

Research Article**Drug Treatment of Hypertension in Older Patients and Its Side Effects****Alsu I. Abdrahmanova¹, Nikolay A. Tsibulkin²,****Juliya V. Oslopova¹ and Rezeda N. Khasanova¹**

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ABSTRACT.

Uncontrolled blood pressure has influence on the incidence of cardiovascular events (CVE), the quality and duration of life. The largest number of deaths related to the irrational pharmacotherapy of hypertension occurs in the age group of 80-90 years. The risk of side effects in patients older than 60 years increases by 2-3 times.

Methods. We have conducted the analysis of scientific publications devoted to the peculiarities of treatment of hypertension in older patients and the possible complications of this therapy.

Results. The presence of hypertension in the elderly is associated with an increased risk of CVE.

The target level for elderly patients with SBP > 160 mm Hg is 150-140 mm Hg. For elderly patients under 80 years old living an active lifestyle and having good treatment tolerability, the SBP target level can be less than 140 mm Hg. And patients over 80 years old with initial SBP \geq 160 mm Hg are recommended to decrease it up to 140-150 mm Hg at satisfactory clinical condition. Older patients are recommended to observe standard approaches to lifestyle changes, and most of them require pharmacological treatment. The main problems of therapy in the elderly is the prescription of multiple drugs due to the presence of concomitant diseases, the long-term treatment due to their chronic course, and inaccurate performance of therapy mode.

Discussion. The main goal of treatment of hypertension in the elderly is to reduce the risk of CVE and development of chronic heart failure (CHF) and chronic renal failure (CRF). The effects of treatment must be weighed against the possible risk of CVE. Treatment should start with a low dose monotherapy with gradual increase at intervals of several weeks until the desired effect. It is necessary to avoid a sharp decline in blood pressure in case of cardiac and renal failure, disorders of cerebral blood flow, and orthostatic hypotension. Selection of therapy is carried out subject to comorbidities, the pathogenesis of hypertension and restrictions for certain groups of drugs. The common therapy complications for the elderly are hypotension, transient ischemic attack, hemorrhagic or ischemic stroke, encephalopathy, pulmonary edema, angina, and myocardial infarction.

Final Report. Knowing the geriatric aspects of cardiology is an important element of knowledge of a modern doctor.

Keywords: arterial hypertension, antihypertensive therapy, side effects, old age

INTRODUCTION

The incidence of hypertension has been increasing, and the further increase in the

number of people suffering from this disease is predicted. In developed countries, less than half

of the patients monitor their blood pressure [1, 2]. This affects the rate of CVE development, the quality and duration of life. The largest number of deaths related to the irrational hypertension pharmacotherapy has been observed in the age group of 80-90 years. In patients over 60 years old, the error rate at taking drugs is about 60% and increases significantly when taking more than three different drugs [3].

METHODS

We have conducted the analysis of recent publications devoted to the peculiarities of treatment of hypertension in older patients and the possible complications of this therapy.

RESULTS.

The main goal of treatment of hypertension in the elderly is to reduce the risk of CVE and development of chronic heart failure (CHF) and chronic renal failure (CRF) [4]. Compared to middle-aged persons, the elderly people have a higher chance of development of drug side effects, adverse drug interactions, they more often receive multicomponent treatment programs [5]. The treatment strategy requires to provide for measures aimed at correction of the potentially modifiable CVE factors identified in patients, including smoking, dyslipidemia, abdominal obesity, and diabetes. The European and national recommendations of the last revision pay a particular attention on target level of blood pressure [1]. The target level for elderly patients with SBP > 160 mm Hg is 150–140 mm Hg. For elderly patients under 80 years old living an active lifestyle and having good treatment tolerability, the SBP target level can be less than 140 mm Hg. And patients over 80 years old with initial SBP \geq 160 mm Hg are recommended to decrease it up to 140–150 mm Hg at satisfactory clinical condition [6]. The main problems of drug therapy in presenile and senile age are: the need for the prescription of more than one drug; prolonged use of medicaments (drugs); violation of pharmacodynamics and pharmacokinetics; incorrect performance of a therapy regime [7, 8]. The doctor must be sure that the indications are

