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EFFECT OF MELATONIN DRUGS ON THE DYNAMICS OF LIPID PROFILE INDICATORS IN PATIENTS WITH ARTERIAL HYPERTENSION AND OSTEOARTHRITIS

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Annotation. *Hypertension (AH) and osteoarthritis (OA) are among the most common diseases in the world, which not only negatively affect the quality of life of patients, but also cause an increase in economic costs for health care.*

Group I patients who received melatonin during the month on the background of the main treatment have better dynamics of lipid profile compared with the corresponding indicators in group II patients. Thus, the level of cholesterol decreased in group I by 13,5%, and in group II – by 12,0%; LDL indicators decreased in group I by 29,2%, and in group II – by 21,4%. At the same time, the indicators of HDL and CA in patients of two groups (I and II) with hypertension combined with OA, were practically unchanged.

The addition of melatonin (3 mg once daily at bedtime for 1 month) to the main therapy has a positive effect on the normalization of lipid metabolism in patients with hypertension associated with osteoarthritis, and facilitates their severe course. Further research will help to optimize the treatment tactics of such patients.

Keywords: *melatonin, hypertension, osteoarthritis, lipid profile.*

Introduction. Hypertension (AH) and osteoarthritis (OA) are among the most common diseases in the world, which not only negatively affect the quality of life of patients, but also increase the economic costs of health care. The triggers of hypertension and OA have not been definitively studied, but their risk factors, occurrence and deterioration are known, among them the leading place is occupied by disorders of lipid metabolism.

According to researchers, the development of dystrophic changes in the vascular wall and articular cartilage, the progression of hypertension and OA may contribute to disorders of lipid metabolism, which become a common pathogenetic mechanism of these diseases [1, 2].

We believe that one of the possible variants of the pathogenetic approach to the treatment of this combined pathology may be melatonin, which is known to act as a biological clock and a cardioprotector, as well as has anti-ischemic and antihypertensive

effects. Additional opportunities and prospects for its use are opened by another, no less important, function – the effect on lipid metabolism [3]. In addition, it has been experimentally demonstrated that melatonin has a chondroprotective potential and may be involved in the pathogenesis of OA due to its effect on circadian rhythms of chondrocytes [4].

The aim is to determine the effectiveness of the course of melatonin therapy in combination with the main treatment on the dynamics of the lipid profile of patients with hypertension combined with OA.

Materials and methods. In accordance with the purpose and objectives of our dissertation research, a total of 130 people of different ages and sexes with hypertension and OA were examined. Of these, hypertension combined with OA had 60 patients, who were divided into two groups. Thus, group I consisted of 30 patients with hypertension combined with OA, who received for a month, in addition to the main treatment, melatonin. Group II included 30 patients who had comorbid conditions of hypertension and OA and who were not given melatonin in their usual treatment. AH without concomitant OA was observed in 30 patients who made up group III. Group IV included 30 people with OA without concomitant hypertension. The control group consisted of 10 healthy people.

Criteria for inclusion of patients in the study were: verified diagnosis of stage – II hypertension in combination with a verified diagnosis of OA Ro-stage II, SFK I – II.

The study did not include patients with concomitant autoimmune diseases, stage III hypertension, heart failure (FC III – IV), OA Ro-stage III – IV, as well as those who took corticosteroids or cyclosporine before the study or planned to take them during its holding. There were no smokers among the subjects. The use of nonsteroidal anti-inflammatory drugs (NSAIDs) was not a criterion for exclusion from the study groups.

According to the study program, all patients underwent serum analysis for lipid metabolism disorders. Lipid profile was re-determined in patients of groups I and II. All patients voluntarily agreed to participate in the study. The study was approved by the Medical Ethics Committee of the Bukovinian State Medical University.

