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Research Article

**THE FEATURES OF ARTERIAL HYPERTENSION
CLINICAL COURSE IN PATIENTS WITH SLEEP
DISORDERS: MELATONIN ROLE**¹Andrey Budnevsky, ¹Nadezhda Rezova, ³Svetlana Kozhevnikova, ⁴Evgeniy Ovsyannikov¹Voronezh State Medical University named after N.N. Burdenko, Voronezh, the Russian Federation**Article Received:** March 2019**Accepted:** April 2019**Published:** May 2019**Abstract:**

The purpose of this study was to analyze the characteristics of arterial hypertension clinical course in patients with sleep disorders for optimization of preventive and curative interventions algorithms, blood pressure control, cardiovascular complications prevention, improvement of patients' life quality. Materials and Methods: We examined 89 patients with arterial hypertension aged from 30 to 70 years. The arterial hypertension diagnosis was based on ESC Clinical Practice Guidelines – ESC/ESH Arterial Hypertension (Management of) (2018). We analyzed the clinical, instrumental and laboratory status of patients with arterial hypertension. All data was evaluated with STATGRAPHICS 5.1, Microsoft Office Excel, Statistica 8.0. Results: the patients with arterial hypertension have expressed dissomnic and psychosomatic disorders which have significant negative influence on the arterial hypertension clinical course and the disease prognosis. Low urine melatonin level is associated with increased blood pressure, blood pressure variability, sleep disorders, psychosomatic disorders, and low life quality of patients with arterial hypertension. Prescription of melatonin in the patients with arterial hypertension with sleep disorders is reasonable to correct dissomnic and psychosomatic disorders, clinical symptoms load of arterial hypertension, improvement of disease prognosis and life quality of patients with arterial hypertension.

Keywords: *arterial hypertension, sleep disorders, psychosomatic disorders, melatonin, quality of life.***Corresponding author:****Nadezhda Rezova,**Voronezh State Medical University named after N.N. Burdenko,
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INTRODUCTION:

Arterial hypertension is a current problem of modern medicine. First of all, arterial hypertension is widespread problem, which leads to permanent functional loss and social and economic losses [1]. Arterial hypertension is a main risk factor of cardiovascular accidents emergence (myocardial infarction, brain attack), which lead to population early disability and determine high mortality rate in the world. According to 2018 ESC/ESH Guidelines for the management of arterial hypertension the prevalence of AH is 43.4% [2]. At simplicity and availability of arterial hypertension treatment, only 14.4% of men and 30.9% of women have effective blood pressure control [3]. However, in spite of high prevalence and significance of arterial hypertension, the etiology and pathogenetic mechanisms are not investigated to the end.

Arterial hypertension is a multifactorial disease in which developing the difficult mechanisms of internal (genetic) and external factors interaction are based [3].

The combination of genetic predisposition to cardiovascular risk factors leads to development of arterial hypertension. The cardiovascular risk factors are psycho-emotional stress, tobacco smoking, abdominal alcohol-related diseases, abdominal obesity, hypodynamia, high dietary salt intake [4].

Now arterial hypertension is a disease which can be controlled. Even insignificant decrease of blood pressure reduces the risks of target organ disease. Meta-analysis of the randomized controlled studies devoted to studying of antihypertensive therapy efficiency showed, the risk of myocardial infarction developing decreases by 22.0% and stroke – by 41.0% if systolic blood pressure decreases by 10 mm Hg. or diastolic blood pressure decreases by 5 mm Hg.

S. Lewington and coauthor (2002) show, the effective treatment of arterial hypertension reduces the cardiovascular diseases mortality by 15.0-20.0% [5].

Today the sleep disorders are the current problem which is found in population. The sleep is one of modulators of different systems at normal also at pathology [6-7].

