HORMONAL CHARACTERISTICS OF RECURRENT ACTH-SECRETING PITUITARY ADENOMAS


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**Introduction:** Cushing's disease (CD) remission after primary surgical treatment is achieved in 70-90%, but recurrence are ranges 18-25% after neurosurgery.

**The aim** of this work to study clinical, hormonal and MRI indicators before and after surgical treatment in patients with recurrent CD to identify possible predictors of recurrence.

**Subjects:** 49 patients with CD (3 men and 48 women aged from 20 to 54 (mean 29.8±12.3) years) in the active stage. The disease duration was up to 3 years. On MRI there were 69.9% microadenomas and in 30.1% Macroadenomas.

**Methods:** Cortisol and ACTH levels in peripheral blood, the concentration of cortisol in saliva and in daily urine were determined by automated system Cobas 601, Roche. Blood samples were taken at 8 a.m. and 11 p.m. to study the diurnal rhythm and to calculate the average daily levels, the sample of saliva was taken at 11 p.m.

**Results:**

Before neurosurgery the average daily ACTH (median 80.0 pg/ml) and cortisol (median 689.5 nmol/l) in blood, free cortisol level in daily urine (median 1336.5 nmol/24h) and the evening free cortisol in saliva (median 18.4 nmol/l) were increased. ACTH levels were correlated with the tumors volume: in patients with microadenomas 69.7±17.3 (52.2-82.9) pg/ml, in patients with macroadenomas 89.9±47.5 (56.3-259.0) pg/ml (p=0.6750, p=0.00000).

Results of small test with dexamethasone (SD2DST) at all patients were negative: a median of decrease in concentration of cortisol for 26.4% (from 8.2 to 35.9%). High dose dexamethasone test (HDDST) was positive at most of patients (65.3%); cortisol level decreased 74.7% (45.2-92.1%). The exception was made by 17 patients (34.7%) (decrease in level of cortisol by 23.0% (12.7-34.5%). At part of patients (24 patients, including at patients from negative HDDST) the selective blood sampling from petrolous sinuses at desmopressin stimulation for an exception of the ACTH-ectopic syndrome has been carried out. The received results have confirmed the central genesis of a hypercortisolism: the tumor was on the left side at 4 patients (A), on the right side - at 9 patients (B), 11 patients have bilateral tumors (C).

According to the results of surgical treatment patients were divided into 2 groups.

1st group – 19 patients (38.8%) had the remission, from them 15 patients had adrenal insufficiency (AI). In 4 patients AI was absent. After remission lasted from 3 to 3.9 years. We observed recurrence of CD. The remission was longer in all patients with AI.

2nd group - 30 patients (61.2%) the remission was not achieved. All of patients underwent the 2nd neurosurgery.

In the group with remission there were a significant decrease ACTH and cortisol concentrations in the early postoperative period (7-10 days) and the normalization of rhythm. ACTH and cortisol levels were markedly decreased in the subgroup with AI.

Cortisol levels reduction in patients with AI was more significant (up to 75%) in HDDST before the operation. All of the patients of 2nd group had negative response after HDDST.

**Conclusion:**

Predictors of longer CD remission can be:

- A more pronounced cortisol reduction during HDDST before the operation
- The presence of AI after the operation
- The average ACTH level below 10.0 pg/ml after surgery