

Combination of two hormones increases height in girls with Turner syndrome

30 March 2011

Giving girls with Turner syndrome low doses of estrogen, as well as growth hormone, years before the onset of puberty, increases their height and offers a wealth of other benefits, say a team of researchers led by Thomas Jefferson University. Their report is published in the March 31st issue of *The New England Journal of Medicine (NEJM)*.

The study, which took more than 20 years to complete, will change the practice of treating girls with [Turner syndrome](#), says the study's lead author, Judith Ross, M.D., professor of Pediatrics at Jefferson Medical College of Thomas Jefferson University and Al DuPont Hospital for Children.

"Our goal is to improve the health and lives of girls and women with Turner syndrome or with other disorders that interrupt normal ovarian function," says Dr. Ross. "This study shows that our strategy accomplishes that."

Currently, most girls with Turner's syndrome receive [estrogen](#) only at the onset of puberty, she says. Turner syndrome, which the National Institutes of Health (NIH) says occurs in 1 out of 2,500 female births worldwide, develops when a female (X) sex chromosome is missing in cells or is abnormal. These girls are typically of short stature and have a loss of ovarian function.

The findings are validation of a theory that Dr. Ross and her colleagues proposed in the *NEJM* 25 years ago. (She was then completing a fellowship at the NIH.) They suggested that typically developing girls produce small amounts of estrogen before puberty, and that in girls with Turner syndrome, a combination of very low doses of estrogen as well as growth hormone would work synergistically to increase height and improve overall cognitive functioning.

"The goal was to mimic what happens with in normal ovarian development, not to induce

puberty," says Dr. Ross.

But the notion was controversial, she adds. "People thought that estrogen use at an early age in these patients could cause growth plates to fuse and to stop development - just as you see in a typically developing teenage girl who has a pubertal growth spurt and then stops growing."

Testing such a theory required a rigorous placebo-controlled clinical trial that could follow girls with Turner syndrome from childhood through adolescence and pubertal development until adult height was attained.

In this study, 149 girls with Turner syndrome, ages 5-12 years old, who were treated at Thomas Jefferson University Hospital or at the National Institutes of Health between 1987 and 2003, were randomized to one of four groups: placebo (no growth hormone or estrogen), growth hormone alone, estrogen alone, or growth hormone and estrogen in combination.

The amount of estrogen administered to girls randomized to receive it was only 1/50th of the dose the girls would be given once they reached puberty, Dr. Ross says.

The study showed that girls who started using the low dose estrogen at the average age of nine and who also used growth hormone grew an average of 3 inches taller than girls who didn't use growth hormone, or girls treated with only low dose estrogen. Girls treated with growth hormone alone were an inch shorter than the combination treatment group. Not only did estrogen increase the girl's height, it also improved psychosocial and [cognitive functioning](#), Dr. Ross says. Once the girls reached puberty, they were all treated with higher doses of estrogen.

According to current standard medical treatment, girls with Turner syndrome are treated with higher

doses of growth hormone, at more frequent intervals, than was used in this study; consequently today's patients are taller than in this study. "It should be noted that adult height within the normal range was attained in 40 percent of growth-hormone-treated patients in this study but in only 4 percent of none-growth-hormone-treated patients," Dr. Ross says. "This research also shows that use of low dose estrogen is synergistic with growth hormone.

"There is a place for estrogen replacement prior to puberty in girls who need it, and we have made the case that replacing it earlier in these children is very beneficial," she says.

The findings may also benefit girls whose ovarian function has been damaged by chemotherapy or surgical removal, or other disorders, Dr. Ross adds.

Provided by Thomas Jefferson University

APA citation: Combination of two hormones increases height in girls with Turner syndrome (2011, March 30) retrieved 19 January 2022 from <https://medicalxpress.com/news/2011-03-combination-hormones-height-girls-turner.html>

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