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Arterial Hypertension and Heart Failure in General Practice

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The Framingham study demonstrated that myocardial infarction (25% of cases) and arterial hypertension (AH) (75% of cases) caused the development of chronic heart failure (CHF). The most significant predictor of CHF development was an increase in systolic blood pressure (SBP) and pulse pressure and each increase in SBP by 20 mm Hg and pulse blood pressure by 16 mm Hg led to an increase in the incidence of CHF by 52% and 55%, respectively.
The presented clinical case of a patient with CHF, developed due to long-term hypertension, considered the mechanisms of CHF development, as well as the issue of pharmacotherapy of AH in combination with chronic heart failure with systolic dysfunction. The key mechanisms that directly lead to the development of CHF in AH are hemodynamic overload, reduction of myocardial contractility, left ventricular hypertrophy (LVH). The likelihood of CHF development in patients with AH is by 4 times higher, whilst in patients with LVH it is by 15 times higher. Along with LVH, one of the early manifestations of LV remodeling in AH is the development of diastolic dysfunction, which precedes the development of systolic abnormalities in AH and LVH. Antihypertensive therapy resulted in reduction of the incidence of CHF by approximately 52% compared to patients who did not receive adequate therapy. The decrease in the incidence of CHF was linearly dependent on the decrease in SBP: each decrease of SBP by 10 mm Hg led to a 26% reduction in the relative risk in CHF development.
It has been established that AH is not only one of the leading etiological factors in CHF development, but also have similar key links in pathogenesis. The strategy for the selection of pathogenetic pharmacotherapy should be determined taking into account the above circumstance. Currently, the European Society of Cardiology recommends prescribing beta-blockers to all patients with stable CHF Class II–IV as a standard treatment in combination with ACE inhibitors and diuretics in the absence of contraindications. In addition to RAAS blockers, medications for patients with AH in combination with systolic CHF can be supplemented with thiazide or loop diuretics, as well as mineralocorticoid receptor antagonists (MRA).
Key words: *heart failure, arterial hypertension, systolic dysfunction, beta-blockers, ACE inhibitors.*

Артеріальна гіпертензія і серцева недостатність у загальнолікарській практиці

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За даними Фремінгемського дослідження, серед хворих на хронічну серцеву недостатність (ХСН) тільки у 25% причиною розвитку був перенесений інфаркт міокарда, а у 75% – артеріальна гіпертензія (АГ). Найбільш значним предиктором розвитку ХСН було збільшення систолічного артеріального тиску (САТ) і пульсового тиску відповідно, кожне збільшення САТ на 20 мм рт.ст. і пульсового АТ на 16 мм рт.ст. призводило до збільшення частоти розвитку ХСН на 52% і 55% відповідно.
На прикладі приведеного клінічного випадку пацієнта із ХСН, яка розвинулася на тлі довготривалої АГ, розглянуто механізми розвитку ХСН, також висвітлено питання фармакотерапії АГ у поєднанні з ХСН із систолічною дисфункцією. Основними механізмами, що безпосередньо призводять до розвитку ХСН при АГ є гемодинамічне перевантаження, зниження міокардіальної скоротливості, гіпертрофія лівого шлуночка (ГЛШ). Так, у пацієнтів з АГ ймовірність у подальшому розвитку ХСН підвищується у 4 рази, а з ГЛШ – у 15 разів. Поряд із ГЛШ одним із ранніх проявів ремоделювання ЛШ в умовах АГ є розвиток діастолічної дисфункції, яка передує розвитку систолічних порушень при АГ і ГЛШ. Антигіпертензивна терапія сприяла зменшенню у середньому на 52% частоти розвитку ХСН порівняно з хворими, які не отримували адекватну терапію. Зниження частоти розвитку ХСН лінійно залежало від зниження САТ: кожне зниження на 10 мм рт.ст. САТ приводило до зменшення на 26% відносного ризику розвитку ХСН.
Встановлено, що АГ є не тільки одним із провідних етіологічних чинників розвитку ХСН, а й має з останньою спільність у ключових ланках патогенезу. Стратегія вибору патогенетичної фармакотерапії визначається з урахуванням цієї обставини. На сьогодні Європейське товариство кардіологів рекомендує призначати b-АВ усім пацієнтам зі стабільною ХСН II–IV ФК в якості стандартного лікування разом із іАПФ і діуретиками за відсутності протипоказань. У хворих із поєднанням АГ та систолічною ХСН можливе застосування додатково до блокаторів РААС тіазидних або петльових діуретиків та антагоністів мінералокортикоїдних рецепторів (АМР).
Ключові слова: *серцева недостатність, артеріальна гіпертензія, систолічна дисфункція* β*-адреноблокатори, інгібітори АПФ.*

