Risk of Hypoglycemia With Alternate-Day Growth Hormone Injections

This paper describes three children with growth hormone deficiency (GHD) who presented with fasting hypoglycemia 36-60 hours after an injection of growth hormone (GH). Each child was receiving thrice-weekly injections of synthetic GH; hypoglycemia no longer occurred once injections were begun on a daily basis.

The first patient was a 5-year-old boy with isolated GHD. He was placed on therapy with nonmethionyl GH (Eli Lilly, Indianapolis), 60 μg/kg IM, three days a week. This child began to experience nightmares 36-60 hours after GH injection, and his plasma glucose values fell below 2.2 mmol/L. Simultaneous insulin-like growth factor-I (IGF-I) levels (measured by Nichols Institute) were 350-500 U/L, compared with 230 U/L prior to the initiation of therapy. Once daily injections of 30 μg/kg IM were instituted, overnight plasma glucose levels rose and remained above 4.7 mmol/L.

The second child, a male with panhypopituitarism diagnosed at birth, was initially treated with thyroxine and cortisol. This resulted in complete resolution of hypoglycemia. When he was 20 months old, he was placed on therapy with methionyl GH (Genentech Inc, San Francisco) for growth failure and received 50 mg/kg subcutaneously three times a week. His blood glucose concentrations

were as low as 1.9 mmol/L 38 hours after GH injections; a simultaneous plasma IGF-I level was 360 U/L, compared with 130 U/L prior to the start of therapy. Fasting plasma glucose levels remained low when the child was given thrice-weekly injections of non-methionyl GH, but he was not hypoglycemic.

The third child, also a male with panhypopituitarism, exhibited hypoglycemia on the first day of life and was treated with thyroxine and hydrocortisone. Thrice-weekly injections of methionyl GH were begun when he was one year old. Like the other two children, he also experienced hypoglycemia, with blood glucose levels as low as 2.3 mmol/L 36 hours after each injection. Treatment with daily injections resulted in complete resolution of hypoglycemic symptoms.

The authors suggest that the high levels of somatomedin-C (IGF-I), which often fail to peak until 19 hours after GH injection, contribute to the total insulin-like activity in the serum since they are not accompanied by GH, which would usually antagonize the glucose-lowering effects of insulin.

Press M, Notarfrancesco A, Genel M. *Lancet* 1987;1:1002-1004.

Editor's comment—*These interesting case reports suggest that all patients requiring GH therapy, even those who do not initially present with hypoglycemia, should be carefully observed for the presence of low blood glucose levels when receiving thrice-weekly GH injections.*

Haymond et al (JCEM 1976;42:846) previously demonstrated that the hypoglycemia observed in untreated patients with panhypopituitarism is substrate-mediated and characterized by low circulating concentrations of plasma alanine and glutamine. However, these patients, when receiving cortisone and daily GH injections, did not become hypoglycemic after 30 hours of fasting. No subject receiving GH every third day was studied. From the data presented by Press et al, it would seem reasonable to repeat Haymond's fasting study with more traditional GH therapy and measurements of IGF-I.

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