

Linear Growth and BMI during Growth Hormone Treatment of Children with Craniopharyngioma Compared to other Organic Growth Hormone Deficiencies: The National Cooperative Growth Study Experience

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Background

Craniopharyngioma (CP) is a benign childhood parasellar tumor that often requires radiation and/or surgical resection. Children treated for craniopharyngioma will generally require recombinant human growth hormone (rhGH) supplementation due to hypothalamic and/or pituitary dysfunction.

The National Cooperative Growth Study (NCGS) contains over 20 years of data on the use of rhGH therapy in children. It includes rhGH dosing and anthropometric data from patients with craniopharyngioma and other organic growth hormone deficiencies (OGHD), as well as other pathologies requiring treatment with rhGH.

Objective

To describe linear growth and body mass index (BMI) changes during the first five years of rhGH therapy in NCGS patients with craniopharyngioma and to compare these measures with those in NCGS patients with other types of OGHD.

Methods

Study Population

- **Age:** 2 years through 14 years of age, pre-pubertal males and females.
- **Target Disease/Population:** Patients with craniopharyngioma treated by surgery, irradiation or a combination of both, subsequently treated with rhGH.
- The other OGHD group consists of congenital or acquired causes of GHD, including a central nervous system (CNS) congenital anomaly, CNS tumor (excluding medulloblastoma), head trauma, or CNS infection.
- **Setting:** Longitudinal data entered into the NCGS registry for at least 5 years from initiation of rhGH treatment between 1985 and June, 2006.

Exclusion Criteria

- Patients were excluded if they met any of the following criteria:
 - Prior rhGH therapy at the time of registry enrollment.
 - Lack of longitudinal data entered and/or insufficient baseline data recorded in registry for analysis.

Limitations

- NCGS registry data do not discriminate between the extent or site of CP surgical resection or the amount or site of tumor irradiation.
- NCGS registry data do not specify how many years have lapsed between CP treatment and rhGH initiation.

Results

Baseline Data

	Craniopharyngioma % or Mean \pm SD (n)	Other OGHD % or Mean \pm SD (n)
Sex, % Male	61% (104 of 170)	66% (795 of 1,206)
Baseline Age	7.8 \pm 2.9 yrs (170)*	7.2 \pm 3.0 yrs (1,206)
Baseline Bone Age	6.1 \pm 2.7 yrs (94)*	5.3 \pm 2.8 yrs (659)
Baseline Height SDS	-2.0 \pm 1.3 (170)**	-2.8 \pm 1.3 (1,206)
Prior Height Velocity	3.8 \pm 2.9 cm/yr (118)	4.1 \pm 2.7 cm/yr (820)
Baseline Weight-for-Age SDS	-0.4 \pm 1.6 (170)**	-2.0 \pm 1.8 (1,206)
Baseline BMI SDS	1.0 \pm 1.2 (170)**	0.0 \pm 1.3 (1,206)
% of Patients with BMI SDS >2	24% (40 of 170)**	6% (70 of 1,206)
Tanner Target Height SDS	-0.1 \pm 0.8 (114)	-0.1 \pm 0.7 (884)

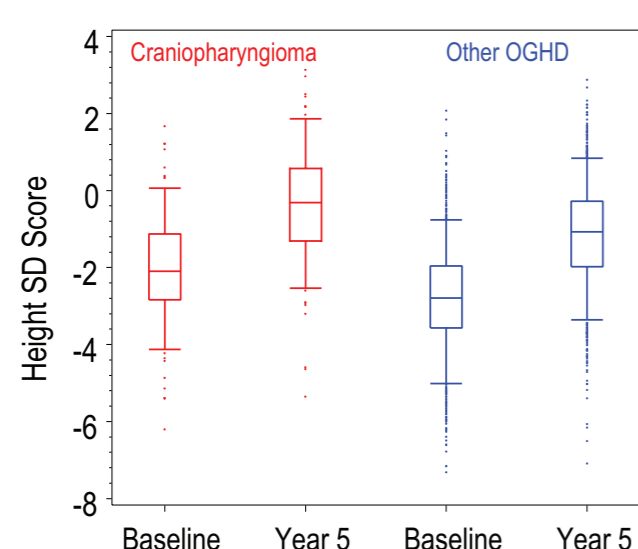
*P <0.05 vs. other OGHD
**P <0.0001 vs. other OGHD

Data at Five Years

	Craniopharyngioma % or Mean \pm SD (n)	Other OGHD % or Mean \pm SD (n)
Average Dose over 5 years	0.25 \pm 0.07 mg/kg/wk (91)**	0.29 \pm 0.06 mg/kg/wk (599)
Height SDS at 5 years	-0.3 \pm 1.4 (170)**	-1.1 \pm 1.3 (1,206)
Weight-for-Age SDS at 5 years	0.8 \pm 1.5 (170)**	-0.5 \pm 1.6 (1,206)
BMI SDS at 5 years	1.1 \pm 1.2 (170)**	0.1 \pm 1.3 (1,206)
% of Patients with BMI SDS >2	25% (43 of 170)**	6% (76 of 1,206)
Five-Year Change in Height	37.4 \pm 7.7 cm (170)*	36.1 \pm 7.4 cm (1,206)
Five-Year Change in Height SDS	1.7 \pm 1.2 (170)	1.7 \pm 1.2 (1,206)
Five-Year Change in Weight-for-Age SDS	1.1 \pm 1.1 (170)*	1.5 \pm 1.4 (1,206)
Five-Year Change in BMI SDS	0.0 \pm 0.8 (170)	0.1 \pm 1.0 (1,206)

