STUDY OF THE EFFECT OF MONO AND COMBINED HYPOTENSIVE DRUGS WITH ANGIOPROTECTIVE PROPERTIES ON THE STIFFNESS OF THE VASCULAR WALL IN HYPERTENSION

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Abstract
This article discusses the study of the effect of mono and combined hypotensive drugs with angioprotective properties on the stiffness of the vascular wall in hypertension.

Keywords: hypertensive disease, angioprotective properties, combined hypotensive drugs, vessel wall.

The main goal of treating arterial hypertension (AH) is to prevent the development of cardiovascular complications and reduce cardiovascular mortality, achieve an optimal level of blood pressure (BP), correct metabolic parameters and other risk factors. One of the most important conditions for ensuring adequate control of blood pressure and increasing patient adherence to treatment is the optimal choice of antihypertensive agent. Combination therapy most effectively prevents target organ damage and leads to a decrease in the number of cardiovascular complications in patients with hypertension.

The advantages of combination therapy, which consist in potentiating the antihypertensive effect and reducing the number of side effects, are inherent only in the so-called rational combinations of antihypertensive drugs.

According to epidemiological studies, the prevalence of arterial hypertension (AH) among the adult population in developed countries ranges from 20 to 40% and increases with age [1]. High blood pressure (BP) is found in more than 50% of men and women over 60 years of age [2]. The urgency of the problem is supported by the increasing processes of urbanization of society, creating the prerequisites for the emergence of factors risk (FR), such as stress, physical inactivity, obesity, bad habits and disturbed ecology.

Elevated blood pressure is one of the main risk factors for the development of cerebral stroke, coronary heart disease (CHD) and other cardiovascular diseases of atherosclerotic origin, with which about 50% of all deaths [3].

Clinical practice and the results of many multicenter studies have shown that the use of monotherapy in the treatment of hypertension rarely leads to the achievement of target blood pressure levels, increases the risk of adverse events and reduces patient adherence to treatment [4-6]. The use of drugs in a rational combined regimen requires compliance with a number of mandatory conditions:

- The safety and efficacy of the components;
- the contribution of each of the components to the expected result;
- different, but complementary mechanism of action of the components;
- the best result in comparison with each of the components;
- balance of components in terms of bioavailability and duration of action;
- strengthening of organoprotective properties;
- impact on the universal (most frequent) mechanisms of increasing blood pressure;
- reduction in the number of adverse events and improved tolerability [7].

According to modern national guidelines [10], the recommendations of the European Society for Hypertension (ESH) and the European Society of Cardiology (ESC) [9], the tactics of treating essential hypertension depend on the level of blood pressure and the risk of cardiovascular complications. The main goal of treatment is to minimize the risk of developing cardiovascular complications (CVE) and death from them.

The main objectives are to normalize the level of blood pressure, prevent complications in the absence or minimum level of adverse drug reactions (ADRs), correct all modifiable risk factors (smoking, dyslipidemia, hyperglycemia, obesity), prevent, slow down the rate of progression and / or reduce damage to target organs, and also treatment of associated and concomitant diseases — coronary artery disease, diabetes mellitus (DM) and others.

In the treatment of patients with hypertension, the value of blood pressure should be less than 140/90 mm Hg. Art., which is the target level. With good tolerability of the prescribed therapy, it is advisable to reduce blood pressure to lower values. In patients with high and very high risk of CVD, it is necessary to achieve a blood pressure level of 140/90 mm Hg. Art. or less within 4 weeks. In the future, subject to good tolerance, it is recommended to reduce blood pressure to 130/80 mm Hg. Art. and less.

Patients with IHD should strive to achieve a blood pressure level of 130/85 mm Hg. Art. In patients with diabetes and / or kidney disease, the target blood pressure level is less than 130/85 mm Hg. Art. [10]. Of course, the treatment of hypertension should begin with lifestyle changes, which include reducing overweight, limiting the consumption of salt and alcohol, increasing physical activity and other activities.

Limiting salt intake is a fairly effective way to reduce blood pressure. It has been noted that salt restriction enhances the effect of many antihypertensive drugs, including angiotensin receptor type 1 antagonists (AT1) and β-blockers (BABs) [10]. One of the most important conditions for ensuring adequate control of blood pressure and increasing patient adherence to

treatment is the optimal choice of an antihypertensive agent as part of mono- or combined pharmacotherapy.

