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THE EFFECTS OF RECOMBINANT HUMAN GROWTH HORMONE ON GLUCOSE METABOLISM AND BODY COMPOSITION IN HIV-POSITIVE SUBJECTS WITH FAT ACCUMULATION SYNDROMES

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BACKGROUND/OBJECTIVES: Low-dose growth hormone (GH) treatment of abdominally obese HIV-negative men reduces visceral adiposity and improves insulin sensitivity, despite initially causing insulin resistance. We hypothesized that GH therapy in HIV-positive subjects with fat accumulation (FA) would similarly result in body fat reduction and a biphasic response in glucose metabolism.

DESIGN: Seven subjects with FA (four buffalo hump, three abdominal obesity) were enrolled in an open-label study of GH (3 mg/day) for 6 months. Insulin sensitivity (euglycemic hyperinsulinemic clamp), oral glucose tolerance (OGT), substrate utilization (indirect calorimetry), and body composition (DEXA) were measured at baseline, 1 and 6 months.

RESULTS: GH was discontinued in one subject at week 3 due to hyperglycemia; baseline OGT revealed pre-existing diabetes despite normal fasting glucose, so subsequent subjects with overt glucose intolerance were excluded. A second subject moved after month 1, and GH was discontinued. Five subjects completed 6 months of GH, with dose reduction to 1.5 mg in one patient at month 2 for arthralgias. All five subjects experienced a therapeutic benefit, with reduction in hump size and/or abdominal girth: fat mass decreased (mean -4.4 kg, 3.7 kg of which was trunk fat) and lean body mass increased (+5.4 kg) in all subjects at month 6. Changes in non-protein respiratory quotient were consistent with a lipolytic effect of GH. As we hypothesized, insulin-mediated glucose disposal decreased at month 1 (mean 6.43 to 3.30 mg/kg LBM min/mU/ml, $P=0.04$) and then increased to baseline at month 6 (6.38,

$P=0.04$). Similarly, glucose AUC increased at month 1 (362 to 443 mg/dl.h, $P=0.01$) but subsequently decreased at month 6 (398, $P=0.07$).

CONCLUSIONS: Short-term GH therapy at 3 mg/day reduced buffalo hump and abdominal girth in subjects with HIV-associated FA. Although insulin sensitivity and glucose tolerance initially worsened, improvement toward baseline was seen at 6 months, possibly due to reduction in body fat. Screening OGT should be obtained to exclude subjects at risk for GH-induced hyperglycemia.

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