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Treatment of sleep disorders in patients with hypertension and obesity

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The aim of the study is to improve the efficacy of the treatment of sleep disorders in patients with arterial hypertension (AH) and obesity.

Materials and methods. In total, 62 patients were examined (mean age 58.3 ± 2.3 years) with AH and obesity. All of the surveyed persons underwent general clinical examination, daily BP monitoring, life quality assessment (General Well-Being Questionnaire). The ICSD-2 (2005) criteria were used to identify sleep disorders (dyssomnia) and subjective sleep characteristics questionnaires – for circadian "sleep –wake" rhythm disturbances assessment. Sleep disorders were found in all the examined patients at baseline. After the baseline data registration, the patients were prescribed basic therapy, 32 (group 1) of whom additionally received melatonin at a dose of 3 mg for 4 weeks; 30 patients were included in group 2.

Results. After treatment, in group 1, the levels of office SBP and DBP were 6.9 % and 6.7 % ($P < 0.05$), and the average daily SBP and DBP (according to DMBP data) were 7.9 % and 6.7 % ($P < 0.05$) lower, respectively, than in group 2. In patients of group 1, positive changes in lipid and carbohydrate metabolism, a significant improvement in subjective sleep characteristics and circadian "sleep – wake" rhythm were registered along with an improvement in the quality of life.

Conclusions. Thus, melatonin add-on treatment in patients with AH and obesity with sleep disorders increases the efficacy of antihypertensive therapy, has a beneficial effect on glucometabolic parameters, subjective assessment of sleep quality and the quality of life.

Key words: sleep disorders, hypertension, obesity, daily monitoring of blood pressure, therapy.

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Лікування порушень сну в пацієнтів з артеріальною гіпертензією та ожирінням

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Мета роботи – підвищення ефективності лікування порушень сну в пацієнтів з артеріальною гіпертензією (АГ) та ожирінням.

Матеріали та методи. Обстежили 62 особи (середній вік – 58,3 ± 2,3 року) з АГ та ожирінням. Усім провели загальноклінічне обстеження, добовий моніторинг АТ, оцінювання якості життя (опитувальник «General Well – Being Questionnaire»). Для виявлення порушень сну (дисомнія) використовували критерії МКРС-2 (2005), а оцінювання порушень циркадного ритму «сон – неспання» – анкети бального оцінювання суб'єктивних характеристик сну. В пацієнтів обох груп у вихідних умовах відзначені порушення сну. Після реєстрації вихідних даних пацієнтам призначали базисну терапію, з них 32 (1 група) отримували додатково препарат мелатонін у дозі по 3 мг протягом 4 тижнів; 2 групу становили 30 пацієнтів.

Результати. Після лікування в 1 групі рівні офісного САТ і ДАТ були на 6,9 % і на 6,7 % ($p < 0,05$), а середньодобові САТ і ДАТ (за даними ДМАТ) – на 7,9 % і 6,7 % ($p < 0,05$) нижчі, ніж у 2 групі. У пацієнтів 1 групи відзначили позитивні зміни показників ліпідного та вуглеводного обміну, вірогідне покращення суб'єктивних характеристик сну та циркадного ритму «сон – неспання» поряд з поліпшенням показників якості життя.

Висновок. Додавання мелатоніну пацієнтам з АГ та ожирінням із порушеннями сну підвищує ефективність гіпотензивної терапії, позитивно впливає на глюкометаболічні параметри, суб'єктивне оцінювання якості сну та якість життя.

Ключові слова: порушення сну, артеріальна гіпертензія, ожиріння, добовий моніторинг артеріального тиску, лікування.

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Лечение нарушений сна у пациентов с артериальной гипертензией и ожирением

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Цель работы – повышение эффективности лечения нарушений сна у пациентов с артериальной гипертензией (АГ) и ожирением.