defined correctly, drug doses comply with the peculiarities of the patient, and the physician's instructions are followed appropriately [7, 8, 9]. These factors determine the approach to antihypertensive therapy (AHT) in the elderly: the control of blood pressure in the sitting and standing position at dose selection; avoidance of a sharp decline in blood pressure, especially at heart failure [10]. The monotherapy treatment should be started with a small dose, gradually increased at intervals of several weeks until the desired effect, which allows avoiding orthostatic disorders, worsening of renal failure and brain. Individual selection of drugs is carried out subject to the associated pathologies, pathogenesis of hypertension, and restrictions for certain groups of drugs. It is recommended to give preference to long-acting drugs with optimal metabolic profile [11, 12]. Five classes of drugs that affect the prognosis are recommended. These are angiotensin-converting enzyme inhibitors (ACEI), angiotensin II receptor blockers (ARB), calcium antagonists (CA), β -adrenergic blockers (BAB) and diuretics. They can be prescribed as either the monotherapy or in combination. All of these classes of drugs may be used in the elderly, but the most preferred are ARB, CA, and thiazide diuretics (TD). AC and TD are more preferred for patients with ISAH [1, 13]. Arterial hypertension complications include arterial hypotension, cerebrovascular disturbance (hemorrhagic or ischemic stroke, encephalopathy), pulmonary edema, angina, myocardial infarction, and tachycardia. Drug-induced hypotension increases the risk of renal, myocardial and cerebral hypo perfusion. The drug-induced hypotension rate reaches 10%. The reasons are the intake of drugs with the effect of vasodilatation or decrease in circulating blood volume (CBV) and spontaneous hypotension at night. Hypotonic reactions are common for drugs with rapid release of the active ingredient with low T/P (Trough/Peak). The T/P index allows us to determine the duration of drug action in respect of the residual (after the last dose intake) activity to the peak activity (action at a maximum blood concentration). At low T/P there is a BP

variability due to hypotension at the peak of action and lack of effect at the end of dosing interval [14]. A decreasing CBV leads to a high concentration of hydrophilic drugs. Excretion of drugs can also slow down upon decreasing renal filtration and reducing activity of the hepatic enzyme systems. A decreasing CBV restricts the use of diuretics. The BP level decrease can occur during combined therapy where the maximum effect is delayed and hypotension occurs within a few hours [15]. The BP variability is a prognostically adverse factor for cardiovascular events (CVE) in hypertensive patients. The patients with vascular diseases showed a paradoxical increase in the frequency of CVE due to excessive reduction in blood pressure. Orthostatic hypotension in patients over 70 years old has been registered in 7%, and their mortality rate is 64% higher than in the control group [16, 17]. Neurological complications of arterial hypertension in the form of reduced physical and mental performance, fatigue, tinnitus and dizziness are observed on the background of cerebrovascular diseases. There are also observed sleep disturbances, emotional lability, and depression. Hypo perfusion conditions may both develop asymptotically in the form of reduced cerebral blood flow, according to the results of Doppler sonography, and cause clinically "silent" strokes. Arterial hypertension complications are also caused by a significant reduction in blood pressure as a result of baroreceptor dysfunction. At normal blood pressure, the cerebral blood flow is maintained at 50 ml/min per 100 g weight of the brain, the lower limit of autoregulation is 60 mm Hg, and the upper limit is 180 mm Hg. Autoregulation of cerebral blood flow in hypertensive patients adapts to the higher values of blood pressure: the higher the usual values of blood pressure are, the higher the lower limit of autoregulation is. Patients with long-term hypertension have the lower limit equal to 90-100 mm Hg. Thus, the rapid decline of SBP to 120-130 mm Hg can lead to a reduction in the perfusion blood pressure and the occurrence of cerebral ischemia. Cerebral hypo perfusion occurs with a

decrease in blood pressure by nearly 10-20% of the "operating" values [17, 18].