The sleep is the process which consists of consecutive functional conditions of a brain. It includes synchronized sleep and REM sleep (rapid eye movement in sleep). The normal sleep is an eight-hour sleep which consists of 4 or 6 undulation cycles by 90 minutes. The sleep significantly has an effect on vegetative nervous system, hemodynamic and a cardiovascular system. Sleep disorders lead to memory and attention impairment, performance

decrement. Sleep disorders are associated with developing of frequent headaches, irascibility. The chronic stress, psychic tension, somatic diseases are triggers for sleep disorders or insomnia. On the one hand, the rare appealability, on the other hand, simplicity of this problem, lead to the fact that only little patients receive the treatment of sleep disorders [8].

Normal the blood pressure is much lower while sleeping in comparison with active waking. Circadian variance of blood pressure most likely are connected with the regulating pineal gland hormone influence – melatonin. Decrease in production of melatonin leads to inadequate lowering of blood pressure while sleeping in patients with arterial hypertension. Besides, pineal gland hormone can play an adaptogen role in patients with increased meteorological and geomagnetic communication [5,9].

The combination of standard arterial hypertension therapy with melatonin intake enables to normalization of sleep quality, decreasing of relation between weather factors, intensity of geomagnetic activity and blood pressure. It results in the expressed hypotensive effect of standard therapy and normalization of blood pressure [10].

At arterial hypertension there are single researches concerning melatonin influence on the disease clinical course, blood pressure control. And researches with the assessment of clinical parameters, psychological status, sleep quality and patients' life quality in dependence on the melatonin level and its participation in blood pressure control were practically not conducted.

In the present work, the goal has been set – to analyse the characteristics of arterial hypertension clinical course in patients with sleep disorders for optimization of preventive and curative interventions algorithms, blood pressure control, cardiovascular complications prevention, improvement of patients' life quality.

To achieve the goal, the following tasks were solved:

1. To analyse the dissonic and psychosomatic disorders in patients with arterial hypertension.
2. To study the characteristics of arterial hypertension clinical course in patients with sleep disorders.
3. To reveal communication between blood pressure level and sleep disorders, urine melatonin level.
4. To study the characteristics of arterial hypertension clinical course depending on urine melatonin level.
5. To define the major factors having an impact on dissonic and psychosomatic

disorders in patients with arterial hypertension in dependence of urine melatonin level.

MATERIALS AND METHODS:

We examined 89 patients with arterial hypertension ((42/47.2% women and 47/52.8% men) aged from 30 to 70 years (mean age, 59.40±0.75 years). The arterial hypertension diagnosis was based on ESC Clinical Practice Guidelines – ESC/ESH Arterial Hypertension (Management of) (2018).

The study was approved by the Ethics Committee of Voronezh State Medical University named after N.N. Burdenko. Written informed consent was obtained from each patient.

A comprehensive clinical examination, functional and laboratory tests included the following procedures:

- Assessment of arterial hypertension severity included the visits to the general practice doctor and the hospital admissions for the past 12 months.
- Quantity assessment of arterial hypertension symptoms (headache, vertigo, seeing spots, general weakness) by the 10-point Visual Analogue Scale.
- Assessment of dissomnic disorders by Pittsburgh Sleep Quality Index (PSQI).
- Assessment of psychosomatic disorders (anxiety level, depression level) by State-Trait Anxiety Inventory (STAI) and Zung Self-Rating Depression Scale.
- Assessment of life quality by Short Form Medical Outcomes Study 36 (SF-36).
- Functional tests: echocardiography (EchoCG), 24-hour blood pressure monitoring.
- Laboratory tests: clinical blood analysis, clinical urine analysis, biochemical blood analysis, urine melatonin level.

All data was evaluated with STATGRAPHICS 5.1, Microsoft Office Excel, Statistica 8.0. Baseline characteristics were summarized as frequencies and percentages for categorical variables and as mean±SD for continuous variables. Student's unpaired t-test was used to compare two groups for data with normal distribution. A probability value of $P < 0.05$ was considered statistically significant.

RESULTS AND DISCUSSION:

We analysed the clinical, instrumental and laboratory status of patients with arterial hypertension.