Артериальная гипертензия и сердечная недостаточность в общеврачебной практике

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По данным Фремингемского исследования, среди больных хронической сердечной недостаточностью (ХСН) только у 25% причиной развития был перенесенный инфаркт миокарда, а у 75% – артериальная гипертензия (АГ). Наиболее значительным предиктором развития ХСН было увеличение САД и пульсового давления соответственно, каждое увеличение САД на 20 мм рт.ст. и пульсового АД на 16 мм рт.ст. приводило к увеличению частоты развития ХСН на 52% и 55% соответственно.
На примере приведенного клинического случая пациента с ХСН, развившейся на фоне длительной АГ, рассмотрены механизмы развития ХСН, а также освещены вопросы фармакотерапии хронической сердечной недостаточности с систолической дисфункцией. Основными механизмами, которые непосредственно приводят к развитию ХСН при АГ, являются гемодинамические перегрузки, снижение миокардиальной сократимости, гипертрофия левого желудочка (ГЛЖ). Так, у пациентов с АГ вероятность развития в дальнейшем ХСН повышается в 4 раза, а с ГЛЖ – в 15 раз. Наряду с ГЛЖ, одним из ранних проявлений ремоделирования ЛЖ в условиях АГ является развитие диастолической дисфункции, которая предшествует развитию систолических нарушений при АГ и ГЛЖ. Антигипертензивная терапия приводила к уменьшению в среднем на 52% частоты развития ХСН по сравнению с больными, которые не получали адекватную терапию. Снижение частоты развития ХСН линейно зависело от снижения САД: каждое снижение на 10 мм рт.ст. САТ приводило к уменьшению на 26% риска развития ХСН.
Установлено, что АГ является не только одним из ведущих этиологических факторов развития ХСН, но и имеет с последней общность в ключевых звеньях патогенеза. Стратегия выбора патогенетической фармакотерапии определяется с учетом этого обстоятельства. На сегодня Европейское общество кардиологов рекомендует назначать β-АВ всем пациентам со стабильной ХСН II–IV ФК в качестве стандартного лечения вместе с иАПФ и диуретиками при отсутствии противопоказаний. У больных с сочетанием АГ и систолической ХСН возможно применение в дополнение к блокаторам РААС тиазидных или петлевых диуретиков и антагонистов минералокортикоидных рецепторов (АМР).
Ключевые слова: *сердечная недостаточность, артериальная гипертензия, систолическая дисфункция,* β*-адреноблокаторы, ингибиторы АПФ.*

Arterial hypertension (AH) remains one of the most ultimate causes of chronic heart failure (CHF) development in all age groups. The Framingham study demonstrated that myocardial infarction (MI) (25% of cases) and arterial hypertension (AH) (75% of cases) caused the development of chronic heart failure (CHF) in patients. In 25 European countries, AH is considered the cause of CHF development in 53% of patients (Euro HeartSurvey, 2002–2003) [8, 13].

In people with blood pressure (BP) greater than 140/90 mmHg the risk for the development of CHF is twice higher compared to individuals who have systolic blood pressure less than 140/90 mmHg. The most significant predictor for the development of CHF was the increase in SBP and pulse pressure and each increase in SBP by 20 mmHg and pulse blood pressure by 16 mmHg increased the incidence of CHF by 52% and 55%, respectively [8]. The summary analysis of the EPRP and DIG studies has found that in patients with CHF and the ejection fraction of 30% – <50% mortality was dependent on the level of SBP in the form of a U-curve, that is, it was maximum at high and low SBP. At the same time, in patients with an ejection fraction of <30%, a linear inverse dependence of mortality on the level of SBP was observed: the higher the SBP the lower the mortality rate and the lower the SBP the higher the mortality in patients with CHF. Other risk factors and diseases as obesity, diabetes, smoking and dyslipidemia, CHD contribute to the development of CHF [5, 10, 13].

