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Deklaracja.
Specyfika i zawartość merytoryczna czasopisma nie ulega zmianie.
Zgodnie z informacją MNiSW z dnia 2 czerwca 2014 r., że w roku 2014 nie będzie przeprowadzana ocena czasopism naukowych; czasopismo o zmienionym tytule otrzymuje tyle samo punktów co na wykazie czasopism naukowych z dnia 31 grudnia 2014 r.
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Refractory arterial hypertension: clinical manifestations and controversies

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Abstract

The study was aimed to assess the clinical manifestations in patients with refractory hypertension. There was demonstrated that refractory arterial hypertension is characterized with hyperactivation of sympathetic nervous system. Patients with RAH used 4,6 ± 0,2 medications to control the pressure. The most common combinations are the combination of blockers, ACE inhibitors and diuretics, ACE inhibitors and diuretics, and, ACC, more rarely, patients received a combination of ARB and a diuretic ACC. Every third patient in therapy included 4 or more antihypertensive drugs, that is, there was a polypharmacy. However the combination of used medications and their dosage regimen does not achieve significant clinical effect.

Key words: arterial hypertension, medication resistance, diagnostics, monitoring.

Arterial hypertension (AH) remains to be one of the most important challenges for public health throughout the world [1]. According to WHO experts' assessment AH is the third leading cause of disability and the first - leading cause of death. They predict that there will be over 1.5 billion hypertensive patients in 2025 [1, 2].

Ulrich Kintscher (2013) indicates that AH is the cause of death of 7.5 million people in the world, accounting for 12.8% of total deaths worldwide, and in 10 years the number of deaths related to AH will exceed 10 million people. AH holds the first place (7% in the general structure of the causes of reduced life expectancy), ahead of such risk factors as smoking and alcohol abuse. [3]

Resistant hypertension is defined as a persistent increase in blood pressure above target, despite administration of three or more antihypertensive medications of different classes in adequate doses, including diuretics [4]. The prevalence of resistant hypertension is 5-30% [1, 4-6].

According to Daugherty A. et al. in patients with resistant hypertension (RAH) the risk of cardiovascular events significantly higher than in the treatment of correctable hypertension - OR = 1.47 (95% CI: 1.33-1.62) [5]. Roberie D. R. et al. (2012) argue that over the last 25 years, the frequency of RAH rose from 8.8% to 20.7% [6].

The study was aimed to assess the clinical manifestations in patients with refractory hypertension.

Material and methods.

The study was performed on the basis of the Regional Clinical Hospital (Odessa, Ukraine) in the period from 2012 to 2015. There were examined 50 patients with resistant hypertension.

We used the following inclusion criteria: refractory to antigipertenzinoy complex therapy of hypertension (blood pressure > 160/90 mm Hg on the background of the appointment of at least three antihypertensive drugs, including a diuretic); GFR over 45 ml/min 1,73 m2. Exclusion criteria for the procedure: verified symptomatic hypertension; type I diabetes; verified significant renal artery stenosis; stenting of the renal artery in the history of the glomerular filtration rate of less than 45 ml/min 1.73 m2.

The examination included a general clinical (medical history, physical examination), clinical and instrumental (ECG, echocardiography, CT, MRI, angiography, Holter ECG and BP monitoring), standard clinical laboratory tests. In all cases, the diagnosis of refractory hypertension was established at the time of admission.

Holter ECG monitoring was performed using the apparatus Phillips Zymed c recording device Philips DigiTrak XT (Netherlands) [7]. Holter blood pressure monitoring was performed using a portable device ABPM-05 Meditech (Hungary) [8]. Programming daily blood pressure monitors and the subsequent analysis of the data from them by means of programs and EasyABPM CardioVisions

Statistical analysis of the results was preformed using the software Statistica 12.5 (StatSoft Inc., USA) [9].

Results of the study

The average age of patients participating in the study was 59.2 ± 0.3 years. Males slightly dominated in the sample (54.0%).

On admission, patients complained of headaches, dizziness, tinnitus, general weakness, sleep disturbances. Nausea at an altitude headaches were complained by 22% of patients. 32% of patients noted visual disorders decribed as flashing "flies" before the eyes. The majority of patients have noted the intensification of complaints after emotional or physical stress.

The average duration of disease was 7,4 ± 0,3 years. Continuous monitoring of blood pressure at home was carried out 56.0% of the patients.

