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THE EFFECT OF COMBINED ANTIHYPERTENSIVE THERAPY ON THE CONDITION OF THE ARTERIAL WALL IN WOMEN WITH ARTERIAL HYPERTENSION AND POSTMENOPAUSAL OSTEOPOROSIS

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60 females (mean age 62.7±3.8 years) with arterial hypertension of stage II, degree 2, postmenopausal osteoporosis (according to the data of osteodensitometry) and not receiving regular antihypertensive therapy were examined. After baseline data registration hypertension therapy with a combination of lisinopril 10–20 mg and indapamide 2.5 mg per day was prescribed to 30 patients (group 1), and lisinopril 10–20 mg plus hydrochlorothiazide 12.5 mg per day for 12 weeks – to 30 patients (group 2). The control group consisted of 20 practically healthy females. All examined persons underwent clinical and laboratory examinations according to the protocols for the examination of patients with arterial hypertension and osteoporosis. Analysis of indicators after 12 weeks revealed the high antihypertensive efficacy of both treatment regimens. In patients with arterial hypertension and postmenopausal osteoporosis, according to the data of office measurement of blood pressure and daily monitoring of blood pressure, 12-week therapy with a combination of lisinopril and indapamide did not significantly differ from the therapy with lisinopril in combination with hydrochlorothiazide in terms of the severity of antihypertensive effect, an ability to normalize the daily profile of blood pressure and reduce pressure load indicators. Propagation velocity of pulse wave and central aortic pressure levels (cSBP and cPP) according to applanation tonometry significantly decreased more during 12-week therapy with lisinopril in combination with indapamide compared to the combination of lisinopril with hydrochlorothiazide, along with good tolerability in both treatment groups.

Key words: hypertension, postmenopausal osteoporosis, central aortic pressure, arterial stiffness, indapamide

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ВПЛИВ КОМБІНОВАНОЇ АНТИГІПЕРТЕНЗИВНОЇ ТЕРАПІЇ НА СТАН АРТЕРІАЛЬНОЇ СТІНКИ У ЖІНОК З АРТЕРІАЛЬНОЮ ГІПЕРТЕНЗІЄЮ ТА ПОСТМЕНОПАУЗАЛЬНИМ ОСТЕОПОРОЗОМ

Обстежено 60 жінок віком (середній вік 62,7±3,8 років) з артеріальною гіпертензією II стадії, 2 ступеня та постменопаузальним остеопорозом за даними остеоденситометрії, які не приймали регулярну антигіпертензивну терапію. Після реєстрації вихідних даних 30 пацієнткам (1 група) призначали терапію артеріальної гіпертезії комбінацією лізиноприлу 10–20 мг та індапаміду 2,5 мг на добу та 30 пацієнткам (2 група) – лізиноприл 10–20 мг плюс гідрохлортіазид 12,5 мг на добу протягом 12 тижнів. Контрольну групу склали 20 практично здорових жінок. Усім обстеженим особам проведено клініко-лабораторне обстеження згідно протоколам обстеження пацієнтів з артеріальною гіпертезією та остеопорозом. Аналіз показників через 12 тижні виявив високу антигіпертензивну ефективність обох схем лікування. У пацієнток з артеріальною гіпертензією та постменопаузальним остеопрозом за даними офісного вимірювання артеріального тиску та добовим моніторингом артеріального тиску, 12-тижнева терапія комбінацією лізиноприлу плюс індапамід за вираженістю антигіпертензивного ефекту, здатності нормалізації добового профілю артеріального тиску, зниженню показників навантаження тиском достовірно не відрізнялася від терапії лізіноприлом у поєднанні з гідрохлортіазидом. Швидкість поширення пульсової хвилі та рівні центрального аортального тиску (цСАТ та цПТ) за даними аппланаційної тонометрії достовірно більше знижувалися на тлі 12-тижневої терапії лізиноприлом у поєднанні з індапамідом порівняно з комбінацією лізиноприлу з гідрохлортіазидом поряд з хорошою переносимістю в обох лікувальних групах.

Ключові слова: гіпертонічна хвороба, постменопаузальний остеопороз, центральний аортальний тиск, артеріальна ригідність, індапамід

The work is a fragment of the research project "Development of methods for early diagnosis and drug prevention of fibrosing processes in patients with comborbid pathology (hypertension and type 2 diabetes mellitus) based on the assessment of cardiohemodynamics and renal function", state registration No. 0120U102062.

