Screening for Growth Hormone Deficiency in Three-year-old Children

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Abstract. We attempted to clarify the efficacy of GH treatment in three-year-old children with GH deficiency. Over 10,000 children aged three were evaluated for their height SD scores at public health centers during 1990 and 1991. Children with height SD scores of less than $-2SD$ were advised to visit children's hospitals. GH secretion was assessed in 19 children by the responses to insulin and arginine, and by GH levels during three hours' sleep. GH treatment was applied in 16 children based on the criteria of the Foundation of Growth Science in Japan. Eight children were treated with hGH for one year. Their height SD scores improved from -3.14 ± 0.83 to -2.17 ± 0.69 ($p < 0.001$).

The results did not show the frequency of GH deficiency among three-year-old children, but of those who were found and treated, their height SD scores improved. Longer-term studies may clarify the benefit of GH treatment initiated at an early age.

Key words: GH deficiency, screening

Introduction

Therapeutic options have increased for short children through the commercial availability of biosynthetic hGH. Though hGH treatment may be more effective for achieving normal height when used in early childhood, there is no generally accepted method for the early detection of GH-deficient children.

We screened short children at their three year medical check and evaluated GH secretion according to the criteria of the Foundation of Growth Science in Japan [1].

Subjects and Methods

The subjects were children who visited a Public Health Center for a three year medical check-up during 1990 and 1991. Children whose height was below -2 SD of the mean were advised to visit children's hospitals. At the first visit, complete blood count, blood chemistry, urinalysis, F-T4, TSH and IGF-I levels were examined.

After confirming normal thyroid function, GH secretion was assessed by insulin ($0.1U/kg$ iv) and arginine ($0.5g/kg$ iv) loading tests (criterion 1), and by the mean GH levels during the first three hours of sleep (criterion 2).

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Patients were treated with biosynthetic recombinant hGH at a total of 0.5U/week, given by five to seven divided sc injections.

Results

GH secretion was examined in 19 out of 24 children who visited the hospital. Table 1 shows the clinical data. Their height SD score was -3.00 ± 0.57 (mean $\pm$ 1SD), and the range was -2.24 to -4.42 . In all cases both

parents were shorter than the average adult Japanese height.

Table 2 shows the peak GH levels after pharmacologic provocation tests. Four patients showed complete GH deficiency and eight had partial deficiency. Table 3 shows the results as defined by criterion 2. One patient showed neurosecretary dysfunction. A summary of the criteria is shown in Table 4. HGH treatment was started in 16 out of 19 short children, of whom eight have already been under treatment for one year. Their

Table 1. Patient data

No.	sex	Age	Height(H)	SD	Father's H	Mother's H
1	F	3yr 3mo	84.0cm	-3.80	172cm	152cm
2	M	3	88.5	-2.31	156	153
3	F	3	86.3	-2.81	169	145
4	F	3	87.1	-2.54	171	150
5	M	3	89.2	-2.38	167	162
6	M	3	86.3	-3.01	172	156
7	M	3	82.3	-4.42	162	153
8	F	3	90.2	-2.69	165	157
9	F	3	86.7	-2.64	165	153
10	M	3	86.1	-3.07	161	151
11	M	3	84.6	-3.54	163	148
12	F	3	86.7	-3.26	166	153
13	M	3	85.5	-3.57	168	154
14	F	3	85.8	-3.14	170	143
15	F	3	88.4	-2.29	160	155
16	F	3	92.2	-2.24	167	148
17	M	3	85.6	-3.07	172	145
18	F	3	85.8	-3.14	167	148
19	F	3	85.0	-3.07	172	151
mean	3	4		-3.00	167	151
SD				0.57	5	5

Table 2. Criterion for GH Therapy (1)

