FEATURES OF PREOPERATIVE PREPARATION, ANESTHETIC MANAGEMENT AND POSTOPERATIVE MANAGEMENT OF PATIENTS WITH HORMONE-ACTIVE ADRENAL TUMORS

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ANNOTATION

Purpose of the study: To improve the results of surgical treatment of patients with hormone-active adrenal tumors by developing optimal options for preoperative preparation, anesthesia and postoperative management.

Research material and methods: The material is based on data from 34 patients with hormone-active adrenal tumors who were operated on in the Samarkand Branch of the Republican Specialized Scientific Practical Medical Center of Oncology and Radiology in the period from 2015 to 2021. The age of the patients varied from 28 to 73 years (mean age 44 ± 11.3 years). Comparative characteristics were carried out among the following groups: Group I, consisting of 11 (32.4%) with adrenal corticosteroma; Group II, consisting of 8 (23.5%) with adrenal aldosteroma (Conn’s syndrome); Group III, consisting of 15 (44.1%), with adrenal pheochromocytoma.

Research results: Preoperative preparation in patients with moderate, mild and moderate arterial hypertension in 23 (67.6%) patients lasted for 5-7 days as an outpatient course. In patients with severe and malignant arterial hypertension, 11 (32.4%) patients lasted for 2-3 weeks as an outpatient course; additionally, a similar weekly stage of inpatient treatment was carried out. As a result of this preparation, 11 (32.3%) patients with hormonally active adrenal tumors with severe or malignant arterial hypertension showed a decrease in systolic blood pressure to 160.4 ± 5.3 and diastolic blood pressure to 100.4 ± 4.1 mm Hg. at baseline systolic blood pressure 220.3 ± 7.4 and diastolic blood pressure 130.5 ± 5.4 mm Hg; Thus, only 11 (32.3%) patients with hormonally active adrenal tumors with severe or malignant arterial hypertension were given 2-3 weeks of preoperative preparation at the outpatient stage.

Conclusion: Thus, hormone-active adrenal tumors are extremely hormoneally aggressive neoplasms, which places high demands on careful preoperative preparation of patients, the level of training of the anesthesia team, equipping the operating room with high-quality monitors, and equipping the operating room with a sufficient amount of necessary drugs.

Key words: adrenalectomy, adrenal tumor, arterial hypertension, hormone-active adrenal tumors, preoperative preparation

I. RELEVANCE:

Cancer of the adrenal cortex (syn.: Adrenocortical cancer; ACC) is a rare malignant tumor of the adrenal cortex, which, as a rule, is characterized by late detection, aggressive clinical course and poor medical prognosis [1]. The annual detection of ACC is 0.5–2 cases per 1 million of the population, in the structure of cancer mortality is 0.04–0.2%. The highest incidence is observed in the southern regions of Brazil, which is explained by the high prevalence of the TP53 gene R337H germline mutation. At the time of diagnosis, the average age of the patient is 50-60 years, but the disease also occurs in children. Women get sick more often, the ratio of women / men is 2.5: 1 [2; 3b 24].
In adult patients, the clinical manifestations of ACC include symptoms of excessive hormonal secretion (50-60%) and nonspecific symptoms associated with tumor growth (30-35%) [2; 5; 6]. In other cases (10-15%), the disease is detected by chance during imaging studies: multispiral computed tomography (MSCT) and or magnetic resonance imaging (MRI) and or ultrasound imaging (USI) as an incidentaloma (Table 1) [4; 5; 6; 7; 8; 9.25].