Currently recommended for the treatment of hypertension five main classes of antihypertensive drugs [10]:

1. angiotensin-converting enzyme inhibitors (ACE inhibitors) (captopril, enalapril, perindopril, lisinopril, fosinopril, quinapril, trandolapril and others);
2. AT1 receptor blockers (ARBs) (valsartan, losartan, telmisartan, candesartan, irbesartan and others);
3. blockers of slow calcium channels (BCCC) (nifedipine, amlodipine and others);
4. BAB (carvedilol, bisoprolol, nebivolol, metoprolol tartrate, metoprolol succinate, atenolol and others);
5. thiazide and thiazide-like diuretics (hydrochlorothiazide, indapamide)

As additional classes of antihypertensive drugs for combination therapy, α-blockers (prazosin, doxazosin), imidazoline receptor agonists (moxonidine), direct renin inhibitor (aliskiren) can be used.

According to these national guidelines [10], the choice of an antihypertensive drug should be determined by the peculiarity of the drug's action, its belonging to a certain class, since the results of clinical trials conducted according to the rules of evidence-based medicine made it possible to establish situations of preferential class choice of drugs.

When choosing an antihypertensive drug, it is necessary first of all to evaluate the likelihood of side effects, the effectiveness and benefits of drugs in a particular clinical situation.

The choice of drug is influenced by many factors, the most important of which are the following:

- the presence of FR in a patient;
- target organ damage;
- concomitant clinical conditions, kidney damage, diabetes;
- concomitant diseases that require the appointment or restriction of the use of antihypertensive drugs of various classes;
- previous individual reactions of the patient for drugs of various classes;
- the likelihood of interaction with drugs that the patient is prescribed for other reasons;
- socio-economic factors, including the cost of treatment.

It is necessary to begin treatment with the use of one Drugs in the minimum daily dose (this recommendation is not applies to patients with severe hypertension or those in whom previous therapy was ineffective). The use of new drugs should begin with the use of low doses, the goal of each next stage of treatment should be to reduce blood pressure by 10-15% [10]. If blood pressure does not drop to the desired level, further treatment is carried out in a gradual way - step by step, step - increasing doses or adding new drugs. Ineffective drugs (not causing

a decrease in blood pressure by 10–15 mmHg Art.) and drugs that cause NLR should be replace [5].

There are no single recommendations as to which means should be used to start treating the patient. The choice of drugs for the initial appointment depends on age, gender and the presence of concomitant diseases.

ARBs are one of the modern and most dynamically developing classes of antihypertensive drugs. ARBs inhibit angiotensin II effect through AT1 receptors. It has been established that angiotensin II hypersecretion leads not only to the development of hypertension, but also to damage to target organs, being one of the main factors in the progression of hypertension and its complications, remodeling of the heart and blood vessels. It is no coincidence that ARBs are classified as essential antihypertensive. Numerous controlled studies such as LIFE, VALUE, MARVAL, PRIME, IDNT, DETAIL have shown that AT1 blockers are effective and safe antihypertensive drugs [13]. ARB blockers have been particularly effective in preventing stroke. For the prevention of stroke in patients with hypertension, ARBs can be used both instead of diuretics or calcium antagonists and together with them. Like ACE inhibitors, they are able to prevent the development of type 2 diabetes, reducing the risk of its occurrence by 20–25% [4].

This suggests that ARBs should be used to treat hypertension primarily in patients at high risk of stroke or DM. Excellent tolerability is an undoubted advantage of ARBs in long-term antihypertensive therapy. The use of drugs of this class can improve the adherence of patients to long-term therapy, since they have to be canceled much less often than other antihypertensive drugs due to the development of side effects. Unlike thiazide diuretics, BSE and ACE inhibitors, antihypertensive

The effectiveness of an ARB does not depend on age, sex, or races of patients [5]. Valsartan is one of the most studied BRA. More than 150 clinical studies conducted with the study of more than 45 points of performance evaluation.

The total number of patients included in clinical trials reaches 100,000, of which more than 40,000 included in incidence studies and mortality. Effect of valsartan on survival patients was studied in a number of large randomized multicenter studies: VALUE, Val-HeFT, VALIANT, JIKEI Heart, NAVIGATOR [3].

