Some features of the perioperative management of patients with a tumor of the chiasmal sellaric region: a review


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Abstract

INTRODUCTION: Tumors of the chiasmal-sellar region (CSR) account for more than 20% of all primary intracranial neoplasms, of which pituitary adenomas account for up to 20% of the world population. Currently, removal of these neoplasms is performed using endoscopic transsphenoidal surgical accesses. OBJECTIVE: Analysis of the results of publications concerning perioperative management of patients with CSF tumors. MATERIALS AND METHODS: Publications were searched and selected in bibliographic databases PubMed, Web of Science, Scopus. To study the approach to perioperative management of patients with CSF tumors, the works published from 2013 to 2023 were analyzed. Search keywords: pituitary surgery, anesthesia. Based on the analysis of current problems in anesthesia planning for patients with CSF tumors, the search was expanded with additional keywords: “pituitary tumor”, “perioperative complications”, “endocrine disorders”, “difficult airway”, “acromegaly”, “cardiologic complications, acromegaly”, “peripheral neuropathy, acromegaly”, “trigemino-cardiac reflex”. 206 publications were additionally analyzed and the main key points in anesthesia planning were summarized. A total of 230 publications were included but 161 were excluded. A total of 69 studies were selected. RESULTS: The main features of patients with CSF tumors are: water-electrolyte disorders, cardiovas-
lar pathology, difficult airway. This determines a multidisci-
plinary approach in preparation for surgery. It is necessary to
take into account these features when planning anesthetic
support and management of the early postoperative period.
In addition, endoscopic transnasal-transsphenoidal access
may cause a number of complications: damage to the hypo-
thalamic region and large vessels, and in the postoperative
period: respiratory disorders, hormonal insufficiency, Water
and Sodium Disturbances. **CONCLUSIONS:** Additional vigil-
ance is required when preparing a patient with CSF formation
for surgery. Perioperative management of a patient with CSO
requires a team approach with participation of neuro-
surgeons, neurologists, ophthalmologists, endocrinologists,
cardiologists, anesthesiologists-resuscitators.

**KEYWORDS:** pituitary neoplasms, endocrine system
diseases, acromegaly, heart diseases, neuropathy

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Introduction

Tumors of the chiasmal-sellar region (CSR), pituitary adenomas (PA), craniopharyngeomas account for over 20% of all primary intracranial neoplasms, of which pituitary adenomas account for up to 16.5% [1, 2]. Surgical removal, in most cases, with the exception of prolactinoma, is considered as the first line of treatment for these formations [3]. To date, most of the operations are performed using endoscopic techniques with transsphenoidal access, which has a number of undeniable advantages: minimally invasive, clear visualization of anatomical structures, low traumatic manipulations and a shorter recovery period [4]. At the same time, the illusion of simplicity and minor traumatism of such surgical interventions is created, which can lead to a decrease vigilance of the anesthesiologist (especially with little clinical experience), underestimation of the severity of the patient’s condition and inadequate pre-operative preparation. In addition, since pituitary adenomas are more common in young and middle-aged people [5], there is often an insufficient assessment of the patient’s somatic status.

Objective

To analyze and summarize the results of publications concerning the perioperative features of the management of patients with chiasmal-sellar region tumors.

Materials and methods

Based on our own experience in the perioperative management of patients with chiasmal-sellar region tumors (about 90–100 operations annually) and using research data published in publicly available databases, we summarized the main key points when planning anesthesia for these patients. A search was conducted for publications in the bibliographic databases PubMed, Web of Science, Scopus and by keywords: “pituitary surgery”, “anesthesia”, “acromegaly”, “hypertension”, “cardiomyopathy”, “difficult airway”, “Cushing disease” over the past 10 years. Publications were included in the review if they met the following criteria: publications including pediatric patients, animal studies, and editorial letters. In total, 69 publications were included in the literature review.