Table 1. Clinical manifestations of ACR in adult patients [4]

<table>
<thead>
<tr>
<th>ACC manifestations</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autonomous hormonal overproduction</td>
<td>50-60%</td>
</tr>
<tr>
<td>Hypercortisolism (Itsenko-Cushing's syndrome)</td>
<td>50-80%</td>
</tr>
<tr>
<td>Overproduction of androgens (virilization in women)</td>
<td>20-30%</td>
</tr>
<tr>
<td>Overproduction of estrogen</td>
<td>5%</td>
</tr>
<tr>
<td>Primary hyperaldosteronism</td>
<td>2-3%</td>
</tr>
<tr>
<td>Non-specific manifestations Primary hyperaldosteronism</td>
<td>30-35%</td>
</tr>
<tr>
<td>Incidentaloma</td>
<td>10-15%</td>
</tr>
</tbody>
</table>

The most common manifestation of hormonal overproduction is hypercortisolism, both isolated (30-50%) and in combination with virilization symptoms (20-30%). Thus, hypercortisolism reaches 50-80% among all cases of hormone-active ACC.

When an adrenal tumor larger than 1 cm is detected, it is first of all recommended to exclude or confirm the hormonal activity of the formation, which can be manifested by hypercatecholaminemia, adrenocorticotropic hormone (ACTH) - independent hypercortisolism, primary hyperaldosteronism [10; 11; 12].

The rarest variant of endocrinopathy in ACC is associated with manifestations of primary hyperaldosteronism, which manifests itself in severe arterial hypertension and hypokalemia. The increased production of aldosterone is noted more often in the framework of mixed hormonal production. In most cases, the ACC is relatively large, on average more than 10 cm; the tumor can grow up to 25 cm or more. Nonspecific symptoms of ACC, such as discomfort or pain, pain in the lumbar and abdominal regions, feeling of fullness in the stomach, are caused by tumor growth in size and compression of adjacent organs [13].

The study of the hormonal activity of the adrenal gland tumor is strictly regulated and it is recommended to take into account its results for each patient when planning preoperative preparation, the volume of surgery, and follow-up [9, 14].

Pheochromocytoma (PC) is a tumor from chromaffin tissue that produces a large amount of biologically active substances catecholamines (adrenaline, norepinephrine, dopamine), clinically manifested by the syndrome of arterial hypertension (AH) of varying severity and various metabolic disorders. [15, 16].

At present, it is not possible to speak about an absolute intravital diagnosis of chromaffin adrenal tumors. It is believed that approximately 1/3 of patients cannot be diagnosed with PC during their lifetime. PC occurs in 0.2–0.6% of patients with persistent arterial hypertension (AH), especially diastolic blood pressure. In the general population, PCs are relatively rare, less than 1 case per 200 thousand of the population per year, and the incidence is no more than 1 person per 2 million of the population. When assessing the detection of PC according to autopsy data, their prevalence is 0.05–0.1%. The tumor can occur at any age (usually between 20-40 years) with the same frequency in men and women. Multiple tumors are found in 8-10% of cases [17, 18].

The study of the hormonal activity of the adrenal gland tumor is strictly regulated and its results should be taken into account for planning preoperative preparation, the volume of the operation, and follow-up of the patient.

For all patients with an adrenal gland tumor, a study of the levels of metanephrine and normetanephrine in the blood or in the daily urine portion should be carried out in order to verify the Pheochromocytoma. Underestimation of the presence of a catecholamine-secreting tumor is associated with a high risk of perioperative development of high-amplitude hypertensive crises, pulmonary edema, fatal arrhythmias, “uncontrolled hemodynamics” syndrome and sudden cardiac death [9, 19, 20, 21].
Objective: To improve the results of surgical treatment of patients with hormone-active adrenal tumors by developing optimal options for preoperative preparation, anesthesia and postoperative management.

II. MATERIALS AND METHODS:

The material is based on data from 34 patients with hormone-active adrenal tumors who were operated on in the Samarkand Branch of the Republican Specialized Scientific Practical Medical Center of Oncology and Radiology in the period from 2015 to 2021. The age of the patients varied from 28 to 73 years (mean age 44 ± 11.3 years). The main mass consisted of patients aged 45.4 ± 10.2 years.