In some of the patients had symptoms of COPD (26.0% of cases), gastroenterological diseases (chronic gastritis, stomach ulcer and duodenum, chronic cholecystitis, chronic pancreatitis, chronic hepatitis, ulcerative colitis) - 22.0% of the cases, the pathology of the musculoskeletal system e.g. deforming osteoarthritis (14.0%), common spinal osteochondrosis (32.0%), rizomelic form of ankylosing spondylitis (1 case) was determined. In the structure of the urinary system diseases there was prevalent chronic pyelonephritis (10.0%) and urolithiasis 8.0%). 4 men observed the phenomenon of chronic prostatitis. Manifestations of chronic disciculatory encephalopathy were observed in 64.0% of patients with visual impairment - at 18.0%.

Type 2 diabetes was observed in 12.0% of patients, thyroid disease - in 3 (6.0%). Obesity was observed in 8.0% of patients with metabolic syndrome - at 26.0%. Gout as comorbidity was detected in 2 patients. 12 (24.0%) patients had symptoms of varicose veins of the lower extremities in 2 (4.0%) cases - hemorrhoids. Proliferative breast disease (diffuse mastopathy, fibroadenoma) were observed in 19 women.

In 5 (10.0%) cases patients had a history of myocardial infarction, 4 (8.0%) - stroke, in 2 (4.0%) - pulmonary embolism. CHD was verified in 26 (52.0%) patients with refractory hypertension.

At the time of initial evaluation of the condition of patients was satisfactory. Overweight (BMI greater than 25 kg/m^2) had 40.0% of the patients and obesity (BMI greater than 30.0 kg/m^2) were 9 (18.0%) patients. Swelling at the time of admission, patients were absent.

BR was averaged 22,2 ± 0,3 min^{-1}. Complaints of shortness of breath on mild exertion imposed on 9 (18.0%) patients.

Heart rate was 77.9 ± 0.2 bpm. Changes in the borders of cardiac dullness to the left side were observed in 52% of patients. Aortic heart blunting configuration was prevailed.

The average daily value of office BPs wasd 164,2 ± 2,5 mm Hg and BPd- 95,3 ± 1,6 mm Hgt. BP on the right and left hand differed by 3-7 mm Hg at 33.0% of patients.

Patients used different medications to control the pressure as average - 4,6 ± 0,2 preparations. The most common combinations are the combination of blockers, ACE inhibitors and diuretics, ACE inhibitors and diuretics, and, ACC, more rarely, patients received a combination of ARB and a diuretic ACC.

Every third patient in therapy included 4 or more antihypertensive drugs, that is, there was a polypharmacy. At the same time, the combination used and the dosage regimen does not achieve significant clinical effect.

Further analysis showed that the maximum daily dosage of drugs were used in 32.0% of patients submaximal - at 59.0%, lower doses of the drugs received only 8.0%.

In this regard, 16.0% patients had various side effects of prolonged use of antihypertensive drugs. So, 3 (6.0%) patients had dry cough, chronic administration of ACE inhibitors, and 5 patients had a variety of allergic reactions (urticaria, vasomotor reactions). Patients treated in the complex treatment of centrally acting agents, in some cases (4.0%) reported the phenomenon of depression, reduce the rate of reaction.

ECG analysis showed that all patients showed signs of LVH in the form of increased QRS voltage in the standard single-pole and the limb leads and chest leads in a single-pole. Slowing of ventricular activity was noted in leads V5, V6, as well as changes in the ST segment and the T wave as an offset relative to the contour lines, and flattening T wave.

In 63 patients the ratio of R-wave amplitude, and T exceeded 10.0 in the extreme left chest leads. The duration of the QRS complex is from 0.10 to 0.11 with the angle set at a deviation to the left and right transition zones RS. These changes were accompanied by an increase in the LIS to 40,5 ± 0,3 mm. Accordingly, CI increased to 2499 ± 9 mm/ms.

ST-segment depression in I greater than 0.5 mm was observed in 44 patients. Frequent (38.0%) was the presence of negative T wave in conjunction with ST-segment depression and

high R-wave in I. Raising the height of the R wave in lead AVL, more than 11 mm was observed in 29 patients. Half of the patients showed flattening of the T wave in lead AVL is the AVF, as well as reducing the height of ST segment in the same leads to 0.5-0.6 mm. In 22 patients observed flattening of the T wave in lead AVL is the AVF, from 9 - T-wave inversion in combination with ST-segment depression and an increase in wave amplitude R, the most pronounced in the left chest leads.

Supraventricular (polymorphic, politopnye, rare and aberrant) ectopic activity prevailing in the lunch hours, recorded by Holter ECG. The average recorded up to 50 episodes of supraventricular ectopic, mainly single activities. Atrial couplets (episodes 4-5) were recorded in 13 patients. The maximum duration of the RR interval was 1400 ms.