The main mechanisms that directly lead to the development of CHF in AH are hemodynamic overload, reduction of myocardial contractility, left ventricular hypertrophy (LVH). Prolonged significant uncontrolled increase in blood pressure leads to overload of the left heart, LVH, left ventricular dysfunction and, as a consequence, the onset of CHF. The development of the latter can be accelerated if AH is combined with coronary heart disease, diabetes mellitus, obesity, increased activity of renin-angiotensin and sympathoadrenal systems. LVH is a sole risk factor for the development of CHF. Thus, in patients with Ah, the likelihood of the follow-up development of CHF is increased by 4 times and with LVH by 15 times. Along with LVH, one of the early manifestations of LV remodeling in arterial hypertension is the development of diastolic dysfunction, which precedes the development of systolic dysfunctions in hypertension and LVH. In patients with arterial hypertension, diastolic dysfunction or its combination with systolic one is more commonly observed [9, 14].

At the initial stage of the left heart remodeling, left ventricular hypertrophy is a compensatory response that allows normalization of myocardial systolic load. Subsequently, dilatation of the left ventricle with a decrease in its function occurs. Another mechanism for the development of CHF in patients with arterial hypertension is the development of atherosclerotic lesions of the coronary arteries and coronary heart disease [13, 14].

Case report

The 54-year-old patient S. was admitted to the Cardiological unit with complaints of tachycardia, dyspnea at rest, peripheral edema, distended stomach.

The patient presented a 10-year history of the disease since 2009, when attacks of tachycardia occurred. The examination revealed the increase in blood pressure up to 180/120 mmHg. He took antihypertensive drugs on irregular basis. He experienced type II diabetes mellitus in 2013. In 2018, dyspnea, peripheral edema, distended stomach occurred.

Physical examination showed moderate overall health state of the patient, forced position, orthopnoea, acrocyanosis, congestive fine rales in the lower parts of the lungs, blood pressure of 150/90 mmHg, heart rate of 110 bpm, arrhythmic, left border of the heart was along the anterior axillary line, the right one was on parasternal line, tones were attenuated, arrhythmic, systolic murmur over the apex and III-IV intercostal space to the left, the liver extended 3–4 cm below the costal margin, free intraabdominal fluid.

Laboratory tests revealed Hb 120 g/L, RBC 3,8×1012/L, WBC 5,0×109/L, ESR 5 mm/h; urinalyses revealed traces of protein, RBC 2–3 FOV, WBC 6–8 FOV; blood biochemistry showed creatinine 133 μmol/l, urea 10 mmol/L, total cholesterol 6,3 mmol/L, LDL 2,4 mmol/L, uric acid 370 mmol/L, fibrinogen 4,0 g/L, glycated Hb 7.5%.

ECG revealed left axis deviation, reduced voltage, atrial fibrillation with the heart rate of 100-120 bpm.

Ultrasound cardioscopy revealed LV end diastolic volume of 70 mm and end systolic volume of 62 mm, left atrium of 46 mm, ejection fraction (EF) 37%, moderate regurgitation on the mitral and tricuspid valve, thickness of the posterior wall of the LV 11 mm , interventricular septum 10 mm. Simpson ejection fraction 40%. The diameter of the left atrium was 6.1 cm.

The chest X-ray revealed cardiomegaly due to the left and right ventricles dilatation, lung congestion.

Clinical diagnosis: stage III hypertension, Class II, very high risk (4). Hypertensive cardiomyopathy, persistent atrial fibrillation. HF Class IIA with LV systolic dysfunction, Class IV. Type II diabetes mellitus in subcompensation stage.

