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Small for gestational age patients in real-life, French clinical practice: what is the difference between good and poor responders to growth hormone treatment?

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Objective

To investigate whether the criteria suggested as predictors of a good response to growth hormone treatment in short children born small for gestational age were, in fact, predictive, based on real-life, ongoing French registry data.

Introduction

- Optimisation and individualisation of growth hormone (GH) treatment in children born small for gestational age (SGA), with growth retardation, is an issue.
- Prediction models, to assess the statural response to treatment, have been developed from large observational studies.[1] Good response to GH treatment is defined as final adult height (FAH) standard deviation score (SDS) >–2.
- Based on available data, the known criteria for a good response in GH deficiency (GHD) are: age and height at treatment start, target height, GH dose and first year treatment response.[2]
- The best predictors in the SGA model during 3 years of follow-up were: GH dose, weight at the start of treatment, mid-parental height SDS and age at treatment start (for age, there was an inverse association).[3]

Methods

- Between 2005 and 2010, 291 children born SGA, treated with Norditropin® (somatropin; Novo Nordisk A/S), were included in a prospective, observational French registry which followed all patients treated with Norditropin® for this indication.
- All patients participated in follow-up until they reached FAH.
- The study is ongoing.
- Of the 90 patients who completed the study, 51 were GH-naïve and were stratified as poor and good responders according to observed FAH SDS ≤–2 or >–2, respectively.
- The criteria that were addressed and compared can be seen in **Table 1**.
- Analysis was descriptive. Student's t-test was used to compare mean quantitative data (standard deviation [SD]) (p-value) and Wilson's test was used to establish 95% intervals for proportions of qualitative data.

Results

- Of the 291 patients, 183 were GH-naïve.
- The mean (SD) treatment duration was 4.4 (2.2) years and for the 90 patients who reached FAH, it was 5.3 (2.2) years.
- To date, 51 GH-naïve patients have completed the study (good responders: 31; poor responders: 20).
- Patient characteristics are presented in **Table 1**.
- A significant difference was observed for the following characteristics in good versus poor responders (data are shown in **Table 1**):
  - Height SDS at treatment start: p=0.0006.
  - Age (years) at treatment start: p=0.0490.
  - Growth velocity SDS 1 year before treatment: p=0.0446.
- A positive trend was observed for the following characteristics:
  - Target height SDS: p=0.0857.
  - Growth velocity SDS in the first year of treatment: p=0.0780.
  - Change in height SDS ≥+0.5 (% patients): p=0.0845.
- Good responders were taller and younger at the beginning of treatment, with better growth velocity in the year preceding treatment.
- There was a trend towards greater growth velocity in the first year of treatment in good responders compared with poor responders.

Table 1 ♦ Patient characteristics: poor and good responders to GH treatment

Parameter	*Statistics*	*Poor responders FAH SDS ≤–2 (N=20)*	*Good responders FAH SDS >–2 (N=31)*	*Good vs. poor responders p-value*
Weight and/or height at birth				
SDS <–2	n (%)	13 (76.5%)	22 (73.3%)	1.0000
	[95% CI]	[52.7%; 90.4%]	[55.6%; 85.8%]	
SDS ≥–2	n (%)	4 (23.5%)	8 (26.7%)	
	[95% CI]	[9.6%; 47.3%]	[14.2%; 44.4%]	
Weight SDS at birth	Mean (SD)	–1.7 (0.6)	–1.5 (1.0)	0.3696
	[95% CI]	[–2.0; –1.4]	[–1.8; –1.1]	
	Median	–1.7	–1.2	
Height SDS at birth	Mean (SD)	–2.5 (0.6)	–2.4 (1.0)	0.8126
	[95% CI]	[–2.8; –2.1]	[–2.8; –2.0]	
Height SDS at treatment start	Mean (SD)	–3.2 (0.4)	–2.7 (0.5)	0.0006
	[95% CI]	[–3.4; –3.0]	[–2.8; –2.5]	
Target height SDS	Mean (SD)	–0.8 (1.0)	–1.3 (0.8)	0.0857
	[95% CI]	[–1.3; –0.4]	[–1.6; –1.0]	
Age at treatment start (years)	Mean (SD)	11.4 (2.2)	10.0 (2.5)	0.0490
	[95% CI]	[10.4; 12.5]	[9.1; 11.0]	
Growth velocity SDS 1 year before GH treatment	Mean (SD)	–1.8 (1.8)	–0.01 (2.1)	0.0446
	[95% CI]	[–3.1; –0.4]	[–1.1; 1.1]	
GH dose at treatment initiation (mg/kg/day)	Mean (SD)	0.039 (0.007)	0.041 (0.010)	0.4270
	[95% CI]	[0.036; 0.043]	[0.038; 0.045]	
GH dose at treatment initiation in classes (mg/kg/day)				
<0.032 (0.035–10%)	n (%)	0 (0.0%)	3 (9.7%)	
	[95% CI]	[0.0%; 16.8%]	[3.3%; 24.9%]	
[0.032; 0.038] (0.035±10%)	n (%)	13 (68.4%)	14 (45.2%)	0.1707
	[95% CI]	[46.0%; 84.6%]	[29.2%; 62.2%]	
>0.038 (0.035+10%)	n (%)	6 (31.6%)	14 (45.2%)	
	[95% CI]	[15.4%; 54.0%]	[29.2%; 62.2%]	
Growth velocity SDS in the first year of treatment	Mean (SD)	1.35 (1.77)	2.33 (1.98)	0.0780
	[95% CI]	[0.52; 2.17]	[1.59; 3.07]	
Δ height SDS in the first year of treatment in classes				
SDS <+1	n (%)	10 (50.0%)	8 (26.7%)	0.1341
	[95% CI]	[29.9%; 70.1%]	[14.2%; 44.4%]	
SDS ≥+1	n (%)	10 (50.0%)	22 (73.3%)	
	[95% CI]	[29.9%; 70.1%]	[55.6%; 85.8%]	
Δ height SDS in the first year of treatment	Mean (SD)	0.42 (0.43)	0.58 (0.32)	0.1247
	[95% CI]	[0.21; 0.62]	[0.46; 0.70]	
Δ height SDS in the first year of treatment in classes				
SDS <+0.5	n (%)	12 (60.0%)	10 (33.3%)	0.0845
	[95% CI]	[38.7%; 78.1%]	[19.2%; 51.2%]	
SDS ≥+0.5	n (%)	8 (40.0%)	20 (66.7%)	
	[95% CI]	[21.9%; 61.3%]	[48.8%; 80.8%]	
GH treatment duration (months)	Mean (SD)	54.55 (19.18)	59.80 (15.53)	0.3044
	[95% CI]	[45.01; 64.09]	[54.01; 65.60]	
GH cumulative dose (mg/kg)	Mean (SD)	58.15 (35.83)	58.58 (27.31)	0.9633
	[95% CI]	[39.73; 76.57]	[48.20; 68.97]	

Δ, change in; FAH, final adult height; GH, growth hormone; CI, confidence interval; SD, standard deviation; SDS, standard deviation score.

Conclusion

- Prospective, observational French registry data show that some of the criteria for a good response to treatment in GHD could also be applicable to patients born SGA, treated with Norditropin®, and useful for clinical practice.
- Nevertheless, the observational design of the study, and the small sample size of patients, could limit the power of analysis.
- Further investigations with more patients completing the study, and additional observational studies, are needed.

References

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Conflict of interest disclosures

MN, RC, BL and JPS are members of the Scientific Committee of, and investigators for, the SGA Registry. EH and BV are employees of Novo Nordisk.

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