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OSTEOPOROSIS AND CARDIOVASCULAR PATHOLOGY: PECULIARITIES OF THE COMBINED DISEASE DEVELOPMENT

ABSTRACT. The article presents the research data devoted to the features of the associated course of coronary heart disease (CHD), arterial hypertension (AH) and osteoporosis (OP). The research covered 82 patients with CHD and AH of mature and senior age and 28 persons in the control group. Analysis of osteoporosis risk factors was carried out on the basis of the unified questionnaires; computer program FRAX was employed.

We have proved that osteoporosis risk factors were more typical of the patients with cardiovascular pathology in comparison with healthy people. The risk of osteoporotic fractures was much higher regarding the patients with cardiovascular diseases which in most cases allows to initiate treatment.

On the basis of a complex clinic-functional research based on the results of bone densitometry, frequency of occurrence of osteopenic syndrome among the patients with cardiovascular pathology was determined.

Patients with coronary heart disease in association with arterial hypertension demonstrated the syndrome of osteopenia in 57,5±9,01% of cases (osteoporosis 35,0±5,45%, osteopenia – 22,5±3,47%); for the patients with AH heh index is 45,23±0,07% (4,76±0,65% and 40,47±6,16%, respectively); in the control group there were only 17,85±3,27% cases of osteopenia.

The lowest indicators of mineral density of bones are registered among the patients with coronary heart disease in association with arterial hypertension, and practically half of the patients had a severe acute form of the disease. The obtained data testify to the need of complex prevention and timely diagnostics of the osteopenic syndrome among the patients with cardiovascular pathology.

KEY WORDS. Osteoporosis, cardiovascular pathology, ischemic heart disease, arterial hypertension.

Osteoporosis (OP) is a systemic skeletal metabolic disease characterized by decrease in bone mass, microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture. OP is one of the most widely spread and socially significant diseases all over the world, in the recent decades its frequency has been constantly growing. In Russia according to the densitometric measurement 30.5-33.1% females and 22.8-24.1% males over 50 have osteoporosis. The most serious medical and social consequences are stipulated by proximal femur fractures. Morbidity rate within the first year after the fracture is 30.8-35.1%; besides over half of the survived patients need nursing care [1].

Nowadays, osteoporosis is more often viewed as a multidisciplinary problem. From the point of view of contemporary medicine it is extremely important to disclose certain interrelations and common pathogenetic mechanisms between different diseases with the purpose of working out a complex and individual approach to treatment and prevention. Special attention should be paid to osteoporosis combined with a cardiovascular pathology as it rates first in the population mortality structure. According to the official data of the Ministry of Health Care and Social Development RF published in 2009 the highest mortality in the country is due to cardio-vascular diseases (CVD), 56.6% to be exact; besides the patients over 50 who died as a result of a cardiovascular pathology have more than three background or co-existing diseases. According to the data of a number of authors vertebral fractures may be predictors of total mortality, also increasing the mortality risk from cardiovascular diseases more than twice [2-5]. Low bone mineral density (BMD) is an independent risk factor of cardiovascular mortality among senior citizens, even more important than the levels of arterial blood pressure and cholesterol [6]. According to the data of an epidemiological survey covering 9704 women over 65 each BMD decrease in the proximal part of the radial bone per one standard norm deviation raised the risk of premature death (not connected with osteoporotic fractures) within the next 2 years by 40% and especially death by stroke [7-8]. In the observations made by other authors it has been stated that more than 70% patients experiencing hip fracture are also diagnosed with a cardiovascular pathology; high death rate has also been registered in cases of combined cardiovascular diseases and hip fractures. Presence of at least one vertebral fracture or OP leads to a triple risk of cardiovascular complications development [9]. In other researches it has been shown that patients with low BMD more often demonstrate an increased lipid level, aggravated coronary atherosclerosis and a much higher risk of stroke and myocardial infarction [10-11]. A number of scientists have claimed that in the early period of post menopause BMD decrease per one standard deviation from the bone mass peak for women is associated with increase in the general mortality by 43% and premature death as a result of a cardiovascular pathology [11].