Medications included 40 mg/day intravenous torasemide, 0.25 mg/day digoxin, 50 mg/day eplerenone, 5.2 mg/day ramipril; on day 4 of therapy the dose was increased to 5.0 mg and on day 7 up to 7.5 mg; 20 mg/ day xarelto, 1000 mg/day metformin.

Within 7 days after stabilization, the patient was prescribed with beta-blocker carvedilol 3.125 mg 2 times a day.

The patient was therefore discharged in a satisfactory condition with recommendation to continue outpatient treatment with 0.25 mg/day digoxin, 7.5 mg/day ramipril, 10 mg/day torasemide, 50 mg/day eplerenone, carvedilol according to the titration scheme (3.125 mg 2 times daily, 12.5 mg 2 times daily), 20 mg xarelto, 1000 mg/day metformin. A follow-up visit after 6 months showed that the patient was in his regular general state with no edema, hemodynamic parameters were satisfactory, heart size was decreased, the patient was taking 25 mg carvedilol (this is a clinically tolerated dose), 7.5 mg/day ramipril; 25 mg/day eplerenone, 0.25 mg/day digoxin, 20 mg/day xarelto.

The reported clinical case gives evidence that untreated hypertension lead to CHF with LV systolic dysfunction. Unlike diastolic dysfunction, in CHF with systolic dysfunction, blood pressure is often decreased, even hypotension is observed, and as a result, it is impossible to use adequate doses of medications.

Another important mechanism by which arterial hypertension leads to the development of CHF is the occurrence of atrial fibrillation, the cause of which is arterial hypertension in 70% of patients. Atrial fibrillation is the sole factor in the development of CHF and, basically, exacerbates the clinical course of the underlying disease [3].

Population and clinical studies have also confirmed correlation between diabetes mellitus and CHF development. Diabetic cardiomyopathy still remains a poorly understood condition, although the role of a number of pathogenetic factors, leading to the development of CHF in diabetes patients, has been proven. Due to hyperglycemia, glucose metabolism changes with increasing beta-oxidation and consequently leads to damage to the myocardium by free fatty acids (lipotoxicity). Insulin resistance, activation of the renin-angiotensin-aldosterone system (RAAS), impaired calcium metabolism, collagen formation, hypertrophy and fibrosis determine the relevant phenotype of diabetic cardiomyopathy [12].

Obviously, early and adequate treatment of hypertension and concomitant diseases is crucial in prevention of CHF, reducing the incidence of its occurrence. A meta-analysis of 12 studies that reported information on the incidence of CHF showed that antihypertensive therapy resulted in reduction of the incidence of CHF by approximately 52% compared to patients who did not receive adequate therapy. The decrease in the incidence of CHF was linearly dependent on the decrease in SBP: each decrease of SBP by 10 mmHg

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led to a 26% reduction in the relative risk in CHF development. Similar results were obtained in later studies. The SOLVD study showed the benefit of reducing blood pressure in patients with systolic CHF and hypertension when using ACE inhibitor (ACEI). The efficacy of ACEI in reducing mortality was higher in patients with hypertension and CHF compared to normotensive patients. The achievements in fundamental and clinical medicine have established that hypertension is not only one of the key etiological factors in the development of CHF, but also have similar key links in pathogenesis. The strategy for the selection of pathogenetic pharmacotherapy should be determined taking into account the above circumstance.

Currently, it is generally accepted that ACEI and beta-blockers are the major means of pathogenetic therapy for CHF, since they alone have evident effect on the rate of progression of cardiac dysfunction and mortality from CHF [2, 4, 15].

Pharmacological effects of ACEI in arterial hypertension and CHF are qualitatively the same. Basically, ACEI influence almost on all components of the pathogenesis of arterial hypertension and CHF, which is usually reflected on positive neurohumoral and hemodynamic effects. Therapy with ACEI in arterial hypertension helped to reduce the risk of CHF by approximately 16%; the HOPE study (2000) showed that ACEI ramipril reduced the risk of the development of CHF, including in patients with arterial hypertension, by approximately 23% [2, 3].

