

Early GH Corrects Growth in Turner Syndrome

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Early treatment with growth hormone can correct growth failure in infants and toddlers with Turner syndrome, allowing many of them to achieve normal height within a few years, Dr. Marsha Davenport and her colleagues reported.

In their randomized placebo-controlled trial, 93% of the girls who received growth hormone achieved a height within normal range before they were 6 years old. The success rate is probably related to early intervention, reported Dr. Davenport, of the University of North Carolina at Chapel Hill, and her associates. "In general, the younger the patient is at growth hormone initiation, the smaller the height deficit to be bridged and the faster height is normalized" (*J. Clin. Endocrinol. Metab.* 2007;92:3406-16).

Dr. Paul Kaplowitz, a member of the American Academy of Pediatrics section on endocrinology, expressed some con-



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DR. KAPLOWITZ

cern about the difficulty of daily injections for such young children.

The investigators randomized 88 girls (mean age 2 years; range 9 months to 4 years) to either no intervention or to 2 years of daily injections with recombinant growth hormone (50 mcg/kg).

At baseline, the mean length/height standard deviation score (SDS) was -1.6. Chronologic age and bone age were not significantly different in any of the girls. Fifty-six had a 45,X karyotype; 14 had a 45,X/46,XX karyotype; and 18 had a variety of other karyotypes.

Compliance with growth hormone treatment was very good, with patients receiving an average of 95% of their scheduled injections.

Treatment corrected growth failure and promoted catch-up growth. In the treatment group, height increased from a baseline SDS of -1.4 to -0.3 at year 2. The control group continued to experience growth failure, falling from a height SDS of -1.8 at baseline to -2.2 by the second year.

During the 2-year study, girls who took growth hormone grew an average of 20.4 cm, compared with an average 13.6 cm in the control group—a significant difference.

The effect of growth hormone was rapid, the investigators noted; by 4 months, the height difference between the groups became significant. In the first year, girls taking growth hormone grew significantly more than those in the control group (11.7 cm vs. 8 cm). The difference was smaller, but still significant, in the second year of treatment (8.4 cm vs. 5.5 cm).

Bone age and chronologic age were similar in both groups at baseline, but by the end of the study, girls in the growth

hormone group experienced a small advance in bone age, compared with chronologic age, whereas bone age had fallen behind in the control group.

Karyotype did not significantly affect response to growth hormone. There were no significant safety concerns; none of the adverse events were deemed related to the study medication.

There are probably few, if any, safety issues with giving growth hormone to girls of this age, Dr. Kaplowitz commented in

an interview. Instead, he expressed some trepidation about problems giving daily injections to such young children.

"I would not be concerned about safety since there is ample data on that for older girls and there is no reason to think younger girls would be different," said Dr. Kaplowitz, chief of endocrinology at the Children's National Medical Center, Washington "The results show clearly that [growth hormone] is safe and effective for girls with Turner syndrome who are be-

tween 9 months and 4 years old. My concern is that a lot of kids and their parents are not psychologically ready for daily injections at this age."

Some girls with Turner syndrome display anxiety and agitation that makes even routine office exams difficult for the physician and traumatic for the child. "I would not want those parents to have to fight with these girls to give them daily injections until they are considerably older and more cooperative." ■



*Model is for illustrative purposes only.

Indications and usage

Levemir is indicated for once- or twice-daily subcutaneous administration for the treatment of adult and pediatric patients with type 1 diabetes mellitus or adult patients with type 2 diabetes mellitus who require basal (long-acting) insulin for the control of hyperglycemia.

Important safety information

Levemir is contraindicated in patients hypersensitive to insulin detemir or one of its excipients. Hypoglycemia is the most common adverse effect of all insulin therapies, including Levemir. As with other insulins, the timing of hypoglycemic events may differ among various insulin preparations. Glucose monitoring is recommended for all patients with diabetes. Levemir is not to be used in insulin infusion pumps. Any change of insulin dose should be made cautiously and only under medical supervision. Concomitant oral antidiabetic treatment may require adjustment. Inadequate dosing or discontinuation of treatment may lead to hyperglycemia and, in patients with type 1 diabetes, diabetic ketoacidosis. Levemir should not be diluted or

mixed with any other insulin preparations. Insulin may cause sodium retention and edema, particularly if previously poor metabolic control is improved by intensified insulin therapy. Dose and timing of administration may need to be adjusted to reduce the risk of hypoglycemia in patients being switched to Levemir from other intermediate or long-acting insulin preparations. The dose of Levemir may need to be adjusted in patients with renal or hepatic impairment.

Other adverse events commonly associated with insulin therapy may include injection site reactions (on average, 3% to 4% of patients in clinical trials) such as lipodystrophy, redness, pain, itching, hives, swelling, and inflammation.

*Whether these observed differences represent true differences in the effects of Levemir, NPH insulin, and insulin glargine is not known, since these trials were not blinded and the protocols (eg, diet and exercise instructions and monitoring) were not specifically directed at exploring hypotheses related to weight effects of the treatments compared. The clinical significance of the observed differences in weight has not been established.

Please see brief summary of Prescribing Information on adjacent page.

References: 1. Meneghini LF, Rosenberg KH, Koenen C, Meriläinen MJ, Lüddecke H-J. Insulin detemir improves glycaemic control with less hypoglycaemia and no weight gain in patients with type 2 diabetes who were insulin naive or treated with NPH or insulin glargine: clinical practice experience from a German subgroup of the PREDICTIVE study. *Diabetes Obes Metab.* 2007;9(3):418-427. 2. Hermansen K, Davies M, Derezinski T, Ravn GM, Clauson P, Home P, for the Levemir Treat-to-Target Study Group. A 26-week, randomized, parallel, treat-to-target trial comparing insulin detemir with NPH insulin as add-on therapy to oral glucose-lowering drugs in insulin-naïve people with type 2 diabetes. *Diabetes Care.* 2006;29(6):1269-1274. 3. Klein O, Lyngge J, Endahl L, Damholt B, Nosek L, Heise T. Albumin-bound basal insulin analogues (insulin detemir and NN344): comparable time-action profiles but less variability than insulin glargine in type 2 diabetes. *Diabetes Obes Metab.* 2007;9(3):290-299. 4. Phyllis-Tsimikas A, Charpentier G, Clauson P, Ravn GM, Roberts VL, Thorsteinsson B. Comparison of once-daily insulin detemir with NPH insulin added to a regimen of oral antidiabetic drugs in poorly controlled type 2 diabetes. *Clin Ther.* 2006;28(10):1569-1581. 5. Data on file. Novo Nordisk Inc, Princeton, NJ. 6. Heise T, Nosek L, Rønn BB, et al. Lower within-subject variability of insulin detemir in comparison to NPH insulin and insulin glargine in people with type 1 diabetes. *Diabetes.* 2004;53(6):1614-1620. 7. Data on file. NDA21-536. Novo Nordisk Inc, Princeton, NJ.