After suffering a brain hemorrhage, the risk of recurrent complications is proportional to the level of DBP, and their lowest rate was at $DAD \leq 80$ mm Hg. Those having suffered the ischemic stroke had the lowest risk of recurrent stroke in the range of DBP 80-84 mm Hg, and at a lower level of blood pressure the risk increased again. After suffering an ischemic stroke, the lowest rate of recurrence of cerebral events was observed at DBP 85-89 mm Hg, after lacunar (ischemic) cerebral infarction - 80-84 mm Hg. In case of intracerebral hemorrhage, it is recommended to gradually reduce the blood pressure to levels normal for the patient, and if such levels are not known, the SBP should be reduced to 150-160 mm Hg, and DBP - to 85-90 mm Hg. 20% of patients having suffered the transient ischemic attack or stroke have a severe stenosis or occlusion of at least one of the carotid artery. Inadequate antihypertensive therapy may impair the cerebral perfusion with respect to normal values of blood pressure and lead to complications. Analysis of the results of several studies that have examined the prognostic values of hypertension and antihypertensive therapy in patients with stenosis or occlusion of the carotid arteries, showed the following results [19, 20]. Patients having suffered the ischemic stroke and with significant stenosis of the internal carotid artery have less risk of stroke during an increase in blood pressure than patients without the pronounced atherosclerosis. Patients with clinically unilateral occlusive carotid lesions have an increased risk of stroke upon a decrease in SBP < 130 mm Hg. In case of bilateral carotid stenosis, the stroke risk also increases with a decreasing blood pressure. This group of patients had the lowest risk of stroke at SBP 150-169 mm Hg, which progressively increased at lower values.

Patients with a history of ischemic cerebral events and suffering from circulatory encephalopathy shall maintain 3 main target SBP levels as the most prognostically significant in relation to the risk of recurrent vascular cerebral complications: SBP 160-150 mm Hg

should be considered the minimum acceptable for patients with grade 3 hypertension or bilateral carotid stenosis $\geq 70\%$; SBP 140-135 mm Hg is optimal for patients with grade 2 hypertension and unilateral carotid stenosis $\geq 70\%$; SBP 120 mm Hg is the minimum possible for patients with grade 1 hypertension and high normal blood pressure in the absence of a pronounced lesion of cerebral arteries [16]. In patients with hypertension and coronary artery disease, the level of diastolic blood pressure below 90 mm Hg is associated with an increased risk of myocardial infarction as compared with the group with the lowest risk of MI at DBP 82.7 mm Hg. Patients with ISAH, the decrease in DBP lower than 70 mm Hg increases the risk of cardiovascular disease, including myocardial infarction, and the CVE risk increases by 2 times at DBP less than 55 mm Hg. Patients with occluded coronary artery disease and/or left ventricular hypertrophy have a higher risk of coronary events at low DBP, although this complication is more typical of patients with degree 1 and 2 hypertension, whose DBP levels dropped by more than 25 mm Hg from the initial one.

The sharp decline in blood pressure results in the development of renal failure. An adequate perfusion of kidneys requires to maintain SBP at a level of 80 to 180 mm Hg. ARBs and ACE inhibitors, by expanding the efferent arterioles, may cause a reduction in the perfusion pressure and a decrease in glomerular filtration rate (GFR). The dependence of the GFR level on angiotensin II becomes particularly pronounced at a decrease in CBV or at bilateral renal artery stenosis. Filtration reduction can lead to increased levels of creatinine or potassium. Hypovolemia and hypotension further exacerbate the reducing filtration [21, 22].

SUMMARY.

The goal of antihypertensive treatment in the elderly is to reduce the risk of cardio-vascular events, CHF and CRF. Their combined use results in high probability of side effects. Treatment should start with a low dose monotherapy with gradual increase until the desired effect. Selection of antihypertensive

therapy is carried out subject to comorbidities, the pathogenesis of hypertension and restrictions for certain groups of drugs. AC and TD are more preferred for patients with ISAH. The typical therapy complications of the elderly are hypotension, transient ischemic attack, hemorrhagic or ischemic stroke, encephalopathy, pulmonary edema, angina, and myocardial infarction. Neurological complications of antihypertensive treatment are manifested in the form of reduced mental performance, rapid fatigue, tinnitus and dizziness. Hypo perfusion conditions may be the cause of asymptomatic strokes.

CONCLUSION.

Knowing the geriatric aspects of cardiology is an important element of knowledge of a modern doctor.

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