

Estrogen Treatment of Tall Girls: Dose Dependency of Effects on Subsequent Growth and IGF-1 Levels in Blood

This retrospective study compares the effects of ethinyl estradiol 250, 500, or 1,000 $\mu\text{g}/\text{d}$ given 3 weeks of each 4-week cycle in very tall girls. Each study consisted of 15 to 21 girls who were in the same age range (13.5 ± 1.1 years), with similar bone ages (12.6 ± 0.9 years), similar height predictions (186.2 ± 3.1 cm), and duration of treatment (1.9 ± 0.6 years). Most received a progesterone analogue during the third week of each cycle.

In the 3 groups, the difference between final and predicted height was similar: 5.5 ± 2.7 , 5.9 ± 3.3 , and 5.6 ± 2.7 years. Follow-up of plasma insulin-like growth factor 1 (IGF-1) levels revealed a significant decrease with 500 or 1,000 $\mu\text{g}/\text{d}$ of ethinyl estradiol but not with 250 $\mu\text{g}/\text{d}$.

The authors conclude that a dose of 250 μg of ethinyl estradiol per day for 3 of every 4 weeks is as potent in reducing final height in tall girls as higher doses.

Savan H, et al. *Acta Paediatr Scand* 1991;80:328-332.

Editor's comment: *The use of large doses of estrogen to reduce stature in tall girls was initiated by Wettenhall in 1955 (J Pediatr 1975;86:602). He used diethylstilbestrol with limited success in reducing stature (an average of -3.5 cm), as the girls he treated had epiphyses that were nearly fused to the metaphyses when treatment was initiated (mean bone age, 13.2 years). The value of his*

study was that 87 girls were followed for >15 years. The only toxicity reported was the development of paraovarian cysts in 2 girls and superficial thrombophlebitis in another.

Bierich (Pediatrics 1978;62:1196 and Gynakologe 1983;16:72) reported his experience with 41 girls whose predicted heights were >180 cm. Conjugated estrogen (7.5 mg/d) was used (plus 7 days of progesterone each 28 days). Fifty percent of the girls were menstruating when treatment started. Because skeletal maturation advanced 3.7 times faster than body height, growth retardation as compared with predicted height was -8.3 ± 2.1 cm in the premenarcheal girls and -6.8 ± 1.6 cm in the menarcheal girls. Doses of 0.3 to 0.5 mg/d of ethinyl estradiol produced similar results. No side

effects were observed in relation to high-dose treatment including no increases in triglycerides and cholesterol. However, Weninger et al subsequently reported (Acta Paediatr Scand 1987;76:500) hyperlipidemia in association with ethinyl estradiol therapy at this dose level.

An important question is: Could a smaller dose of ethinyl estradiol be as effective as the usually recommended larger dose? Bartsch et al (Eur J Ped 1988; 147:59) evaluated the use of

0.1 mg/d for 2 years in 25 tall girls. They reported that the reduction in predicted adult height achieved by estrogen treatment averaged 7.4 cm in girls whose bone ages were >12.5 years. They concluded that the higher dosages offer little advantage. Gruters et al (Eur J Ped 1989;149:11) studied 2 comparable groups of tall girls: the first group receiving 0.3 - 0.5 mg/d ethinyl estradiol, and the second 0.1 mg/d ethinyl estradiol. The different doses had similar effects on final height reduction.

The current abstract compares several intermediate doses (0.25, 0.50, and 1.0 mg/d) and concludes that the effects are comparable. The consensus seems to be that doses prescribed to treat tall girls over the past 20 years may be unnecessarily high. A response from the readers through the "Letters to the Editor" column is welcome.

Jean-Claude Job, MD