The number of visits to the general practice doctor was 2.39±0.07 per year, hospital admissions – 0.60±0.06 per year.

The subjective assessment of arterial hypertension symptoms, according to the 10-point Visual

Analogue Scale, demonstrated, headache was 4.60±0.09, vertigo was 3.19±0.09, seeing spots were 2.50±0.07, general weakness was 6.15±0.11.

According to EchoCG the left ventricular hypertrophy were revealed. Left ventricle posterior wall was 1.1±0.01 cm, interventricular septum thickness was 1.2±0.02 cm. 78/87.6% patients have not luxus heart, and 11/12.4% patients have luxus heart. Systolic left ventricular function was kept at all patients; left ventricular ejection fraction was 56.39±0.59%.

According to 24-hour blood pressure monitoring average daily blood pressure was 151±3.4/84±2.9 mm Hg, average day-time blood pressure was 157±2.8/89±3.1 mm Hg, and average night-time blood pressure was 140±2.5/78±2.9 mm Hg. There are 4 types of patients depending of systolic blood pressure night decrease: 2/2.3% patients were dipper, 39/43.8% patients were non-dipper, 47/52.8% patients were night-dipper, and 1/1.1% patients was over-dipper. There are 4 types of patients depending of diastolic blood pressure night decrease: 3/3.3% patients were dipper, 42/47.2% patients were non-dipper, 42/47.2% patients were night-dipper, and 2/2.3% patients were over-dipper.

According to clinical blood analysis, clinical urine analysis, biochemical blood analysis nothing abnormal detected.

The assessment of serum lipid profile was revealed dyslipidemia. Total cholesterol was 6.09±0.09 mMol /L, low density lipoprotein cholesterol was 4.01±0.12 mMol /L, high density lipoprotein cholesterol was 0.88±0.03 mMol/L, and triglyceride was 2.05±0.08 mMol/L.

Urine melatonin level was 10.60±1.24 ng/ml.

We analysed the dissomnic and psychosomatic disorders of patients with arterial hypertension. Assessment of dissomnic disorders was by Pittsburgh Sleep Quality Index (PSQI). PSQI was 7.44±0.20.

The patients with arterial hypertension showed the various complaints connected with sleep disorders. They are fatigue when awakening after night sleep (75/84.3% patients), difficulty in falling asleep (60/67.4% patients), superficial sleep with night awakenings (58/65.2% patients), superficial sleep with a set of dreams (51/57.3% patients), sleeplessness more than 30 minutes (56/62.9% patients), night awakenings with headache complaints (37/41.5% patients), ghastly dreams (25/28.1% patients), daytime sleepiness (23/25.8% patients), daytime sleep (13/14.6% patients), rhythmical movement while sleeping (9/10.1% patients), sleep deficiency (5/5.6% patients)

We analysed the arterial hypertension clinical course

and dissonmic disorders in patients of the general group. If the arterial hypertension degree, stratification risk of complications, systolic blood pressure, diastolic blood pressure are higher, disease is long-continued, then dissonmic disorders are significant more severity ($p < 0.05$). Also the irregularity of hypotensive therapy significantly influences on patients sleep quality ($p < 0.05$).

Assessment of psychosomatic disorders was by State-Trait Anxiety Inventory (STAI) and Zung Self-Rating Depression Scale.

In the general group there are patients with high state anxiety (53/59.6%) and patients with high trait anxiety (49/55.1%). 36/40.5% patients were with medium state anxiety. 40/44.9% patients were with medium trait anxiety. There are not patients with low state and trait anxiety levels in the general group. State anxiety level was 44.63 ± 0.66 . Trait anxiety level was 44.17 ± 0.66 .

In the general group there are patients without depression (18/20.2%). 41/46.1% patients have mild (neurotic) depression, 30/33.7% patients have masked depression. There are not patients with true depression in the general group. Depression level was 55.29 ± 0.94 .

