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Antihypertensive therapy in patients with coexisting hypertension and bronchial asthma

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Abstract

The aim of the research was to study the peculiarities of cardiac and pulmonary hemodynamics, the mechanisms of formation of endothelial dysfunction, as well as their correction with angiotensin converting enzyme inhibitor, Ramipril and angiotensin-II receptor blocker, Irbesartan, in patients with arterial hypertension (HTN) combined with bronchial asthma (BA). **Design and methods.** Altogether 80 patients with BA of moderate severity combined with HTN of 1. 2 degrees were enrolled in the study. The average age of the patients was 52.9 ± 4.2 years. The eligible patients were randomized for treatment with either Ramipril 5 mg/day or Irbesartan 150 mg/day in combination with bronchodilator inhalation and anti-inflammatory medications for BA (Formoterol/Budesonide 160/4.5 mcg 2 inhalations twice, Ipratropium bromide and Ambroxol through nebulizer devices). The program of instrumental examination included echocardiography (Aloka 1700, Japan; LOGIQ 500, Germany) with ultrasonic sensors of 3.5 MHz. The plasma level of endothelin 1 (ET-1) was estimated by immune-enzyme assay (Biomedica set, category № 442–0052, Arkray, Japan). Results. Two-month monotherapy with Irbesartan allows to achieve the target blood pressure (BP), leads to the regression of cardiac remodeling and has a positive effect on endothelial function and bronchial patency. **Conclusions.** Irbesartan is able to provide a stable and reliable control of BP, and delays the progression of pathological cardiovascular changes; it has a favorable impact on the respiratory function, is well tolerated, easy to use, and may be considered as the best antihypertensive drug in patients with co-morbid HTN and BA.

Key words: arterial hypertension, bronchial asthma, diastolic heart dysfunction, endothelial dysfunction, Ramipril, Irbesartan

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Антигипертензивная терапия у больных с сочетанием гипертонической болезни и бронхиальной астмы

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Резюме

Цель исследования — изучить особенности сердечной и легочной гемодинамики, механизмы формирования эндотелиальной дисфункции и их коррекция ингибитором ангиотензинпревращающего фермента рамиприлом и блокатором рецептора ангиотензина II ирбесартаном у пациентов с артериальной гипертензией (АГ) в сочетании с бронхиальной астмой (БА). **Материалы и методы.** В исследование было включено 80 больных БА средней степени тяжести в сочетании с АГ 1, 2 степени. Средний возраст больных составил 52,9 ± 4,2 года. При дальнейшем углубленном обследовании пациенты распределены на две рандомизированные группы для лечения: рамиприлом 5 мг/сутки и ирбесартаном в дозе 150 мг/сутки на фоне ингаляционной бронхолитической и противовоспалительной терапии БА (формотерол/будесонид 160/4,5 мкг 2 ингаляции × 2 раза, ипратропия бромид / фенотерол и амброксол через небулайзер). Программа инструментального обследования включала: эхокардиограмму на аппаратах «Aloka 1700» (Япония), «LOGIQ 500» (Германия) с использованием ультразвуковых датчиков с частотой 3,5 мГц. Оценивали уровень эндотелина-1 в плазме с этилендиаминтетраацетатом (ЭДТА) с помощью иммуноферментного анализа — набор «Biomedica», категория № 442–0052 (Arkray, Япония). **Результаты.** Установлено, что монотерапия в течение 2 месяцев ирбесартаном позволяет достичь целевого уровня артериального давления (АД), способствует регрессу патологического ремоделирования миокарда, а также благоприятно влияет на эндотелиальную функцию, бронхиальную проходимость у больных с данной коморбидной патологией. **Выводы.** Ирбесартан эффективно обеспечивал стабильный и надежный контроль АД, замедлял прогрессирование патологических изменений со стороны сердечно-сосудистой системы, положительно влиял на функцию внешнего дыхания и характеризовался наиболее высокой приверженностью пациентов к лечению, поэтому может быть оптимальным выбором препарата при лечении АГ у больных БА.

Ключевые слова: артериальная гипертензия, бронхиальная астма, диастолическая дисфункция сердца, эндотелиальная дисфункция, рамиприл, ирбесартан

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Introduction

The most important internal diseases, such as hypertension (HTN), bronchial asthma (BA) currently are the leading causes of morbidity, disability and mortality in the economically developed countries. In recent years, comorbidities are being actively investigated.