The study consisted in the study of the clinical features of preoperative preparation, anesthetic management and postoperative management of patients with hormonally active adrenal tumors based on clinical observations and the study of archival case histories.

The groups of patients were compared depending on the level of arterial hypertension. Arterial hypertension was observed in 100% of patients. Conditionally patients were divided into five groups. (table number 2).

To determine the nature and level of arterial hypertension (AH), the classification of the World Health Organization (WHO) was used.

Table 2

<table>
<thead>
<tr>
<th>The severity of arterial hypertension</th>
<th>Blood pressure level (mm Hg)</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Border</td>
<td>140-149 and 90-94</td>
<td>12 (35.3%)</td>
</tr>
<tr>
<td>Soft</td>
<td>150-159 and 95-99</td>
<td>6 (17.6%)</td>
</tr>
<tr>
<td>Moderate</td>
<td>160-179 and 100-109</td>
<td>5 (14.7%)</td>
</tr>
<tr>
<td>Heavy</td>
<td>200-220 and 115-130</td>
<td>8 (23.5%)</td>
</tr>
<tr>
<td>Malignant</td>
<td>more than 300 and 170</td>
<td>3 (8.8%)</td>
</tr>
</tbody>
</table>

Five groups of patients were conditionally identified:

Group I, consisting of 12 (35.3%) patients with borderline hypertension (fluctuations in systolic blood pressure 143.5 ± 4.6 diastolic blood pressure 92.3 ± 2.4 mm Hg);

Group II, consisting of 6 (17.6%) patients with mild hypertension (fluctuations in systolic blood pressure 158.4 ± 2.6 and diastolic blood pressure 97.4 ± 3.5 mm Hg);

Group III, consisting of 5 (14.7%) patients with moderate hypertension (fluctuations in the numbers of systolic blood pressure 173.5 ± 5.6 and diastolic blood pressure 105.2 ± 3.8 mm Hg);

Group IV, consisting of 8 (23.5%) patients with severe hypertension (fluctuations in the numbers of systolic blood pressure 209.7 ± 8.1 and diastolic blood pressure 122.4 ± 7.3 mm Hg);

Group V, consisting of 3 (8.8%) patients with malignant hypertension (systolic blood pressure over 300 ± 22.9 and diastolic blood pressure 170 ± 18.6 mm Hg);

Distribution of operated patients by sex and age: among the operated patients, 23 women (67.6%) prevailed, 11 men (32.4%).

Taking into account the fact that preoperative preparation and management of anesthesia should be based on the hormonal activity of the adrenal gland to be removed, the specific manifestations of the underlying disease and the nature of the accompanying pathology, 3 groups of patients were identified:

Group I, consisting of 11 (32.4%) with adrenal corticosteroma

Group II, consisting of 8 (23.5%) with adrenal aldosteroma (Conn’s syndrome).
Group III, consisting of 15 (44.1%), with adrenal pheochromocytoma.

**In patients of group I, it consisted of 11 (32.4%) with adrenal corticosteroma.**

Preoperative preparation included the correction of metabolic disorders by inhibiting excessive secretion of glucocorticoids. This was achieved by prescribing drugs that block the biosynthesis of steroids in the adrenal glands: mitotane 500 mg 2-3 r / day. If necessary, the indicated doses were increased to the level of the maximum tolerable, and once every 7-10 days, the excretion of cortisol in daily urine was monitored in order to diagnose the possible development of adrenal insufficiency. In the presence of steroidal diabetes, the blood sugar level was corrected by diet and administration of simple insulin. In severe osteoporosis, anabolic steroid hormone was used - retabolil 50 mg / ml 1 time in 1-3 weeks. At the same time, sufficient intake of calcium (600–1200 mg) and vitamin D into the body was ensured. Considering the fact of activation of the angiotensin-converting enzyme by glucocorticoids, its inhibitors captopril 25 mg were used under the control of blood pressure.