We analysed the arterial hypertension clinical course and psychosomatic disorders in patients of the general group. If the arterial hypertension degree, stratification risk of complications, systolic blood pressure, diastolic blood pressure are higher, disease is long-continued, then psychosomatic disorders are significant more severity: state and trait anxiety, depression level are higher ($p < 0.05$). Also the irregularity of hypotensive therapy significantly influences on psychosomatic disorders expressiveness in patients of the general group ($p < 0.05$).

The life quality assessment by SF-36 revealed the low health status of patients with arterial hypertension. The lowest average values had 4 scales. Role-Physical Functioning (RP) was 41.07 ± 1.71 , Bodily Pain (BP) was 42.69 ± 1.46 , and Role Emotional (RE) was 40.49 ± 1.46 .

We carried out the correlation analysis to identify the dependences and statistic relation between the studied characteristic.

The data of correlation analysis confirmed the results of our research. The frequent visits to the general practice doctor, the frequent hospital admissions, the high arterial hypertension degree, high stratification risk of complications, long-continued disease, irregularity of hypotensive therapy, marked arterial hypertension symptoms, blood pressure variability, dyslipidemia, low urine melatonin level are

correlated with more severity dissonmic and psychosomatic disorders (high PSQI, high state and trait anxiety levels, high depression level), low quality of life.

We carried out the One-Way ANOVA to assess the influence of independent variable (factors) on the end result (sign).

One-Way ANOVA was carried out to identify the influence of the behavioral performances (smoking, regularity of hypotensive therapy), dissonmic and psychosomatic disorders (PSQI, state and trait anxiety, depression), urine melatonin level on the arterial hypertension clinical course (arterial hypertension degree, visits to the general practice doctor, hospital admissions, stratification risk of complications, long-continued disease).

According to One-Way ANOVA smoking, PSQI, state and trait anxiety, depression, urine melatonin level significant influence on arterial hypertension degree.

The 3rd degree of arterial hypertension was diagnosed for the smoking patients significant more often ($F=21.96$; $p=0.0000$).

In patients of the general group PSQI, state and trait anxiety level, depression level, urine melatonin level significant differed depending on arterial hypertension degree.

At the 1st degree of arterial hypertension PSQI was 4.8 ± 0.20 ; at the 2nd degree of arterial hypertension PSQI was 6.86 ± 1.19 ; at the 3rd degree of arterial hypertension PSQI was 9.03 ± 0.40 ($F=23.96$; $p=0.0000$).

At the 1st degree of arterial hypertension state anxiety level was 36.8 ± 1.07 ; at the 2nd degree of arterial hypertension state anxiety level was 42.45 ± 0.86 ; at the 3rd degree of arterial hypertension state anxiety level was 49.18 ± 0.53 ($F=23.80$; $p=0.0000$).

At the 1st degree of arterial hypertension trait anxiety level was 37.4 ± 1.12 ; at the 2nd degree of arterial hypertension trait anxiety level was 41.57 ± 0.79 ; at the 3rd degree of arterial hypertension trait anxiety level was 49.21 ± 0.59 ($F=30.70$; $p=0.0000$).

At the 1st degree of arterial hypertension depression level was 40.8 ± 0.58 ; at the 2nd degree of arterial hypertension depression level was 51.22 ± 0.88 ; at the 3rd degree of arterial hypertension depression level was 63.79 ± 0.77 ($F=70.75$; $p=0.0000$).

At the 1st degree of arterial hypertension urine melatonin level was 31.89 ± 1.21 ng/ml; at the 2nd degree of arterial hypertension urine melatonin level

was 11.48 ± 1.19 ng/ml; at the 3rd degree of arterial hypertension urine melatonin level was 2.92 ± 0.55 ng/ml ($F=49.07$; $p=0.0000$).

According to One-Way ANOVA PSQI, state and trait anxiety, depression have significant influence on visits to the general practice doctor.

In patients of the general group PSQI, state and trait anxiety level, depression level significant differed depending on visits to the general practice doctor.

