PECULIARITIES OF PHARMACOTHERAPY IN ARTERIAL HYPERTENSION AND COMORBID PATHOLOGY

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PECULIARITIES OF PHARMACOTHERAPY IN ARTERIAL HYPERTENSION AND COMORBID PATHOLOGY (Abstract): In patients with arterial hypertension (AH) pharmacotherapy often remains ineffective because of comorbid pathology. Research of haemodynamic and metabolic processes in such patients allows prescribe effective antihypertensive medicines, improve life quality and prognosis. **Material and methods:** 60 patients with AH, coronary artery disease and obesity were divided into three groups: 1st group was treated with lisinopril + atorvastatin + aspirin (regimen I); 2nd group was treated with lisinopril + atorvastatin + bisoprolol + aspirin (regimen II); 3rd group was treated with lisinopril + bisoprolol + indapamide + atorvastatin + aspirin (regimen III). Laser correlation spectrometry (LCS) was used to evaluate the homeostatic alterations. **Results:** All regimens were equally effective in normalization of systolic blood pressure and did not influence the ejection fraction. Only in the 3rd group was determined significant increase of glomerular filtration rate (92.73±2.12 vs 79.62±13.62 ml/min/1.73m^2). The LCS test showed that these patients had high level of light scattering particles IV, which may be caused by activation of anabolic processes. In other groups, spectral alterations were not so expressive. **Conclusions:** Prescription of antihypertensive therapy cause homeostatic and metabolic alterations, which may influence the efficacy of treatment. **Keywords:** PHARMACOTHERAPY, COMORBID PATHOLOGY, LASER CORRELATION SPECTROMETRY.

A considerable growth of cardiovascular diseases, especially among the elder patients, is observed all over the world and in Ukraine. Primary hypertension (PH) and coronary artery disease (CAD) are the main causes of cardiovascular morbidity (41.8% / 38.3, accordingly) [1]. PH combined with CAD make worse patient's prognosis and lead to adverse outcomes [2]. High level of systolic blood pressure is one of the main risk factors of CAD and its complications [3]. Thus, addition of CAD to PH increases cardiovascular risk to high level [4]. It was proved by PROGRESS investigation, which confirmed that every 4th death from CAD is caused by increased blood pressure [3]. In elderly patients, PH is complicated with CAD in 67.7% cases [1].

In patients with CAD combined with PH obesity is one of the most common comorbidities [5]. Our previous investiga-

tions determined negative impact of the obesity in heart failure, atrial fibrillation and decompensation of the patient state [6]. Patients with obesity and PH have high cardiac preload caused by the growth of circulating blood volume and high postload caused by high arterial stiffness [7].

In the elderly patients, choice of effective pharmacotherapy (PT) is complicated with numerous comorbidities, pharmacokinetic and pharmacodynamic peculiarities [8, 9, 10]. Nowadays there are not enough methods, which allow to determine the influence of PT on metabolic processes [8, 11]. This leads to low efficacy of antihypertensive treatment [3]. So it is important to provide complex sanogenetic monitoring in all patients with PH. Laser correlation spectrometry (LCS) is one of the most common methods, which allows quickly determine and analyze the metabolic disorders [12, 13, 14].

MATERIAL AND METHODS

In Odessa University Clinic (Ukraine) 60 patients with PH, CAD and obesity were treated according to clinical recommendations [4, 15, 17, 18]. All patients were divided into three groups: the 1st (n=20) was given lisinopril + atorvastatin + aspirin (regimen I), the 2nd (n=20) was given lisinopril + atorvastatin + bisoprolol + aspirin (regimen II); the 3rd (n=20) was given lisinopril + bisoprolol + indapamide + atorvastatin + aspirin (regimen III). Exclusion criteria: myocardial infarction and stroke in anamnesis. Body mass index (BMI) and glomerulal filtration rate (GFR) were calculated in all patients.

The special research method for estimation of plasma metabolic features was LCS [13]. It helps to measure spectral characteristics of the induced monochromatic coherent radiation in biological liquids. That makes possible to register particles with hydrodynamic radius 1 - 10000 nanometers. Results are presented as a histogram.

According to our previous studies [13], to the I zone (0-10 nanometers) are included low-molecular monomeric albumins and glycolipid free complexes; to the II zone (11-30 nanometers) are included globulin proteins and low-molecular lipoprotein complexes; to the III zone (31-70 nanometers) are included high-molecular lipoprotein complexes, RNP-, DNP molecules, the low-molecular immune complexes; to the IV zone (71-150 nanometers) are included mainly constitutive immune complexes of the average size. Huge particles ($\geq$ 150 nanometers, the V zone) are present in patients with allergization and an autoimmune sensibilization. The particle distribution and their molecular interaction characterizes different pathological states. The presence of xenobiotics (e.g. medicines) causes specific changes of the initial distribution and may characterize the treatment efficacy. Metabolic features were determined in blood plasma before and on the 10th day of PT. The investigation was carried out according to the method after Bazhora J.I. and Noskin L.A. [14].