**In patients of group II, consisting of 8 (23.5%) with adrenal aldosteroma (Conn’s syndrome).**

The following drugs were included in the preoperative preparation in order to correct arterial hypertension (daily dosages are indicated): hydrochlorothiazide 100 mg, atenolol 50 mg, enalapril 10-20 mg, nifedipine 10 mg each. For hypokalemia, potassium preparations - 4% potassium chloride solution 10 ml per 400 ml of 0.9% sodium chloride solution once a day, Panangin -10.0 ml per 400 ml of 5% dextrose solution once a day and a potassium-sparing diuretic - veroshpiron 50-200 mg per day under the control of blood pressure, central venous pressure and potassium levels in the blood.

**Group III consisting of 15 (44.1%) with adrenal pheochromocytoma.**

Drug preparation was aimed at correcting the disorders identified during the examination and stabilizing hemodynamics. To lower blood pressure, doxazosin a-blockers were used at a dose of 4 to 16 mg per day in 2 doses daily under blood pressure control, in the presence of an initial tachycardia or the appearance of compensatory tachycardia while taking a-blockers, selective B1-blockers bisoprolol were prescribed at a dose of 2.5 to 10 mg per day under control of blood pressure. These drugs not only effectively lower blood pressure, but also reduce peripheral vascular resistance, which reduces afterload and facilitates heart function. In addition, they increase the secretion of insulin by the pancreas and alleviate the course of diabetes. For persistent hypertension, b + a-blockers (labetalol), calcium channel blockers (nifidipine, nitrendipine) and angiotensin-converting enzyme blockers (captopril, enalapril). If necessary, cardiac glycosides, diuretics (mainly potassium-sparing), nitrates, neoton, riboxin, panangin were used to correct heart failure. When correcting water-electrolyte disorders, special attention was paid to the normalization of potassium metabolism. In emotionally labile patients, tranquilizers were prescribed to create mental peace.

**The features of the anesthesia were different, we conditionally divided the patients into 3 groups.**

**Features of anesthesia in group I, consisting of 11 (32.4%) patients with adrenal corticosteroma.**

Hypertension during the lifting of the roller, as well as at the time of isolation and removal of the tumor was corrected by the administration of a-adrenoblocker (10–20 mg of tropafen). For this purpose, ganglion blockers were used in the form of intravenous drip infusion. Immediately after tumor resection, the administration of ganglion blockers was discontinued and adequate compensation for blood loss and BCC deficiency was provided.

Depending on the severity of the initial condition, the total volume of intravenous infusion ranged from 1.5 to 3 liters.

**Features of anesthesia in group II, consisting of 8 (23.5%) patients with adrenal aldosteroma (Conn’s syndrome).**

To stabilize hemodynamics, first of all, infusion therapy was enhanced with the use of plasma substitutes for hemodynamic action, blood preparations, and only if they were ineffective, vasopressor drugs were used norepinephrine at a dose of 0.05 mg / kg / min.

When a tumor of the adrenal glands was isolated, hypertension occurred, the required level of blood pressure was maintained by intravenous administration of verapamil (2.5 mg per 100 ml of saline) and isosorbital dinitrate (isoket) - 2-3-4 mg / hour by continuous infusion under the control of blood pressure. Taking into account the
electrolyte metabolism disorders, careful monitoring of the ECG, heart rate, blood pressure was carried out for the timely diagnosis of possible cardiac arrhythmias.

**Features anesthesia in group III, consisting of 15 (44.1%) patients with adrenal pheochromocytoma.**

To prevent and correct hypertension, we use a-blockers, in particular ebrantil. Ebrantil 10-50 mg IV slowly under blood pressure control and / or continuous infusion was carried out using a perfusion pump at an average of 9-15 mg / h, the dose was adjusted depending on the severity of arterial hypertension.