At one visit a year PSQI was 6.12 ± 0.61 ; at two visits a year PSQI was 6.93 ± 0.28 ; at three visits a year PSQI was 8.23 ± 0.39 ; at four visits a year PSQI was 8.50 ± 1.32 ($F=3.97$; $p=0.0107$).

At one visit a year state anxiety level was 37.12 ± 0.97 ; at two visits a year state anxiety level was 41.97 ± 0.44 ; at three visits a year state anxiety level was 49.26 ± 0.51 ; at four visits a year state anxiety level was 47.00 ± 2.35 ($F=22.17$; $p=0.0000$).

At one visit a year trait anxiety level was 36.88 ± 0.71 ; at two visits a year trait anxiety level was 40.79 ± 0.78 ; at three visits a year trait anxiety level was 49.35 ± 0.54 ; at four visits a year trait anxiety level was 47.00 ± 1.96 ($F=37.69$; $p=0.0000$).

At one visit a year depression level was 40.63 ± 0.59 ; at two visits a year depression level was 51.52 ± 0.94 ; at three visits a year depression level was 62.14 ± 0.94 ; at four visits a year depression level was 64.25 ± 0.85 ($F=46.66$; $p=0.0000$).

According to One-Way ANOVA PSQI and depression have significant influence on hospital admissions.

Patients with expressed dissomnic disorders in the anamnesis had one or two hospitalization a year, and patients with less expressed dissomnic disorders had no more than one hospitalization a year.

If patients didn't have hospitalization a year, PSQI was 6.5 ± 0.27 . If patients have one hospitalization a year, PSQI was 8.07 ± 0.26 . If patients have two hospitalizations a year, PSQI was 11.00 ± 0.58 . Only 1 patient has three hospitalizations a year, his PSQI was 15 ($F=17.79$; $p=0.0000$).

If patients didn't have hospitalization a year, depression level was 47.92 ± 1.03 . If patients have one hospitalization a year, depression level was 60.67 ± 0.73 . If patients have two hospitalizations a year, depression level was 68.63 ± 0.33 . Only 1 patient has three hospitalizations a year, his depression level was 69 ($F=43.56$; $p=0.0000$).

It should be noted, state and trait anxiety have not significant influence on hospital admissions.

According to One-Way ANOVA PSQI, state and trait anxiety have significant influence on stratification risk of complications.

In patients of the general group PSQI, state and trait anxiety level significant differed depending on stratification risk of complications.

At the 2nd stratification risk of complications PSQI was 4.90 ± 0.21 ; at the 3rd stratification risk of complications PSQI was 6.51 ± 0.97 ; at the 4th three stratification risk of complications PSQI was 8.31 ± 0.56 ($F=37.88$; $p=0.0021$).

At the 2nd stratification risk of complications state anxiety level was 34.40 ± 0.25 ; at the 3rd stratification risk of complications state anxiety level was 38.75 ± 0.60 ; at the 4th three stratification risk of complications state anxiety level was 47.27 ± 0.64 ($F=39.65$; $p=0.0000$).

At the 2nd stratification risk of complications trait anxiety level was 34.60 ± 0.25 ; at the 3rd stratification risk of complications trait anxiety level was 39.05 ± 0.58 ; at the 4th three stratification risk of complications trait anxiety level was 46.52 ± 0.69 ($F=27.88$; $p=0.0000$).

It should be noted, depression has not significant influence on stratification risk of complications. Smoking is the main risk factor of cardiovascular pathology. According to One-Way ANOVA PSQI, state anxiety level and depression level have significant influence on smoking.

In patients of the general group PSQI, state anxiety level and depression level significant differed depending on smoking.

In non-smoking patients PSQI was 5.25 ± 0.31 , at refused smoking patients PSQI was 6.61 ± 0.21 , at smokers PSQI was 8.82 ± 0.37 ($F=21.58$; $p=0.0000$).

In non-smoking patients state anxiety level was 37.12 ± 0.97 , at refused smoking patients state anxiety level 41.93 ± 0.72 , at smokers state anxiety level was 49.26 ± 0.26 ($F=36.15$; $p=0.0000$).