In the case of stage II hypertension, patients were prescribed a comprehensive standard treatment in accordance with the recommendations of the International Society of Hypertension (ISH) (2020) [5], the European Society of Hypertension (ESH) and the European Society of Cardiology (ESC) (2018) [6], Ukrainian Association of Cardiologists (2017), in particular: angiotensin-converting enzyme (ACE) inhibitors (lisinopril – 10 – 20 mg/day), combining them with thiazide diuretics (hydrochlorothiazide –12.5 – 25 mg/day). In the case of hyperlipidemia, statins (rozurvostatin – 10 – 20 mg / day) were added until the target levels of blood pressure (BP) and total cholesterol were reached. Patients with OA were prescribed NSAIDs (ibuprofen, diclofenac sodium in appropriate doses), chondroitin sulfate drugs in accordance with the clinical guidelines of the Association of Rheumatologists of Ukraine and the Association of Orthopedic Traumatologists of Ukraine (2017). At the same time, patients of group I were added to the complex treatment melatonin (“Vita-melatonin», JSC «Kyiv Vitamin Plant”, Kyiv, Ukraine) 1 tablet (3 mg per day) for 1 month.

The lipid profile study package included the determination of cholesterol (cholesterol) (N = up to 5.2 mmol/l) by colorimetric, enzymatic methods using esterase and cholesterol oxidase; low-density lipoprotein (LDL) (N = up to 2.59 mmol/l), high-density lipoprotein (HDL) (N = 1.04–1.55 mmol/l) by the direct method of elimination of chylomicrons. All laboratory tests were performed on an automatic biochemical analyzer Accent 200. The coefficient of atherogenicity (CA) was calculated by the following formula: CA = (cholesterol – HDL cholesterol) / HDL cholesterol) (N = female to 3.5; male to 3.2)

The obtained data were processed by methods of variation statistics using the program Statistica 10.

Results of the research. According to the study plan, lipid profile parameters were first determined for all patients. Patients in groups 1 and 2 were advised not to drink alcohol, coffee and drugs (corticosteroids, cyclosporine), which affect the melatonin-forming function of the pineal gland. Then patients in group 1, in addition to the main treatment, were prescribed a monthly course of melatonin at a dose of 3 mg / day. All patients in this group after re-treatment with the addition of melatonin re-performed serum tests to determine the parameters of the lipid profile of the blood. Patients in group 1 also re-determined the following indicators. Laboratory results at the beginning of the study are given in table 1.

Table 1

Indicators of lipid profile in patients at the beginning of the study (M±m)

Indicator	Group1 AH+OA	Group 2 AH+OA	Group 3 AH	Group 4 OA	Control
Cholesterol, mmol/l	5.90±1.41	5.87±1.28	5.61±1.28	5.52±1.11	3.76±0.83
HDL, mmol/l	1.43±0.38	1.40±0.30	1.37±0.38	1.37±0.27	1.26±1.12
LDL, mmol/	4.45±1.48	4.19±1.17	4.13± 1.24	4.19±1.17	2.12±0.22
CA	3.27±1.39	3.38±1.38	3.35±1.22	3.14±1.18	2.0±0.67

*Note: * – the difference is significant compared to the figure in almost healthy individuals ($p<0.05$).*

Table 1 show that disorders of lipid metabolism are present in all four groups. It should be noted that in patients of groups 1 and 2, who have a comorbidity of hypertension and OA, these indicators are worse than in patients of groups 3 and 4, who do not have a combination of these pathologies. This confirms our hypothesis about the mutually burdened course of hypertension and OA.

Figure 1 shows the dynamics of lipid profile after treatment of patients with comorbid hypertension and OA, who for a month, in addition to the main treatment, received additional melatonin (group 1), and who, in addition to the main treatment, did not receive melatonin (group 2).