Arterial hypertension (AH) is currently one of the most significant medical and social problems due to its widespread prevalence and the fact that hypertension is the most important risk factor for most cardiovascular diseases [1]. Another no less significant problem of modern healthcare is osteoporosis (OP). According to the WHO approximately 75 million people worldwide suffer from OP [7]. The main risk group (approximately 80 %) consists of women in the postmenopausal period. The high prevalence of OP and cardiovascular diseases in old age is not explained only by aging processes [2]. The general patterns of development of these diseases have been actively studied in recent years.

It has been established that an important marker of vascular remodeling is an increase of stiffness of the arterial wall, what increases the risk of complications of cardiovascular diseases and determines the difficulty of treatment [14]. It was established that the stiffness of the vascular wall is recognized as an independent risk factor for cardiovascular diseases and is included in the list of mandatory examinations of AH patients. Antihypertensive drugs have different effects on both the character of the pulse wave and indicators of central hemodynamics, despite the similar ability to lower blood pressure (BP) in the brachial artery. The study of changes of the arterial wall parameters, as well as effectiveness of AH treatment in women with postmenopausal OP under the influence of thiazide (hydrochlorothiazide) and thiazide-like (indapamide) diuretics in combination with the ACE inhibitor lisinopril, is quite relevant.

The purpose of the study was to estimate the effect of combined antihypertensive therapy with the addition of indapamide or hydrochlorothiazide on the indices of arterial stiffness and central aortic pressure in women with a combination of arterial hypertension and postmenopausal osteoporosis.

Materials and methods. 60 women from 46 to 69 years old (mean age 62.7±3.8 years) with AH stage II, degree 2 and postmenopausal OP (based on the osteodensitometry results) and not receiving regular antihypertensive therapy were examined. The average AH duration was 8.3±2.7 years. The diagnosis of AH was established by the recommendations of the European Society of Hypertension and the European Society of Cardiology (ESH/ESC, 2018). The diagnosis of the postmenopausal OP was established according to European recommendations (ESCEO, 2019), including BMD indices of the femoral neck. All examined persons gave informed consent to participate in the study.

The control group comprised 20 practically healthy females (average age 61.3±3.5 years).

The study did not include patients with secondary forms of AH, coronary artery disease, diseases of the respiratory system, kidney disorders, liver or endocrine pathology, oncological pathology, or surgical or medical menopause. The patients did not receive hormone replacement therapy.

All examined persons underwent a general clinical examination, fracture risk assessment (FRAX), office blood pressure (OBP) measurement with the determination of systolic blood pressure (SBP), diastolic (DBP) and heart rate (HR), determination of serum glucose concentration, lipid profile parameters, levels of calcium, phosphorus, alkaline phosphatase, creatinine, estimated glomerular filtration rate [eGFR] (CKD-EPI formula), deoxypyridinoline, parathyroid hormone, 25(OH) vitamin D, osteocalcin, Type I Collagen C-Terminal Telopeptide – CTX-I in blood plasma.

Daily monitoring of blood pressure (BP) was performed with the device ABPM-02 (Meditech, Hungary). The following parameters were evaluated: average values of SBP, DBP, pulse pressure (PP), aver. BP per day (24 hours), day and night, Hypertensive Time Index (PTEI) – % measurements of SBP ≥140 and DBP ≥90 mm Hg awake; and respectively ≥120 and ≥70 mm Hg asleep. The intensity of the day-night rhythm biphasic BP was assessed by the diurnal index (DI), which was calculated according to the formula:

DI = 100 % x (BPd – BPn) / ATd,

where ATd is the average BP awake; BPn – the average BP asleep.

Four groups of patients were distinguished according to the value of DI:

– dipper (DI – 10 – 20 %) – optimal nocturnal BP reduction;

– non-dipper (DI – 0 – 10 %) – insufficient night BP decrease;

– night-picker (DI < 0) – persistent increase of night BP;

– over-dipper (DI > 20) – excessive nocturnal BP decrease.