Arterial vasodilation with reduced afterload and blood pressure is of particular importance in arterial hypertension and venous vasodilation with reduced preload in CHF. The regression of cardiac remodeling is important in both pathologies [6]. The advantage of ACEI over some other classes of antihypertensive medications is in their metabolic effects, aimed at improvement of glucose metabolism, increase the sensitivity of peripheral tissues to insulin, the presence of antiatherogenic and anti-inflammatory properties. ACEI have the best nephroprotective activity compared to other antihypertensive drugs with the ability to regress the remodeling of the left ventricle, prevent ischemic and reperfusion myocardial damage, decelerate the rate of progression of nephropathy, reduce the clinical manifestations of CHF in prolonged use.

The resulting data on the ability of the above drugs to decelerate the progression of CHF, reduce mortality, increase the life expectancy of patients, improving its quality, allowed to recommend them as a mandatory basic therapy for CHF or in combination with arterial hypertension, regardless the severity and functional class.

ACEI are indicated for all patients regardless of etiology, stage, type of decompensation.

ACEI are effective even at the initial stages of CHF with asymptomatic LV dysfunction, as well as in CHF with preserved systolic heart function.

non-administration of ACEI to patients with CHF cannot be justified and leads to a conscious increase in the risk of mortality.

ACEI are recommended as the first-line drugs in patients with reduced LV systolic function (EF <40-45%) both in the presence and absence of symptoms (Class IA).

ACEI therapy should be started at low doses, gradually (no more than once every 2–3 days, and with systemic hypotension even less frequently: once a week, titrating them to achieve optimal effect, i.e., to the target effect);

asymptomatic patients with documented LV dysfunction should receive ACEI therapy to regress/ prevent the development of HF. They reduce the risk of MI and sudden death in patients with Class IA. ACEI dose titration is a completely individual process, and each patient has his/her optimum and maximum effective and tolerable doses. However, it should be emphasized that staying at the minimum doses of ACEI (except in cases of hypotension development) is simply erroneous. ACEI can be prescribed to patients with outgoing hypotension, by 2 times reducing the starting dose [1, 2, 4].

Currently, beta-blockers/ACEI combination therapy is the main treatment for CHF in patients with systolic CHF dysfunction. For the treatment of CHF carvedilol, bisoprolol, metoprolol of prolonged action are approved. Beta-blockers therapy in CHF should be started with caution. Doses should be increased slowly (no more than 1 time per week, and with doubtful tolerance and excessive reduction of blood pressure: once every 2 weeks or even a month) [1, 4].

In such cases, other therapy can be tried: to increase the dose of diuretics and, where possible, ACEI, as well as to titrate beta-blockers doses more slowly.

Currently, the European Society of Cardiology recommends prescribing beta-blockers to all patients with stable CHF Class II-IV as a standard treatment in combination with ACEI and diuretics in the absence of contraindications. It is known that, basically, patients with CHF have a permanent form of atrial fibrillation, and beta-blockers are the drugs of choice for heart rate control in tachysystolic form.

However, in practice, many physicians do not follow these recommendations: only 1/3 of patients with CHF are prescribed with beta-blockers, while 2/3 of patients receive ACEI therapy.

In addition to RAAS blockers, medications for patients with AH in combination with systolic CHF can be supplemented with thiazide or loop diuretics, as well as mineralocorticoid receptor antagonists (MRA). Diuretics should always be used in combination with ACEI (or ARB), beta-blockers, and MRA in HF patients with low systolic function until signs of fluid retention disappear.

Thiazide diuretics can be used in patients with persistent renal function and mild symptoms of stagnation. However, most patients require prescription of loop diuretics (or their combination with thiazide diuretics, MRA) because of the severity of HF symptoms and the constant progression of renal dysfunction. Deceleration of ventricular contraction by digoxin in CHF patients with systolic LV dysfunction and concomitant AF is recommended only when no other medications can be prescribed.

CONCLUSIONS

1. Currently, arterial hypertension is one of the ultimate causes in the development of CHF.

2. Early adequate therapy of arterial hypertension and comorbid conditions (diabetes mellitus, dyslipidemia, atrial fibrillation) is crucial in the prevention of CHF development in the conditions of general medical practice.

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