GROWTH HORMONE DEFICIENCY IN NOONAN SYNDROME: DOES IT INFLUENCE CLINICAL RESPONSE TO GH THERAPY?

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Background

Short stature is a main feature of Noonan syndrome. Although rhGH is commonly administrated in Noonan syndrome patients, it is not known whether a defect in GH secretion influences the response to rhGH therapy.

Objective and hypotheses

The aim of this study was to evaluate the efficacy and safety of rhGH treatment in Noonan syndrome patients, according to the presence of GH deficiency at the baseline.

Method

We retrospectively collected data of 35 patients with Noonan syndrome. Genetic test was positive in 29 cases (25 with PTPN11 mutation). Before starting treatment with rhGH, at an average dose of 0.031±0.005 mg/kg/day, patients undertook GH secretion test after stimulation. With normal secretion test (peak >8 ng/ml), rhGH was administered off-label. Height was expressed as Standard Deviation Score (SDS) according to chronological age calculated using the Italian National Growth Charts. Growth was evaluated as change in height (Delta-Height-SDS) at one, two and three years after the start of therapy.

Results

At the baseline 13 patients had a deficiency of GH secretion (GHD), while 22 showed no failure (NoGHD). The two groups were homogeneous for baseline characteristics (except for GH peak, Table 1).

The mean follow-up time was 2.5±0.8 years.

Therapy with rhGH was effective in improving linear growth in the entire population (Figure 1) with one third of patients with height>-2SDS after three years of therapy. Between the two groups we found no significant difference in growth at 1, 2 and 3 years from baseline (Figure 2). No difference was found according to the presence of PTPN11 mutation (Figure 3). As persistent side effects, insulin resistance (HOMA-IR>2.5) was reported in 5 subjects (GHD: 3, 23.1%; NoGHD: 2, 9.1%).

	Total	GHD	No GHD	
	n=35	n=13	n=22	p
Age (year)	9.1 ± 3.3	7.9 ± 3.4	9.8 ± 3.1	0.11
Gender (M, %)	18 (51%)	5 (39%)	13 (59%)	0.31
Puberal (%)	6 (18%)	2 (15%)	4 (18%)	1.00
Height (SDS)	-3.08 ± 0.86	-3.07 ± 0.87	-3.10 ± 0.87	0.75
Target Height (SDS)	-0.49 ± 1.09	-0.32 ± 1.20	-0.58 ± 1.05	0.77
Underline chronic disese (%)	4 (11%)	0 (0%)	4 (18%)	0.27
GH peak (ng/ml)	8.5 ± 3.1	5.5 ± 1.1	10.4 ± 2.3	< 0.0001
IGF-1 (low level, %)	20 (57%)	7 (54%)	13 (59%)	1.00
Bone age delay (year)	1.7 ± 1.3	1.2 ± 1.1	2.1 ± 1.4	0.07
GH dosage (mcg/kg/day)	30.9 ± 5.1	32.4 ± 3.5	30.0 ± 5.7	0.06

Table 1: Baseline characteristics of the studied pupulations

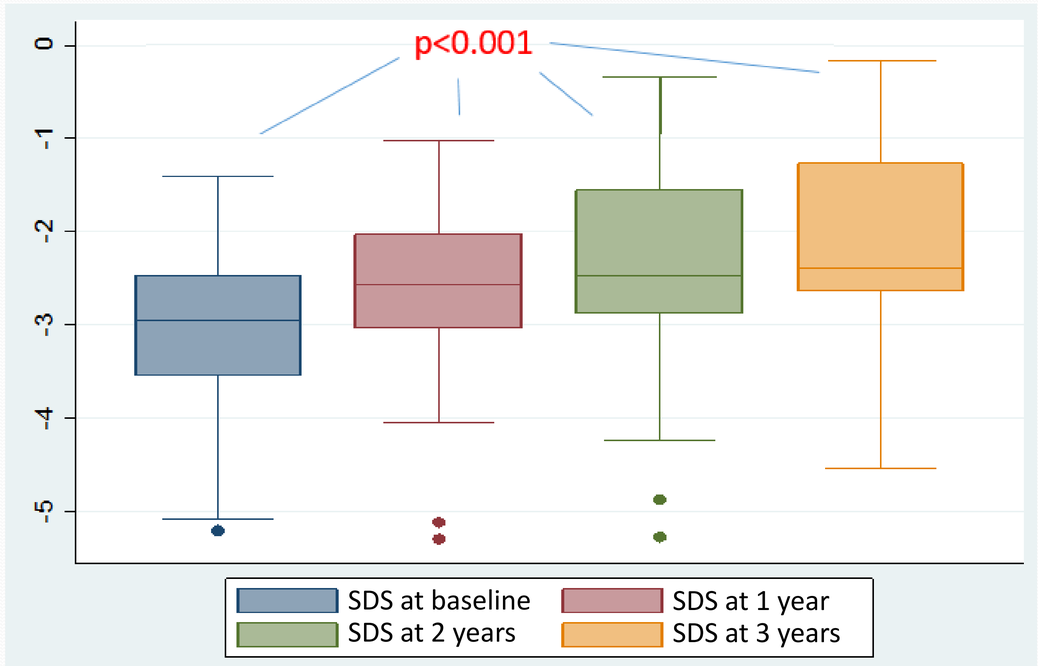
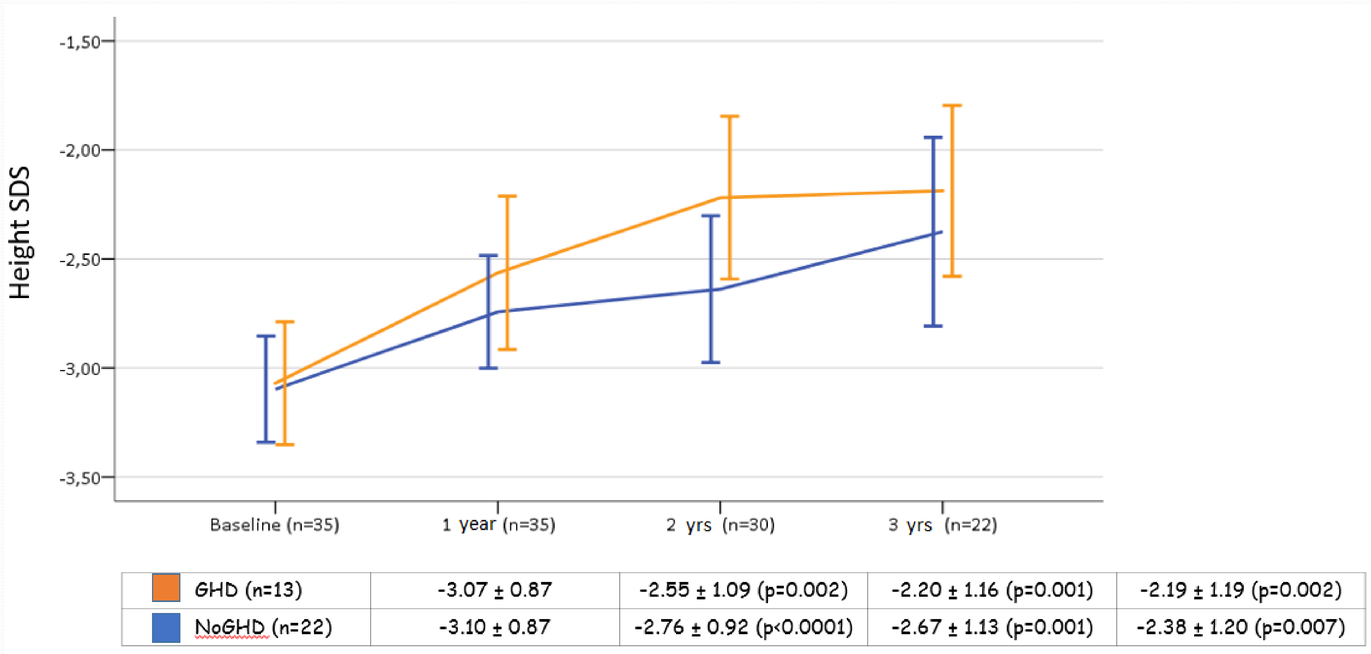