In 1970, an American doctor Feinstein A. R. defined "comorbidity" for the first time [1]: "comorbidity — is any single pre-existing, existing or potential nosology in a patient with the known disease of interest."

Later, Kate Nadal-Ginard gave another definition of comorbidity: "A comorbidity is a combination of two or more interrelated and co-existent chronic diseases in one patient independently of the activity of each of them ". [2] This definition is definitely a more comprehensive one, because it allows to diagnose the co-existence of multiple diseases in one patient. Moreover, it can be considered as an additional factor contributing to the nature and severity of complications, preventing from timely and correct diagnosis and treatment.

The co-existence of cardiac and pulmonary disease leads to the additional burden requiring novel diagnostic and management approaches [3, 4]. Today, cardiovascular disease is the most frequent and serious co-existent pathology in patients with respiratory diseases [5, 6].

According to the World Health Organization, Russia holds the leading place in terms of HTN-related morbidity and mortality, found in 40 % of the adult population.

In co-existent HTN and BA, central and pulmonary hemodynamics is abnormal leading to the remodeling of the left and right heart chambers. In addition, endothelial dysfunction (ED) [7–9] is a common pathogenetic link between cardiovascular and cardiorespiratory complications. In patients with co-existent cardiorespiratory pathology, antihypertensive and anti-inflammatory therapy is cimplicated due to the negative bronchopulmonary effects of β-blockers and unfavourable cardiovascular effects of glucocorticosteroids and β2-agonists.

Available data do not provide clear evidence regarding cardiovascular disorders and mechanisms of ED development in co-existent cardiorespiratory disease. The interaction with systemic inflammation and ED require further research [10]. Our previous studies showed that endothelium-dependent vasodilation is affected by a combination of factors, including impaired myocardial function, obesity, duration of HTN and BA.

Thus, the issue of ED and pulmonary hypertension (PHTN) in patients with co-existent HTN and BA remains relevant, as well as the choice of optimal antihypertensive therapy in this large cohort of patients.

The purpose of our study is to assess cardiac and pulmonary hemodynamics, mechanisms of ED and the impact of treatment by angiotensin converting enzyme inhibitor (ACEI) (Ramipril, "Tritatse", "Sanofi-Aventis", Italy) and angiotensin receptor blockers to II (ARB) (Irbesartan, "Aprovel", "Sanofi", France) in hypertensive patients with BA.

Design and methods

We examined 126 patients. Patients were familiar with the study design, purpose, objectives, and were informed about the diagnostic procedures. The study was conducted as a simple randomized, prospective, open study. Randomization was performed by the following stratification criteria: age and gender characteristics, duration and disease severity. The main group included 80 patients with moderate BA in combination with HTN 1–2 degree. Further, the patients were divided into two groups: those treated by Ramipril ("Tritatse") 5 mg/day (n = 40) and the Irbesartan ("Aprovel") at a dose of 150 mg/day (n = 40). Antihypertensive therapy was administered along with the inhaled bronchodilators and anti-inflammatory treatment of BA (formoterol + budesonide, "Symbicort" 160/4.5 mcg, 2 inhalations twice daily, ipratropium bromide + fenoterol "Berodual" and ambroxol, "Lasolvan" nebulized). A week later, if target blood pressure (BP) was not achieved (i. e. BP remained > 140/90 mm Hg) the dose of Ramipril or Irbesartan was increased (up to 10 and 300 mg/day, respectively).

The average age of patients was 52.9 ± 4.2 years. Women were predominant (68 %), the comorbid conditions were more frequent in elderly people.

To evaluate the clinical and functional characteristics of the co-existent HTN and BA, three control groups were formed: subjects with HTN

1–2 grade (n = 15), normotensive patients with moderate BA, (n = 15), healthy subjects without HTN and BA (n = 16).

Instrumental examination included echocardiography ("Aloka 1700", Japan; "LOGIQ 500", Germany) with the use of ultrasonic sensors with a frequency of 3.5 MHz. Structural and functional parameters of the left and right ventricles were assessed: end-systolic dimension (ESD, cm), end-diastolic dimension (EDD, cm), myocardial interventricular septum thickness (IVS, cm), the thickness of the left ventricular posterior wall (TLVPW, cm), the thickness of the anterior wall of the right ventricle (TAWRV, cm); left ventricular mass (LVM, g), left ventricular myocardial mass index (LVMMI, g/m^2), ejection fraction (EF %), end-systolic volume (ESV, ml), end-diastolic volume (EDV, ml), peak velocity phase in the phase of early diastolic filling (E, m/sec), peak velocity phase in the phase of late diastolic filling (A, m/sec), the ratio of peak velocities (E/A), mean pulmonary arterial pressure (MPAP, mm Hg), and others.

