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Research Article

The Value of Replacement Therapy with Genetically Engineered Growth Hormone Djintropin in Patients with Pituitary Adenomas after Selective Hypophysectomy

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Abstract

The need for this study is based on the International Recommendations for the treatment of growth hormone deficiency (GHD) in adults (2007), since the lack of GHR substitution has many complications, including after transnasal adenomectomy of the pituitary gland.

Aim: The aim of the study was to study the clinical efficacy (normalization of quality of life and GH level) and the tolerability of genetically engineered growth hormone Gentropine (Europharm) in case of somatotropic insufficiency after selective pituitary adenomectomy in patients with pituitary adenomas.

Material and Methods of Investigation: Patients - men (n = 10) and women (n = 3) - aged 2 to 55 years) who were on a stationary and outpatient examination in the RSMPS Endocrinology of the Ministry of Health of the Republic of Uzbekistan named by Acad. J.H. Turakulov, were selected in a group of patients with diagnosed somatotropic insufficiency (n = 13) and received treatment with the study drug Jintropin for 6 months.

Results of the Study: Against the backdrop of GY "JINTROPIN" substitution therapy, there was a significant increase in baseline low IGF-1 and GH levels in the blood ($p < 0.05$) after 3 months of treatment, and an increase in STH ($p < 0.05$) at 6 months. Evaluation of the change in anthropometric indicators against the background of ongoing therapy GR "JINTROPIN" showed the normalization of QoL AGHD: 10.2 ± 2.5 points (over a 6-month period).

Keywords: Growth Hormone Deficiency (GHD) in Adults; Postsurgery Hypopituitarism; Therapy by Growth Hormone

Relevance

Growth Hormone Deficiency Syndrome (GHD) is a well-defined clinical condition in adults, causing abnormalities in metabolism, body structure, physical and psychosocial functions, which improve after replacement therapy with genetically engineered GH [1-4, 8].

According to prof. Grossman A.B. (2005), the frequency of hypopituitarism reaches from 12 to 42 new cases per 1,000,000 population every year and there is an increase in prevalence (300-455 cases per 1,000,000 [5].

According to data from a multicenter study conducted from 2008 to 2011, devoted to the study of cardiovascular risk markers with DGR in 80 patients (from 18 to 25 years old) with non-secretory pituitary tumors, after transsphenoidal pituitary adenomectomy (TAG) - in the early postoperative period in these patients, unlike those who were not subjected to TAG, were observed markers of cardio-vascular risk: dyslipidemia, increased CRP, IL6, homocysteine [19].

Numerous triple studies have shown that GHD in adults significantly aggravates the course of the disease and affects both quality

and longevity in patients with pituitary adenomas after surgical or radiation therapy [6,7,9,16-18].

According to neuroendocrinologists from the UK [14], who studied the efficacy of GH therapy in the postoperative period for 5 years in patients with GHD due to NFPA - non-functional pituitary adenomas (42 patients), Cushing's disease and prolactinoma, the need to treat GHD in this category of patients was confirmed.

KIMS Publications (Pfizer International Metabolic Database) expands on previous clinical trial data confirming that adults with GHD have an unfavorable cardiovascular risk profile [18].

All of the above emphasizes the relevance of this study. The aim of the study was to study the clinical efficacy and tolerability of the genetically engineered growth hormone Djintropin (Europharm) in somatotropic insufficiency after selective pituitary adenomectomy in patients with pituitary adenomas.

Material and Research Methods

Patients - men (n = 10) and women (n = 3) - at the age of 2 to 55 years old, who were on inpatient and outpatient examinations at RSNPMC Endocrinology of the Ministry of Health of the Republic of Uzbekistan named Acad. Y.H. Turakulov of Ministry of Health of the Republic of Uzbekistan, were selected in the group of patients with diagnosed somatotropic insufficiency (n = 13) and received treatment with the drug Djintropin for 6 months. This study was carried out with the support of the EuroFarm pharmaceutical company.