Other data claim a close pathogenetic link between OP and cardiovascular diseases. It should be underlined that some authors relate BMD loss to a category of CVD predictors, to be exact coronary arterial diseases [12]. This is explained by a certain similarity of the OP and atherosclerosis pathogenesis when the damaged monocytic cells in one case differentiate in the vascular wall into macrophage-looking 'foam' cells; in the other into osteoclasts. Apart from that the bone and vascular tissue have a number of other general morphological and molecular properties. Vascular calcification has the same elements as the bone tissue: calcium salts, phosphates combined with hydroxyapatite, osteopontin, bone morphogenetic protein, matrix Gla-protein, collagen type I, osteonectin, osteocalcin etc. [13-14]. Moreover the arterial wall affected by atherosclerosis consists of osteoblats' predecessors which are capable of synthesizing mineral components characteristic of bone tissue. Several researchers note the common pathogenesis of arterial hypertension (AH) and osteoporosis. In particular activation of renin-angiotensin system (RAS), on the one hand, due to the influence on the local blood

circulation and bone blood supply causes vasoconstriction of the microcirculatory bloodstream and, on the other hand, directly influences on angiotensin II production. The latter is the growth promoting factor directly stimulating proliferation of osteoclasts and increasing the level of endotelin-1 the concentration of which at RAS activation rises not only in endothelium but also in osteoclasts. These data are clinically confirmed by the osteoprotective action of inhibitors of angiotensin converting enzyme. These substances promote less resorption of osteoclasts of the bone tissue by suppressing activity of angiotensin II and thus reducing BMD loss [15-17].

Resulting from the profound atherosclerosis and osteoporosis there are data indicating possible mechanisms of pathophysiological interconnection between these diseases. With age the OP and CVD incidences increase due to atherosclerosis. There is an interconnection between the biological CVD risk factors due to atherosclerosis and the bone mass. It has been demonstratively proved that calcium metabolic disorders lie in the pathologic basis of these diseases. We observe a one-way change of hormone systems which regulate calcium metabolism including increase in the levels of parathyroid hormone and angiotensin-II and decrease in vitamin D and estrogen.

The common links of the pathogenesis of OP and CVD conditioned by atherosclerosis are explained by the presence of the markers simultaneously influencing on the vascular and bone cells. Osteoprotegerin, leptin, oxidized lipids and C-reactive protein can be such markers.

It should also be pointed out that inflammation plays the key role in all the stages of atherosclerosis development accompanied by a significant increase in the concentration of inflammation markers in blood plasma – cytokines (interleikin-1, tumor necrosis fartor *a*), which in turn induce bone resorption.

Consequently nowadays researchers have at their disposal data providing evidence of a possible interconnection between osteoporosis and CVD; although the existing researches are few and contradictory. In connection with this study of the link between OP and CVD have a big scientific and practical value as it can facilitate discovery of the factors influencing on OP development accompanied by AH and ischemic heart disease (IHD), promote earlier diagnostics, prevention and effective ethiopathogenetic treatment of OP for such patients.

The aim of this study is to state the interrelation of risk factors related to CVD and OP, estimate the frequency of incidences of osteopenic syndrome among the patients with cardiovascular pathology.

Materials and methods of research. We have examined 82 patients with cardiovascular diseases. Taking into account the nature of pathology we have divided the patients into the following groups: group I included 40 patients with IHD and AH, among them there are 24 women and 16 men aged 63.3±0.89. Group II included 42 patients with AH (31 women and 11 men), the average age 58.07±0.87. Group III (control) consisted of 28 people (21 women and 7 men) without somatic pathologies, the average age 58.13±0.92. The patients in all the three groups are comparable in age, gender composition and body mass index ($p>0.05$). The research does not cover patients suffering from: chronic heart failure IV functional class (NYHA); a permanent

form of atrial fibrillation; cardiac valve diseases; non-coronary myocardial diseases and other diseases which could themselves produce an impact on the bone tissue metabolism (endocrine, rheumatic diseases, pathology of digestive system, chronic kidney failure etc.); patients taking medications affecting mineral metabolism (glucocorticoids, cytostatics, anticonvulsants). Before the examination the patients did not undergo any specific therapy for OP treatment and prevention.

Verification of IHD and AH diagnostics was made on the basis of recommendations of the All-Russian scientific society, fourth revision. For BMD analysis we used the standardized osteodensitometric method of peripheral dual-energy X-ray absorptiometry of L spine and proximal femur on the apparatus "Lunar DPX" (USA). For the complex evaluation of the cardiovascular system condition we carried out a functional examination: electrocardiography, echocardiography, and 24-hour blood pressure monitoring. The biochemical blood tests including definition of the values of mineral metabolism (levels of total calcium, ionized calcium, phosphor, and alkaline phosphatase), lipid metabolism (levels of total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides), and glucose have been performed.

