INTERNATIONAL MEDICAL PRESS

3rd International Workshop on Adverse Drug Reactions and Lipodystrophy in HIV

23-26 October 2001, Athens, Greece

EFFECTS OF GROWTH HORMONE ON HEPATIC LIPID AND CARBOHYDRATE METABOLISM IN HIV-INFECTED PATIENTS WITH FAT ACCUMULATION

Antiviral Therapy 2001; 6(Suppl. 4):19 (abstract no. 26)

JM Schwarz[1,2], K Mulligan[2], J Lee[1], JC Lo[2], M Wen[1], MA Noor[2], C Grunfeld[2] and M Schambelan[2]

[1] Departmentof Nutritional Sciences, University of California, Berkeley.Calif., USA; and [2] Department of Medicine, University of California, SanFrancisco, Calif., USA

BACKGROUND: We recently reported that treatment with a pharmacological dose of recombinant human growth hormone (GH) resulted in a significant loss of fat and gain in lean tissue in HIV-infected subjects with syndromes of fat accumulation. However, insulin-mediated glucose disposal decreased transiently after 1 month of GH, suggesting impaired peripheral insulin sensitivity.

OBJECTIVE: To evaluate the effects of GH on hepatic insulin sensitivity and lipid metabolism in the same subjects.

METHODS: Stable isotope tracer studies, indirect calorimetry, and measurements of lipid concentrations were performed under both fasting and hyperinsulinemic-euglycemic clamp conditions, before and after 1 and 6 months of GH (3 mg/day) in five patients.

RESULTS: Fasting hepatic glucose production (GP) increased significantly at 1 month (12.0±0.7 to 14.9±0.9 μmol/kg/min, $P<0.03$), and the increase was sustained after 6 months of treatment (14.0±1.1 μmol/kg/min, NS). This increase in GP was driven largely by significantly increased gluconeogenesis (GNG) (3.5±0.9 to 5.2±0.9 and 5.8±1.2 μmol/kg/min, $n=4$, $P<0.01$ and $P<0.01$ at 1 and 6 months, respectively). Sustained increases in whole-body lipolysis and progressive decreases in hepatic fractional de novo lipogenesis (DNL) occurred with GH. These changes were accompanied by an improved lipid profile (significant increase in HDL cholesterol and decreases in total and LDL

cholesterol and triglyceride levels), the latter consistent with the decrease in hepatic DNL. During a hyperinsulinemiceuglycemic clamp, GP and GNG were markedly suppressed relative to the corresponding timepoints under fasting conditions, albeit less so when measured after 1 month of GH.

CONCLUSIONS: In HIV-infected subjects with fat accumulation, GH improved lipid profiles but worsened glucose homeostasis, under both fasting and hyperinsulinemic conditions. These results suggest that treatment with a pharmacological dose of GH is associated with hepatic, as well as peripheral insulin resistance that might lead to hyperglycemia. The combined implications of these positive and negative metabolic effects for cardiovascular disease risk remain unknown.

011023
26

Copyright © 2001 - International Medical Press Ltd. Reproduction of this abstract (other than one copy for personal reference) must be cleared through the International Medical Press Ltd. 2-4 Idol Lane, London EC3R 5DD UK.