The following spectrum of studies was performed on the patients before, in the dynamics and at the end of the study: 1) anthropometric indicators: standing height, proportionality index, weight, SDS height and weight, BMI: 2) general clinical studies: complete blood count, urinalysis 3) biochemical analyzes: lipid spectrum, calcium, phosphorus, total protein in the blood, ALT, AST, bilirubin, creatinine, alkaline phosphatase, cancer embryonic antigen) instrumental examinations: MRI or CT of the pituitary gland, 5) hormonal examinations: blood STH, IGF-1, TSH, LH, FSH, ACTH, cortisol - in the blood, 6) oculist consultation: examination of the fundus and visual fields for all colors, 7) questioning using the questionnaire for assessing the quality of life of adults with GDR QoLAGHD

Scheme of the administration of medicine. Patients in the study group received the drug Dzhintropin for 6 months under the control of objective examination data. The dose of the drug was prescribed at the rate of 0.033 mg/kg/day, daily s/c, at bedtime (21-22.00).

The Results of the Study and their Discussion

Table 1 shows the distribution of patients by sex and age. From table 1 it can be seen that the majority of patients were over 16 years old - 11 observations (84.6%).

The age, years	The number of women	The number of men	Total
2 - 4	-	2	2
16 - 29	1	5	6
30 - 44	1	1	2
45 - 59	1	2	3
60 - 74	-	-	-
75 и ст.	-	-	-
total: n = 13	3	10	13

Table 1: The distribution of patients by sex and age (according to WHO).

According to the etiology, the patients were distributed as follows: NFPA - 7, BIC -1, craniopharyngioma (CF) - 5. All patients were subjected to TAG, of which 2 + radiation therapy (1 with CF and 1 with NFPA). The diagnosis of GHD was established on the basis of indicators of the level of STH, IGF-1, as well as determining the deficit of basal values of another 2-3 tropic hormones. All patients had multiple deficiency of adenohypophysis hormone (MDAH).

An analysis of the initial anthropometric indicators revealed a harmonious development: the ratio of the upper and lower segments, the average value of BMI are within normal values. Against the background of the therapy, the normal proportions of the body remain. The growth rate after 6 months of treatment did not change, while the BMI decreased from 31.38 ± 0.9 to 25.6 ± 0.3 kg/m2. In addition, the weight significantly decreased, as well as the OT, OA, OT/OB indicators - after 6 months of treatment of GH.

Next, we studied the dynamics of indicators of the questionnaire Qo: L AGHD e 13 operated patients 3 months and 6 months after

the TAG operation and hormonal data. These data are presented in tables 2 and 3.

As can be seen from the data presented in Tables 2 and 3, in 13 patients, after 3 months and 6 months after TSE, a decrease in

The number of patients	Average score before TAG	Average score after TAG	STH before TAG	STH after TAG	IGF-1 before TAG	IFG-1 after TAG
(n= 13)	23,0 ± 3,2	14,4 ± 3,4	0,11 ± 0,03	1,13 ± 0,04	84,10 ± 11,6	154,3 ± 22,6
Control	7,3 ± 0,4	7,3 ± 0,4				
Norm	< 11 б	< 11 б	2-5 ng/ml		134 - 836 ng/ml	
P	> 0,05	< 0,05	< 0,05		< 0,05	

Table 2: Dynamics of indicators of the QoL AGHD questionnaire for assessing the quality of life of 13 operated patients and hormonal data 3 months after the TAG operation.

Note: P - significance of differences with control, before and after surgery

Number of patients	Average score 3 months after TAG	Average score 6 months after TAG	STH 3 months after TAG	STH 6 months after TAG	IGF -1 3 months after TAG	IGF -1 6 months after TAG
(n= 13)	14,4 ± 3,4	10,2 ± 2,5	1,13 ± 0,04	2,03 ± 0,05	154,3 ± 22,6	208,9 ± 21,3
Control	7,3 ± 0,4	7,3 ± 0,4				
Norm	< 11 б	< 11 б	2 - 5 ng/ml		134 - 836 ng/ml	
P	> 0,05	< 0,05	< 0,05		< 0,05	

Table 3: Dynamics of indicators of the QoL AGHD questionnaire for assessing the quality of life of 13 operated patients and hormonal data 6 months after the TAG operation.

Note: P - significance of differences with control, before and after surgery

the average score was observed in the AGR questionnaire against the background of a significant increase in the mean GH and IGF-1 values.

Conclusions

- Assessment of changes in anthropometric indices against the background of the therapy with growth hormone "Djintropin" showed the normalization of life quality indicators on the QoL AGHD questionnaire: 10.2 ± 2.5 points (over a period of 6 months).
- Against the background of the replacement therapy for GR "Djintropin", a significant increase in the initial low values of the levels of IGF-1, GH in the blood ($p < 0.05$) after 3 months of treatment, as well as an increase in GH ($p < 0.05$) after 6 months.

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