Results

Review and multicenter randomized trials helped to identify the most specific features of anesthesia for patients with CSR tumors. These included: endocrine and water-electrolyte disorders, assessment of the upper respiratory tract, concomitant pathology of the cardiovascular system and related complications, peripheral neuropathy and patients positioning on the operating table, trigeminal-cardiac reflex, intraoperative blood loss, extubation difficulties.

Endocrine and water-electrolyte disorders

CSR tumors can be the cause of neurohumoral disorders that aggravate the course of the perioperative period and require special patient arrangements [6, 7]. Thus, hormonally active pituitary adenomas, such as corticotropinoma and somatotropinoma, can lead to serious disorders of the cardiovascular system, hemostasis, carbohydrate and protein metabolism, and cause water-electrolyte disorders. Pituitary macroadenomas and craniopharyngeomas are often the cause of hypopituitarism, overt or covert [8]. Compression of the pituitary pedicle and the posterior lobe of the pituitary gland can lead to the development of diabetes insipidus, which, in the absence of thirst and substitution therapy, can cause hypovolemia and hypernatremia [9]. In patients with somatotropinoma, acromegaly, splanchomegaly, hypertension, diabetes mellitus, insulin resistance lead to a high risk of cardiovascular complications, difficulties in correcting hyperglycemia [9, 10]. In patients with corticotropinomas, hypertension, diabetes mellitus, insulin resistance, and myopathies pose a high risk of cardiovascular complications, difficulties in correcting hyperglycemia, and problems with weaning from invasive mechanical ventilation [9, 11, 12]. Patients with CSR tumor should be examined by an endocrinologist before surgery in order to timely detect excessive hormonal activity or insufficiency. Preoperative secondary adrenal insufficiency is registered in 10–27% of patients with CSR tumor [11, 13]. Patients with macroadenomas and craniopharyngiomas in the postoperative period have a high risk of adrenal insufficiency developing (AI) [8, 14]. In patients with initial AI, corticosteroid therapy should be started at least 5–7 days before surgery. On the eve of the intervention, patients are transferred to parenteral corticosteroids, their management in the perioperative period is the same as in patients with primary AI, except that the administration of mineralocorticoids is extremely rarely required [7, 12]. With initially preserved adrenal function, postoperative AI usually develops in the first 24-48 hours in 4–9% of patients, and up to 18% demonstrate early transient AI [12]. The risk of developing postoperative AI is associated with the size of the tumor, its spread to surrounding structures, as well as the experience of the surgeon [15]. The restoration of the function of the pituitary-adrenal system takes place within 14 days. In the presence of preoperative AI, resto-
ration of function occurs in 15–20 % of patients, and this is usually associated with a younger age, a smaller tumor size (< 2 cm), and hormonally inactive tumors [15]. Patients who received oral forms of corticosteroids are transferred to parenteral forms of drugs for the entire perioperative period. On the evening before the operation, 100 mg of hydrocortisone is administered intravenously, and then 100 mg every 8 hours. In the uncomplicated postoperative period, as a rule, 300–500 mg of hydrocortisone per day parenterally is sufficient. After stabilization of the condition, the dose is quickly reduced (in 3 days) and transferred to oral forms of drugs [15–17].

Secondary hypothyroidism usually occurs in a mild form. If the function of the thyroid gland is not impaired before surgery, the incidence of postoperative hypothyroidism is approximately 3 % [12]. Only in 7 % of patients with pre-existing secondary hypothyroidism, thyroid function is restored [12, 13]. If early postoperative thyroid dysfunction is suspected, both free thyroxine and the index of free thyroxine and thyroid-stimulating hormone are examined. In the immediate postoperative period, early hypernatremia may be an indicator of thyroid dysfunction [6–8]. Levothyroxine should be started with a low dose (25–50 mcg per day) and titrated in increments of 25 mcg to achieve a full replacement dose [10,18]. Special attention should be paid to the assessment of the water-electrolyte balance and its disorders. Among the water-electrolyte disorders, the most common are central diabetes insipidus (DI), syndrome of inadequate secretion of antidiuretic hormone and, somewhat less frequently, cerebral salt loss syndrome [9]. Postoperative DI occurs in 10–30 % of patients with CSR tumor [9, 10]. The cause of central DI is a deficiency of antidiuretic hormone (ADH). Due to the large losses of free water, a hypovolemic hyperosmolar state develops. Compensation of ADH and fluid deficiency are the key points of DI therapy [19]. Excess ADH in the syndrome of inadequate secretion of antidiuretic hormone leads to hypervolemic hypoosmolarity due to plasma hemodilution. Treatment consists in temporary restriction of fluid administration [20].