Материалы и методы. Обследовано 62 больных (средний возраст – 58,3 ± 2,3 лет) с АГ и ожирением. Всем обследованным лицам проведено общеклиническое обследование, суточный мониторинг АД, оценка качества жизни (опросник «General Well – Being Questionnaire»). Для выявления нарушений сна (диссомния) использовали критерии МКРС-2 (2005), а оценки нарушений циркадного ритма «сон – бодрствование» – анкеты балльной оценки субъективных характеристик сна. У пациентов обеих групп в исходных условиях отмечены нарушения сна. После регистрации исходных данных пациентам назначали базисную терапию, из них 32 (1 группа) дополнительно получала препарат мелатонин в дозе 3 мг в течение 4 недель; 30 пациентов составили 2 группу.

Результаты. После лечения в 1 группе уровни офисного САД и ДАД были на 6,9 % и на 6,7 % ($p < 0,05$), а среднесуточные САД и ДАД (по данным СМАД) – на 7,9 % и 6,7 % ($p < 0,05$) ниже, чем во 2 группе. У пациентов 1 группы отмечены позитивные изменения показателей липидного, углеводного обмена и достоверное улучшение субъективных характеристик сна и циркадного ритма «сон – бодрствование» наряду с улучшением показателей качества жизни.

Ключевые слова: нарушение сна, артериальная гипертензия, ожирение, суточный мониторинг артериального давления, лечение.

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Вывод. Таким образом, назначение мелатонина пациентам с АГ и ожирением с нарушениями сна повышает эффективность гипотензивной терапии, положительно влияет на глюкометаболические параметры, субъективную оценку качества сна и качество жизни.

It has been found that arterial hypertension (AH) and metabolic disorders are associated with high cardiovascular morbidity and mortality [1]. On the other hand, an extremely pressing issue today is an increase in prevalence of obesity and associated metabolic disorders, that is the basis for the development of many chronic non-communicable diseases [2]. The association between AH and obesity significantly increases the risk of cardiovascular complications development. Thus, weight gain of 1 kg increases the risk of developing cardiovascular complications by 3.1 % and diabetes by 4.5–9.0 % [3].

Many studies have demonstrated the relationship between sleep disorders, sleep duration and obesity [4]. Thus, the results of meta-analysis [5] confirmed that in individuals with short sleep duration, the risk of obesity development was 1.55 times increased. The influence of sleep duration, insomnia and obstructive sleep apnea syndrome on the increased risk of metabolic syndrome, cardiovascular morbidity and mortality, determining the clinical and social significance of sleep disorders, has been established [6].

Disturbances in the system of circadian biorhythms associated with sleep disorders, in particular, changes in the melatonin secretion – a hormonal mediator between the suprachiasmatic nucleus of the hypothalamus and peripheral tissues, contribute to the development of a number of diseases, including obesity, hypertension, type 2 diabetes [7]. However, an important and protective role of melatonin in case of obesity are regulation of body mass due to the stimulation of lipolysis and thermogenesis, normalization of lipid and carbohydrate metabolism, slowing the development of atherosclerotic processes [8]. Changes in melatonin secretion, circadian disorders, desynchronosis can play a significant role in the pathogenesis and progression of metabolic syndrome in patients with sleep disorders, so their detection and evaluation from the diagnostic standpoint, as well as the correction of melatonin deficiency is important in optimizing therapy for this pathological condition. In that regard, the aim of our study was to improve the treatment efficacy of sleep disorders in patients with AH and obesity.

Materials and methods

In total, 62 patients (12 females and 40 males, mean age 58.3 ± 2.3 years) with stage 2 AH and obesity were examined. Based on body mass index (BMI), 46 and 16 patients were diagnosed with obesity class I and II, respectively. AH was diagnosed in accordance with the recommendations of the European Society of Hypertension and the European Society of Cardiology (ESH/ESC, 2013) as well as the Ukrainian Association of Cardiology for the Prevention and Treatment of AH (2013).

