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# **HYPERTENSIVE CRISIS IN MODERN GUIDELINES: HOW TO AVOID MISTAKES IN DIAGNOSIS AND TREATMENT. BASED ON THE MATERIALS OF THE RUSSIAN NATIONAL «HUMAN AND MEDICINE» CONGRESS AND THE III CARDIOLOGY SUMMIT**

**Abstract**

The prevalence of hypertension is about 40 % according to Russian and world statistics. Approximately 1–2 % of patients with hypertension have high blood pressure throughout their lives, which requires urgent or emergency care. Hypertensive crisis is an acute condition caused by a sudden increase in blood pressure to individually high values, accompanied by clinical symptoms and requiring a controlled reduction to prevent target organ damage. According to the severity of clinical symptoms, hypertensive crisis is divided into uncomplicated and complicated. Typical signs of hypertensive crisis include malignant hypertension, severe hypertension associated with other clinical conditions, a sudden increase in blood pressure due to pheochromocytoma associated with organ damage, severe hypertension during pregnancy or preeclampsia. Hypertensive crisis is associated with various acute conditions, most often stroke (ischemic and hemorrhagic), acute cardiogenic pulmonary edema, acute heart failure, acute coronary syndrome, acute kidney injury, acute aortic dissection and eclampsia. The main goals of the treatment of hypertensive crisis are relief of the crisis, post-crisis stabilization, and prevention of repeated hypertensive crises. In patients with an uncomplicated hypertensive crisis, a decrease in mean blood pressure by 10 % during the first hour and by another 15 % during the next 2–3 hours is recommended. Therapy of complicated hypertensive crisis consists in the mandatory use of intravenous drugs with a predictable and controlled effect. The prognosis in patients with a hypertensive crisis, especially complicated one, is not favorable due to the high risk of short-term and long-term mortality. Patients who have undergone a hypertensive crisis require long-term follow-up.

**Key words:** *hypertension, hypertensive crisis, stroke, acute coronary syndrome, aortic dissection, pulmonary edema, hypertensive encephalopathy, target organ*

**Conflict of interests**

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BP — blood pressure, DIC-syndrome — disseminated intravascular coagulation syndrome, CAD — coronary artery disease

*From April 8 to 11, 2019, the XXVI Russian National «Human and Medicine» Congress and the III Cardiology Summit were held in Moscow. Hypertension has become one of the key topics of the Congress and the Summit. The physicians paid great attention to the problem of diagnosis and therapy of urgent and emergency conditions caused by hypertension.*

## Relevance

According to the World Health Organization, there are 1.13 billion patients with hypertension in the world [1]. Russian epidemiological studies indicate that the prevalence of hypertension is an average of 40 % [2]. Approximately 1–2 % of these patients have high blood pressure (BP) throughout their lives, which requires urgent or emergency care. It should be noted that of all calls to the ambulance service, 15–25 % were related to high blood pressure.

*Hypertensive crisis* — this is a condition caused by a sudden increase in blood pressure to individually high values, accompanied by clinical symptoms and requiring a controlled decrease in blood pressure to prevent damage to target organs.

Typical manifestations of hypertensive crisis include malignant hypertension, severe hypertension associated with other clinical conditions, sudden increase in blood pressure due to pheochromocytoma associated with organ damage, severe hypertension during pregnancy or preeclampsia.

Hypertensive crisis is of great importance in elderly patients, especially since in many of them severe uncontrolled hypertension is asymptomatic. The study, which included 1,546 elderly patients (mean age 69 years) who were hospitalized for a hypertensive crisis, showed that 56 % of patients experienced nonspecific symptoms such as dizziness, palpitations, and headache. While symptoms indicative of target organ damage, chest pain and focal neurological symptoms were observed only in 28 % and 16 % of patients, respectively [3].

## Risk factors and causes of hypertensive crisis

During sessions at the “Human and Medicine” Congress and the Third Cardiology Summit, factors that provoke a hypertensive crisis and methods for their correction were discussed. The triggers of hypertensive crisis include: non-adherence to antihypertensive therapy regimen, ineffective antihypertensive therapy, psychoemotional stress, excessive intake of salt and liquid, intake of psychoactive substances, alcohol abuse, history of preeclampsia. One study showed that factors potentially associated with the development of hypertensive crisis are female gender, high obesity, hypertension or coronary artery disease (CAD), the presence of somatoform disorders, a large number of antihypertensive drugs, poor adherence to therapy. At the same time, the lack of adherence to antihypertensive therapy was the most significant risk factor and was associated with an increase in the risk of hypertensive crisis by 6 times [4]. In another recent study, it was demonstrated that old age, CAD, congestive heart failure and chronic renal failure are associated with hypertensive crisis [5].

