

Reduced Growth Hormone Secretion With Maintained Periodicity Following Cranial Irradiation in Children With Acute Lymphoblastic Leukaemia

Lannering et al obtained growth hormone (GH) determinations every 20 minutes for 24 hours in a group of 34 children with acute lymphoblastic leukemia (ALL) who had received cranial irradiation with 18 to 24 Gy. These children (12 boys and 22 girls) had been diagnosed 4 to 10 years previously; their mean age at diagnosis was 3.9 years. Fourteen (5 boys and 9 girls) were prepubertal at the time of the study (using Tanner staging). Height was expressed as standard deviation scores (SDS) in comparison with Swedish reference values for healthy children. A control group of 208 children was utilized. The GH profiles were analyzed using the Pulsar pulse detection program and Fourier time-series analysis.

The estimated GH secretion rate in all irradiated ALL children was below the median of that of controls for pubertal stage and sex. The difference between patients and controls was more pronounced in late puberty than before puberty. GH secretion as expressed by the area under the curve was also reduced in irradiated children. However, the number of GH peaks over

24 hours was within the normal range for both boys and girls. Before puberty a broad range of cycles per 24 hours was seen; these synchronized during puberty to approximately 1 every 3 to 4 hours. Lower peak amplitudes were observed in the irradiated children. There was no correlation between time from diagnosis and GH secretion or the maximal GH level during the 24-hour period. There were no obvious influences of the time of diagnosis on GH secretion. Children who were still prepubertal at the time of the study had lost an average of 0.2 SDS. Children who had entered puberty lost an average of 1.0 SDS.

The authors state that their results indicate not only that cranial irradiation in the range of 20 to 24 Gy alters GH secretion (as determined by Moell et al, 1988), but also that irradiation with 18 Gy both before and during puberty reduces GH secretion. Specifically, there was lower pulse amplitude in the irradiated patients, suggesting a physiologic GH insufficiency. Height of the children at a mean follow-up age of 7 years fell within the normal range for the Swedish population. Final heights were not reached in a majority of patients. The authors further state that the impairment observed in growth is small before puberty. The recommendation is made that ALL patients should be studied repeatedly as adults to evaluate the effects of decreased GH secretion on organs other than the growth plate.

Lannering B, et al. *Clin Endocrinol* 1995;42:153-159.

Editor's comment: More and more information regarding the effects of cranial irradiation on pituitary function is becoming known. Although most pediatric endocrinologists recognize that irradiation with 24 Gy could be expected to be associated with pituitary dysfunction, it is not generally felt that lower dosages will be detrimental. However, few investigators have performed the careful type of analysis that Lannering and coworkers presented. Their data suggest that there are indeed significant reductions in GH secretion with smaller doses of radiation that may not be clinically observable (no obvious reduction in stature) until puberty, and that there is little difference between the effects of 18 and 24 Gy. It will be interesting to review final heights in the patients reported in this study. One may then be able to better counsel families whose children have received even modest doses of cranial irradiation.

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