The statistical analyze was provided with Statistica 7.0. To measure differences between values before and after the treatment we used t-test; p-value of < 0.05 was considered to be statistically significant. Values are presented as Mean ± Standard deviation (SD).

RESULTS

Mean age (MA) of the investigated patients was 67.2±5.1 years. Among them were 28 males (MA 66.2±8.9 years) and 32 females (MA 68.3±7.4 years). All of them had obesity with BMI corresponding to the

first stage (BMI: 30-35 kg / m2). Diabetes mellitus was diagnosed in 26.31% patients in the 1st group, in 15% in the 2nd group and in 25% in the 3rd group.

Before and after the prescription of antihypertensive therapy we determined changes of heart rate (HR), systolic and diastolic blood pressure (SBP, DBP), ejection fraction (EF), total cholesterol and levels (tab. I).

After the treatment in the 1st group was determined the decrease of SBP (by 35.0 mm Hg), DBP (by 12.4 mm Hg) and HR (by 14/min). EF, GFR and glucose levels remained without any changes. Total cholesterol decreased by 1.68 mcmol/L.

In the 2nd group SBP decreased by 20.91 mm Hg. DBP, HR and EF remained the same. Cholesterol reached the normal values (4.78 mmol/L) but glucose level increased by 1.14 mmol/L ($p>0.05$).

In the 3rd group SBP decreased by 29.8 mm Hg, DBP by 14 mm Hg, HR by 9.73/min. Cholesterol level reached the target borders (4.68 mmol/l). EF and glucose level remained the same. GFR rate increased to 92.73 ml/min/1.73m^2.

LCS data showed that only regimen III caused a significant growth of light scattering particles (LSP) IV (on 11.1%), which characterize anabolic reactions. Before the prescription of regimens I and II prevalence of LSP II, III and IV was observed. It is typical for catabolic, toxic and allergy-directed reactions.

These alterations remained without any significant changes after the treatment (tab. II).

Concerning spectral alterations, we determined that hydrolytic alterations remained the same after the prescription of regimen I. Normological type even decreased by 15.0% and anabolic type increased the same value due to autoimmune reactions. Regimen II caused the decrease of hydrolytic reactions by 25.0% and growth of anabolic reactions by 15.0%. Regimen III was characterised by increase of hydrolytic and anabolic type reactions (10.0% / 25.0%, accordingly) (tab. III).

TABLE I

Clinical data of all the investigated groups before and after PT

Clinical data	Regimen I		Regimen II		Regimen III	
	Before the treatment	During the treatment	Before the treatment	During the treatment	Before the treatment	During the treatment
SBP, mm Hg	163.2±16.1	128.0±8.6*	151.3±6.2	130.4±6.0*	160.7±11.5	130.9±9.1 *
DBP, mm Hg	87.3±8.5	75.0±4.6*	83.0±6.6	85.0±6.3	94.0±7.1	80.0±6.6 *
HR, bpm	79.6±13.1	65.6±9.0*	72.3±5.1	68.2±11.2	81.1±14.7	71.7±13.0 *
EF, %	64.8±6.6	65.6±6.3	59.8±8.2	60.6±8.1	59.3±9.3	58.8±8.7
Cholesterol, mcmol/L	6.3±1.8	4.6±0.4*	6.4±1.2	4.8±0.4*	5.9±0.9	4.6±0.6*
Glucose, mmol/L	6.0±1.7	6.3±1.3	5.4±0.7	6.5±1.4	6.5±1.9	6.7±0.8
GFR, ml/min/1.73m^2	81.7±13.7	78.4±12.6	79.4±14.8	76.6±12.1	79.6±13.6	92.7±12.1 *

*, $p< 0.05$ vs before treatment.

TABLE II

Subfractional redistribution before and after PT

LSP redistribution	Regimen I		Regimen II		Regimen III	
	Before PT, %	During PT, %	Before PT, %	During PT, %	Before PT, %	During PT, %
I zone	8.5	7.3	9.4	9.4	10.3	9.2
II zone	27.4	22.9	37.4	29.2	29.7	26.7
III zone	27.6	32.5	21.4	25.2	27.0	20.6
IV zone	33.3	30.9	22.6	26.2	19.3	30.4*
V zone	3.2	6.4	9.2	10.0	13.7	13.1

*, p< 0.05 vs before treatment.

