Anorexie mentale de l'enfant: efficacité du traitement par l'hormone de croissance dans les formes avec atteinte sévère de la croissance

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Introduction

- Anorexia nervosa (AN), a state of chronic nutritional deprivation prevalent in children and young adolescents, is associated with major changes to the hypothalamic-pituitary axis including the GH-IGF-I axis, thyroid function, hypercortisolemia and hypogonadotropic-hypogonadism, with delayed puberty and a low height velocity (HV) at a time critical for the pubertal growth spurt, potentially affecting adult height.
- After nutritional and mental improvements, reports describing catch-up growth range from complete catch-up growth of less frequently failure to gain any height. We previously have shown that about 1/3 of girls with severe early onset AN have a risk of adult height deficit (Rose C et al; Clin Endocrinol 2007). Patients may take several years to recover, and physical and mental disorders may persist into early adulthood. Therefore, these patients have limited time window for potentially effective treatment to improve HV.

- The effects of supraphysiological human GH on HV and improvement on adult height are currently unknown.

Aim of the Study

We aimed to investigate the effect of hGH on HV and until adult height in children with AN and profound height velocity impairment.

Patients and Methods

Ten girls diagnosed with AN (DSM IV) at a mean chronological age of 10.0 ± 1.9 years were treated for severe prolonged height failure (HV< 2 cm/yr for at least 18 months) at a mean age of 13.3 ± 1.1 years and a bone age of 10.9 ± 1.7 years, Tanner stage I (n=7), II (n =1) or III (n =2), and 2.0 years after the lowest reached BMI (SDS), with open-label hGH until adult height was achieved.

The initial characteristics of these patients and auxological data are shown in Table I and II.

Table I - Pre therapy clinical characteristics of the 10 girls with AN included in the study

Age at onset of AN (yrs)	10.0±1.9
Lowest BMI reached (SDS)	-3.1 ±1.1
Age at lowest BMI reached (yrs)	12.3 ±1.6
Duration of hospitalization before study entry (w)	30.4 ±20.0*
Use of overnight nasogastric feeding (w)	4 (40%)
Associated comorbidity	9 patients [depression (n=5), anxiety (n=7), obsessive-compulsive disorder (n=3)]

* Never hospitalized n=1 - Results are expressed as mean (±SD)

Results

A significant increase in HV directly attributed to GH therapy was observed in all children, resulting in adult height close to target height after a mean duration of GH treatment of 3.9 ± 1.9 years, with no side effects.
IGF-I concentration normalized without exceeding the reference ranges.

	Baseline	+1 yr	+2 yrs	Adult height
HV cm/yr	1.5 ± 1.2	7.8 ± 2.4*	5.8 ± 3.3*	
Height cm	141.7±8.9	149.3±8.1	153.2±7.5	161.2±4.6
Height SDS	-2.2±1.3	-1.6±1.3	-1.2±1.6	-0.2±0.9*
Height - Target Height SDS	-2.6±1.3	-2.0±1.2	-1.7±1.4	-0.6±0.9*

*p< 0.001 vs baseline

Table II - Individual patient characteristics before and during rhGH therapy (mean ± SD)