With tachycardia over 120 per minute, especially when ventricular tachycardia occurs, intravenous administration of beta-blockers was performed. After isolating the tumor from the blood circulation, it is necessary to have norepinephrine ready for intravenous infusion, we started the injection of norepinephrine at the stage of vascular excretion using a perfusion pump, with a constant correction of the injection rate, depending on the degree of hypotension. A good effect can also be achieved by intravenous drip infusion of dopamine at a dose of 5 - 7 μg / kg / min. In addition, approximately 5 minutes before isolating the tumor from the blood circulation, we began intravenous administration of Solu-medrol 250 mg, immediately after removal of the formation, another 250 mg of Solu-medrol (methylprednisalone) was injected.

It is known that the course of pheochromocytoma is accompanied by a decrease in the BCC. To prevent the development of hypovolemic shock, we carried out infusion therapy at the initial stages of the operation, on average up to 1500-2000 ml of water-salt solutions. During the operation, blood loss was strictly taken into account and compensated for with a significant excess of volume (3-4 times). CVP was monitored regularly to avoid overloading the damaged heart. In order to conduct adequate fluid therapy, it is necessary to catheterize 2 veins.

III. EARLY POSTOPERATIVE PERIOD.

**In group I patients with adrenal corticosteroma.**

In the complex of intensive care measures after total adrenalectomy, when symptoms of adrenal insufficiency appeared, glucocorticoid replacement therapy was prescribed. Considering that the half-life of hydrocortisone in the organism is 1.5-2 hours, hormone replacement therapy was started 2-3 hours after (water-soluble hydrocortisone 125-250 mg / day or prednisolone 1 mg / kg).

**In group II patients with adrenal aldosteroma.**

After the intervention, potassium and spironolactone infusion was gradually canceled, antihypertensive therapy was minimized. Postoperative fluid therapy consisted mainly of isotonic saline solutions without potassium chloride, except in situations with persistent hypokalemia (<3.0 mmol / L). Postoperative hyperkalemia may result from hypoaldosteronism due to chronic suppression of the mineralocorticoid function of the contralateral adrenal gland. In rare cases, temporary treatment with fludrocortisone (cortineff 200mcg / day) was required.

**In group III patients with adrenal pheochromocytoma.**

In the early postoperative period, patients needed intensive observation and rational therapy with steroid hormones, correction of electrolyte metabolism, the need for constant monitoring of the level of glycemia, sufficient administration of fluids, alkaline solutions, drugs that improve metabolism and myocardial contractility.

After the operation, the patients could serve themselves and be free in 2-3 days.

IV. RESEARCH RESULTS.

When examining patients with hormone-active adrenal tumors and making a diagnosis, complaints, anamnesis, data from physical, instrumental and laboratory examinations were taken into account.

In all patients, the operational and anesthetic risk according to the classification of the American Association of Anesthesiologists –ASA– was III. Diagnosed and removed during surgery, hormonally active adrenal tumors were localized in 20 (58%) patients on the right, in 13 (42%) patients on the left. The sizes of the removed hormonally active formations of the adrenal glands ranged from 40 to 164 mm, and their average size was 55.5 ± 5.1 mm. It was noted that as the duration of the disease increased, the size of the hormonally active formations of the adrenal gland also increased.
Preoperative preparation in patients with moderate, mild and moderate arterial hypertension in 23 (67.6%) patients lasted for 5-7 days as an outpatient course.

In patients with severe and malignant arterial hypertension, 11 (32.4%) patients lasted for 2-3 weeks as an outpatient course; additionally, a similar weekly stage of inpatient treatment was carried out.

In 21 (61.8%) patients, before the initiation of antihypertensive therapy, the heart rate increased to 110.5 ± 10.2 per minute. The conducted preoperative preparation contributed to a decrease in heart rate to 87.4 ± 5.3 per minute in all patients with pre-existing tachycardia.