Sleep disorders were diagnosed in accordance with the International Classification of Sleep Disorders ICSD-2 criteria [9], which were manifested by difficulties with falling asleep or staying asleep, daytime functioning associated with poor sleep quality, or the above listed complaints in any combination.

All patients underwent general clinical and physical examination, office blood pressure (BP) and heart rate (HR) were measured, clinical blood test, urinalysis, biochemical blood test to determine fasting serum glucose (FSG), levels of glycosylated hemoglobin (HbA1c) in whole blood, insulin, fasting blood levels of lipids (total cholesterol – TC, low density lipoprotein cholesterol – LDL-C, high density lipoprotein cholesterol – HDL-C, triglycerides – TGs) were performed; insulin resistance was assessed by HOMA-IR index.

BMI was calculated according to the formula:

BMI = body weight (kg)/height (m^2).

According to the 1997 WHO classification [10], the following was considered: normal body weight if BMI – 18–24.9; overweight if BMI – 25–29.9 and obesity class I, II if BMI – 30–34.9 and 35–39.9 kg/m^2, respectively. According to the same guideline, abdominal obesity was defined as waist circumference (WC) of 102 cm or more for men and 88 cm or more for women.

Daily blood pressure monitoring (DBPM) was performed using an "ABPM-02" equipment (Meditech, Hungary). The following parameters were assessed: average values of SBP, DBP, pulse pressure (PP), $BP_{aver.}$ per day (24 hours), day and night, BP rate variability during day and night, time index (TI) of hypertension – percentage of daytime SBP ≥140 and DBP ≥90 mm Hg and nighttime ≥120 and ≥70 mm Hg, respectively [11]. We evaluated the severity of BP two-phase pattern by daily index (DI) – day – night difference in BP defined as a percentage decline using the formula:

DI = 100 % x (BPd – BPn)/BPd,

where BPd – mean BP during daytime; BPn – mean BP during nighttime.

The patients were divided into four groups by the value of DI:

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

– "non-dipper" (DI – 0–10 %) – insufficient nocturnal BP drop;

– "night-peaker" (DI <0) – nocturnal increase in BP;

– "over-dipper" (DI >20) – extreme nocturnal BP drop.

The ICSD-2 (2005) criteria were used to identify sleep disorders (dyssomnia):

1) complaints of sleep disorders ≥3 nights per week;

2) sleep disorders despite the presence / availability of adequate opportunity and circumstances for sleep;

3) symptoms associated with daytime impairment are due to the sleep difficulty.

In addition, at the screening stage, the patients completed the Berlin questionnaire and the Epworth Sleepiness Scale and were excluded from the study in case of obstructive sleep apnea syndrome signs presence.

In order to assess circadian "sleep – wake" rhythm in addition to anamnesis data, point assessment questionnaires were used to evaluate subjective characteristics of sleep [12]. Patients were asked to complete the questionnaires and to evaluate the following sleep parameters on a five-point scale: time of sleep onset and sleep duration, number of night awakenings and dreams, quality of sleep and morning awakening. The interpretation of the test results was performed according to the total number of points:

22 and above – sleep was rated as normal, 18 points and less – disturbed sleep, 19–21 points – boundary values. The study included the patients who scored 19 points or less according to the results of the questionnaire.

To assess the patients' life of quality, the "General Well – Being Questionnaire" of Marburg University (GWBQ, J. Siegrist et al., 1989) was used. The questionnaire includes 7 clinical scales: patients' assessment of their physical well-being (I), ability to work (II), positive (III) or negative (IV) psychological health, psychological abilities (V), interpersonal relationships (VI) and social abilities (VII). During assessment the dynamics of the GWBQ questionnaire scales, it was considered that a decrease in scales I and IV and an increase in other scales indicated an improvement in the quality of life.