Vascular endothelium-dependent vasodilation was assessed according to the method by D. S. Celermajer et al (1992) [11]. Linear transducer 10 MHz was used to measure vasomotor response of the brachial artery as implied in the test of the cuff reactive hyperemia. The plasma levels of endothelin-1 (ET-1) (plasma samples with ethylenediaminetetraacetate) were assessed by enzyme immunoassay (kit "Biomedica", category № 442–0052; "Arkrey", Japan) [12].

Statistical analysis was performed using Statistica 6.0 software package, and "Microsoft Excel". Normally distributed quantitative variables are presented as means and standard deviations. Student t-test was used to compare two independent groups in case of normally distributed variables. The rates were compared by χ^2 Pearson-test. Differences were considered significant at p-level < 0.05; the differences at $0.05 <$ p-level < 0.1 were considered as tendency.

The relations between the studied parameters were evaluated by the nonparametric Spearman correlation analysis. The strength and direction of the associations were assessed by the magnitude and sign of the regression R coefficient. The differences were considered significant at p-level < 0.05.

Results

As some of the examinations (Echocardiography, Doppler Echocardiography and others) were not easy to perform during the exacerbation of BA in patients with severe respiratory failure, we used data obtained when the status was stable, after the dyspnea episodes got more rare, the forced expiratory volume at the first second (FEV1) and peakflowmetry parameters improved, and the compliance increased. When comparing groups of BA patients with and without HTN, we found that the rate of uncontrolled or partially controlled BA (GINA, 2007, 2013) [13] was 3.2-times higher in comorbid disease. Therefore, BP control in BA patients is required for a quicker and better asthma control.

Clinical signs of PHTN were found in some of BA patients, i. e. the shift of the right border of the heart (one third of patients, 35.2 %), epigastric pulsation (27.3 %), the accent of the 2nd tone above the pulmonary artery (PA) (32.3 %). In the group with comorbid disorders (n = 80) the abnormal change of these indicators was more prevalent: the expansion of the right border of the heart was diagnosed in half of patients (52.1 %), epigastric pulsation — in 38.4 %, the accent of the 2nd tone above pulmonary artery — in 42.4 %. Heart rhythm disorders were found rarely, which corresponds to the other data (Chuchalin A. G., Nikitin Y. P.) [14, 15]. Atrial fibrillation was found in 0.8 %, right ventricular premature beats — in 2.8 %. However, on coexistent BA and HTN, their frequency significantly increased: atrial fibrillation was found in 9.8 %, right ventricular premature beats — in 12.8 %. Right deviation of the heart electrical axis was the most common sign in patients with combined pathology (25.2 %). Thus, the analysis of medical records of patients with BA and with coexistent BA and HTN demonstrates higher rate of PHTN signs (based on the physical examination, ECG and ultrasound data) in patients with comorbid disorders rather than in those with one disease. However, the diagnostic opportunities in routine practice are limited to detect PHTN at the early stages.

Echocardiography showed changes of the following parameters in patients with HTN and BA: increased left atrium (LA) to 3.7 ± 0.05 cm, thickness of the interventricular septum (IVS) — 1.14 ± 0.02 cm, and left ventricular

Table 1

LEFT VENTRICULAR DIASTOLIC FUNCTION IN PATIENTS WITH ARTERIAL HYPERTENSION AND BRONCHIAL ASTHMA

Parameter	HTN 1–2 degree and moderate BA (n = 80)	HTN 1–2 degree (n = 15)	Moderate BA (n = 15)	Healthy respondents (n = 16)
VE, m/c	0.68 ± 0.04*^#	0.71 ± 0.04*#	0.78 ± 0.07*	0.62 ± 0.06
VA, m/c	0.81 ± 0.03*^	0.86 ± 0.04*#	0.81 ± 0.02*	0.35 ± 0.03
E/A	0.78 ± 0.02*^#	0.87 ± 0.02*#	0.96 ± 0.04*	1.48 ± 0.03

