Results of growth hormone treatment in childhood brain tumors survivors

Mazerkina NA[1], Gorelyshev SK[1], Geludkova OG[2].

[1]Burdenko Neurosurgery Institute and [2]Research Institute for Pediatric Hematology, Moscow, Russia

Background

GH deficiency is the most common endocrine abnormality in childhood brain tumours survivors. It may occur as the result of a tumor's direct effect on hypothalamic and pituitary structures or as the result of surgical or radiation treatment. Craniospinal radiation is included in treatment protocols of many malignant tumors. Although exogenous GH is frequently used to treat the short stature, these patients have great variability in their response to GH therapy.

Materials and methods

118 patients with GHD after brain tumor treatment:

72 Craniopharyngioma (CP), 17 germ cell tumors (GCT), 29 medulloblastoma (MB) (Table 1)

At start of the treatment mean chronological age was 13.2±3.2 yrs, bone age 10.8±2.4 yrs, remission 2.8±1.4 yrs, height SDS -2.8±1.2

All patients received substitution GH treatment (Rastan, JSC «Pharmstandard» manufactured, Russia) in dose 0.03-0.034 mg/kg/day

Patients with pituitary deficiency received hydrocortison, L-thyroxine and desmopressin

Methods:

-Anthropometric data

-GH stimulation tests (clonidine, insulin, glucagon) before treatment

- IGF-1 level before and during treatment

- Statistical analysis was done using STATSTICA 8.0, all data in mean±SD. Students's T-test and Kruskal-Wallis ANOVA tests were used for comparison between groups

Objectives

To evaluate the effectiveness and safety of GH treatment in patients with childhood brain tumours.

Results

-Growth velocity was significantly increased on GH treatment: in CP group from 2.3 to 9.4 cm/yr ($p<0.001$), GCT group from 1.2 to 7.4 cm/yr ($p=0.01$), MB group from 2.3 to 6.3 cm/yr ($p<0.01$) (Table 2).

- Growth velocity on GH treatment was significantly ($p<0.01$) higher in CP patients, than GCT and MB patients (Pic1).

-Regression analysis revealed that effectiveness of GH therapy was affected by chemotherapy treatment ($P<0.05$) and CSI ($p<0.01$) growth velocity in patients treated with CSI was 5.9 cm/yr, in patients without CSI - 9.6 cm/yr. (Pic 2).

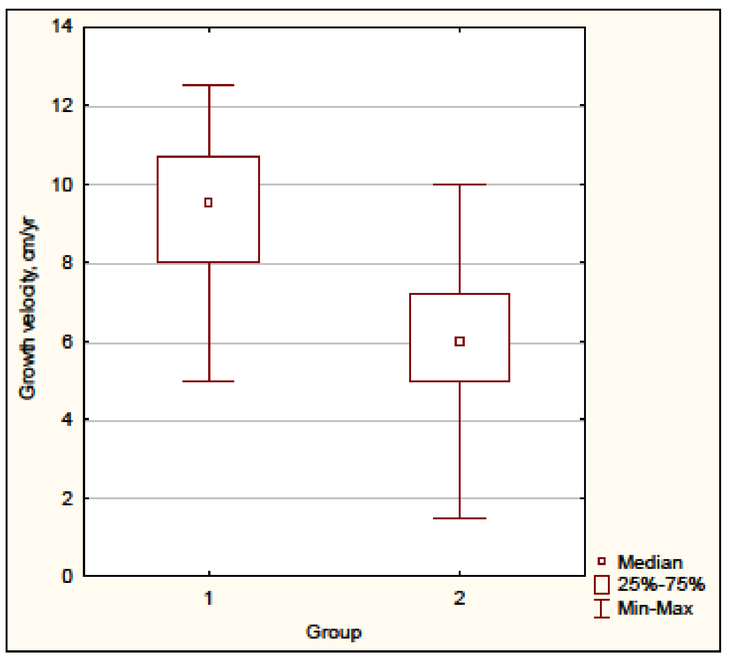
- Despite higher GH dose and IGF-1 level during GH treatment MB patients had worse growth response than CP and GCT patients: Height SDS increased +0.7 SD in CP and GCT and didn't improve in MB after 1st yr treatment (Table 2).

-One MB patient developed epileptic seizures during the 1st month of GH therapy

-There were no tumor recurrence GCT group during GH treatment,

- 1/29 MB patient relapsed after 5.4 years tumor treatment and 1.9 years of GH treatment

- Tumor recurrence in CP group was 29% (21/72 pts), which was similar to untreated group.