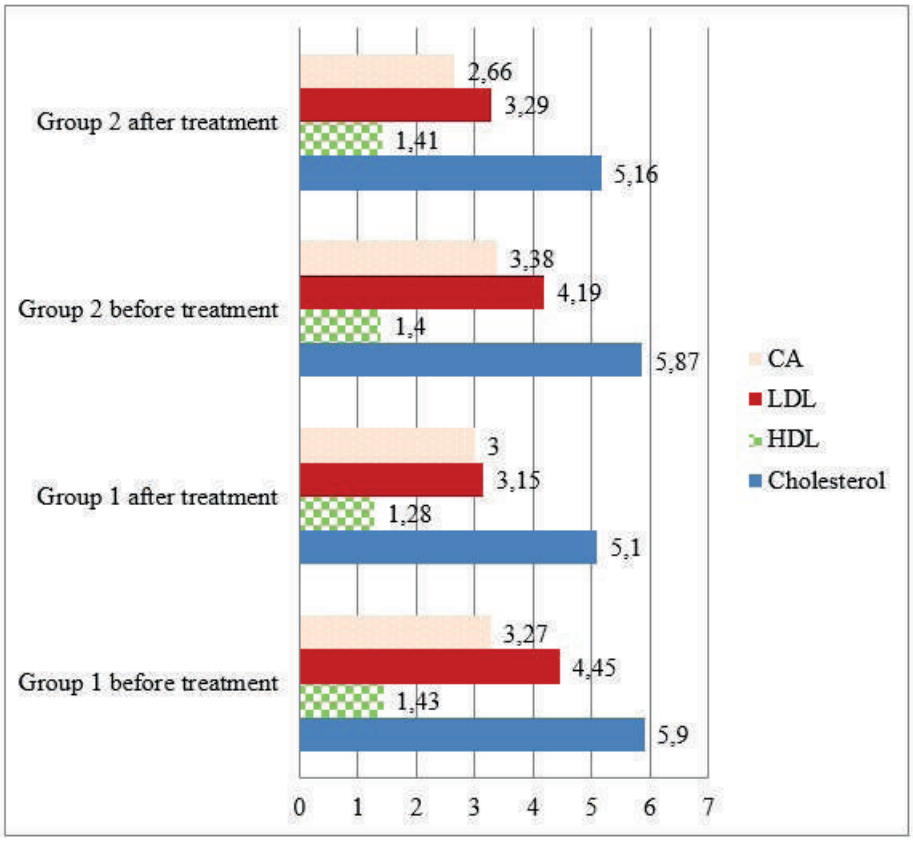

Fig. 1. Dynamics of lipid profile after treatment.
*Note: * – the difference is significant compared to almost healthy individuals ($p < 0.05$).*
*** – the difference is significant compared to the rate in persons before treatment ($p < 0.05$).*

The image in Fig. 1 demonstrates a positive effect of treatment of patients with combined pathology of the two study groups. However, patients in group 1 who received melatonin during the month on the background of the main treatment have better results compared with the corresponding indicators in patients of group 2. Thus, the level of cholesterol decreased in group I by 13.5%, and in group 2 – by 12.0%; LDL indicators decreased in group I by 29.2%, and in group II – by 21.4%. At the same time, the indicators of HDL and CA in patients of two groups (1 and 2) with hypertension combined with OA, did not change. It should be noted that the use of melatonin did not affect the changes in the lipid profile of the blood of patients in whom the lipid profile was within normal limits.

The obtained results give grounds to speak about the effectiveness and expediency of adding melatonin to the main treatment to combat hypercholesterolemia, which is one of the key factors in the development of atherosclerosis and the progression of

hypertension.

Discussion. The importance of finding and choosing the optimal treatment regimens for the above-mentioned comorbid diseases is due to their prevalence and socio-economic consequences. After all, during these diseases, even against the background of treatment, hormonal and metabolic changes deepen, atherogenic hyperlipidemia and insulin resistance increase, which are known to contribute to obesity (or its progression). Then such patients need more intensive antihypertensive therapy to obtain target blood pressure levels. It should be noted that these diseases have a number of common mechanisms of progression. These include chronic systemic generalized immunological inflammation (in particular, adipose tissue), insulin resistance, dyslipidemia, endothelial dysfunction [7]. That is why it is promising to study the effect of melatonin as one of the components of complex treatment on the course of hypertension with OA.

If we take into account all the effects of melatonin both as a hormone and as a drug, it is most consistent with the principles of physiological regulation and normalization of blood pressure in the human body. Direct antihypertensive action opens additional opportunities and prospects for the use of melatonin as monotherapy and its treatment in combination with antihypertensive drugs. In addition, melatonin affects lipid metabolism. There is evidence in the literature that the accumulation of lipid peroxidation products, including hydroperoxides, oxidized low-density lipoproteins (LDL) and anti-LDL, can lead to the progression of OA [8]. These compounds are able to modify and damage the lipid components of LDL, as well as cause depletion of low molecular weight oxidants [9]. It is believed that oxidized lipids can become autoantigens, resulting in the formation of anti-LDL, which adversely affects the articular cartilage.

Conclusions. The addition of melatonin (3 mg once daily at bedtime for 1 month) to the main therapy has a positive effect on the normalization of lipid metabolism in patients with hypertension associated with osteoarthritis, and facilitates their severe course. Further research will help to optimize the tactics of treatment of such patients.

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