After registration of baseline data, basic therapy for AH was administered to 32 patients of the main group (group 1) (Lisinopril, Amlodipine) and melatonin medication ("Vita-Melatonin", Kyiv Vitamin Plant, Ukraine) at a dose of 3 mg, 30 minutes before bedtime for 4 weeks. Group 2 included 30 patients who received basic therapy for AH. Patients in both groups also received Metformin, statins, antiplatelet therapy. These patient groups were age- and gender-matched. The control group consisted of 20 healthy individuals (4 females and 16 males, mean age 58.1 ± 2.9 years).

All patients successfully completed the study according to the protocol. The second examination (assessment) was performed after 4 weeks of treatment. There were no side and adverse effects reported in that period.

The computer processing of the study results was carried out using the software package Statistica 8.0 (StatSoft Inc., USA).

A Lilliefors-corrected Kolmogorov-Smirnov test was used to determine the distribution normality. Differences between groups were tested for statistical significance using Student's t test for unpaired data when the data passed the normality test and a Mann–Whitney U test when it did not. Continuous quantitative variables were expressed as M ± SD, where M was the arithmetic mean and SD was the standard deviation. Dichotomous and ordinal qualitative data were expressed as frequencies (n) – the number of objects with the same attribute value and fraction (%). To determine the differences in qualitative variables, contingency tables were analyzed using the exact Fisher criterion. The differences were considered statistically significant at $P < 0.05$.

Results

In our study, after the treatment course in patients with AH and obesity, a significant decrease in BP was observed according to the office BP measurement and DMBP (*Table 1*).

It was found that after the course conducted in the group of patients who received melatonin as add-on to basic therapy, the levels of office SBP and DBP were 6.9 % and 6.7 % ($P < 0.05$) lower, respectively, than in group 2.

Analysis of DMBP after 4 weeks revealed high antihypertensive efficacy of both treatment regimens (*Table 2*), but more pronounced in case of melatonin add-on therapy. Thus, average daily SBP and DBP were 7.9 % and 6.7 % ($P < 0.05$) lower, respectively, in patients of group 1 in comparison to group 2.

Indicators of pressure load, SBP and DBP TI of hypertension, were significantly decreased in all the patients on the combined treatment with melatonin add-on at all time intervals and did not exceed the norm, indicating a stable 24-hour antihypertensive effect.

Analysis of the BP daily profile showed that in group 1, there was a significant increase in the number of "dippers" from 5 (15.6 %) to 22 (68,8 %) ($P < 0.05$), and the number of "non-dippers" decreased from 19 (59.3 %) to 10 (31.2 %) ($P < 0.05$). 8 patients "night-peakers" moved to the "dipper" group. Less pronounced changes were found in group 2: the number of "dippers" increased from 4 (13.3 %) to 15 (50 %) 1($P < 0.05$), the number of "non-dippers" decreased from 20 (66.6 %) to 12 (40 %) ($P < 0.05$). 3 patients moved to the "dippers" group from 6 "night-peakers" patients.

After the treatment, an improvement of metabolic profile indicators (*Table 2*) was found.

After treatment, it was found that there were positive changes in the lipid metabolism indicators in both groups of patients with AH and obesity, but more pronounced decrease in TC, triglycerides and LDL cholesterol levels along with a statistically significant increase in HDL cholesterol ($P < 0.05$) level demonstrated the group received melatonin add-on to basic therapy (*Table 2*).

Changes in the carbohydrate profile after the treatment confirmed a significant decrease in FBS levels in patients received melatonin add-on to basic therapy (*Table 2*). The levels of HbA1c, insulin and HOMA-IR were decreased in group 1 patients, indicating that fasting serum glucose was under control and manifestations of insulin resistance were reduced. No significant changes in carbohydrate metabolism were observed in group 2.