In most guidelines, the clinical classification of hypertensive crisis based on the severity of clinical symptoms and the presence of complications is preferred. Based on this classification, uncomplicated and complicated hypertensive crises are identified.

Uncomplicated hypertensive crisis is characterized by a significant increase in blood pressure with relatively intact target organs. Uncomplicated hypertensive crisis is of 2 types:

without sympathoadrenal activity and with sympathoadrenal activity (tachycardia, hyperthermia, etc.).

Complicated hypertensive crisis is accompanied by acute or progressive damage to target organs (brain, heart, kidneys, liver) and is a threat to the patient's life, which requires controlled intensive antihypertensive therapy. Hypertensive crisis accompanies various acute conditions. With cerebral infarction the frequency is 24.5 %, with hypertensive encephalopathy — 16.3 %, with intracerebral hemorrhage or subarachnoid hemorrhage — 4.5 %. Acute pulmonary edema is accompanied by a hypertensive crisis in 22.5 % of cases, acute heart failure — in 14.3 % of cases, and acute coronary syndrome — in 12 % of cases. Acute kidney injury in <10 % of cases is accompanied by hypertensive crisis. It must be remembered that an increase in hepatic enzymes, in most cases due to HELLP-syndrome (hemolysis, thrombocytopenia, liver damage, usually occurs in the III trimester of pregnancy), can also be accompanied by hypertensive crisis in 0.1–0.8 % of cases. In addition, hypertensive crisis can accompany retinal hemorrhage in 0.01–0.02 % of cases. Among the vascular causes of hypertensive crisis, eclampsia (4.5 %) and acute aortic dissection (2 %) are identified [6].

At the “Human and Medicine” Congress, the topic of malignant hypertension was discussed in detail, given the poor prognosis of patients and high mortality. In these patients, severe hypertension (usually of the 3rd degree) associated with changes in the fundus (hemorrhage and/or optic papilla edema), microangiopathies and syndrome of disseminated intravascular coagulation (DIC), as well as encephalopathy (in about 15 % of cases), acute heart failure and sudden deterioration of renal function is generally revealed. The basis of this condition is fibrinoid necrosis of the small arteries of the kidneys, retina and brain. The term “malignant” reflects an extremely unfavorable prognosis of this condition if untreated [7].

It is noteworthy that in many patients in emergency departments with pain or other conditions, there may be an acute increase in blood pressure, which independently returns to normal values

when the pain decreases and will not require special measures to reduce it.

## Examination of patients with hypertensive crisis

A training course was set up for practitioners at the “Human and Medicine” Congress where approaches to the diagnosis of emergency conditions caused by hypertension were discussed.

During the history taking and direct examination of a patient with an abnormal increase in blood pressure, the presence of symptoms and signs of target organ damage should be assessed. In particular, it is necessary to carefully review headache, dizziness, shortness of breath, chest pain, vomiting and changes in vision.

In patients with hypertensive crisis, it is important to assess the duration and severity of previous hypertension, as well as ongoing drug therapy, including the use of OTC drugs such as sympathomimetics, and drug abuse (in particular cocaine).

During the direct examination of the patient, it is important to correctly measure blood pressure using a cuff of the appropriate size. In addition, the presence of signs of heart failure should be assessed in patients: elevated pressure in the jugular veins, wheezing in the lungs, gallop rhythm, peripheral edema. In case of hypertensive crisis, detailed neurological examination with cerebellar tests, as well as fundus examination, is mandatory.

Patient complaints may be specific to target organ damage. Chest pain may indicate the presence of ischemia or myocardial infarction, back pain may be evidence for aortic dissection, dyspnea may indicate pulmonary edema or congestive heart failure. The presence of neurological symptoms, including convulsions, visual impairment and impaired consciousness may indicate the presence of hypertensive encephalopathy. It should be taken into account that in patients with hypertensive encephalopathy somnolence, lethargy, tonic-clonic convulsions and cortical blindness can precede loss of consciousness. However, focal neurological symptoms rarely occur

and stroke should be excluded when said symptoms occur.