Indices of central aortic pressure and arterial stiffness were studied by the method of applanation tonometry with the device SphygmoCor-PVx, AtCor Medical Pty Ltd, Australia) according to the standard methods recommended by the experts in the assessment of arterial stiffness (Laurent S., 2006). The program automatically calculated the levels of SBP, DBP and PP in the aorta and main characteristics of the central pulse wave (augmentation pressure (AG) in the aorta, amplitudes of systolic peaks P1, P2, augmentation index (AIx = TP/PT P2/P1), including a normalized one for HR of 75 bpm (AIx @HR 75). Pulse wave velocity in the aorta (PWV) was measured using the same device by the method of sequential recording of the pulse wave on the carotid and femoral arteries simultaneously with the recording of the ECG signal in three chest leads. To calibrate the waveforms of the carotid arteries, the indices of average and diastolic BP in the aorta, obtained during measurement on the radial artery, were input into the system. The value of PWV was calculated according to the formula:

$PWV = D/\Delta t$,

where D is the distance between the jugular notch and the level of the navel (m);

Δt – the difference between the time from the Q wave to the beginning of the signal in the ascending and abdominal aorta (s).

BMD was investigated in two areas: the lumbar vertebrae and the proximal part of the thigh – using dual-energy X-ray absorptiometry on the "Discovery W QDR Series X-Ray Bone Densitometer" (HOLOGIC Inc., USA) according to the standard methods. The analysis of BMD data, assessed by the T-criterion in the femoral neck and lumbar region, made it possible to determine regular intergroup differences (all $p<0.01$). Patients with a normal BMD have a lower risk of major fractures and femoral neck fractures compared to patients with OP.

After registration of baseline data AH therapy with a combination of lisinopril 10–20 mg (Lisinopril Teva, Merkle GmbH for Teva Ukraine, LLC, Germany/Ukraine) and indapamide 2.5 mg per day (Indapen, Polpharma, Poland) was prescribed to 30 patients (group 1) and lisinopril 10–20 mg (Lisinopril Teva, Merkle GmbH for Teva Ukraine, LLC, Germany/Ukraine) plus hydrochlorothiazide (HCTZ) 12.5 mg per day (Hydrochlorothiazide, JSC NVC Borshchagiv Chemical and Pharmaceutical Plant, Kyiv, Ukraine) were administered to 30 patients (group 2). Patients in both groups also received statins and antiplatelet therapy. The mentioned groups of patients were comparable in age. A follow-up examination, in addition to dual-energy X-ray absorptiometry, was made after 12 weeks of treatment. Side effects and undesirable events were not registered during this period.

Mathematical computer processing of the research results was performed using the software package Statistica 9.0 (Statsoft Inc, USA) with standard algorithms of variational statistics.

Results of the study and their discussion. The clinical characteristics of the patients allowed to establish of the absence of statistical differences between the groups according to the baseline clinical and demographic characteristics. No significant differences were found between the groups of patients according to AH duration and lipid metabolism disturbances.

The effect of drug therapy on the indicators of office BP and DMBP is presented in Table 1.

Table 1

Dynamics of BP indices according to the data of office BP and DMBP measurements in female patients with AH and OP in the therapy time profile (M±m)

Indices	Group 1 (n=30)		Group 2 (n=30)	
	Before treatment	After treatment	Before treatment	After treatment
Sphygmomanometry:				
SBP, mm Hg	163.5±2.5	136.8±2.6*	162.8±2.8	138.8±2.9*
DBP, mm Hg	100.3± 2.7	87.5±2.6*	100.7± 2.8	88.6±2.7*
DMBP				
SBP24, mm Hg	152.1± 2.5	120.8±2.5*	152.9±2.6	122.5±2.8*
DBP24, mm Hg	91.5±2.6	74.3±2.5*	91.7±2.7	77.1±2.8*
TI SBP day, %	61.7±3.5	35.2±3.2*	62.3±3.7	35.1±3.2*
TI DBP day, %	50.5±3.2	15.9±3.5*	51.3±3.3	15.7±3.5*
TI SBP night, %	65.8±3.5	48.2±3.2*	65.9±3.6	48.5±3.3*
TI DBP night, %	43.5±3.5	20.8±3.3*	43.3±3.7	20.6±3.5*

Notes: 1. * – reliability of differences in comparison to the original data; 2. * – $p<0.001$.

During the office BP measurement after the course of treatment, no significant differences in the reduction of office blood pressure were not found between the therapy groups of patients. SBP index decreased by 16.3 % ($p<0.001$) in the group receiving the combination of lisinopril and indapamide, and by 14.7 % ($p<0.001$) in the group receiving the combination of lisinopril and hydrochlorothiazide. The level of DBP decreased by 12.8 % in the group receiving the combination of lisinopril and indapamide, and by 12.0 % in the group of patients receiving the combination of lisinopril and hydrochlorothiazide (all $p<0.0001$). The average HR decreased by 7.7 % over 12 weeks in group 1, and by 5.1 % in group 2, but the change of this parameter did not reach statistical significance in any group.