Table 1. Indicators of blood pressure according to the office measurement and DMBP in patients with AH and obesity before and after treatment (M ± m)

Indicators, units	Group 1 (n = 32)		Group 2 (n = 30)	
	before treatment	after treatment	before treatment	after treatment
Sphygmomanometry:				
SBP, mm Hg	164.3 ± 2.3	130.5 ± 1.8***	165.1 ± 2.4	139.5 ± 1.8***
DBP, mm Hg	93.8 ± 2.5	80.3 ± 1.8***	94.1 ± 2.6	85.7 ± 1.8**
DMBP				
SBP24, mm Hg	151.6 ± 2.6	120.3 ± 1.6***	151.9 ± 2.5	129.8 ± 1.8***
DBP24, mm Hg	91.7 ± 2.2	75.1 ± 1.7***	91.6 ± 2.3	80.1 ± 1.8***
TI SBP day, %	61.5 ± 2.3	35.1 ± 1.1***	62.1 ± 2.4	36.3 ± 1.1***
TI DBP day, %	50.3 ± 2.1	15.9 ± 1.4***	51.1 ± 2.3	26.7 ± 1.3***
TI SBP night, %	65.5 ± 2.3	48.1 ± 2.1*	65.3 ± 2.1	49.5 ± 2.3*
TI DBP night, %	43.3 ± 2.3	20.9 ± 2.1***	43.2 ± 2.4	21.9 ± 2.3***

Significance of differences compared to the baseline data; *: $P < 0.05$; **: $P < 0.01$; ***: $P < 0.001$.

Table 2. Dynamics of glucose metabolism parameters in patients with arterial hypertension and obesity before and after treatment (M ± m)

Indicators, units	Group 1 (n = 32)		Group 2 (n = 30)	
	before treatment	after treatment	before treatment	after treatment
TC, mmol/l	5.4 ± 0.11	5.0 ± 0.08*	5.5 ± 0.11	5.2 ± 0.05*
LDL-C, mmol/l	3.4 ± 0.12	2.5 ± 0.10**	3.5 ± 0.13	2.8 ± 0.10**
HDL-C, mmol/l	0.98 ± 0.06	1.23 ± 0.02**	0.95 ± 0.05	1.05 ± 0.03*
TGs, mmol/l	2.28 ± 0.07	1.79 ± 0.06**	2.35 ± 0.07	1.98 ± 0.05**
FSG, mmol/l	5.6 ± 0.15	5.2 ± 0.10*	5.5 ± 0,16	5.4 ± 0.11
HbA1c, %	5.5 ± 0.12	5.1 ± 0.10*	5.4 ± 0.14	5.4 ± 0.11
Insulin, mcU/ml	19.1 ± 0.49	15.3 ± 0.45**	18.2 ± 0.49	18.1 ± 0.47
HOMA-IR, mcU/ml	4.9 ± 0.46	3.4 ± 0.42*	3.9 ± 0.459	3.5 ± 0.47

Significance of differences compared to the baseline data: *: P < 0.05; **: P < 0.01; ***: P < 0.001.

Table 3. Subjective sleep characteristics in the control group and in patients with AH and obesity before and after treatment

Indicators	Period of study	Group 1 (n = 32)	Group 2 (n = 30)	Control (n = 20)
Time of falling asleep	Before treatment	2.8 ± 0.3	2.7 ± 0.4	4.0 ± 0.2
	After treatment	3.8 ± 0.2**	2.7 ± 0.2	
Duration of sleep	Before treatment	2.4 ± 0.5	2.5 ± 0.5	4.3 ± 0.3
	After treatment	3.7 ± 0.2*	2.6 ± 0.3	
Number of nighttime awakenings	Before treatment	2.25 ± 0.3	2.25 ± 0.3	3.8 ± 0.2
	After treatment	3.2 ± 0.2**	2.25 ± 0.1	
Number of dreams	Before treatment	2.4 ± 0.5	2.5 ± 0.3	4.0 ± 0.2
	After treatment	3.8 ± 0.4*	2.5 ± 0.2	
Sleep quality	Before treatment	2.6 ± 0.3	2.7 ± 0.4	4.5 ± 0.4
	After treatment	3.7 ± 0.4*	2.8 ± 0.3	
Quality of morning awakening	Before treatment	2.8 ± 0.3	2.9 ± 0.4	4.3 ± 0.3
	After treatment	3.8 ± 0.2**	2.9 ± 0.3	

Significance of differences compared to the baseline data; *: P < 0.05; **: P < 0.01.

