

Hypochondroplasia (HC) treatment with growth hormone (GH): a pilot study of discontinuous, IGF1-dosing regimen.

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BACKGROUND

In patients with HC due to the N540K FGFR3 mutation, adult height spontaneously ranges 138-155 cm (men) and 128-145 cm in women. We previously reported that a mean 75 µg/k.d rGH dose started at 2.6±0.7 yrs of age allowed a gain of 1.9 SD of height over 6.1 yr. This GH dosage was 1.5-2-fold higher than those used in HC. Trunk leg disproportion was improved (SHR decreased from 6.8 to 4.5 SD) but was still grossly abnormal; head circumference remained + 1,8 SD. Bone age gained 1.04 yr per yr. IGF-1 levels averaged 1.3 SD). At age 8.7 yrs, mean height was -1.1 SD.

OBJECTIVES

To report additional data in 4 patients (2 young ones and Two older boys)
To report the evolution of growth rate with advancing age in those children treated in early childhood.
To report final height results in 7/10 children (5 treated in early childhood) and 2/10 treated at 12 and 14.5 yrs of age. in

CONCLUSIONS

rGH treatment in patients with HC

- i) show clearcut positive results when started early
- ii) provided large doses of GH given through a discontinuous regimen are used (serum IGF1 not very high though)
- iii) growth gain is more limited if started in mid-childhood
- iv) cannot maintain growth acceleration at adolescence
- v) seems to end its effect around age 13 yrs.

The current observations are preliminary and should be confirmed in larger studies of this rare chondrodysplasia. This report can serve as a warning for a very early treatment trying to maximize rGH effects in infancy and early childhood.

References

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METHODS

Starting at 1.8-7 yr of age, 10 HC patients received a cumulative dosage of 81±0.009 µg/k.d rGH with repeated planned 6-9 month breaks from treatment and frequent measurements of height, body proportions, and serum IGF1.

At a mean age of 10 yrs of age in 4 girls and 11 yrs in 3 boys, GnRH analogs were used to delay puberty and epiphyseal closure.

RESULTS

Among the first 6 children, 5 were aged 8.1, 8.6, 9.5, 9.6 and 9.9 yrs at the end of the 6.1 yrs of treatment. They started GH at age 2, 2, 3.2, 3.2; 3.3 yrs respectively. Their heights were -1.3, -1.3, -0.8, -1.2, - 1 SD.

Four yrs later, with ages ranging from 12 to 14 yrs, mean height was only -2-2.5 SD from the mean meaning they have not been able to maintain the previously observed acceleration of growth: instead, height loss reached 1 SD approximately between 11 and 13-14 yrs of age, due to the accelerated fusion of epiphyseal plates of the femur and tibia (despite the prescription of GnRH antagonists in 4/6 children. Given the currently low growth rate, we expect the girls to be reaching an adult height of 145-150 cm and the boys 155-158 cm. This remains to be observed.

The younger child, who was only 6.8 yrs old at the end of the first period of observation still has maintained his height at -1 SD at age 10.8.

Four additional children have started treatment at 1.8, 3, 12 and 14.5 yrs. The height of the two older boys was -4SD and -4.5 S at initiation of GH treatment. Both have received GnRH antagonists for 18 months at initiation of GH therapy. They both have reached an adult height at 158 and 154 cm and are no longer growing.