The European guidelines for the treatment of patients with hypertension provide examinations that must be performed in patients with emergency conditions due to hypertension [8]. Standard examinations include: 12-lead electrocardiography, fundoscopy, tests for hemoglobin, platelets, fibrinogen, creatinine, glomerular filtration rate, electrolytes, lactate dehydrogenase, haptoglobin, urine albumin/creatinine ratio, urinary sediment microscopy (erythrocytes, leukocytes, casts) as well as pregnancy test in women of reproductive age. In addition to these studies, some tests are performed according to indications. Troponin, MB-fraction of creatine phosphokinase and the N-terminal pro-brain natriuretic peptide (NT-proBNP) are determined in cases of suspected myocardial damage, for example, with chest pain or acute heart failure); chest X-ray with volume overload; echocardiography with suspected aortic dissection, heart failure, ischemia; computed angiography of the chest and/or abdominal cavity with suspected aortic dissection; computed tomography or magnetic resonance imaging of the brain with suspected damage; ultrasound examination of the kidneys in cases of suspected kidney damage or renal artery stenosis; urine drug screen in cases of suspected use of amphetamine or cocaine.

## The choice of optimal therapy for hypertensive crisis

The main objectives of hypertensive crisis therapy are: relief of crisis, post-crisis stabilization and prevention of repeated hypertensive crises.

The rate of decrease in blood pressure in hypertensive crisis is a debatable issue. The ideal rate of decrease in blood pressure in uncomplicated hypertensive crisis has not been precisely determined. In clinical guidelines, a decrease in mean BP by 10 % during the first hour and by another 15 % during the next 2–3 hours is recommended. It should be remembered that a more rapid decrease in blood pressure can lead to ischemia of organs. A gradual decrease in the level of blood pressure is recommended to be carried out with

tablet antihypertensive drugs sublingually. In the absence of an effect from the tablet form and/or the presence of nausea and vomiting, parenteral drugs may be administered.

Therapy of complicated hypertensive crisis has become an important topic of discussion at the “Human and Medicine” Congress. Treatment of complicated hypertensive crisis consists in the mandatory use of intravenous drugs with a predictable and controlled effect. In complicated hypertensive crisis, BP reduction should be carried out as follows: in the first hour, mean BP decreases by 25 % (target level of diastolic BP  $\geq$  100 mm Hg), during 2 to 6 hours — to the target systolic BP of 160 mm Hg and/or diastolic BP of 100–110 mm Hg, during 6 to 24 hours — blood pressure should be maintained at the level achieved in the first 2–6 hours, during 24 to 48 hours — maintenance of blood pressure figures according to the latest clinical recommendations.

It is important to remember that BP reduction according to this principle is performed in all patients except for acute aortic dissection, acute ischemic or hemorrhagic stroke, eclampsia/pre-eclampsia, acute coronary syndrome, acute cardiogenic pulmonary edema. Urapidil, nitroglycerin, nitroprusside, esmolol, metoprolol and some other drugs are currently used for intensive antihypertensive therapy.

The choice of drug depends on the clinical manifestation. In patients with acute coronary syndrome, an immediate decrease in systolic blood pressure to <140 mm Hg is necessary. The first-line drug is nitroglycerin (dose of 5–200 mg/min with increase by 5 mg/min every 5 min), urapidil is its alternative (12.5–25 mg by bolus, 5–40 mg/h as continuous infusion). In the case of acute cardiogenic pulmonary edema, systolic blood pressure should be immediately reduced to <140 mm Hg. The drug of first choice is nitroglycerin with furosemide, and the alternative drug is urapidil. In patients with acute aortic dissection, an immediate rapid decrease in systolic blood pressure to <120 mm Hg within 5–8 minutes and a decrease in heart rate to <60 beats/min have been shown to be effective. The drugs of first choice are esmolol (0.5–4 mg/kg