Note: HTN — hypertension; BA — bronchial asthma; VE — the velocity of early diastolic filling of the left ventricle; VA — the velocity of late diastolic filling; * — $p < 0.01$ compared with healthy respondents; ^ — $p < 0.01$ compared with the HTN group; # — $p < 0.01$ compared with the BA group.

posterior wall thickness (LVPW) 1.62 ± 0.02 cm, end-diastolic volume (EDV) — 148.55 ± 3.0 ml (vs. 118.30 ± 2.1 ml in the control group), end-systolic volume (ESV) — 42.94 ± 1.73 ml, elevated mean pulmonary artery pressure (MPAP) — 28.19 ± 2.32 mm Hg, high LV myocardial mass index (LVMMI) — 140.58 ± 29.17 g/m^2, right atrium dimension (RA) 3.08 ± 0.06 cm, right ventricular dimension (RV) — 2.92 ± 0.05 cm. Table 1 shows the baseline indices of diastolic function.

In the group of patients with HTN and patients with coexistent HTN with BA, the peak E was reduced and as a compensation mechanism peak A was increased, resulting in the decreased ratio E / A (0.78 ± 0.02 in the group with comorbidities), indicating LV diastolic dysfunction.

In patients with comorbidities, the baseline diameter of BA was decreased (3.4 ± 0.7 mm), the systolic and diastolic blood flow were significantly reduced, and at 1st, 2nd and 3rd minutes after the cuff removal pathological vasoconstriction was found in 2.3 % of the patients that was 3.5-times higher than in the control group. These findings indicate an important role of BA in the development of vascular injury. Abrupt baseline deceleration of flow velocity in the narrow BA in patients with HTN and BA indicate ED associated with the irreversible endothelial structural changes, with the severity of inflammation, and with the hypoxia-related increase in blood viscosity.

The ET-1 level (0.74 ± 0.07 fmol/l), which is the main indicator of ED, was higher in patients with the more profound impairment of the endothelial response to reactive hyperemia (i. e. in patients with coexistent HTN and BA): 3.3-times exceeding the normal values.

Our study showed that endothelial function is affected by a combination of factors, including impaired myocardial function, obesity, duration of HTN and BA, severity of broncho-obstruction, increase of the mean pulmonary pressure, ET-1 level [2].

In patients with HTN and BA with abnormal vasoconstriction, higher MPAP was registered (35.3 ± 0.2 mm Hg) compared with the group of patients with abnormal vasodilation as shown by the reactive hyperemia test (MPAP 26.0 ± 1.1 mm Hg, $p < 0.01$).

Two-month therapy with Irbesartan or Iamipril led to a significant BP decrease in both groups. Patients with coexistent HTN and BA who received Irbesartan showed a significant reduction in systolic BP from 162 to 129 mm Hg, and diastolic BP — from 97 to 83 mm Hg. In the group receiving Ramipril systolic BP decreased from 164 to 139 mm Hg, and diastolic BP — from 98 to 88 mm Hg. Within two months of treatment, compliance of patients in the Irbesartan group was 91 %.

In both groups, there was a 8 % reduction in the volume of left atrium (6 %); EDV decreased by 10 % (9 %); ESV decreased by 11 % (10 %), respectively; MPAP decreased by 30 % (29 %) (Table 2).

In patients with coexistent HTN and BA, 2-month therapy with Ramipril led to the improvement of endothelial function: the frequency of pathological vasoconstriction decreased by 50 %, vasodilatation of BA more than 10 % was found in 52 %. At the same time, Irbesartan demonstrated even better results: 2.2-fold increase in the number of patients with normal endothelial function (from 30 to 68 %), and 5.5-times lower frequency of vasoconstriction (from 39 to 7 %).

Thus, the use of Ramipril and Irbesartan is associated with the improvement of endothelial function in patients with coexistent HTN and BA.

At baseline, the ET-1 level was similar in both groups: 0.73 and 0.73 fmol/ml in the subgroup Ramipril and Irbesartan, respectively. After 2 months of treatment ET-1 significantly decreased in both groups to 0.30 fmol/ml in Ramirpil group, and to 0.29 fmol/ml in Irbesartan group (Table 3).

In the studied subgroups of patients with HTN and BA the peak E increased to a similar extent aftert he treatment (0.04 cm/s) indicating the decrease in the LV stiffness during LA diastole. At the same time, in the Ramipril group, a more pronounced decline of transmitral blood flow during atrial systole was found. The pronounced effect of Ramipril on the diastolic dysfunction might be linked to the lipophilic properties of this drug and its good penetration into the heart muscle resulting in the efficient blockade of the tissue renin-angiotensin-aldosterone system.

