P2-P175

The impact of Growth hormone treatment in patients with Noonan syndrome and growth hormone deficiency

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Disclosure of conflict of interest None of the authors have any conflict of interest to disclose.

INTRODUCTION

- Noonan syndrome (NS) is a genetic disorder characterized by specific features including short stature, cardiac defect, and distinctive facial dysmorphism.
- Human growth hormone (GH) has been used to improve growth in children with NS but there is little information how GH treatment affects height.
- The aim of this study is to investigate efficacy of GH treatment in Korean children with NS compared to sex and age-matched patients with growth hormone deficiency (GHD).

METHODS

•Seventeen prepubertal children (10 boys, 7 girls) with NS who received rhGH therapy for at least 3 years between 2008 and 2015 were included.

•The recombinant human was administered at a dose of 33–66 μg/kg/day for 6 days a week subcutaneously.

•We analyzed height and height velocity before and during GH treatment. The height and height velocity were compared with children with GH deficiency (n=31) matched for age, sex as a control group.

Table 1. Baseline characteristics and comparison of the rhGH response in patients with NS and GHD

	NS (N=17)	GHD (N=31)	p-value
Age (year)	6.35 ± 2.32	6.35 ± 1.84	0.996
Sex (Male: Female)	10:7	22:9	0.524
Height SDS	-2.63 ± 0.73	-2.24 ± 0.40	0.050
BMI SDS	-0.34 ± 1.14	-0.26 ± 1.06	0.811
IGF-1 SDS	-0.27 ± 1.09	-0.56 ± 1.06	0.371
Bone age (year)	5.22 ± 1.93	4.77 ± 1.60	0.416
BA-CA	-1.35 ± 0.95	-1.57 ± 0.64	0.417
Height SDS			
1st	-1.85 ± 0.90	-1.41 ± 0.43	0.073
2nd	-1.44 ± 0.96	-1.06 ± 0.41	0.148
3rd	-1.25 ± 0.89*	-0.77 ± 0.45*	0.060
Δ height SDS	1.42 ± 0.61	1.47 ± 0.46	0.800
Growth velocity (cm)			
1st	8.8 ± 1.9	9.3 ± 1.7	0.372
2nd	7.4 ± 1.1	6.9 ± 1.2	0.240
3rd	6.7 ± 1.1	6.8 ± 1.8	0.902
GH dose (ug/kg/d)	44.7 ± 6.8	30.7 ± 1.6	<0.001

RESULTS

•Mean age of patients with NS was 6.34 ± 2.32 years.

•Mutations in PTPN11, RAF1, and SHOC2 genes were identified in 11 (64.7%), 1 (5.8%), and 1 patient (5.8%), respectively; no mutations were found in 4 patients (23.5%).

•Height standard deviation score (SDS) in patients with NS increased from -2.64 ± 0.73 before starting treatment to -1.24 ± 0.89 after treatment ($P < .001$). Height SDS in patients with GHD increased from -2.24 ± 0.40 before starting treatment to -0.77 ± 0.45 after treatment. There were no significant differences in growth velocity or change in height SDS with rhGH therapy between patients with NS and GHD (Table 1).

•There were no significant differences in clinical or laboratory findings between patients with and without *PTPN11* mutation at the start of rhGH therapy (Table 2).

Table 2. Baseline and treatment data according to the mutation type for patients with NS

	Non-PTPN11* (N=6)	PTPN11 (N=11)	p-value
Age (year)	7.07 ± 2.86	5.96 ± 2.02	0.362
Sex (Male: Female)	3: 3	7: 4	0.643
Height SDS	-3.00 ± 0.99	-2.44 ± 0.48	0.129
Weight SDS	-2.43 ± 0.63	- 1.89 ± 1.39	0.388
BMI SDS	-0.46 ± 0.37	-0.27 ± 1.41	0.748
IGF-1 SDS	-0.83 ± 1.45	0.04 ± 0.75	0.116
Bone age (year)	6.18 ± 2.19	4.86 ± 1.80	0.254
BA-CA	-2.06 ± 1.15	-1.09 ± 0.77	0.080
Height SDS			
1st	-2.50 ± 1.00	-1.49 ± 0.63	0.023
2nd	-2.07 ± 1.06	-1.08 ± 0.75	0.041
3rd	-1.71 ± 1.04	-0.94 ± 0.68	0.084
Δ height SDS	1.25 ± 0.82	1.53 ± 0.46	0.400
Growth velocity (cm)			
1st	7.3 ± 2.0	9.6 ± 2.8	0.013
2nd	7.4 ± 1.4	7.3 ± 1.0	0.909
3rd	6.9 ± 1.6	6.5 ± 0.8	0.589
GH dose (ug/kg/d)	41.0 ± 0.7	46.7 ± 5.5	0.097

* Non-PTPN11 group included patients for which PTPN11 mutations was not found.

CONCLUSION

- The rhGH therapy in patients with NS increased height SDS and growth velocity after 3 years of treatment.
- Also, the response to rhGH therapy was similar between patients with NS and GHD.
- Our study provides evidence that rhGH therapy is very helpful to promote growth in these patients.

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