As a result of this preparation, 11 (32.3%) patients with severe and malignant hypertension showed a decrease in systolic blood pressure to 160.4 ± 5.3 and diastolic blood pressure to 100.4 ± 4.1 mm Hg; at baseline systolic blood pressure 220.3 ± 7.4 and diastolic blood pressure 130.5 ± 5.4 mm Hg: Thus, only 11 (32.3%) patients with hormonally active adrenal tumors with severe or malignant arterial hypertension were given 2-3 weeks of preoperative preparation at the outpatient stage.

Total adrenalectomy with tumor was performed in 34 (100%) patients.

The average duration of the operation was 55.4 ± 8.6; the average volume of blood loss was 110.5 ± 10.4 ml.

The patients underwent multicomponent intravenous anesthesia with total myoplegia and mechanical ventilation.

All adrenalectomies were unilateral. The intraoperative period can be divided into 2 stages.

The first stage is induction into anesthesia and operative access until the central adrenal vein is ligated.

The second stage is after vein ligation.

Mandatory conditions are: cardiac monitoring at all stages of the operation, dynamic control of blood pressure and central venous pressure.

We used invasive arterial monitoring through the radial artery, which made it possible to quickly and accurately assess the changes occurring in the patient.

In all patients, the central and peripheral veins were cathetized before the operation.

Postoperative complications, most of them 5 (14.7%) are due to short-term hypotension in the postoperative period for 8-16 hours with a gradual rise and stabilization of blood pressure, partial pneumothorax on the side of surgery 2 (5.9%). After operations, patients could fully serve themselves for 2-3 days. The average postoperative bed-day was 10 ± 2 days.

V. DISCUSSIONS:

Neimark M.I. et al., (2003); Knuttegen D. et al., (2007) report anesthetic benefits during surgery for hormone-active adrenal tumors are not well understood. Until now, there are no clear recommendations regarding the duration of preoperative preparation in patients with hormone-active adrenal tumors, the priority objects of correction of changes associated with electrolyte metabolism disorders have not been specified, there are no specific recommendations regarding the advisability of using mineralocorticoid drugs when removing hormone-active adrenal tumors. In addition, there is no clear data on the choice of the method of pain relief, on the advisability of using certain narcotic drugs, such as muscle relaxants, during operations for hormone-active adrenal tumors; the features of the immediate postoperative period in patients of this group have not been specified [22; 23].

In patients with hormone-active tumors in the early postoperative period of all groups, the pathologically increased level of hormones decreased, and there was a tendency to a decrease and stabilization of blood pressure numbers. Assessing the hormonal status of patients in the early postoperative period, we can speak of the sufficiency of the volume of surgery in the treatment of hormonally active tumors. Persistent adrenal insufficiency after surgery was observed only in patients with corticosteroids. At the same time, the volume of the operation did not matter, since
the cause of this complication was ACTH deficiency against the background of its prolonged suppression by a hyperfunctioning tumor. This mediation was corrected with conclusion.

**VI. CONCLUSION:**

Thus, hormone-active adrenal tumors are extremely hormonally aggressive neoplasms, which places high demands on careful preoperative preparation of patients, the level of training of the anesthesia team, equipping the operating room with high-quality monitors, and equipping the operating room with a sufficient number of necessary drugs. The number of complications after surgery to remove hormonally active adrenal tumors are few.

There was no mortality in the postoperative period in the group of 34 operated patients with hormonally active adrenal tumors.

During the operation to remove hormonally active adrenal tumors, no critical changes in blood pressure were noted. The maximum level of systolic blood pressure was 170.4 ± 10.5 diastolic - 107.3 ± 3.4 mm Hg. Arterial hypertension was easily corrected with standard doses of antihypertensive drugs.

Considering that at present the most effective method of treating adrenal tumors is surgical, the main task is to identify and promptly treat these tumors in the early stages of the disease, which makes it possible to improve the results of relapse-free and tumor-specific survival.

**REFERENCES**