Supraventricular group maximum duration recorded mainly in the evening.

QT interval averaged over the period of the daily monitoring ranged from 300 to 400 ms, averaging 364 ± 8 ms. Over a period of significant ECG monitoring pauses (RR interval 2500 ms), dislocation of ischemic ST segment, of a violation of the AV and intraventricular conduction on the sinus rhythm was recorded.

Frequently (87.0%) there was detected EHA deviation to the left. Signs of cardiosclerosis were observed in 39 patients with left bundle branch block - in 22 patients.

The findings suggest that patients with RAH noted the repeated increase in blood pressure during the day (fig. 1).

It was found that patients with RAH has hyperactivation of sympathetic-adrenal system, whereas degree of sympathicotonia correlated with the systolic blood pressure ($r = 0.73$).

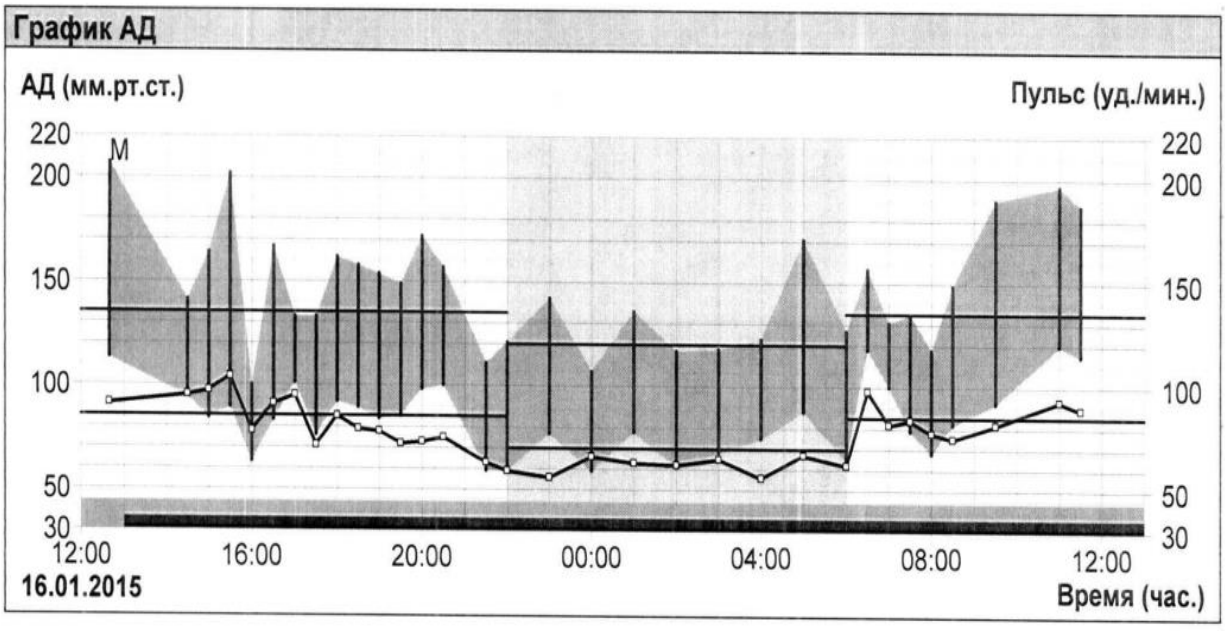

Fig. 1 The episodes of BP increase in RAH (patient V., male, 66 y.o. Treatment: in the morning - Eqautor 10/5 (10 mg of lysinoprile + 5 mg of amplodipine) - 1 tablet after meal, after lunch – Arifon-retard (Indapamide) 1,5 mg, 1 tablet, in the evening – bisoprolole 5 mg, 1 tablet)

A more detailed analysis of the characteristics of autonomic regulation in patients with refractory hypertension found that 78.0% of the patients took place sympathicotonia, the Kerdo's index averaged 1,14 ± 0,02. Eytonia was recorded in 22.0% of patient.

Conclusion.

1. Refractory arterial hypertension is characterized with hyperactivation of sympathetic nervous system
2. Patients used different medications to control the pressure as average - 4,6 ± 0,2 preparations.
3. The most common combinations are the combination of blockers, ACE inhibitors and diuretics, ACE inhibitors and diuretics, and, ACC, more rarely, patients received a combination of ARB and a diuretic ACC.
4. Every third patient in therapy included 4 or more antihypertensive drugs, that is, there was a polypharmacy.
5. The combination of used medications and their dosage regimen does not achieve significant clinical effect.

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