Analysis of DMBP indices after 12 weeks revealed high antihypertensive efficiency of both treatment regimens, but no significant difference between the treatment groups was found. Thus, average daily SBP and DBP were reduced by 20.6 % and 18.8 % in patients receiving the combination of lisinopril and indapamide and by 19.8 % and 15.9 %, respectively, in the group receiving lisinopril and hydrochlorothiazide (all $p<0.001$).

Indices of pressure load in all patients of both treatment groups after therapy of hypertension TI according to SBP and DBP significantly decreased in all time intervals but did not exceed the norm, which proves a stable 24-hour antihypertensive effect.

Analysis of the daily BP profile showed that in the group receiving the combination of lisinopril and indapamide, the number of dippers significantly increased from 5 (16.7 %) to 25 (83.3 %) ($p<0.05$), the number of non-dippers decreased from 20 (66.6 %) to 5 (16.7 %) ($p<0.05$). 5-night picker patients were

transferred to the group of dippers. Similar changes were observed in the group receiving the combination of lisinopril and hydrochlorothiazide: the number of dippers increased from 4 (13.3 %) to 26 (86.7 %) ($p<0.05$), the number of non-dippers decreased from 22 (73.4 %) to 4 (13.3 %) ($p<0.05$). All 4-night picker patients were moved to the group of dippers. The time frame of the characteristics of the central pulse wave in the examined patients under the influence of antihypertensive therapy is presented in Table 2.

Table 2

Changes in the parameters of the central pulse wave in the examined persons

Indices	Group 1 (n=30)		Group 2 (n=30)	
	Before treatment	After treatment	Before treatment	After treatment
cSBP, mm Hg	161.4±2.9	130.3±2.6*	160.9±2.9	138.1±2.5*
cPP, mm Hg	56.5±2.9	40.3±2.5**	55.9±2.6	47.1±2.2*
AIx, %	27.8±1.3	24.1±1.2*	26.0±1.2	27.3±1.1
AIx @HR 75, %	25.6±1.3	22.0±1.2*	24.1±1.3	25.5±1.2
PWV, m/s	12.6±0.9	8.9±0.8**	12.7±0.8	10.8±0.5*

Notes: 1. * – reliability of the differences compared to the baseline data; 2. * – $p < 0.05$; 3. ** – $p<0.001$

During the analysis of the parameters of the central pressure in the aorta, the initial intergroup indicators of the patients were comparable. After treatment, in both treatment groups a significant reduction in central SBP (cSBP) was observed – by 19.3 % in the group receiving the combination of lisinopril and indapamide and by 14.2 % in the group receiving lisinopril plus hydrochlorothiazide. At the same time, in the group receiving the combination of lisinopril and indapamide, a greater reduction was observed (cSBP by 5.9 % ($p<0.05$) compared to the group receiving lisinopril plus hydrochlorothiazide (Table 2). In both treatment groups, a decrease of cPP was observed, however, the reduction in the group of lisinopril with indapamide exceeded that in the group of lisinopril in combination with hydrochlorothiazide, and made up to 28.7 % vs 15.7 %, respectively ($p<0.05$ for comparison with baseline data and intergroup comparison).

Speaking about the dynamics of such an index of vascular stiffness as the augmentation index (AIx), it is worth noting that in the group of lisinopril with indapamide it significantly decreased by 13.3 % ($p<0.05$ compared to the baseline data and intergroup comparison), while in the group of lisinopril and hydrochlorothiazide, the level of this parameter, on the contrary, unreliably increased by 5.0 %. Nevertheless, the difference between the groups according to this indicator was statistically significant. A similar time profile was observed for the reflected wave augmentation index adjusted to the heart rate (AIx @ HR 75): in the group receiving the combination of lisinopril and indapamide, a decrease of 14.1 % was established ($p<0.05$ compared to the initial data and intergroup comparison), while in the group of lisinopril with hydrochlorothiazide, an unreliable increase of this indicator by 5.8 % was noted, which was 13.7 % significantly higher than in the patients of group 1.

An improvement in the visco-elastic properties of arteries was also revealed due to a statistically significant decrease in PWV compared to the baseline level in both treatment groups. At the same time, on the background of the therapy with a combination of lisinopril and indapamide, a more pronounced decrease of this indicator was observed – by 29.4 % compared to the therapy with lisinopril and hydrochlorothiazide, on the background of which the PWV decreased by 14.9 % ($p<0.05$ compared to the baseline data and between-groups comparison).

