

# Differential Effects of Prednisone and Growth Hormone on Fuel Metabolism and Insulin Antagonism in Humans

Horber et al have previously reported (*J Clin Invest* 1990; 86:265) that recombinant human growth hormone (rhGH) therapy may have a role in preventing the protein losses associated with the administration of glucocorticoids in humans. This study is also reviewed in this issue of *GGH*. The present paper reports additional data regarding fat and carbohydrate metabolism obtained during the original study. Glucose and fat oxidation were determined utilizing isotopic dilution studies and indirect calorimetry. Four groups of normal adult males (N=8, each group) treated with (1) prednisone alone (0.8 mg/kg/d); (2) rhGH alone (0.1 mg/kg/d); (3) prednisone and rhGH; or (4) placebo were studied.

Fasting plasma glucose concentrations increased in the groups treated with prednisone and prednisone plus rhGH but fasting plasma insulin levels were higher only during combined treatment. Protein oxidation was decreased in the postabsorptive state in subjects receiving rhGH alone and increased in subjects receiving prednisone alone, but there was no difference in protein oxidation observed between the placebo-treated subjects and subjects treated with combined prednisone and rhGH. However, fasting fat oxidation was decreased in subjects treated with prednisone but not significantly increased in subjects treated with rhGH alone. The ratio of protein to fat

oxidation was increased in subjects on prednisone alone, decreased in subjects treated with rhGH alone, and unchanged in subjects given the combined treatment as compared with controls. No differences in carbohydrate oxidation were observed among the different groups. The prednisone-treated subjects oxidized more protein but less fat than the controls, whereas the subjects treated with rhGH alone oxidized more fat but less protein than the controls. Subjects treated with both rhGH and prednisone oxidized more fat and less protein than controls.

The authors state that this study suggests that rhGH and prednisone induce insulin antagonism by independent mechanisms. Their conclusions are based on the observations that the increases in concentrations of glucose, insulin, and C peptide with combined rhGH and prednisone were synergistic. Secondly, prednisone alone decreased the plasma concentrations of free fatty acids and ketone bodies in the postabsorptive state but decreased fat oxidation and increased protein oxidation and plasma lactate and pyruvate in both the fed and fasted states. In contrast, therapy with rhGH alone increased fat oxidation, decreased protein oxidation, and had no effects on plasma concentrations of free fatty acids, ketone bodies, lactate, and pyruvate. Finally, although the combined treatment normalized protein and fat oxidation, the

plasma concentrations of free fatty acids, lactate, and pyruvate remained elevated in the fed state. The authors further suggest that the mechanism for carbohydrate intolerance in subjects treated with prednisone alone appears to be a decrease in glucose clearance possibly related to a post-receptor defect. The mechanism for the inverse relationship between fatty acids and protein oxidation observed in this study remains unclear, but may be a result of reciprocal effects of the 2 drugs on enzymes that regulate the mobilization and oxidation of fatty acids and amino acids.

Horber F, Marsh H, Haymond M. *Diabetes* 1991;40:141-149.

**Editor's comment:** *This is an extremely detailed study that extends a previous report on the effects of rhGH and/or prednisone on protein homeostasis in normal adults. The authors have presented data suggesting that the insulin antagonism of rhGH and prednisone is probably caused by independent mechanisms, since it would appear that rhGH and prednisone reciprocally regulate the oxidation of protein and fat while decreasing the efficiency of glucose disposal. This paper along with the previously reported article should be read and studied together.*

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