SURGICAL TREATMENT OF PITUITARY ADENOMAS VIA THE TRANS-SPHENOIDAL ROUTE IN UZBEKISTAN

Pituitary adenomas, noncancerous tumors that occur in the pituitary gland, represent from 7% to 24% of all primary intracranial neoplasms. Worldwide the trans-sphenoidal approach is the preferred and more widely spread one. The work was initiated to study early and late complications in patients undergoing surgical treatment for pituitary adenomas via the trans-sphenoidal route at the Neuroendocrinology Department with pituitary neurosurgery, Center for the Scientific and Clinical Study of Endocrinology, Uzbekistan Public Health Ministry.

Keywords: Complication, pituitary adenomas, neurosurgery, trans-sphenoidal approach

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Introduction

Pituitary adenomas, noncancerous tumors that occur in the pituitary gland, represent from 7% to 24% of all primary intracranial neoplasms occurring in persons of both sexes more frequently in the middle age; 75% of the tumors fall at the active working age and have various clinical presentations depending on their hormonal and proliferative activity (Asa, 2009; Chang, 2000). An estimated prevalence of pituitary adenomas is 16.7%; 14.4% in autopsy studies and 22.5% in radiologic studies (Ezzat, 2004). Studies in Switzerland, Belgium and the United Kingdom demonstrated that the pituitary adenoma prevalence is from 78 to 94 cases per 100,000 of population, that is, 3-5 times higher than that previously thought. Data from Northern Finland shows that the overall standardized rate of incidence has increased by 4 cases per 100,000 of population (Karavitaki, 2012).

Worldwide the trans-sphenoidal approach, sometimes called trans-sphenoidal pituitary hypophysectomy, is the preferred and more widely spread one (Goudakos, 2011; Kumar, 2012; Locatelli, 2013; Winder, 2011; Yang, 2012). Of all publications on the pituitary neurosurgery trans-sphenoidal and transcranial approaches are reported to be used in 70% and 12%, respectively, a combination of the approaches being performed in 18% (Cherebillo, 2007). At the Center for the Scientific and Clinical Study of Endocrinology, Uzbekistan Public Health Ministry, pituitary neurosurgical operations started in 2004, neuroendocrinologist Ashley Grossman providing all-sided support and neurosurgeon Professor Michael Powell (both the United Kingdom) performing the operations. Starting from 2011 this type of surgical operations has been performed by personnel of the Center. This seems to be high time to sum up outcomes of the operations performed.

The work was initiated to study early and late complications in patients undergoing surgical treatment for pituitary adenomas via the trans-sphenoidal route.

Materials and methods

We have managed to analyze outcomes of clinical examination and treatment of 151 patients with pituitary adenomas aged from 15 to 67 (mean age 38.9±1.04 years), 60 (39.7%) men and 91 (60.3%) women among them, undergoing surgical treatment for pituitary adenomas at the Neuroendocrinology Department with pituitary neurosurgery, Center for the Scientific and Clinical Study of Endocrinology, Uzbekistan Public Health
Ministry, within the period from 2004 to 2012. The disease median duration was found to be 3 years [Inter Quartile Range (IQR) 2.0-10.0]. Microscopic and endoscopic techniques were used in 108 (71.5%) and 43 (28.5%) patients, respectively.

All patients underwent ocular fundus examination and Goldmann kinetic perimetry and had their hormonal parameters measured. Visualization of hypothalamo-hypophyseal area by means of computer tomography (CT) and magnetic resonance imaging (MRI) was performed prior to the operation and after it. The adenomas were classified according to classification of Kadashev (2007). Serum levels of somatotrophic hormone (STH), prolactin (PRL), insulin-like growth factor-1 (IGF-1), thyroxin (T₄), thyroid-stimulating hormone (TSH), cortisol, adrenocorticotropic hormone (ACTH), triiodothyronine (T₃) testosterone, luteinizing hormone (LH), follicle-stimulating hormone (FSH), estradiol and progesterone were measured, radio-immune assay (RIA) being used to measure pituitary hormones by means of commercially available kits (Immunotech a.s., Czech Republic).

All data was processed by means of a Microsoft Excel, STATISTICA 6 and BIOSTAT software packet. Logistic regression was used to calculate odds ratio (OR) and 95% confidence interval (CI). Statistical significance of differences between parameters was assessed by means of non-parametric χ² test (Pearson’s criterion). The data is presented as M±m as well as Median (Me) and 25th and 75th percentiles as the Inter Quartile Range (IQR). Intergroup differences were considered significant at p < 0.05.

**Results and discussion**

Spectrum of pre-operative patients’ complaints was quite wide and included headaches (n=123, 81.5%), weakness (n=102, 67.6%), fatigue (n=96, 63.6%), vertigo (n=90, 59.6%), sleep disorders (n=82, 54.3%), memory impairment (n=18, 11.9%) and pains of various localization (n=80, 53.6%). Considerable number of patients (68.9%) suffered visual deterioration, restriction of visual fields (9.9%) as well as diplopia and strabismus (2.7%). Gonadal disorders, such as, amenorrhea and lactatorrhea were registered in 51.7% of female patients; reduction in sexual potency and libido as well as erectile dysfunction being found in 8.6% of men. Infertility was diagnosed in 7.3% of patients. Specific complaints included enlargement of the extremities and changes in appearance (9.3%) as well as weight gain (12.6%).