	Baseline							Duration treatment (years)	GH dose (µg/kg/d) start-end	Last evaluation at adult height				
	Age at start (years)	BMI SDS	Pubertal status	Bone Age (years)	HV (cm/y)	Height (cm)	Height SDS			Adult Height (cm)	Adult Height SDS	Target Height (SDS)	BMI SDS end	Menarche (age (years) at M+)
1	14.2	-1.2	B1	11.5	0.9	149.9	-1.6	4.6	26 - 37	165.5	0.4	2.3	-1.4	Mo
2	13.0	-0.6	B3	13.0	2.7	145.7	-1.6	2.1	49 - 36	154.5	-1.2	-0.3	-0.8	M+ (14.5)
3	11.0	-1.5	B1	8.8	1.0	135.0	-1.0	3.7	29 - 31	163.0	0.5	-0.2	0.4	M+ (13.0)
4	12.6	0.2	B1	10.0	0.5	136.0	-2.5	3.3	41- 32	166.9	0.7	0.1	0.9	Mo
5	13.8	-0.2	B2	11.5	4.0	139.0	-3.3	4.1	37 - 47	154.7	-1.5	-1.7	-1.8	M+ (16.7)
6	14.0	-1.1	B1	12.0	0.7	148.0	-2.0	2.8	27 - 26	163.5	0.1	1.2	0.4	Mo
7	12.3	-0.8	B1	8.8	0.9	133.0	-2.7	5.9	44 - 42	159.8	-0.6	0.3	-3.2	Mo
8	13.6	-0.2	B1	8.8	0.0	127.0	-5.2	4.5	34 - 35	157.5	-1.0	-0.1	-1.5	M+ (17.4)
9	15.1	-1.3	B3	13.0	2.1	152.0	-1.6	1.0	38 - 33	160.2	-0.5	1.4	0.7	M+ (15.9)
10	13.3	-1.1	B1	12.0	2.0	152.5	-0.7	1.9	32 - 27	166.5	0.9	1.2	-1.6	Mo
Total	13.3±1.1	-0.8 ±0.6	B1 (n=7) B2 (n=1) B3 (n=2)	10.9±1.7	1.5±1.2	141.7±8.9	-2.2±1.3	3.9±1.9	37.0 - 35.0	161.2±4.6	-0.2±0.9	0.4±1.1	-0.8±1.3	M+ 15.5±1.8

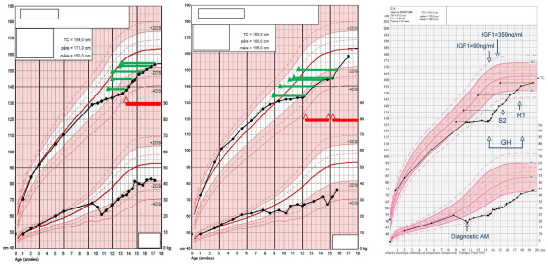

Figure 5
Growth curve in three patients (n° 5, 7, 8). The curves clearly show the positive effect of GH treatment.

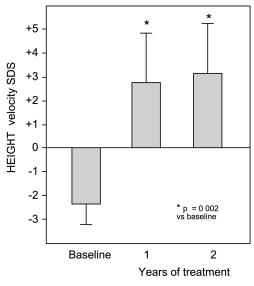

Figure 1
Mean (± SD) annual height velocity (SDS) for chronological age in 10 patients with AN just before and following 1 and 2 years of hGH treatment.

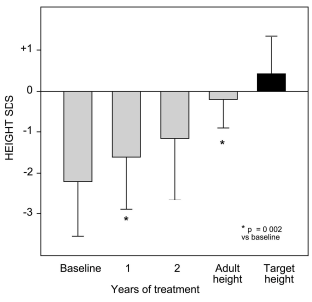

Figure 2
Mean (± SD) height SDS in 10 patients with AN at baseline, following 1 and 2 years after the start of hGH treatment and at adult height.

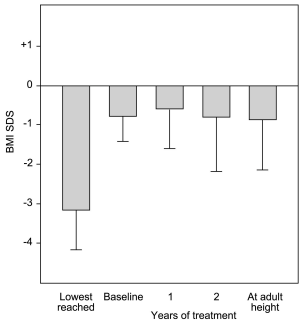

Figure 3
Mean (± SD) Body Mass Index (BMI) SDS in 10 girls with AN before and during GH treatment.

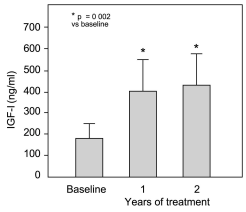

Figure 4:
Effects of GH therapy on serum IGF-I levels in all patients.

Summary

After onset of GH treatment, height velocity and serum IGF-I concentrations significantly increased leading to improvement of height and near normalization of adult height in all patients.

Conclusions

Our pilot, proof of concept study provide a promising treatment to improve height velocity and adult height in severely growth affected children and adolescents with AN.
A randomized controlled trial vs placebo is now required to determine the ultimate impact of GH treatment in this severe and rare condition.

No conflict of interests