Table 4. Changes in the quality of life indicators (M ± m, in points) in the dynamics of treatment in patients with AH and obesity

GWBQ scales	Period of study	Group 1 (n = 32)	Group 2 (n = 30)
I	Before treatment	7.61 ± 0.43	7.63 ± 0.43
	After treatment	6.05 ± 0.41*	6.07 ± 0.41*
II	Before treatment	13.51 ± 0.41	13.52 ± 0.40
	After treatment	15.09 ± 0.36**	14.73 ± 0.33**
III	Before treatment	8.26 ± 0.41	8.29 ± 0.40
	After treatment	8.87 ± 0.36	8.86 ± 0.37
IV	Before treatment	11.08 ± 0.39	11.0 ± 0.37
	After treatment	8.50 ± 0.34**	9.83 ± 0.35*
V	Before treatment	14.43 ± 0.35	14.40 ± 0.35
	After treatment	16.48 ± 0.30**	15.37 ± 0.32*
VI	Before treatment	7.53 ± 0.45	7.52 ± 0.43
	After treatment	7.39 ± 0.41	7.40 ± 0.41
VII	Before treatment	12.72 ± 0.55	12.70 ± 0.54
	After treatment	13.98 ± 0.43*	13.35 ± 0.45*
C	Before treatment	3.76 ± 0.11	3.78 ± 0.12
	After treatment	3.99 ± 0.16	3.95 ± 0.15
H	Before treatment	4.17 ± 0.18	4.15 ± 0.21
	After treatment	4.43 ± 0.19	4.40 ± 0.23

C: general condition a week before the survey; **H:** mood the week before the survey.
Significance of differences compared to the baseline data; *: P < 0.05; **: P < 0.001.

Patients of both groups reported sleep disorders at baseline, according to the anamnesis data and the results of subjective sleep characteristics assessment. The questionnaire survey data of the examined patients and the control group are presented in *Table 3*. It was found that the examined patients had pronounced sleep disorders according to the questionnaire results of subjective sleep characteristics evaluation. Thus, the mean score in patients with AH and obesity was significantly lower compared to healthy persons (15.4 ± 0.4 vs 24.9 ± 0.3; P < 0.001).

After 4 weeks of therapy, group 1 patients showed significantly improved subjective sleep characteristics: decreased duration of falling asleep and number of nighttime awakenings, improved quality of sleep and quality of morning awakening that reasonably resulted in a significant increase in the total point score from 15.25 ± 0.5 up to 22.0 ± 0.6 (P < 0.001) points. Moreover, the total score reached the normal values in 24 patients (75 %) (P < 0.05).

Analysis of the therapeutic effect on the subjective assessment of sleep quality in the patients of group 2 showed no significant changes in any evaluated indicators of the somnological status (the total score was slightly increased from 15.5 ± 0.5 to 15.7 ± 0, 4).

Prescription of combined treatment with melatonin resulted in an improvement of the indicators characterizing the quality of life in patients with AH and obesity (*Table 4*).

Significant improvement in the indicators I, II, IV, V and VII of the questionnaire scales was revealed, covering nearly all components of the quality of life in both groups of patients. However, group 1 demonstrated a more significant (P < 0.05) improvement in the psychological component of the quality of life: psychological abilities (scale V) and degree of negative psychological condition severity in the examined patients (scale IV). The improvement of physical health (scale I) in patients of both groups was estimated (apparently due to BP correction). In addition, the tendency to more positive effect of combined therapy with melatonin add-on on the ability for work (scale II) and ability for social contacts (scale VII) was found in patients with AH and obesity.