*FIGURE 1. DISTRIBUTION OF PATIENTS WITH VARIOUS TYPES OF ADENOMAS*

CT and MRI were used to assess the size and direction of pituitary adenomas’ growth in the examinees. Macroadenomas were diagnosed in most patients (n=102, 67.8%), microadenomas and gigantic adenomas being registered in 32 (21.2%) and 17 (11.3%) patients, respectively (Figure 1). Among macroadenomas observed in the significantly predominant number of the patients (OR 4.33; 95%CI 2.68 - 7.02; P<0.0001) most were
characterized with extrasellar growth (62.8 versus 37.3% of those with intrasellar growth) (OR 2.84; 95%CI 1.61-5.0; P<0.0001).

As to hormonal activity of the tumors diagnosed, clinically non-functioning adenomas and somatotropinomas were registered more frequently, in 60 (39.7%) and 51 (32.1%) patients, respectively; pituitary corticotropinomas (n=20, 13.3%) and prolactinomas being registered confidently less frequently (OR 0.10; 95%CI 0.06-0.17; P<0.0001). Neoplasms in chiasmatic-sellar area, such as, craniopharyngiomas, choleteatomas, Rathke’s pouch tumors and tumors of mixed types occurred less frequently (2-3%). Monohormonal pituitary adenomas could be seen in 99.3% of patients, in one patient both STH and PRL excessive secreting being found. Thus, most patients (60.3%) had hormonally active adenomas.

Mean hormone parameters were found increased in 80.1%. Normal levels of hormones in 19.9% of patients could be attributed to a drug therapy they received pre-operatively. At diagnosis median basal STH was found exceeding reference values (0-20 mIU/l) more than by 2 times, median basal ACTH (<50ng/ml) and PRL being higher almost by 1.5 and more than by 1.5 times, respectively. Early post-operative (3-12 months) STH, ACTH, PRL and cortisol were confidently reduced to fall within the normal range (Table 1).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before operation</th>
<th>After operation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal STH, mIU/l</td>
<td>57.7±7.67</td>
<td>16.4±6.37</td>
</tr>
<tr>
<td>ACTH, ng/ml</td>
<td>65.9±4.08</td>
<td>27.8±2.85</td>
</tr>
<tr>
<td>PRL, ng/ml</td>
<td>42.1±6.95</td>
<td>6.94±1.19</td>
</tr>
<tr>
<td>Cortisol (morning), nmol/l</td>
<td>444.1±37.5</td>
<td>227.9±51.2</td>
</tr>
<tr>
<td>IGF-1, ng/ml</td>
<td>339.4±57.1</td>
<td>198.9±26.7</td>
</tr>
</tbody>
</table>

Note: Me - median, IQR - Inter Quartile Range

It should be noted that achievement of target values for STH in acromegaly, for cortisol and ACTH in Cushing’s disease as well as for PRL in patients with prolactinomas post-operatively took place in 78.6%, 71.4 and 64.3% of the patients, respectively. Post-operative complications occurred in 56 (23.8%) patients, to name diabetes insipidus (6.0%), post-operative rhinitis (5.3%), liquorrhea (4.0%), amaurosis (2.0%) as well as oral cavity aphthous ulcers, epidural hematomas, post-operative uvulitis, intramural hematomas and acute rhinopharyngeal hemorrhage in 1.3% of patients.

Late complications of trans-sphenoidal resection of pituitary adenomas included secondary hypothyroidism (21.9%), osteopenia (15.2%), panhypopituitarism (12.6%), hypocortisolism (12.6%), osteoporosis (11.9%) and hypogonadism (11.3%). Menstrual disorders were diagnosed in 9 (9.9%) women, intracranial hypertension being found in 7 (4.6%) patients, empty sella syndrome in 4 (2.6%) and GH deficiency in 2 (1.3%). The disease recurrence was registered in 36 (23.8%) patients, recurrent tumor growth found more frequently in those with gigantic adenomas (35.3%; OR 8.18; 95%CI 1.43-46.8; P=0.03) and in those with macroadenomas (27.5%; OR 5.68; 95%CI 1.27-25.3; P=0.02)
as compared with the patients undergoing surgery for microadenomas (6.3%). Analysis of recurrences by pituitary adenoma types demonstrated that in 21.7% the disease recurrences took place in patients with non-functioning pituitary adenomas, in 29.4% of patients with somatotropinomas, in 13.3% of patients with prolactinomas and in 25% of patients with corticotropinomas.

**Conclusion**

Pituitary adenomas were diagnosed in most examinees (67.8%), predominantly those with extrasellar growth (62.8%). Most tumors were hormonally active (60.3%), predominantly somatotropinomas (32.1%). Frequency of post-operative complications is 23.8%, among them diabetes insipidus found in 6.0%, post-operative rhinitis in 5.3%, liquorrhea in 4.0% and amaurosis in 2.0%. Late post-operative complications included endocrine disorders, such as, secondary hypothyroidism (21.9%), osteopenia (15.2%), panhypopituitarism (12.6%), hypocortosolism (12.6%), osteoporosis (11.9%) and hypogonadism (11.3%). The tumor recurrences were predominantly found in patients with gigantic adenomas and macroadenomas as compared with patients having microadenomas (6.3%).

**References**


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