*P <0.05 vs. other OGHD
**P <0.0001 vs. other OGHD

Figure 1: NCGS Naïve Pre-Pubertal Patients
Baseline and Year 5 Height SD Score
Patients with Craniopharyngioma and with other OGHD



Horizontal lines in each box plot define the 5th, 25th, 50th, 75th and 95th percentiles.

Figure 2: NCGS Naïve Pre-Pubertal Patients
With Craniopharyngioma
Year 5 BMI SD Score vs. Baseline BMI SD Score

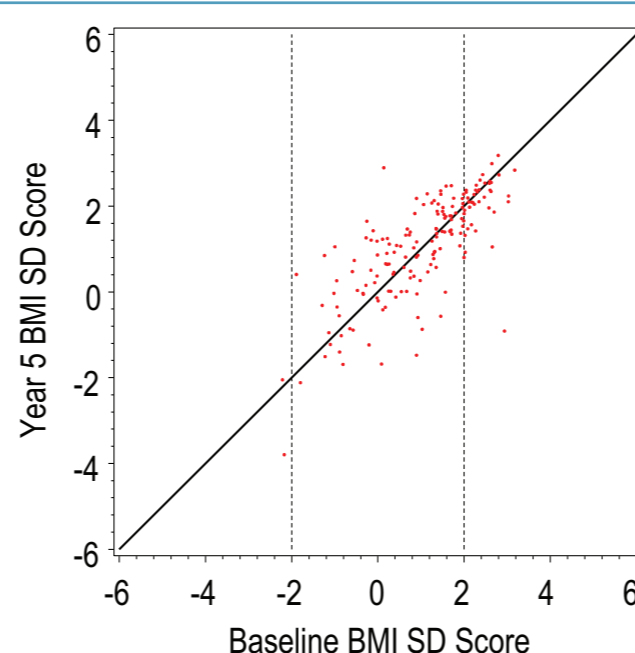
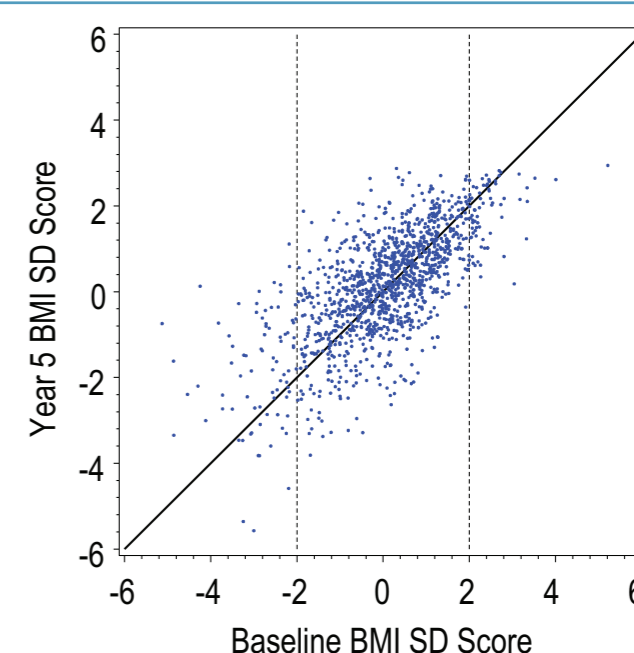


Figure 3: NCGS Naïve Pre-Pubertal Patients
Other OGHD (without Craniopharyngioma)
Year 5 BMI SD Score vs. Baseline BMI SD Score



Summary

- CP patients tended to be slightly older with higher BMI at baseline.
- CP patients had a greater mean height SDS both at baseline and at 5 years compared with other OGHD patients.
- CP patients had notably greater mean BMI SDS both at baseline and at 5 years compared with other OGHD patients. Little or no BMI benefit was evidenced in CP with rhGH therapy.
- Mean changes in height-for-age SDS, weight-for-age SDS and BMI SDS over 5 years of rhGH therapy were similar in the two groups.

Summary (continued)

- The linear growth response to 5 years of rhGH therapy was similar in the two groups, despite the fact that the CP group had a notably greater mean height SDS and BMI SDS at baseline.
- Other studies of CP patients place the incidence of hypothalamic obesity at 50-70%.¹ The majority of CP patients in NCGS do not appear to have hypothalamic obesity based on BMI.

Reference

¹Lustig R, Post SR, Srivannaboon K et al. J Clin Endocrinol Metab 88:611-616, 2003.