Growth hormone is used to treat twice as many short boys than girls in the US and Asia

April 17 2008

Boys are twice as likely as girls in the U.S. and Asia (mostly Japan) to receive recombinant human growth hormone (rhGH) for growth hormone deficiency, illnesses that affect height, and short stature of a non-medical nature. A smaller gender difference exists in Europe, Australia and New Zealand, but in the rest of the world short boys and girls are treated at the same rate. This indicates a likely cultural bias for male height in some countries.

The study, by researchers from The Children's Hospital of Philadelphia and Pfizer, is electronically available prior to publication in the *Journal of Clinical Endocrinology and Metabolism*.

All children entered in the Pfizer International Growth Study (KIGS), a database designed to document long-term outcomes and safety of Genotropin®, one of the three leading commercial brands of rhGH, were categorized by gender, location, date and age of therapy initiation, and diagnosis. Measures of national health status, health care expenditures, general economic indices and mean adult heights were also compared. Children were categorized into four geographic regions including the U.S., Europe/Australia/New Zealand, Asia and the "Rest of the World."

Recombinant human growth hormone has been available since 1985. "Because reports found more U.S. males receiving rhGH in its first years

of availability, and rhGH use has increased considerably over the past 20 years, we thought it was important to get an up-dated look at the gender-based patterns of use in the U.S. and how they compared to other countries," said Adda Grimberg, M.D., lead author of the study and a pediatric endocrinologist at The Children's Hospital of Philadelphia. "We suspect that social and cultural pressures, combined with financial constraints, contribute to the international differences in the gender distributions of children treated with rhGH."

Historical trends revealed a consistent overall male predominance among U.S. pediatric rhGH recipients at a nearly two-to-one ratio. The gender ratio did not change significantly across the more than 20 years of rhGH use. Males outnumbered females at all ages, especially during the second decade of life. Because boys typically start puberty later than girls and hit their growth spurt at a later stage of puberty, boys who lag behind their peers are more likely to be perceived as having a growth problem.

The factor that most consistently affected the gender distribution was the diagnostic indication for rhGH therapy. The greatest gender disparities occurred for diagnoses without an identifiable cause, such as idiopathic short stature and idiopathic GH deficiency because of the complexity of the diagnostic tests. Prader-Willi syndrome, a genetic disease with multiple benefits from rhGH therapy besides height, was the only indication with gender equality in the U.S. Dr. Grimberg hypothesized, "when the decision to treat involves an indication that relies more heavily on clinical judgment, treatment patterns are more likely to highlight underlying differences in social pressures for tallness."

Comparing the U.S. experience with global patterns revealed that Asia (mostly Japan) had the greatest male predominance at 65 percent, followed closely by the U.S. at 64 percent. Europe/Australia/New Zealand came third at 55 percent. All three world regions exceeded 50 percent males, while the rhGH recipients in the rest of the world regions,

where rhGH is used far less frequently, were 47 percent male. Similar to the U.S. data, global gender distributions of rhGH depended on the specific reason the therapy was initiated. The United Kingdom had the lowest male percentage of the top 10 country-based children prescribed Genotropin®.

Dr. Grimberg's earlier research in referral patterns for growth failure evaluations at a U.S. pediatric endocrinology clinic showed a disturbing statistic: that 41 percent of the girls were found to have an underlying disease that made them short, compared to 15 percent of the boys. Conversely, 38 percent of the boys were within normal height ranges, compared to 20 percent of the girls, and boys were referred for evaluation about twice as often as girls.

A variety of diseases may cause growth failure – among them, hormone deficiencies, Turner syndrome (a chromosome abnormality found only in females) and gastrointestinal conditions such as celiac disease or inflammatory bowel disease. For some, growth failure is the only symptom. "Gender differences in the use of rhGH may be indicative of more general gender differences in the diagnostic rates of diseases that present solely with growth failure," cautioned Dr. Grimberg. Not all of these diseases are treated by rhGH. For example, celiac disease is treated with a gluten-free diet. If a short girl is less likely to be perceived as needing rhGH treatment, she may also be less likely to undergo the diagnostic evaluation that reveals her underlying celiac disease.

The manufacture of rhGH in 1985 changed the treatment of pediatric growth failure. Prior to 1985, only children with the most severe growth hormone deficiency were treated because of the very limited supply of human pituitary GH. In 2003, the U.S. Food & Drug Administration (FDA) approved the use of rhGH for the treatment of idiopathic short stature, for children who are significantly shorter than their peers yet do not have an identifiable underlying disease.

Source: Children's Hospital of Philadelphia