Discussion

The theoretical basis of the developed treatment complex is the concept that changes in the production of melatonin, which go beyond physiological fluctuations, lead to a discrepancy of the body's own biological rhythms between themselves (internal desynchronosis) and the rhythms of the organism with the environmental rhythms (external desynchronosis) [13]. Chronobiological disorders have been shown to occur in case of hypertension, diabetes mellitus, and other pathological conditions [14]. It is important to study the chronotropic activity of melatonin, as a potent biochemical marker of circadian rhythm and a regulator of the most important metabolic processes in the body. It has been experimentally established that melatonin exhibits endothelioprotective properties, in particular, increases the bioavailability of nitric oxide, increases activity of antioxidant enzymes and reduces oxidative damage, has a positive effect on carbohydrate and lipid metabolism, as well as the profile of BP, decreases insulin resistance, accelerates weight loss [15]. Melatonin has been shown to be effective in reducing BP in patients with metabolic syndrome and chronic non-communicable inflammation [16], but such studies are insufficient and controversial regarding efficacy and safety of such therapy. In our study, melatonin add-on to the traditional antihypertensive therapy resulted in a significantly greater decrease in the levels of office BP and average daily data, pressure load time and normalization of the daily BP profile.

It is also worth mentioning that antihypertensive therapy choice is difficult in patients with obesity, since drugs for such patients treatment should have a prolonged effect during the day, contribute to the regression of target organs damage, be easy-to-use and provide an opportunity for a rational drug combinations as well as should not have a negative effect on carbohydrate and lipid metabolism. The research based on the systematic approach methodology will allow developing a strategy for treatment optimization taking into account individual characteristics of patients with sleep disorders combined both with AH and obesity, and it seems promising and justified.

We have found a more pronounced significant decrease in the HOMA index and basal insulinemia, FBS and HbA1 levels in subjects taking melatonin appeared to indicate the pathogenetic evidence of such therapy. The data obtained meet the results of the previous studies [17,18]. Possible mechanisms of these effects can be an activation of peripheral receptors to insulin by means of phosphorylation of tyrosine kinase, as well as the normalization of the circadian rhythm of the adipose tissue secretory activity [19]. Combined therapy with melatonin add-on resulted in a slight but significant decrease in the blood levels of TC, LDL and TG and a significant increase in HDL ($P < 0.05$), that was apparently linked the antiatherogenic pleiotropic effect of melatonin. Moreover, melatonin add-on to the basic therapy in AH patients with obesity and insomnia showed an improvement in sleep quality and normalization of the sleep-wake rhythm giving advantages in the treatment for this category of patients. Both groups demonstrated improved physical and mental characteristics of the quality of life at the end of the study.

Conclusions

1. Melatonin add-on to the therapeutic complex in case of sleep disorders in patients with AH and obesity improves subjective assessment of sleep quality and is manifested in the improvement of the circadian rhythm sleep-wake.

2. Melatonin add-on to the treatment regimen for patients with AH, obesity and sleep disorders increases the effectiveness of antihypertensive therapy, improves BP daily profiles, positively influences glucometabolic parameters and the quality of life in this category of patients.

3. Complex therapy with melatonin add-on has a positive impact on the quality of life in AH patients with obesity and sleep disorders. This is evident in improvements in the indicators of scales reflecting physical well-being, performance efficiency, psychological skills, the degree of intensity of psychological well-being and social skills.

Currently, one of the most promising strategies is the influence on chronobiological mechanisms triggering cascade of metabolic disorders with an outcome of insulin resistance. Our research showed that melatonin enhances the hypotensive effect of basic therapy, especially in case of inability to adequately reduce BP at night. It seems to us that melatonin is still underestimated by doctors and should be wider used for the therapy of internal diseases in the future.

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