The pathophysiology of cerebral salt loss syndrome remains unclear. Natriuresis contributes to the loss of a significant amount of fluid and the development of hypovolemic hypoosmolar state. Therapy of this syndrome is aimed at replenishing the loss of sodium and the volume of circulating blood [20, 21].

Thus, the minimum protocol for examining patients with CSR tumor before surgery, in addition to the standard one, should include: assessment of cortisol level, free thyroxine and thyroid-stimulating hormone level, plasma sodium and potassium levels, and Zimnitsky’s test. Patients with corticotropinoma are recommended to be examined by a cardiologist, undergo kidney function assessment, and patients with somatotropinoma, in addition to the above mentioned, need ultrasound examination of abdominal organs and echocardiography [6, 14].

Assessment of the Airway

Worldwide, changes in the anatomy, caused by acromegaly, are considered to be the leading cause of difficulties in ensuring the airway [22–24]. Anatomical features that develop in patients cause problems with mask ventilation, laryngoscopy, tracheal intubation and extubation [25, 26]. The most significant anatomical changes that cause difficulties in providing mask ventilation through a facial mask in acromegaly are: pathological changes in the facial skeleton, enlargement of the nose, tongue, lips, proliferation of soft tissues of the oral cavity and larynx, in addition, the cartilages of the larynx are enlarged, the vocal cords are hypertrophied [27]. These hypertrophied tissues are prone to swelling and contact bleeding. The size of the laryngeal aperture decreases and the visualization of the glottis worsens during laryngoscopy. In addition, patients with long-term acromegaly may develop diffuse damage to the musculoskeletal system (arthrosis, arthropathy), which leads to a deterioration in mouth opening (if the temporomandibular joint is affected) and stiffness in the cervical-thoracic spine, limited neck extension. This exacerbates the difficulties of intubation and creates conditions for critical situations such as “it is impossible to ventilate — it is impossible to intubate” [28]. And even in cases where an external examination does not give grounds to anticipate these complications, intubation may be difficult [22]. Therefore, studies are being conducted to search for specific and sensitive laboratory markers of difficult airways, and the possibilities of X-ray diagnostics of oropharyngeal features are being studied [29, 30]. There is some data that show the correlation of the level of insulin-like growth factor with airway difficulties [31]. In addition to the obvious external anatomical features in patients with acromegaly, attention should be paid to the description of the abdominal ultrasound. They often describe hepatomegaly and splenomegaly, as well as an enlarged atonic stomach. This should be taken into account when recommending preoperative fasting and, in any case, consider these patients as having a full stomach. Anatomical prerequisites for difficult airways are also present in patients with Itsenko-Cushing’s disease [32]. A “moon-shaped” face can make mask ventilation difficult, fat folds in the base of the neck often create an obstacle for comfortable placement of the patient for intubation, make it difficult to unbend the head, and pronounced fatty tissue in the abdominal area mechanically prevents ventilation. But with direct laryngoscopy, the visualization in patients with Cushing’s disease often turns out to be quite good, corresponding to 1–2 degrees on the Cormack scale. Therefore, intubation of the patient should be planned in advance. Prepare a video laryngoscope, laryngeal masks, blades of various configurations. If significant difficulties in intubation are evident during the preoperative examination of the patient, it is necessary to prepare for elective endoscopic
intubation and explain the details of this manipulation to the patient [29, 30].