In the Irbesartan group, positive changes in respiratory function, i.e. a significant increase in lung vital capacity (VC), the Tiffno index and forced expiratory volume at the 1st second. At the same time therapy with Ramipril was associated with the dry cough intensification in 12% of patients with AH and BA, while this side effect was not registered in the Irbesartan group. Therefore, Irbesartan miht be a more suitable treatment option for patients with BA and HTN.

Discussion

Coexistence of BA and HTN exacerbates myocardial dysfunction, is associated with more severe ED, resulting in the higher frequency of uncontrolled BA and prolongation of target

Table 2

PARAMETERS OF LEFT AND RIGHT VENTRICLES IN PATIENTS WITH HYPERTENSION AND BRONCHIAL ASTHMA

Parameter	Before treatment with Ramipril (n = 40)	After treatment with Ramipril (n = 35)	Before treatment with Irbesartan (n = 40)	After treatment with Irbesartan (n = 38)
LA, cm	3.6 ± 0.03	3.3 ± 0.03*	3.7 ± 0.02	3.5 ± 0.02*
IVS, cm	1.3 ± 0.02	1.23 ± 0.02	1.34 ± 0.12	1.29 ± 0.16
EDV, ml	148.4 ± 3.6	133.1 ± 2.9*	145.2 ± 4.3	131.7 ± 4.1*
ESV, ml	58.8 ± 3.2	52.4 ± 3.8*	60.1 ± 3.2	54.3 ± 2.8*
RV, cm	2.6 ± 0.22	2.5 ± 0.25	2.7 ± 0.25	2.6 ± 0.30
RA, cm	3.3 ± 0.28	3.1 ± 0.3	3.5 ± 0.28	3.3 ± 0.5
MPAP, mm Hg	29.9 ± 3.1	20.9 ± 3.4*	31.2 ± 3.0	22.1 ± 3.6*

Note: LA — left atrium; IVS — interventricular septum; EDV — end-diastolic volume; ESV — end-systolic volume; RV — right ventricle; RA — right atrium; MPAP — mean pulmonary artery pressure; * — $p < 0.05$, significant differences before and after treatment.

Table 3

THE EFFECTS OF IRBESARTAN VS. RAMIPRIL ON THE LEFT VENTRICULAR DIASTOLIC FUNCTION AND ENDOTHELIN-1 IN PATIENTS WITH HYPERTENSION AND BRONCHIAL ASTHMA

Parameter	Ramipril		Irbesartan	
	Before treatment (n = 40)	After treatment (n = 35)	Before treatment (n = 40)	After treatment (n = 38)
ET-1, fmol/ml	0.73	0.30*	0.73	0.29*
VE, m/c	0.77 ± 0.17	0.81 ± 0.11*	0.76 ± 0.16	0.80 ± 0.14*
VA, m/c	0.87 ± 0.15	0.80 ± 0.14*	0.86 ± 0.14	0.83 ± 0.13*
E/A	0.78 ± 0.17	1.01 ± 0.18*^	0.79 ± 0.15	0.98 ± 0.21*

Note: ET-1 — endothelin-1; * — $p<0.05$ significant differences before and after treatment; ^ — $p <0.05$ significant intergroup differences.

BP achievement. Our study demonstrates that comorbid diseases affect each other, but the extent of this impact is likely to be different.

Doppler dynamic assessment of systolic and diastolic dysfunction and the degree of PHTN is recommended in all patients with comorbid diseases (a combination of BA and HTN) for the early diagnostics and treatment of heart failure.

It is first study to demonstrate the positive impact of a complex antihypertensive monotherapy by Ramipril ("Tritatse", Sanofi) in patients with HTN 1–2 degrees and coexistent moderate treated BA regarding the improvement of endothelial function as following: the reduction of the plasma level of ET-1, normalization of vasodilator BA function in 52% patients, a 2-fold decrease of the pathological vasoconstriction (from 40% to 20%), a significant increase of early diastolic filling velocity of the left (15%) and right (12.4%) of ventricles and deceleration of late diastolic filling velocity by 8.8 and 14%, respectively, leading to the increase of E / A ratio.

However, Ramipril is not always well tolerated in BA patients: 12% patients develop dry cough, which might be associated with an unreasoned strengthening of bronchodilator therapy and low adherence to treatment.