by bolus; 50–300 mg/kg/min — continuous infusion) and nitroprusside (0.3–10 mg/kg/min with increase by 0.5 mg/kg/min every 5 min until the target BP is achieved), or nitroglycerin, or nicardipine (5–15 mg/h via continuous infusion, initial dose of 5 mg/h with increase every 15–30 min by 2.5 mg until target BP is achieved, then it should be reduced to 3 mg/h); their alternative is metoprolol (15 mg i. v., usually 5 mg i. v. with repeat dosing at 5-minute intervals) or labetalol (0.25–0.5 mg/kg; 2–4 mg/min until target BP is achieved, then 5–20 mg/h). However, in patients with cerebral stroke, the reduction of blood pressure should be extremely careful. The initial decrease in blood pressure should be no more than 10–15 % of the initial value under continuous monitoring of the patient's neurological status. In patients with unspecified stroke, antihypertensive therapy in the acute period is carried out only in the case of systolic blood pressure above 200 mm Hg. In patients with diagnosed subarachnoid hemorrhage of non-traumatic origin, antihypertensive therapy is carried out only with systolic blood pressure above 170 mm Hg. In patients with baseline systolic BP  $\geq 220$  mm Hg, BP is reduced to  $<180$  mm Hg. In the case of malignant hypertension accompanied by acute kidney injury or without it, blood pressure should be reduced within a few hours, and mean BP should be reduced by 20–25 %. The drugs of first choice are labetalol and nicardipine, and nitroprusside and urapidil are alternative drugs. In patients with diagnosed hypertensive encephalopathy, an immediate decrease in mean BP by 20–25 % with labetalol or nicardipine is recommended (nitroprusside is an alternative drug). In patients with eclampsia and severe pre-eclampsia/HELLP syndrome, systolic blood pressure should be immediately reduced to  $<160$  mm Hg and diastolic blood pressure — to  $<105$  mm Hg. For this purpose, labetalol or nicardipine and magnesium sulfate are recommended. When prescribing drug therapy, in addition to efficacy, possible contraindications and adverse events should be taken into account. For example, esmolol is contraindicated in atrioventricular blockade of the 2nd or 3rd degree, systolic heart failure, asthma and bradycardia, and nitroprusside should be used with caution in renal and hepatic insufficiency [7].

## The prognosis of patients after hypertensive crisis

Mortality among patients with hypertension, and in particular, hypertensive crisis, decreased significantly after the widespread introduction of antihypertensive drugs into clinical practice. The results of the studies indicate that the survival rate in patients with malignant hypertension increased from 37 % in the 1960s to 94 % in the 2000s. However, the long-term prognosis of patients who experienced a hypertensive crisis remains not very favorable. The results of a retrospective study with 670 adults with hypertensive crisis demonstrate that the increase in short-term mortality is due to neurovascular causes, and long-term mortality for 12 months — due to cardiovascular causes. The mean survival period in patients in whom the hypertensive crisis was due to a neurovascular cause was 14 days, in patients with a cardiovascular cause of hypertensive crisis — 50 days [8]. According to an extensive multicenter study, which included patients with hypertensive crisis who received intravenous therapy, nosocomial mortality was 6.9 %, followed by a 90-day mortality rate of 4.6 %. More than half of these patients (59 %) had new development or worsening of organ failure, most often kidney injury, acute heart failure, ischemia or myocardial infarction and encephalopathy [9]. According to another analysis in the European registry, 30-day mortality in patients with hypertensive crisis requiring parenteral therapy was 4 %, and the overall risk of damage to vital organs was 19 % [10].

In clinical guidelines, it is recommended, after discharge from the hospital once BP reaches a safe stable level during oral therapy, to perform follow-up with a monthly medical visit until the optimal target BP level is reached, and long-term follow-up by specialists subsequently.

## Conclusion

Diagnosis and therapy of emergency conditions caused by hypertension became the subject of scientific discussion at the National "Human and Medicine" Congress and the III Cardiology Summit. Hypertensive crisis is a life-threatening condition that requires a controlled decrease in blood

pressure to prevent damage to target organs, usually with the help of intravenous therapy.

At the “Human and Medicine” Congress and the III Cardiology Summit, clinical algorithms for managing patients at the level of primary health care were tested. Today, algorithms for dyspepsia, non-alcoholic fatty liver disease, hypertension, hypercholesterolemia, stable coronary artery disease, tobacco dependence, type 2 diabetes mellitus, acute and recurrent cystitis, acute otitis media, acute and recurrent tonsillopharyngitis, acute bronchitis, acute and chronic rhinosinusitis and vaccination are approved and available for use in clinical practice.

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