In cases with severe acromegaly where it is possible to examine a patient who is scheduled for surgical treatment in advance, the possibility of prescribing somatostatin analogues can be discussed with the attending physician [31, 32]. These drugs reduce the swelling of hypertrophied oropharyngeal tissues and thus can help improve visualization during laryngoscopy. However, there is a study that shows the absence of a positive effect of somatostatin analogues on visualization during laryngoscopy in patients with acromegaly [33].

Cardiovascular system disorders

Many patients with Itsenko-Cushing’s disease and acromegaly have persistent, poorly correctable hypertension. These patients usually receive combined antihypertensive therapy, but despite this, high blood pressure figures are observed during examination [34, 35]. Many patients do not immediately consult a doctor or, for various reasons, could not get qualified consultation and have persistent high arterial hypertension for a long time [36, 37]. It should be remembered that in this case, mechanisms of long-term compensation for hypertension in the form of remodeling of the cardiovascular system and myocardium may be involved [38, 39]. And severe hypotension, which can develop in the early postoperative period against the background of hormonal changes, which is often observed with total corticotropinoma removal, can lead to severe cardiovascular complications. Therefore, it is very important to plan perioperative hormone replacement therapy together with an endocrinologist. With long-term hypersecretion of somatotropic hormone, patients develop cardiomegaly, hypertrophy of the left ventricle, acromegalic cardiomyopathy — diffuse changes in the myocardium, leading to a violation of its blood supply. In some patients, this causes the development of chronic heart failure [40–47]. Acromegaly is an indication for performing echocardiography before surgery. This examination could reveal systolic dysfunction, decreased cardiac output and, importantly, diastolic myocardial dysfunction, which is often the very first sign of acromegalic cardiomyopathy and is completely asymptomatic for the patient. Myocardial contractility and cardiac output are not affected, but the patients with diastolic dysfunction are particularly sensitive to the cardiodepressive effects of anesthetic drugs. This manifested by persistent, poorly correctable arterial hypotension and bradycardia. Therefore, it is necessary to plan an anesthesia induction without rapid bolus administration of hypnotics analgetics. Cardiomyopathies associated with Cushing’s disease are less common [48, 49]. There is evidence that prolactin-secreting tumors may also be associated with a higher risk of developing cardiovascular diseases [50].

The intraoperative period

Positioning on the operating table

Usually patients lie on their backs with the head end raised, and therefore the anesthesiologist does not expect difficulties. But in patients with acromegaly, degenerative changes in the periarticular areas and excessive collagenization of tendons lead to a violation of the normal location of peripheral nerves [50–52]. It is important to avoid complete extension of the joints of the upper and lower extremities when laying the patient, as this can lead to overstretched peripheral nerves and their compression by soft tissues with the development of peripheral neuropathies [53, 54].

Surgical access

Both traditional surgical access and micro-access require the anesthesiologist to ensure sufficient flexibility of the brain so that the surgeon can perform precise, accurate manipulations in the wound [54, 55]. Hyperemia and edema pose a risk of traction tissue damage and local ischemia. The ways to provide a malleable brain are well known: careful laying of the head — an elevated head end and a neutral position of the head to ensure venous outflow; the use of hyperosmolar solutions — mannitol or hypertonic sodium chloride solution; in emergency cases — short-term hyperventilation; lumbar drainage of the cerebrospinal fluid.

With endoscopic accesses, it is important to monitor the preparation of the nasal mucosa by surgeons for the introduction of an endoscope before surgery. Usually, tampons with a local anesthetic and trace doses of epinephrine are used for this purpose. Data have been published that local administration of epinephrine at a concentration of 1:1,000 does not lead to systemic effects [55, 56]. With an increase in the amount of epinephrine, its systemic absorption may be accompanied by cardiovascular reactions [56, 57]. In patients with reduced cardiovascular reserve, these hyperdynamic reactions can lead to myocardial ischemia.