In several studies [8] the data confirming a relationship between the processes of bone remodeling and cardiovascular pathology were obtained. Common pathogenetic mechanisms unite them: calcium deficiency, oxidative stress, which triggers osteoclastogenesis and mineralization in the vascular wall and bone tissue mediated by oxidized lipoproteins. OP and AH have common risk factors. There is an evidence that timely and systematic treatment of AH prevents loss of bone mineral density in women in the postmenopausal period [15].

The value of thiazide diuretics has been proven in many controlled clinical trials in the field of AH, in which they were used as first-line medication or as a necessary component to achieve the target BP [1]. An additional administration of thiazide diuretic significantly improves BP control regardless of the class of antihypertensive drugs with which the treatment started [4].

Under the action of thiazide diuretics, reabsorption is inhibited in proximal tubules and NaCl transport is blocked in distal tubules [9]. The thiazide-like drug indapamide has a natriuretic effect, characteristic for all thiazide diuretics, and additional vasodilating properties. The antihypertensive effect of indapamide is provided, on the one hand, by the natriuretic effect, which eliminates the sodium overload of the vascular wall and reduces its hyperreactivity to various vasopressor agents (catecholamines, angiotensin II, etc.), on the other hand, by a direct vasodilating effect due to the blockage of slow calcium channels in smooth muscle cells of the vascular wall, increase of the synthesis of prostacyclin in the vascular wall and prostaglandin E2 (PGE2) in the kidneys and inhibition of the synthesis of endothelium-dependent vasoconstrictor factor [10]. So, indapamide, in addition to the properties of a classic thiazide

diuretic, has the properties of a calcium antagonist, which determines its higher efficiency and organ protection in AH due to the double mechanism of implementation of antihypertensive effect.

In addition to the reduction of blood pressure thiazides control calcium homeostasis and increase mineral density of the bone tissue. Thiazides reduce urine calcium excretion and stimulate the differentiation of osteoblasts and formation of minerals in bones [11]. The mechanism by which thiazides reduce calcium excretion is not fully studied. Reduction of calcium loss helps to increase bone calcium content and bone density. It has been established that thiazides can reduce the frequency of hip fractures [5]. But other studies have not confirmed these data.

Meta-analysis data showed that AH has been associated with bone mass loss and increased risk of fractures [13]. AH is associated with severe loss of bone minerals, including calcium, and its metabolism, what leads to accelerated bone resorption [3]. Antihypertensive drugs such as thiazides have now been found to reduce the risk of fractures by replenishing bones with minerals. In addition, activated osteoclasts through angiotensin II induced receptor NF-kB (RANKL) can be inhibited by angiotensin II inhibitors, which significantly reduce the risk of osteoporotic fractures [13]. In this regard, the adverse effect of AH on bones can be controlled with the help of antihypertensive drug schedules [12].

Studies have shown that thiazide diuretics are effective in AH with OP [6]. The effect of thiazide and thiazide-like diuretics on the condition of the arterial wall seems interesting. In our study high antihypertensive efficiency of combined therapy, which included the ACE inhibitor lisinopril and indapamide or hydrochlorothiazide, was observed. Moreover, antihypertensive effectiveness according to the data of office measurement and DMAT indicators did not reliably differ between the treatment groups. But the data analysis of applanation tonometry revealed more pronounced ($p<0.05$) changes in central aortic pressure indicators: central SBP and cPP on the background of lisinopril therapy in combination with indapamide. It was established that the augmentation index (Aix), the reflected wave augmentation index, adjusted for the heart rate (AIx @ HR 75), significantly decreased during intake of lisinopril in combination with indapamide and increased in patients of the group receiving lisinopril plus hydrochlorothiazide. A significant decrease in PWV was observed in patients of both treatment groups, significantly more pronounced on the background of therapy with lisinopril in combination with indapamide. Side and adverse effects were not registered during this period.

Conclusions

1. In patients with arterial hypertension and postmenopausal OP, according to the data of office measurement of BP and DMAT, 12-week therapy with a combination of lisinopril plus indapamide in terms of the severity of antihypertensive effect, an ability to normalize the daily profile of BP and reduce pressure load indicators did not reliably differ from the therapy with lisinopril in combination with hydrochlorothiazide

2. Pulse wave propagation speed and central aortic pressure levels (cSBP and cPP) according to applanation tonometry data decreased more significantly on the background of 12-week therapy with lisinopril in combination with indapamide compared to the combination of lisinopril with hydrochlorothiazide along with good tolerability in both treatment groups.

