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ORIGIN, DIAGNOSIS AND MODERN CLINICAL DIAGNOSTIC METHODS OF HYPERTENSION

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Relevance of the problem: Many RCTs have shown that monotherapy reduces blood pressure only in a limited number of hypertension cases, and most patients require a combination of at least two drugs for satisfactory blood pressure control. A meta-analysis of more than 40 studies has shown that a rational combination of two drugs from any two classes of antihypertensive agents significantly improves the degree of blood pressure reduction than increasing the dose of a single drug. Another advantage of combination therapy is that there may be physiological and pharmacological synergy between drugs from different classes, which not only leads to a significant decrease in blood pressure and good tolerability. Combination therapy also allows you to suppress counter-regulatory mechanisms of blood pressure increase. Rational combinations of antihypertensive drugs are ACE inhibitors + TD; BRA + TD; ACE inhibitor + AC; BRA + AK; dihydropyridine AC + BB; AK + TD; BB + TD [1].

Research methods and materials: Taking into account the clinical course of the disease, comorbid pathology, tolerability of treatment and side effect profile, as well as the presence of benefits associated with the patient's personal positive or negative experience and, accordingly, the expected adherence to treatment, the doctor has the right to prescribe any antihypertensive drug registered in Russia, both in monotherapy and in combination therapy, if clinically appropriate. In this case, deviations from standard treatment regimens require an appropriate explanation in the anamnesis [1].

When the combination is not sufficiently effective, "stepping up" within the AHT framework involves using higher doses of the combination or immediately switching to a 3-component treatment regimen. Both approaches are acceptable in the phase of using a secondary combination of antihypertensive agents, but they should ensure that the target blood pressure is achieved within 3 months, with a dose titration phase of approximately 4 weeks [1].

When assessing the need for extended AHT, it should be borne in mind that target blood pressure levels are recommended to be achieved in each subgroup of patients, but the most

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important principle for achieving them is to ensure safety and maintain the patient's quality of life. Therefore, the speed of achieving target values and the degree of blood pressure reduction can be adjusted for a particular patient depending on the specific clinical situation. In this case, poor tolerance of blood pressure reduction may be a reason for a slower titration of doses and the number of drugs prescribed; as with good tolerance to AHT, BP can be reduced to values lower than the average recommended [1]. Failure to achieve target blood pressure within 3 months is not considered AHT failure if this is associated with clinical necessity. If the physician considers that poor compliance of the patient is an obstacle to achieving target BP, this should be reflected in the medical record and measures should be taken and recorded to improve compliance. In such cases, failure to achieve target levels should not be considered a failure of care [1]. Recommended combinations of three antihypertensive drugs include ACE inhibitor + AC + diuretic and ARB + AC + diuretic. Other combinations may be used, depending on the indication and in special circumstances: ACE inhibitor + dihydropyridine AC + BB; BRA + dihydropyridine AC + BB; ACE inhibitor + diuretic + BB; ARB + diuretic + BB; dihydropyridine AC + diuretic + beta-blocker [1].

Low-dose aspirin (75–150 mg) is recommended for patients with hypertension and a history of cardiovascular disease [1, 21]. Long-term use as part of secondary prevention reduces cardiovascular mortality by 15% and nonfatal vascular events by 30% [1, 22]. In patients after MI, acetylsalicylic acid use for 2 years is associated with an absolute reduction in the risk of cardiovascular events of $33 \pm 7\%$ per 1000 patients treated within 1 month and $39 \pm 5\%$ per 1000 patients treated. After stroke or transient ischemic attack, the reduction in cardiovascular events is $27 \pm 8\%$ per 1000 patients treated for 34 months [1, 23]. In a study of patients with stable angina, taking acetylsalicylic acid (75 mg daily) for 15 months compared with placebo reduced the overall incidence of MI and sudden death by 34%, and other vascular events and cardiovascular death by 22-32% [1, 24].

Conclusions: In 15–20% of patients, blood pressure control may not be achieved with three drugs. In this case, a combination of ≥4 antihypertensive drugs (preferably in two tablets) is used. However, in cases of resistant hypertension, the effectiveness of each new drug should be monitored with the addition of their effect, and ineffective antihypertensive drugs should be discontinued as part of a stepwise titration of multi-component AHT [1].

In case of intolerance to spironolactone, other diuretics (eplerenone, loop diuretics, including high doses), beta-blockers, alpha-blockers, or centrally acting drugs can be used as the 4th component of hypertension therapy [1, 26].

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Eplerenone, like spironolactone, has shown positive effects in heart failure and resistant hypertension. Spironolactone and eplerenone are used in the treatment of hypertension at low daily doses (25–50 mg). Their use is absolutely contraindicated in patients with a creatinine clearance <30 ml/min/1.73 m2, as this increases the risk of hyperkalemia and worsening renal function [1].

The imidazoline receptor agonist moxonidine increases tissue insulin sensitivity in overweight patients with mild hypertension, insulin resistance, and impaired carbohydrate metabolism. It is recommended for use in the treatment of patients with hypertension and metabolic syndrome or obesity [1, 27]. In this group of patients, moxonidine may be considered in combination with RAAS blockers (ACE inhibitors or ARBs), CA antagonists, or diuretics [1].

Conclusion: According to the Eurasian Clinical Guidelines for the Prevention and Treatment of Cardiovascular Disease in Patients with Diabetes and Prediabetes (2021), it is recommended to consider the use of moxonidine + RAAS inhibitor (ACE inhibitor or ARB) + AC or diuretics in patients with hypertension to control blood pressure: UUR - IIb, UDL - C [26]. We should add that in patients with arterial hypertension with diabetes mellitus, it is recommended to start antihypertensive therapy when the blood pressure measured in a medical institution is ≥140/90 mm Hg. The target blood pressure levels and the principles of stepwise therapy in this case correspond to the hypertension treatment regimen presented in this material (Part I) [1, 26].

The use of moxonidine is contraindicated in cases of sick sinus syndrome, sinoatrial, atrioventricular block 2-3 degrees, severe bradycardia with a heart rate <50 beats per minute, CHF III-IV functional class [1].

The preferred indication for alpha-blockers (doxazosin, prazosin) is benign prostatic hyperplasia in patients with hypertension. They improve carbohydrate and lipid metabolism, increase tissue sensitivity to insulin, and improve renal hemodynamics. These drugs are used with caution in patients with diabetic neuropathy and in patients over 65 years of age because they can cause postural hypotension [1].

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