating levels of 22 kDa- to 20 kDa-GH remained constant after GHRH plus ARG both in obese/non-obese and GHD/non-GHD groups, thus suggesting the preservation of a normal balance in GH isoforms in PWS.