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THE INFLUENCE OF ANXIETY LEVEL AND PAST COVID-19 ON SLEEP QUALITY AND INSOMNIA SEVERITY

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Based on recent studies, we put forward a hypothesis about the synergistic effect of anxiety disorders and previous COVID-19 on the deterioration of the quality of sleep and occurring of insomnia. The purpose of the study was to investigate the impacts of anxiety disorders, and COVID-19 on anamnesis and its combined effect on sleep disturbances. We conducted a case-control study, which included 60 patients, who were divided into 3 groups depending on the occurrence of anxiety disorders and COVID-19 in their medical history during the last 6 months. Patients were assessed by the Beck anxiety inventory, Pittsburgh Sleep Quality Index, and the Insomnia Severity Index. We found a worsening sleep quality and a higher frequency of insomnia in patients with COVID-19. Along with this, concomitant anxiety disorders worsened both the quality of sleep and the level of insomnia in these respondents. It was determined that patients with an anxiety disorder with a history had a lower subjective assessment of sleep quality, higher sleep latency, and more pronounced diurnal dysfunction, while patients without a history had better sleep efficiency and a lower frequency of sleeping pills. Anxiety disorders and having experienced COVID-19 are associated with poorer sleep quality and more severe insomnia. Their combination significantly reduces the quality of sleep and increases the degree of insomnia. These findings suggest a potential role for COVID-19 in exacerbating the association between anxiety and sleep disorders.

Key words: anxiety, mood disorders, sleep disorders, insomnia, sleep quality, COVID-19.

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ВПЛИВ РІВНЯ ТРИВОГИ ТА ПЕРЕНЕСЕНОГО COVID-19 НА ЯКІСТЬ СНУ ТА ТЯЖКІСТЬ ІНСОМНІЇ

На підставі останніх досліджень, нами було висунуто гіпотезу про синергічний вплив тривожних розладів та перенесеного COVID-19 на погіршення якості сну та виникнення безсоння. Метою дослідження було вивчення впливу тривожних розладів, COVID-19 в анамнезі та їх комбінованого впливу на порушення сну. Ми провели дослідження «випадок-контроль», яке охопило 60 осіб, що були розділені на 3 групи залежно від наявності тривожних розладів та COVID-19 в анамнезі протягом останніх 6 місяців. Пацієнти були оцінені за допомогою опитувальника тривожності Бека, Пітсбургського індексу якості сну та Індексу тяжкості безсоння. Нами було виявлено погіршення якості сну та вищу частоту безсоння у пацієнтів, що перехворіли на COVID-19. Поряд з цим супутні тривожні розлади погіршували як якість сну, так і рівень безсоння у цих респондентів. Було визначено, що у пацієнтів з тривожним розладом та перенесеним в анамнезі нижча суб'єктивна оцінка якості сну, вища його латентність та більш виражена добова дисфункція, в той час як пацієнти без в анамнезі мали кращу ефективність сну та нижчу частоту використання снодійних. Виявлено, що тривожні розлади та перенесений COVID-19 мають зв'язок із погіршенням якості сну та більш важким безсонням. Їх поєднання суттєво знижує якість сну та підвищує ступінь безсоння. Ці результати вказують на потенційну роль COVID-19 у посиленні зв'язку між тривогою та розладами сну.

Ключові слова: тривога, розлади настрою, розлади сну, інсомнія, якість сну, COVID-19.

The study is a fragment of the research projects: "The study of the pathogenetic role of the circadian molecular clock in the development of metabolic diseases and systemic inflammation and the development of treatment methods aimed at these processes", state registration No. 0120U101166 and "Clinical-psychopathological and paraclinical examinations and optimization of medical and rehabilitation measures at the common forms of mental and comorbid disorders", state registration No. 0121U108235.

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) causes a coronavirus respiratory disease (COVID-19) with a variety of clinical syndromes and severity that has affected health systems worldwide [6].

In the early stages of studying treatments for COVID-19, many researchers explored the possibility of non-pharmaceutical interventions to limit the spread of SARS-CoV-2, for example, attempts were made to study the effect of heliometeorological factors, such as sunlight and temperature, on virus strains [5].