Growth Hormone Therapy Often Needed Into 20s

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BOSTON — To maintain skeletal health and reach optimal bone development, patients with childhood-onset growth hormone deficiency should continue therapy as they approach young adulthood, according to new treatment guidelines that have been issued by The Endocrine Society.

"The mindset in the past has been that you treat these children until they stop growing," Dr. Mark Molitch said at the society's annual meeting. "But the bones don't mature until the mid-20s, so they may still need the hormone as they transition into adulthood."

In addition, he said, skeletal maturity may occur more slowly in patients with delayed onset of puberty or decreased gonadotropin secretion, so continuation of treatment is even more important for this population. Bone mineral density testing may provide additional valuable information for the decisions about continuing therapy.

Bone mineral density testing may facilitate decisions about whether to continue therapy.

DR. MOLITCH

The new guidelines, which were presented for the first time at the meeting, recommend retesting all children with idiopathic growth hormone deficiency as soon as possible after discontinuing the medication.

Although many will have normal values, therapy should be quickly reinstituted for those who remain deficient.

The guidelines are based on 166 published studies examining the prevalence and diagnosis of growth hormone deficiency in adults, as well as treatment strategies and their long-term risks and benefits, said Dr. Molitch, chairman of the guidelines committee and professor of endocrinology at Northwestern University, Chicago.

The recommendations are aimed only at adults with clinically proven deficiency. "There is a lack of evidence for treating for any other reason, including longevity or athletic performance," he said in a press conference.

In adults, growth hormone deficiencies may result from genetic defects, radiotherapy, structural lesions, or trauma. Only rarely is adult deficiency idiopathic, the guidelines state.

In the past, the insulin tolerance test was the favored diagnostic tool. However, this test carries an increased risk in patients with seizure disorders and cardiovascular disease, and requires close monitoring of even healthy patients. Recently, Dr. Molitch said, stimulation testing with growth hormone releasing hormone-arginine (GRHR-arginine) has gained favor. The test is less affected by age or obesity.

In a recent study of five different tests, including stimulation with GHRH-arginine and insulin tolerance, the stimulation test had 95% sensitivity and 91% specificity at the growth hormone cutoff level of 4.1 mcg/L; insulin testing was 96% sensitive and 92% specific at the cutoff level of 5.1 mcg/L.

Testing is indicated for adults with pituitary disease; surgery, trauma, or radiation in the pituitary area; or other pituitary deficiencies.

Although children with idiopathic growth hormone deficiency should be retested as they approach adulthood, testing may be unnecessary for those with low insulinlike growth factor-1 and known defects, lesions, surgery or radiation of the hypothalamic-pituitary region, or a proven genetic defect of their capacity to secrete growth hormone.

"This [combination] generally suffices to document continuing growth hormone deficiency," the guidelines state.

The evidence strongly supports individualized growth hormone dosing regimens. Generally, treatment should start low and should be titrated upward based on clinical response, side effects, and IGF-1 levels.

Younger patients are likely to need higher doses, as are women, especially those on oral contraceptives, Dr. Molitch said. Patients aged 30-60 years can usually start at 300 mcg/day; dosing should be increased by 100-200 mcg/day every 1-2

months, with a therapeutic target of an IGF-1 level in the upper half of the normal range.

Older patients should be started on 100-200 mcg/day, while those younger than 30 years may benefit from initially higher doses (400-500 mcg/day).

Although no studies have linked growth hormone therapy with malignancies, the guidelines recommend against using the hormone in anyone with an active cancer. There is no evidence that treatment affects the recurrence of pituitary tumors. Patients with diabetes may need adjustments to their diabetes medications when on growth hormone.

The side effects of growth hormone therapy are usually dose-related and can be alleviated by adjusting the medication. The most common are related to fluid retention. These effects occur in up to 18% of patients and include paresthesias, joint stiffness, peripheral edema, arthralgia, and myalgia. Increased blood pressure is sometimes seen, but can be avoided with appropriate dosing.

Therapy offers significant benefits, including a decrease in fat mass and its attendant risk reductions of improved lipid levels and decreased insulin resistence. The modest increases in muscle mass improve exercise tolerance, which in turn has beneficial effects on blood pressure and cardiac function. Patients with childhood-onset growth hormone deficiency also may experience improvements in left ventricular muscle mass and end diastolic volume, as well as stroke volume. Therapy also benefits bone health with both anabolic and antiresorptive effects.

However, no studies have confirmed a mortality benefit with growth hormone therapy, Dr. Molitch said.

"Some do suggest that mortality is increased in those with hypopituitarism, but it's never been proven that hypopituitarism is the cause of this, or that growth hormone decreases it," he said. ■

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