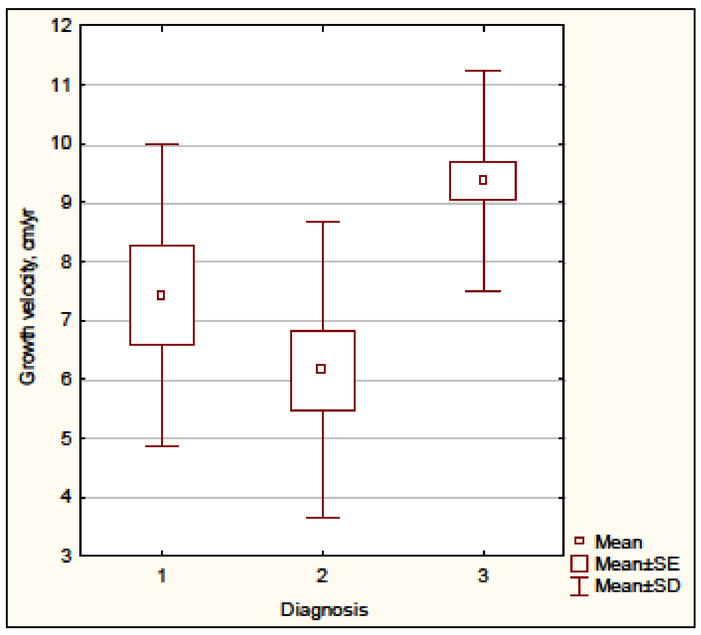
Pic.2 Growth velocity on GH treatment in patients with brain tumors.
Groups: 1 - no CSI, 2 - CSI 24-35 Gy1

	CP (n=72)	GCT (n=17)	MB (n=29)
Surgery	31 – transnasal removal 33 transcranial removal 12- stereotaxic Omaya	6 – stereotax biopsy 7 – transcran biopsy 4 – no surgery	All – transcranial removal
Radiation therapy	18 – LI 42-56 Gy	All – LI 24-55 Gy 5 – CSI 24 Gy	All- LI 55 Gy All CSI – 35 Gy
Chemotherapy	none	4 cycles PE-regimen VP-16 + CDDP	8 cycles VCR+CDDP + CCNU
Remission, yrs	2.1 ± 2.6	2.2 ±1.2	3.4±2.1
Age, yrs	12.1 ± 3.2	13.2± 2.4	12.8±2.1
BA, yrs	9.1 ± 2.2	10.7 ± 2.1	11.9±2.5
Height SDS	-2.7± 1.3	-3.2 ± 1.4	-2.1 ± 1.2
Growth velocity before GH, cm/yr	2.3 ± 1.6	1.2 ± 0.9	2.3±1.5
Tanner stage	70 pts -1 2 pts -2	All -1	17 pts -1 12 pts -2
GH peak on tests, ng/ml	2.2±1.1	2.1±1.3	3.9±1.7
IGF-1, SDS	-2.9±1.4	-3.0±1.2	-2.1±1.5

Table 1. All data in Mean ± SD
CP – craniopharyngioma, **GCT** – germ cell tumor, **MB** – medulloblastoma, **LI** – local irradiation, **CrI** – cranial irradiation, **CSI** – craniospinal irradiation, **ChT** - chemotherapy

	CP (n=35)	GCT (n=15)	MB (n=18)	p
GH treatment dose, mg/kg/day	0.03 ± 0.003	0.033 ± 0.003	0.034± 0.003	<0.05
Growth velocity 1ST yr GH treatment	9.4 ± 1.9	7.4 ±2.6	6.2±2.6	<0.01
IGF-1 1ST yr GH treatment, ng/ml	-0.4±1.1	0.1±0.9	1.1±1.1	<0.05
Δ Height SDS after 1st yr GH treatment	+0.7± 0.2	+0.7 ± 0.1	0.0 ± 0.1	<0.01

Table 2 All data in Mean ± SD
CP- craniopharyngioma, **GCT** – germ cell tumor, **MB** - medulloblastoma



Pic.1 Growth velocity on GH treatment in patients with brain tumors.
Groups: 1 – **GCT**, 2 – **MB**, 3- **CP**

Conclusions

-GH treatment in GHD patients with brain tumors significantly increase growth velocity

- CP patients have better response to GH therapy, than GCT and MB patients

-Despite higher GH doses MB patients had worse GH treatment results, than GCT and CP patients

- Spinal irradiation is the most prominent factor causing poor growth response to GH treatment in childhood brain tumor survivors

- Chemotherapy may be additional risk factor for poor response to GH therapy in childhood brain tumor survivors

- There is no data of increase of tumor recurrence while GH treatment in patients with brain tumors

References

1. Adan l., Sainte-Rose C., Souberbielle J.C., et al. Adult height after growth hormone (GH) treatment for growth hormone deficiency due to cranial irradiation. Med Pediatr Oncol; 2000, 34, 14-19.
2. Brownstein C.M., Mertens A.C., Mitby P.A., et al. Factors that affect final height and change in height standard deviation scores in survivors of childhood cancer treated with growth hormone: A report from the Childhood Cancer Survival Study. J Clin Endocrinol Metab; 2004, 89, 4422-4427
3. Gleeson H.K., Stoeter R., Ogilvy-Stuart A.L., et al. Improvements in final height over 25 years in growth hormone (GH)-deficient childhood survivors of brain tumors receiving GH replacement. J Clin Endocrinol Metab; 2003, 88, 3682-3689
4. Swerdlow A.J., Reddingus R.E., Higgins C.D., et al. Growth hormone treatment of children with brain tumors and risk of tumor recurrence. J Clin Endocrinol Metab; 2000, 85, 4444-4449

JSC "Pharmstandart", Russia

ESPE 2015
814--P3
Misc 1
Nadia Mazerkina
DOI: 10.3252/pso.eu.54espe.2015
Poster presented at: 54th Annual Meeting 1-3 October ESPE 2015 BARCELONA European Society for Paediatric Endocrinology