Trigeminal-cardiac reflex

It can be caused by stimulation of any sensitive branch of the trigeminal nerve in the nasopharyngeal mucosa, facial skin, dura mater of the anterior cranial fossa [58]. The afferent signal passes through the Gasser node into the sensitive nucleus of the trigeminal nerve, and the efferent link is provided by the fibers of the vagus nerve. The reflex is manifested by a decrease in heart rate and a decrease in blood pressure. On average, the reflex is observed in about 15% of cases during operations for a CSR tumor. The clinical significance of this reflex is still being discussed [59]. Most often, it is stopped on its own, and does not lead to any neurological consequences. However, several descriptions of clinical cases have been published, which describe persistent arterial hypotension and bradycardia up to asystole, which required cardiopulmonary resuscitation [60, 61]. In addition, with transnasal access, the trigeminal-cardiac reflex occurs in a peripheral form in the form of a “diver’s reflex” [62]. It man-
Ifests itself with bradycardia and hypertension, which can lead to increased bleeding in the area of the surgical wound and significantly worsen visualization. Therefore, it is important to reduce the manifestations of this reflex as much as possible, primarily by maintaining sufficient depth of anesthesia and normoventilation.

**Intraoperative bleeding**

Modern neurosurgical interventions are most often accompanied by minimal blood loss [63]. But during surgical manipulations in CSR, it is necessary to remember about the possibility of the internal carotid artery injury. This is an extremely rare complication [64]. Its frequency varies from tenths to hundredths of a percent according to various sources. This is due to the good capabilities of modern neuroimaging methods — the features of anatomy are usually known in advance to the surgeon, which allows to plan access in the least traumatic way. However, special caution should be maintained in patients with repeated interventions in CSR and in patients who have been taking bromocriptine for a long time. Scars and adhesions that occur in the area of intervention increase the risk of injury to the artery [63].

In case of massive arterial bleeding, only surgical hemostasis will be effective, therefore, our clinic provides the possibility of rapid communication with endovascular surgeons. In the event of such an emergency, the neurosurgeon performs temporary hemostasis by any method available to him, and then the final hemostasis (and, if possible, reconstruction of the vessel) is performed by endovascular surgeons.

**The end of the operation and extubation**

The concept of difficult airways also includes difficulties in extubation, which is often demonstrated to us by patients with CSR tumors. Acromegaly, obesity, and Itsenko-Cushing’s disease can cause problems with extubation. Excess adipose tissue and hypertrophied oropharyngeal tissues increase the risk of obstructive sleep apnea. In patients with Itsenko-Cushing’s disease, respiratory disorders may be aggravated due to muscle weakness associated with hypercatabolism of muscle tissue and impaired its synthesis [65, 66]. Ineffective breathing after extubation leads to hypoxia, attempts by the anesthesiologist to provide a mask ventilation, which often also turns out to be ineffective, but at the same time significantly increases the risk of complications such as postoperative liquorreah and pneumocephaly [67–69]. Therefore, extubation should be planned as carefully as intubation [66].

