Leiden University Medical Center

C.A. Hoekx[1], D. Bresters[1], S. Le Cessie[3], C. Scholte[1], W. Oostdijk[1], S.E. Hannema[1]
[1]Dept. of Paediatrics, Leiden University Medical Center, Leiden
[2]Dept. of Ethics and Law, Leiden University Medical Center, Leiden

The effect of growth hormone treatment in children after hematopoietic stem cell transplantation

Introduction

Hematopoietic stem cell transplantation (HSCT) has become more common in treating malignant and non-malignant diseases in children. However, HSCT is associated with several late effects that can affect growth, such as insufficient growth hormone (GH) secretion, growth plate damage and hypogonadism. Growth hormone treatment may improve growth, but limited data are available on its effect on adult height (AH).

Methods

Thirty-four patients who had an HSCT between 1988 and 2010, were treated with GH for ≥ 1 year and had reached AH were included in this retrospective study. Each patient was matched with two control HSCT patients, who did not receive GH treatment, based on [1] indication of HSCT (malignancy, benign hematological or immune deficiency), [2] gender, [3] age at HSCT and [4] total body irradiation (TBI). Information on HSCT, growth and puberty was extracted from the medical files.

Results

Twenty three boys and eleven girls received GH treatment at a standard dose of 1.33 mg/m2/day for a median duration of 3.8 years (range 1.7-9.2). Malignancy was the most common indication for HSCT (82%) and 71% received TBI before HSCT. Growth parameters are shown in table 1.
From the start of GH treatment until AH, height SDS decreased by 0.3 ± 0.9 in GH treated versus 1.0 ± 0.9 SDS in untreated patients (p<0.001). AH was closer to PAH in GH treated children compared to those without GH treatment (difference -0.2 ± 0.8 SDS vs -1.0 ± 1.1 SDS, p<0.001) (figure 1). However AH was below the target height (TH) in both groups (difference -2.0 ± 1.0 SDS vs -1.8 ± 1.0 SDS, p=0.48) (figure 2).
Within the GH treated group boys had lower AH compared to PAH than girls (-0.5 ± 0.7 vs 0.5 ± 0.6, p<0.001) (figure 1). Children treated with TBI had a lower AH compared to PAH than those without TBI (-0.4 ± 0.7 vs 0.4 ± 0.8 SDS, p=0.005) and AH further below TH (-2.4 ± 0.8 vs -1.0 ± 0.6, p=0.001).

Table 1. Patient characteristics and growth data

	GH treated patients (n=34)	Control patients (n=68)	P value
Age at HSCT (years)	6.8 (4.0)	8.2 (3.7)	n.s.
Height at HSCT (SDS)	-1.5 (1.2)	-0.6 (1.4)	P<0.001
Bone age at HSCT (years)	6.1 (3.6)	8.0 (3.4)	P<0.05
Age at start GHRx (equivalent age in non-GH treated) (years)	12.0 (2.6)	12.0 (2.6)	
Height at start GHRx (SDS)	-1.9 (1.1)	-0.7 (1.3)	P<0.001
Bone age at start GHRx (years)	11.3 (2.2)	11.4 (2.6)	n.s.
Duration GHRx[a] (years)	3.8 (1.7 - 9.2)	-	
PAH at start GHRx (SDS)	-2.0 (1.2)	-0.7 (1.4)	P<0.001
Target height (SDS)	-0.2 (1.0)	0.1 (0.9)	n.s.
Adult height (SDS)	-2.2 (1.3)	-1.7 (1.2)	n.s.

Data are presented as mean (SD). [a] median (range), HSCT, hematopoietic stem cell transplantation; GHRx, growth hormone treatment; SDS, standard deviation score