No.	GH(peak)		score	total
	insulin	arginine		
1	1.7ng/ml	3.3ng/ml	4+4	8
2	6.1	5.3	4+4	8
3	1.8	5.5	4+4	8
4	4.0	6.7	4+4	8
5	4.8	7.4	4+3	7
6	7.5	7.3	3+3	6
7	8.6	7.5	3+3	6
8	9.2	7.2	3+3	6
9	8.2	8.4	3+3	6
10	8.2	7.7	3+3	6
11	8.1	7.7	3+3	6
12	8.2	8.4	3+3	6
13	21.0	8.6	0+3	3
14	10.4	2.2	0+4	4
15	16.0	3.6	0+4	4
16	12.5	2.9	0+4	4
17	17.0	3.2	0+4	4
18	13.1	9.7	0+3	3
19	10.6	10.7	0+0	0

Table 3. Criterion for GH Therapy (2)

No.	Perinatal Abnormality	mean GH (sleep) (ng/ml)	urine GH (pg/mgCr)	IGF-I (U/ml, ng/ml •)	BA/CA %	score
1	+(1)	1.8(3)	ND	0.24	31(1)	5
2	-(0)	4.1(3)	ND	0.38	82(0)	3
3	-(0)	3.2(3)	27(0)	0.26	59(1)	4
4	-(0)	3.0(3)	4(1)	0.42	47(1)	5
5	-(0)	4.2(2)	27(0)	1.32	62(1)	3
6	-(0)	4.2(2)	ND	0.19	46(1)	3
7	-(0)	3.5(3)	ND	0.11	45(1)	4
8	-(0)	6.3(0)	33(0)	0.51	49(1)	1
9	-(0)	5.3(0)	15(0)	0.84	46(1)	1
10	-(0)	2.8(3)	ND	0.41	38(1)	4
11	-(0)	5.4(0)	ND	0.47	46(1)	1
12	-(0)	5.1(0)	46(0)	0.84	46(1)	1
13	+(1)	3.1(3)	ND	0.78	64(1)	5
14	-(0)	3.1(3)	ND	0.21	60(1)	4
15	-(0)	4.0(3)	12(0)	0.77	60(1)	4
16	-(0)	4.6(2)	29(0)	62.1 *	65(1)	3
17	-(0)	5.6(0)	ND	0.89	39(1)	1
18	-(0)	7.0(0)	40(0)	0.48	69(1)	1
19	-(0)	2.8(3)	36(0)	79.0 *	55(1)	4

ND: not done.

Table 4. Criteria for GH Therapy

No.	Criterion(1)	Criterion(2)	Evaluation
1	8	5	therapy
2	8	3	therapy
3	8	3	therapy
4	8	5	therapy
5	7	4	therapy
6	6	3	therapy
7	6	4	therapy
8	6	1	therapy
9	6	1	therapy
10	6	4	therapy
11	6	1	therapy
12	6	1	therapy
13	3	5	therapy
14	4	4	therapy(6mo)
15	4	4	therapy(6mo)
16	4	3	therapy(6mo)
17	4	1	follow-up
18	3	1	follow-up
19	0	4	follow-up

Screening for Growth Hormone Deficiency

Fig 1. Height SD score changes after 1 year of hGH treatment.

height SD scores were significantly improved from -3.14 to -2.17 ($p < 0.001$) (Fig.1). There was no significant difference in improvement of the height SD scores between patients with complete or partial GH deficiency.

Discussion

HGH is now easily obtainable because of advances in biosynthetic techniques. Several studies have documented the beneficial effects of hGH treatment in short children who do not meet the criteria for GH deficiency [2]. This raises the question: is the early diagnosis

of GH deficiency important? Screening for GH deficiency was performed at the age of three; of 24 short children who were investigated, 16 were found to be GH-deficient; HGH therapy proved effective for these patients. Josefsberg *et al.* [3] reported a greater effect of hGH therapy in children below five years of age. There are few reports about the early detection of GH deficiency, and we attempted to evaluate a screening program for this. Our results also showed an early improvement of height SD scores within one year of treatment. Longer-term experience may confirm the usefulness of the three year medical check at public health centers.

References

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