Figure 1: Growth (height SDS) in the entire population



GHD (n=13)	-3.07 ± 0.87	-2.55 ± 1.09 (p=0.002)	-2.20 ± 1.16 (p=0.001)	-2.19 ± 1.19 (p=0.002)
NoGHD (n=22)	-3.10 ± 0.87	-2.76 ± 0.92 (p<0.0001)	-2.67 ± 1.13 (p=0.001)	-2.38 ± 1.20 (p=0.007)

Figure 2: Growth in the two groups (GHD: growth hormone deficiency)

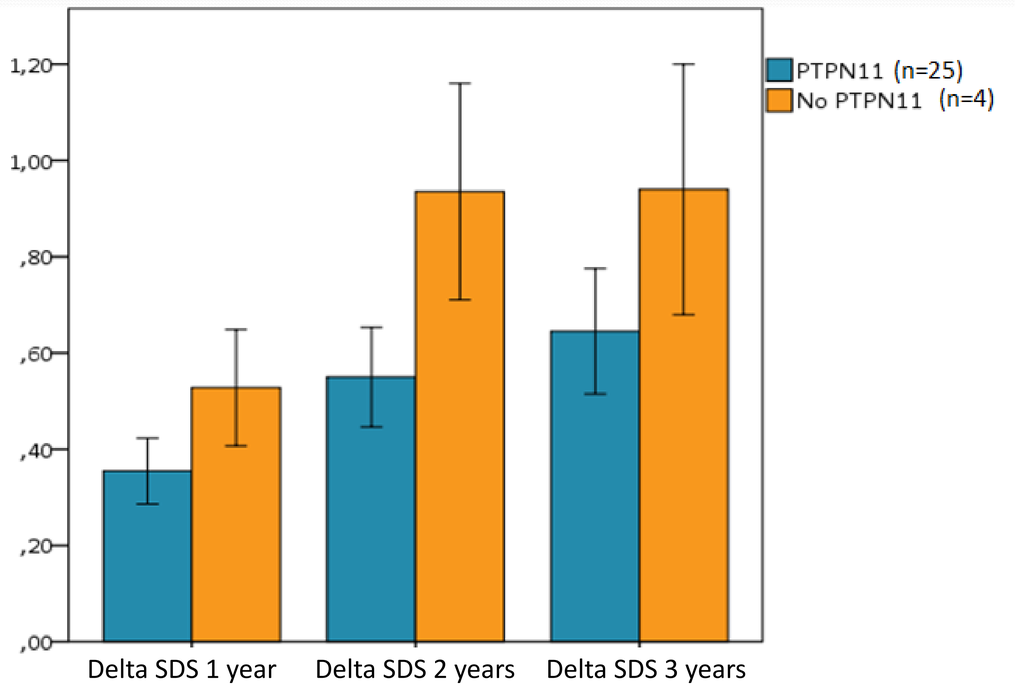


Figure 3: Changes in height standard deviation scores according to presence of PTPN11 mutation

Conclusions

Therapy with rhGH significantly increases growth in patients with Noonan syndrome, regardless of the initial presence of a GH deficiency and in the absence of significant side effects even in subjects with normal stimulation test.

Reference list

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