| Table 1. Studies included in the review, their design and main results |
|--------------------------|-----------------|-----------------|-----------------|
| **Features of perioperative management** | **Authors** | **Design** | **Number of patients** | **Brief cases description** |
| Endocrine and water-electrolyte disorders | Carosi G. et al. [8] | A retrospective study | 218 | It is recommended to carry out a complete assessment of the basal and dynamic function of the pituitary gland, regardless of the size of the tumor |
| Buttan A. et al. [12] | Review | — | Assessment and monitoring of hormone levels are crucial after surgery for CSR tumors. Proper management can have a significant impact on postoperative outcome, mortality and long-term outcome indicators |
| Nie D. et al. [14] | Meta-analysis 1992–2022 | 69 | In patients with somatotropic tumors after endoscopic surgery, the risk of pituitary dysfunction and insufficiency tends to increase, while preoperative thyroid insufficiency, gonadal insufficiency and hyperprolactinemia tend to regress |
| Dunts P. et al. [17] | Review | — | If adrenal insufficiency is suspected, preoperative examination and careful preoperative preparation are necessary, followed by the use of corticosteroids |
| Alexandraki K. et al. [18] | Review | — | In patients with CSR tumors in the perioperative period, it is necessary, first of all, to assess the function of the adrenal glands and thyroid gland, and to carry out replacement therapy on time |
| Tomkins M. et al. [19] | Review | — | It is important to pay special attention to consumption control. Specific clinical syndromes such as adiptic diabetes insipidus and diabetes insipidus during pregnancy, as well as the management of a perioperative patient with diabetes insipidus |
| Cui H. et al. [20] | Review | — | The issues of diagnosis, differential diagnosis and pathogenesis of the syndrome of inadequate secretion of ADH and cerebral salt loss syndrome are considered |
| Oh H. et al. [21] | Review | — | Modern views on the diagnosis, pathogenesis, and treatment of cerebral salt loss syndrome are presented |
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<td>A prospective single-center study</td>
<td>45</td>
<td>3 out of 45 patients had liquorrhea on the background of cough during extubation</td>
</tr>
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<td></td>
<td>Jain D. et al. [69]</td>
<td>A prospective controlled single-center study</td>
<td>50</td>
<td>The goal is to stop coughing during extubation. 50 patients, 25 intravenous lidocaine, there was no difference in the smoothness of the exit from anesthesia</td>
</tr>
<tr>
<td>Features of the perioperative manage- ment of patients with chiasmal sellar region tumors</td>
<td>Esfahani K. et al. [6]</td>
<td>Review</td>
<td>—</td>
<td>Transsphenoidal pituitary surgery poses unique challenges for the anesthesiologist. Emerging data on monitoring, surgical techniques and multimodal analgesic therapy, among other things, shed light on ensuring optimal care for patients with non-functioning and functioning pituitary adenomas</td>
</tr>
<tr>
<td></td>
<td>Cote D.J. et al. [7]</td>
<td>A retrospective study</td>
<td>928</td>
<td>Patients with sellar lesions undergoing transsphenoidal surgery require complex, multidisciplinary postoperative care to monitor common adverse events and improve outcomes</td>
</tr>
</tbody>
</table>
Findings

In addition to the standard minimum examination before elective surgery, it is mandatory to perform a number of additional examinations and diagnostic measures:

- assessment of hormone plasma levels (adrenocorticotropic hormone, cortisol, thyroid-stimulating hormone, free thyroxine, somatotropic hormone insulin-like growth factor type 1, prolactin);
- examination of the patient by an endocrinologist and correction of hormone replacement therapy; ensuring the continuity of hormone replacement therapy during the perioperative period;
- echocardiography for all patients with acromegaly and consultation with a cardiologist for patients with hormone-producing tumors;
- evaluation of serum electrolytes (sodium, potassium, chlorine): before surgery and in the postoperative period;
- preparation for airway difficulties;
- planning tactics in case of intraoperative artery damage, discussion of the possibility of participation of X-ray endovascular surgeons for endovascular interventions in emergency situations;
- planning “soft” extubation of patients.

Publications on the features of perioperative management of patients with a CSR tumor included in the review are presented in Table 1.

Conclusion

Despite the apparent low-traumatic nature of transsphenoidal surgical interventions, each patient with a CSR tumor can become a serious challenge to the professional skills of an anesthesiologist and intensive care specialist.

Performing extended preoperative preparation and anesthesiological support is the key to a successful outcome of surgery and minimizing the frequency of postoperative complications.

Perioperative management of a patient with a CSR tumor requires a team approach involving neurosurgeons, neurologists, ophthalmologists, endocrinologists, cardiologists, anesthesiologists and intensive care specialists. All specialists should be well aware of the characteristics of these patients. Therefore, as a rule, the best treatment results are shown by specialized centers where more than a hundred operations are performed per year. However, there are not so many such centers in Russia, in addition, such patients often require emergency surgical interventions, so we hope that our article will be interesting and useful to those of our colleagues who work in emergency hospitals.

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