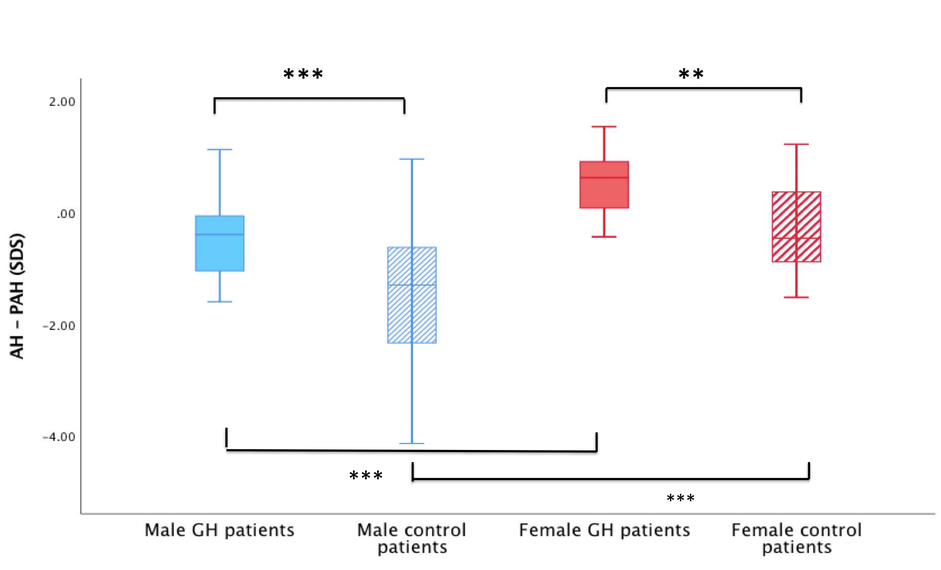

Fig. 1 Difference between AH and PAH at start GH treatment in boys and girls with GH treatment compared to control patients without GH treatment. ** p<0.01 *** p<0.001

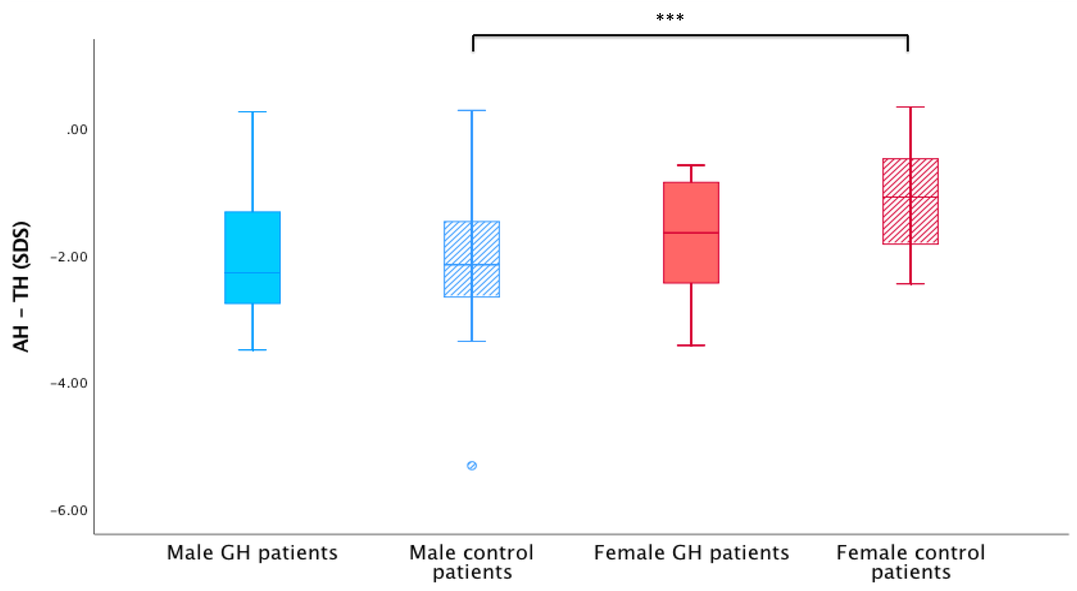

Fig. 2 Difference between AH and TH in boys and girls with GH treatment compared to control patients without GH treatment. *** p<0.001

Discussion and conclusions

Without GH treatment a height loss of 1 SDS was observed following HSCT, which is similar to findings from other studies [1-2]. GH treatment reduces this height loss and results in an AH closer to PAH. This confirms the positive impact of GH found by others [1-4]. However, AH was lower than previously reported which may be related to lower height SDS at HSCT and lower TH. Boys had a lower AH compared to PAH and TH than girls, in line with previous studies [3,4]. The cause of this gender difference is unclear but might be related to differentially affected pubertal growth, differences in pubertal induction or possibly in adherence to GH treatment. TBI was associated with lower AH compared to PAH and TH consistent with its detrimental effects on both the growth plate and the endocrine system.
In conclusion, GH treatment improves AH in children with impaired growth after HSCT although AH remains far below TH.

References

1. Bakker B, et al. Growth hormone (GH) secretion and response to GH therapy after total body irradiation and haematopoietic stem cell transplantation during childhood. Clin. Endocrinol. 2007;67(4):589-97..
2. Frisk P, et al. Pubertal development and final height after autologous bone marrow transplantation for acute lymphoblastic leukaemia. Bone Marrow Transplant. 2004;33(2):205-10.
3. Sanders JE, et al. Final adult height of patients who received hematopoietic cell transplantation in childhood. Blood. 2005;105(3):1348-54.
4. Isfan F, et al. Growth hormone treatment impact on growth rate and final height of patients who received HSCT with TBI or/and cranial irradiation in childhood: a report from the French Leukaemia Long-Term Follow-Up Study (LEA). Bone Marrow Transplant. 2012;47(5):684-93

57ESPE 156--P1
GH and IGFs
Sabine Hannema
Poster presented at: 57th ESPE 2018 Meeting ATHENS GREECE 27-29 September 2018