Valsartan is a drug that combines high efficacy with good tolerability, no risk of significant drug interactions and ease of use. The action of valsartan leads to a stable blockade of AT1 receptors. Over time, there is no increase in the number of blocked receptors or a decrease in their sensitivity.

Valsartan does not change the heart rate and rhythm, orthostatic adaptation after changing the position of the body, as well as hemodynamic reactions due to sympathetic stimulation after exercise. To realize the therapeutic effect of the drug, metabolic transformations are required. He is effective regardless of gender and age of patients, both for short-term and long-term use.

For the treatment of hypertension, valsartan is used once. In most patients, the onset of its antihypertensive action is noted within 2 hours, maximum - 4-6 hours, duration of action - more than 24 hours, which allows you to take it once a day [2].

In patients with severe hypertension and in case of ineffectiveness of treatment with one drug, combinations of drugs are used.

Combination antihypertensive therapy has many advantages:

- enhancement of the antihypertensive effect due to the multidirectional action of drugs on the pathogenetic mechanisms of the development of hypertension, which increases the number of patients with a stable decrease in blood pressure;
- reduction in the incidence of side effects, both due to lower doses of combined antihypertensive drugs, and due to the mutual neutralization of these effects;
− ensuring the most effective organ protection and reducing the risk and number of CVCs.

Numerous randomized clinical trials and real clinical experience
showed all the advantages of combination therapy, which
can be summarized as follows [3]:

- the simultaneous use of drugs of two different pharmacological groups more actively reduces blood pressure due to the fact that there is an effect on various pathogenetic mechanisms of hypertension;
- combined use of lower doses of two drugs acting on various regulatory systems, allows better control of blood pressure, given the heterogeneity of the response of hypertensive patients to antihypertensive drugs;
- the appointment of a second drug may weaken or to balance the launch of mechanisms to counteract the decrease in blood pressure that occurs when prescribing one drug;
- a steady decrease in blood pressure can be achieved smaller doses of two drugs (than with carrying out monotherapy);
- smaller doses avoid dose-dependent side effects that are more likely high with a higher dose of a particular drug (during monotherapy);
- the use of two drugs can prevent target organ damage to a greater extent (heart, kidneys) due to hypertension;
- the appointment of the second drug can, to a certain extent, reduce (and even completely eliminate) the undesirable effects caused by the first (even if quite effective) drug;
- the appointment of a second drug (in particular, a diuretic) allows you to get a quick antihypertensive effect, since most antihypertensive drugs (ACE inhibitors, CBCCs, ARBs and partly BAB) show their full effect only in the second or third week of administration (and even later).

The most important conditions for increasing adherence patients to treatment are their understanding of the goals, objectives, modern methods and principles of treatment, as well as correct choice of antihypertensive treatment option doctor. The tactics of using combination

therapy with the selection of drugs with different mechanisms of action already at the beginning of treatment gives a much greater chance of a successful control of blood pressure and the risk of developing CVS.

The advantages of combination therapy are to potentiate the antihypertensive effect and reduce the number of side effects and are inherent only in the so-called rational combinations of antihypertensive drugs. For adequate treatment of hypertension, combination therapy should be used, starting with low doses of drugs.

ARBs, in particular valsartan (Valsacor), are characterized by high efficacy, good tolerability, the minimum number of side effects, the possibility protective effect on target organs and associated with this reduction in morbidity and mortality, as well as high adherence of patients to treatment due to convenient dosing regimen. These properties of valsartan (Valsacora) and other ARBs make these drugs indispensable and convenient in the treatment of patients with hypertension.

According to the results of many clinical international studies, the influence of blood pressure (BP) and associated risk factors on cardiovascular, renal complications and mortality in patients with arterial hypertension (AH) has been proven [1].

Assessment of cardiovascular risk in hypertension along with risk factors, clinically manifest cardiovascular diseases, diabetes and chronic kidney disease includes asymptomatic target organ damage resulting from changes in the vascular bed [2].

One of the links in the pathogenesis of hypertension is the functional and morphological restructuring of arterial vessels - remodeling, which aggravates the course of the disease. Changes in the vascular bed supplying the brain, heart, and kidneys contribute to early damage and progression of organ disorders in AH and cause the development of associated clinical conditions [3].

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