Our comparative study showed a positive effect of angiotensin II receptor blocker Irbesartan ("Aprovel", Sanofi) in patients with treated BA on the ED as following: normalization of the plasma level of ET-1, improvement of BA vasodilation in 68% patients, 5.6-fold reduction of pathological vasoconstriction. Irbesartan led to a positive change in diastolic function: an increase in the E / A ratio, rapid achievement of target BP, a decrease in PHTN degree, improvement of respiratory function, increase in the quality of life.

Both Irbesartan and Ramipril delayed the progression of cardiovascular remodeling, but there was a clear trend towards poorer treatment tolerability in Ramipril group compared to Irbesartan group due to a negative impact on the lung function and more frequent dry cough (12%). Therefore, ACE inhibitors in effective doses show lower safety profile in patients with bronchopulmonary pathology compared to ARBs in maximal doses, while their efficiency is comparable.

Conclusions

Irbesartan enables efficient BP control, delays the progression of cardiovascular remodeling, has a favourable effect on respiratory function, and is characterized by a higher compliance. Therefore, it can be considered the best choice in patients with coexistent HTN and BA.

Conflict of interest
The authors declare no conflict of interest.

References

1. Feinstein AR. Pretherapeutic classification of comorbidity in chronic disease. J Chron Disease. 1970;23(7): 455–468.

2. Nadal Ginard K. When one interferes with the other — comorbidity on the topic of the day. New medicine of the millennium. 2012;6:22–24.

3. Shirinsky VS, Shirinsky IV. Comorbid diseases as a topical issue in clinical medicine. Siberian Medical Journal. 2014;29(1):7–11. In Russian.

4. Pavlenko VI, Kolosov VP, Naryshkina SV. Peculiarities of comorbid course, prognosis and treatment of chronic obstructive pulmonary disease and coronary heart disease. Blagoveshchensk. 2014. In Russian.

5. Gavrisyuk VK. Cardiovascular system disorders in patients with bronchial asthma. Ukrainian Pulmonology Journal. 2000;2:31–32. In Russian.

6. Pronichenko LV, Mal GS. Morphological and functional features of cardiovascular and respiratory systems in patients with arterial hypertension and chronic obstructive pulmonary disease. Fundamentalnye Issledovaniya = Fundamental Studies. 2011;10(1):144–147. In Russian.

7. Eliseeva ES, Sizykh TP. Hemodynamics and diastolic function of the right ventricle in patients with bronchial asthma. Therapeutic Archives.1995;67(8):39–42. In Russian.

8. Pribylov SA, Zhidkikh BD, Prusakova OI, Mustak A. Pulmonary hypertension and diastolic dysfunction of the heart in elderly patients with bronchial asthma and COPD. Kursk Journal of Research and Practice «Man and Health». 2009;4:80–89. In Russian.

9. Prusakova OI. Correction of endothelial dysfunction, pulmonary hypertension in patients with arterial hypertension with coexisting bronchial asthma. Modern Problems of Science and Education. 2011;6. Available at: http://www.science-education.ru/100–4957. In Russian.

10. Kravchun PG, Delevskaia VI. The relation of bronchial obstruction with diastolic dysfunction of the left ventricle in patients with arterial hypertension with coexisting chronic obstructive pulmonary disease. Bulletin of Vitebsk State Medical University. 2014;13(4):48–53. In Russian.

11. Celermajer DS, Sorensen KE, Gooch VM, Spiegelhalter DJ, Miller OI, Sullivan ID et al. Non-invasive detection of endothelial dysfunction in children and adults at risk of atherosclerosis. Lancet. 1992;340(8828):1111–1115.

12. Bakhtiiarov RZ. Modern methods of studying endothelial function. Rossiiskij Kardiologicheskij Zhurnal = Russian Journal of Cardiology. 2004;2(46):20–24. In Russian.

13. Global strategy for asthma management and prevention (updated 2014): Global Initiative for Asthma (GINA). URL: http://www.ginasthma.org; 2014.

14. Bronchial asthma. In 2 v. ed. by A. G. Chuchalin. Moscow: Agar, 1997. p. 432. In Russian.

15. Nikitin YP, Kuznetsov AA, Malyutina SK, Simonova GI Prognostic value of duration and variability of Q-T and R-R intervals in general population of Novosibirsk. Kardiologiia. 2002;2:76–83. In Russian.

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