TABLE III

Direction of spectral alterations before and after PT

Type of spectral alteration	Regimen I		Regimen II		Regimen III	
	Before PT, %	During PT, %	Before PT, %	During PT, %	Before PT, %	During PT, %
Normological	25.0	10.0*	0	5.0	15.0	10.0
Hydrolytic	40.0	40.0	65.0	55.0*	35.0	45.0*
Anabolic	15.0	30.0*	15.0	30.0*	5.0	30.0*
Mixed	20.0	20.0	20.0	10.0*	45.0	15.0*

*, p< 0.05 vs before treatment.

DISCUSSION.

As we observed from abovementioned data, all the three regimens equally caused stabilization of SBP, which is the main target of antihypertensive PT [19]. DBP was significantly lowered with the Ist and IIIrd regimens, but in the IInd regimen it remained without changes. Significant lowering of HR was achieved after the prescription of lisinopril. We did not determine any influence of used PT on EF rate.

In all three groups, total cholesterol level was brought to the normal values. Regimen II increased glucosa level, but not statistically significant. GFR rate didn't changed after regimens I and II, but regimen III caused growth of GFR. Thus, as we see, such a step-by-step prescription of each new drug is very convenient for observing of it's influence and helps us to optimise the treatment.

LCS data showed that regimens I and II didn't change the subfractional structure and only regimen III caused the growth of anabolic reactions. To estimate PT influence on metabolic processes we have to take into account not only subfractional structure but also directions of spectral alterations.

We also have to take into account initial alterations and compare them with alterations after the PT. Otherwise, the received data could be incorrectly interpreted.

So, regimen I caused lowering of normological type and in spite of anabolic reactions growth, hydrolytic type remained the same as before the treatment. Thus, regimen I is not effective in correction of hydrolytic reactions. Addition of bisoprolol (regimen II) caused decrease of hydrolytic reactions and simultaneous increase of

anabolic ones. So, regimen II change hydrolytic as anabolic processes. Regimen III (which included indopamide) caused increase of hydrolytic and anabolic reactions. So, as we see, we have to compare both LCS data: LSP redistribution and spectral alterations in order to estimate PT influence on metabolic processes. In our investigation spectral alterations appeared to be more informative because of proved statistical significance.

CONCLUSIONS.

All the prescribed regimens are optimal for SPB stabilization but they do not influence EF. In elderly patients with PH and comorbid pathologies PT should be individualized. LCS is very sensitive method, which allows determine homeostatic alterations and metabolic transformations in the process of treatment. Addition of LCS to basic clinical, laboratory, and instrumental data helps to choose an appropriate PT.

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NEWS

EVALUATION OF CLINICAL OUTCOMES IN PATIENTS UNDERGOING DUAL VESSEL PERCUTANEOUS CORONARY INTERVENTION USING SIROLIMUS-ELUTING CORONARY STENT SYSTEM IN INDIA

The safety and efficacy of percutaneous transluminal coronary angioplasty (PTCA) has been demonstrated in selected patients with symptomatic coronary artery disease. Application of PTCA in patients with multiple vessels or in more extensive coronary artery disease has been limited, and the safety and short- and long-term efficacy are less clear. Stent implantation has added an important dimension to percutaneous re-vascularization strategies and has been shown to be an effective rescue device after acute or threatened vessel closure after failed PTCA. However, some studies with multivessel disease reported higher restenosis and repeat revascularization rates in patients treated with bare metal stents (BMS) than in those after surgical treatment. The introduction of drug-eluting stents (DES) indicating advantage over bare-metal stents in reducing the restenosis incidence and has narrowed the re-intervention gap between percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG) surgery in multivessel coronary artery disease (CAD). Additionally, performing multivessel PCI in a single index procedure has potential economic and social advantages. Here, we present our experience of the use of the Supralimus-Core sirolimus-eluting stent (SES) in patients with dual vessel CAD in an unselected real-world population. No study was especially designed to evaluate the safety and effectiveness of SES in patients with dual vessel disease. The study shows that, dual vessel Supralimus-Core SES implantation allows safe and effective treatment with low rates of TLF at one year follow-up in Indian population (Chandwani P, Prajapati J, Porwal S,et al. Evaluation of Clinical Outcomes in Patients Undergoing Dual Vessel Percutaneous Coronary Intervention Using Sirolimus-Eluting Coronary Stent System in India. Journal of Clinical and Diagnostic Research. 2015, Vol-9(2): 5-9).

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