In non-smoking patients depression level was 40.63 ± 0.59 , at refused smoking patients depression level was 51.54 ± 0.92 , at smokers depression level was 62.63 ± 0.83 ($F=75.09$; $p=0.0000$).

It should be noted, trait anxiety level has not significant influence on smoking. The obtained significant data confirm patients with arterial hypertension use smoking as one of the easiest ways to reverse the psychoemotional stress.

According to One-Way ANOVA state and trait anxiety level and depression level have significant

influence on regularity of hypotensive therapy

State anxiety level was 41.49 ± 0.82 in patients with arterial hypertension which are regularly taking the antihypertensive medicines; state anxiety level was 49.25 ± 0.49 in patients which did not take medicine ($F=51.80$; $p=0.0000$).

Trait anxiety level was 40.69 ± 0.72 in patients with arterial hypertension which are regularly taking the antihypertensive medicines; trait anxiety level was 49.28 ± 0.54 in patients which did not take medicine ($F=75.67$; $p=0.0000$).

Depression level was 49.96 ± 0.43 in patients with arterial hypertension which are regularly taking the antihypertensive medicines; depression level was 63.14 ± 0.79 in patients which did not take medicine ($F=102.54$; $p=0.0000$).

The data of One-Way ANOVA confirmed the results of our research. The behavioral performances (smoking, irregularity of hypotensive therapy), dissomnic and psychosomatic disorders (high PSQI, high state and trait anxiety levels, high depression level), laboratory indicators (low urine melatonin level) have significant negative influence on the arterial hypertension clinical course (arterial hypertension degree, visits to the general practice doctor, hospital admissions, stratification risk of complications).

Thus, psychosomatic ratios in patients with arterial hypertension are characterized by influence of psychological status on the arterial hypertension clinical course. Psychosomatic influences at arterial hypertension are characterized by increase of psychosocial disability and mixed anxiety-depressive disorders.

Further, we carried out the One-Way ANOVA to assess the influence of sleep quality on social and demographic, behavioural, psychological, clinical, instrumental, and laboratory characteristics of patients with arterial hypertension.

According to One-Way ANOVA sleep quality (dissomnic disorders) have significant negative influence on smoking status (a large number of smoking patients), a large number of visits to the general practice doctor and hospitalizations, irregularity of hypotensive therapy, periodically headaches, blood pressure variability, psychosomatic disorders (high state and trait anxiety levels, high depression level), low quality of life (low scales Physical Functioning (PF), General Health (GH), Vitality (VT), Role Emotional (RE), and Mental Health (MH)).

Also, we carried out the One-Way ANOVA to assess the influence of urine melatonin level on social and

demographic, behavioural, psychological, clinical, instrumental, and laboratory characteristics of patients with arterial hypertension and dissomnic disorders.

According to One-Way ANOVA low urine melatonin level has significant negative influence on elevated arterial hypertension degree, blood pressure variability, sleep quality (high PSQI), psychosomatic disorders (high state and trait anxiety levels, high depression level).

Proceeding from results of our investigation we could allocate the most significant factors having an impact on the arterial hypertension clinical course and also define the significant factors having an impact on dissomnic disorders in patients with arterial hypertension.

CONCLUSION:

In conclusion, the patients with arterial hypertension have expressed dissomnic and psychosomatic disorders which have significant negative influence on the arterial hypertension clinical course and disease prognosis. Low urine melatonin level is associated with increased blood pressure, blood pressure variability, sleep disorders, psychosomatic disorders (high state and trait anxiety levels, high depression level), and low life quality of patients with arterial hypertension. Prescription of melatonin to the patients with arterial hypertension with sleep disorders is reasonable to correct dissomnic and psychosomatic disorders, clinical symptoms load of arterial hypertension, improvement of disease prognosis and life quality of patients with arterial hypertension.

Competing interests

The authors declare that they have no competing interests.

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