To estimate OP risk factors we used uniform questionnaires. The estimation of a ten-year probability of fractures was carried out with the help of FRAX software according to the recommendations of the International Association on Osteoporosis and the World Health Organization (WHO). This methodology implies a qualitative estimation of the total risk on the basis of mathematical analysis of the existing OP risk factors. In case there is a possibility of femoral neck BMD measurement its results can be taken into account for the calculation. Calculation of the risk of OP complications (fractures) with FRAX lets us define the choice of medical interventions without additional diagnostic methods as well as disclose a bigger number of patients needing treatment and diagnostics.

For OP diagnostics we used WHO criteria: BMD values deviating from the bone mass peak (by T-criterion) by less than 1 standard deviation (SD) were considered as the norm; values ranging from -1 SD to -2.5 SD as osteopenia; less than -2.5 SD as osteoporosis [18].

Statistical processing of the results was carried out with the use of parametric and non-parametric methods depending on the character of distribution of variational series with the help of statistical software Statistica 6.0.

Research findings. Analysis of the obtained data has shown that OP risk factors were quite frequent among the patients in each group. In 1st and 2nd groups correspondingly 61.87±9.67% and 55.50±8.48% of the people under study have risk factors, which is more often than in the control group – 47.01±8.78%. Such risk factors as smoking (about 40% patients in each group), low physical activity, low daily calcium consumption with food and fractures in the medical background of the closest relatives are as frequent. Alcohol abuse is not registered among the patients in question.

Atraumatic bone fractures and growth decrease are significantly more frequent among the patients suffering from IHD in association with AH. Thus, the experienced

atraumatic fractures have been diagnosed for 47.5±7.43% patients in the 1st group, 30.95±4.67% in the 2nd group and 14.28±2.60% in the 3rd group, and growth decrease by more than 3 cm in 52.5±8.22%, 21.42±3.22% and 3.57±0.57%, correspondingly ($p_{I-III}<0.001$).

The most often localization of osteoporotic fractures among the patents with CVD is spinal compression fracture.

Hypercholesterolemia and LDL increase is also more frequent in the 1st group ($p_{I-III}<0.05$). Lipid profile values in 1st-2nd and 2nd-3rd groups were not significantly different ($p<0.05$).

The ten-year risk of osteoporotic fractures (by FRAX) is significantly higher among the patients with cardiovascular pathology and is on average in 1st group 15.11±4.07%, in 2nd group 10.01±1.27% and in 3rd group 7.02±0.54% ($p_{I-II}<0.05$, $p_{I-III}<0.001$, $p_{II-III}<0.05$). The average values of the proximal femur risk fracture are the following: 3.95±0.74%; 1.34±0.37% and 0.37±0.08% correspondingly ($p_{I-II}<0.001$, $p_{I-III}<0.001$, $p_{II-III}<0.05$).

BMD values for the patients with IHD combined with AH are significantly lower (-1.72±0.55) SD than for the patients in the 2nd group (-0.48±0.24) SD and 3rd group (-0.01±0.015) SD ($p<0.001$). It should be noted that IHD and AH patients (group 1) more often have osteopenic syndrome 57.5±9.01% (osteoporosis 35.0±5.45%, osteopenia 22.5±3.47%); in 2nd group 45.23±0.07% (4.76±0.65% and 40.47±6.16% correspondingly); only osteopenia has been found in the control group in 17.85±3.27% cases.

While estimating mineral metabolism no significant differences have been registered between the groups.

Conclusion. OP and CVD risk factors are more frequently diagnosed among the patients with cardiovascular pathology. Moreover such category of patients has the lowest BMD values and practically half of them have been diagnosed with severe OP.

The data we have garnered indicate a high incidence rate and severe degree of osteoporosis among the patients of middle and old age suffering from ischemic heart disease combined with arterial hypertension which allows considering these diseases as risk factors.

Cardiovascular pathology considerably raises probability of fractures in the next 10 years of life which means that it requires prompt diagnostics, complex prevention and treatment of osteopenic syndrome in this category of patients.

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