

## Short-Term Metabolic Effects of Recombinant Human Insulin-Like Growth Factor (IGF-I) in Healthy Adults

Recombinant human IGF-I was administered intravenously (IV) at a dose of 100 µg/kg to eight healthy adult volunteers after a ten-hour fast. In addition, on a separate day, 0.15 U/kg of IV insulin were administered to the same subjects. Serum was obtained after the fast and after each injection for determinations of total and free circulating IGF-I, glucose, growth hormone (GH), cortisol, lactate, epinephrine, norepinephrine, glucagon, and free fatty acids.

The mean fasting blood glucose level was  $4.65 \pm 0.30$  mmol/l. Similar reductions in blood glucose were observed with either IGF-I or insulin ( $1.98 \pm 0.44$  and  $1.78 \pm 0.29$  mmol/l, respectively, 30 minutes after injection). Blood glucose levels returned to  $3.50 \pm 0.56$  and  $3.48 \pm 0.25$  mmol/l within 120 minutes of IGF-I and insulin administration, respectively. The glycaemic curves for those studies were not significantly different. Serum IGF-I rose from  $144 \pm 38$  ng/ml to  $424 \pm 56$  ng/ml 15 minutes after administration and fell to  $261 \pm 56$

ng/ml after 60 minutes and remained at that level for seven hours. Serum levels of free IGF-I rose within 15 minutes after injection from  $26 \pm 8$  ng/ml to  $343 \pm 87$  ng/ml and then decreased to its initial value within seven hours. Blood glucose values returned to normal after two hours, although total IGF-I was still elevated. Peak GH values were reached at 45 minutes ( $19.3 \pm 9.4$  ng/ml) after IGF-I injection and at 90 minutes ( $29.8 \pm 14.3$  ng/ml) after insulin injection. No statistically significant differences between the two GH curves were observed. Serum insulin fell below the limit of sensitivity of the radioimmunoassay ( $< 8.0$  ng/ml) after injection of IGF-I. Glucagon, epinephrine, norepinephrine, cortisol, and lactate levels were similar after both injections. In addition, free fatty acids were suppressed by both hormones, and they reached a nadir 30 minutes after injection. Free fatty acid levels at 60 and 90 minutes, however, were significantly lower ( $P < 0.01$ ) after injection with insulin than with IGF-I.

The authors conclude that IGF-I, when administered in a supra-physiologic dose, is a hypoglycemic agent in human beings. The potency of IGF-I in producing hypoglycemia was 7.5% of that of

insulin on a molar basis. The disappearance curve of free IGF-I between 15 and 60 minutes after injection was similar to that of insulin, but the apparent half-life of free IGF-I was twice as long as that of insulin (20 minutes v 10 minutes). The authors state that the kinetic features of disappearance of IGF-I are similar to those of insulin in subjects with substantial levels of anti-insulin antibodies. In addition, the effect of free IGF-I on free fatty acids is in keeping with in vitro data obtained in rat adipose tissue, demonstrating that insulin is about 100 times more potent than IGF-I in inhibiting lipolysis. Finally, these data do not support the hypothesis of a negative feedback loop of IGF-I on GH secretion.

Guler H-P, Zapf J, Froesch ER. *N Engl J Med* 1987;317:137-140.

**Editor's comment**—This carefully performed study provides much information concerning both the metabolic and the pharmacokinetic effects of recombinant human IGF-I. Further studies will be required to determine the long-term effects of this hormone in individuals with GH deficiency and, possibly, insulin-dependent diabetes.

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## Effect of Growth Hormone Releasing Hormone (GHRH) on Growth Hormone (GH) Secretion in Type II (Non-Insulin-Dependent) Diabetes Mellitus

Pietschmann and Schernthaner studied GH response to GHRH in 21 non-obese and 26 obese patients with Type II diabetes mellitus. Subjects received an intravenous bolus injection of 1 µg/kg GHRH (1-44) following an overnight fast. In addition, nine Type II diabetic patients received hpGHRH during hyperglycemia and after reductions in blood sugar with insulin. The increase in

GH levels following GHRH administration was less marked in obese Type II diabetic patients compared to non-obese Type II diabetic patients ( $P < 0.02$ ). However, the GH response to GHRH in non-obese Type II diabetic patients was not significantly different from that in control subjects. In addition, reduction in mean fasting plasma glucose values from 247 mg/dl to 131 mg/dl did not influence GH response to GHRH.

Pietschmann P, Schernthaner G. *Diabetologia* 1987;30:13-15.

**Editor's comment**—GH response to GHRH in normal subjects has been shown to be influenced by age and obesity. This

paper suggests that obesity might be the factor that is predominantly responsible for the GH responses to GHRH in obese Type II diabetics. The authors suggest that GH responses to GHRH may be due to enhanced secretion of hypothalamic somatostatin, since rats with genetic obesity have a greater release of somatostatin from the hypothalamus than do non-obese rats. In addition, the finding that improvement in glucose control does not alter GH response to GHRH is consistent with similar findings in patients with Type I diabetes. Those individuals failed to exhibit glucose-mediated suppression of GHRH-induced GH levels.

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