

RUDN Journal of MEDICINE. ISSN 2313-0245 (Print). ISSN 2313-0261 (Online)

DOI: 10.22363/2313-0245-2021-25-4-282-289

RESEARCH ARTICLE
HAYYHAЯ СТАТЬЯ

Blood pressure time load formation in patients with arterial hypertension without metabolic syndrome

TatjanaYu. Zotova De Anastasiya A. Lukanina De Mikhail L. Blagonravov

Abstract. Relevance. The study of the daily dynamics of blood pressure in arterial hypertension both on the basis of the daily index and on the basis of the time load is a relevant task, since, these indicators are associated in the literature with stable changes in the neurohumoral regulation of the cardiovascular system in arterial hypertension. The aim of the study was to compare data of the time load in patients with arterial hypertension, depending on the nocturnal blood pressure profile, with integrative indicators of the activity of the cardiovascular system in the form of a Circadian index, a structural point of blood pressure, double product. *Materials and Methods*. The study included 72 patients who were treated at the City Clinical Hospital No 13 in Moscow and signed a voluntary consent to participate in the research and the processing of personal data. Inclusion criteria: arterial hypertension. Exclusion criteria: metabolic syndrome, secondary forms of arterial hypertension and concomitant pathology. Depending on the daily index (DI≥10% and DI≤10%) patients were divided into 2 groups: 1 group (N= 32): patients with arterial hypertension without nocturnal decrease in blood pressure (non-dippers and night-pickers100%); Group 2 (N = 40): patients with arterial hypertension who had a nocturnal decrease in blood pressure (dippers and over dippers 100%). All patients and members of the control group (N=15) underwent daily monitoring of blood pressure (24-hour Arterial Blood Pressure Monitoring). The data were statistically processed to determine the 5% level of significance of differences ($p \le 0.05$) (Student's test). In the comparative analysis of integrative indicators at day and at night, a variance analysis was applied. *Results* and Discussion. As a result of the study, it was found that the values of Circadian Index for blood pressure vary depending on the type of night decrease in blood pressure and the blood pressure time load, while daily index and structural point of blood pressure remain on the same level as a reflection of the hemodynamic allostasis existing in both groups. *Conclusion*. Reflection of the allostatic load on hemodynamics is change of values of double product and of the structural point of blood pressure compared with the control group. These changes are not associated with the peculiarities of the nocturnal blood pressure profile in patients with hypertension without metabolic syndrome.

Key words: arterial hypertension, AH without metabolic syndrome, blood pressure profile, allostasis, circadian index for blood pressure

Author contributions. All authors contributed to the study: conceptualization, methodology — T.Z.; software, analysis, investigation — A.L.; validation — M.B.; writing, draft preparation — T.Z.; writing and editing — M.B.; supervision — T.Z., M.B.; project administration and funding acquisition — M.B. All authors have read and agreed to the published version of the manuscript.

© Zotova T.Yu, Lukanina A.A., Blagonravov M.L., 2021



This work is licensed under a Creative Commons Attribution 4.0 International License https://creativecommons.org/licenses/by/4.0/

Funding. The investigation has been supported by the RUDN Program "Priority-2030".

Conflicts of Interest: The authors declare no conflict of interest.

Received 07.08.2021. Accepted 25.10.2021.

For citation: Zotova TYu, Lukanina AA, Blagonravov ML. Blood pressure time load formation in patients with arterial hypertension without metabolic syndrome. *RUDN Journal of Medicine*. 2021;25(4):282—289. doi: 10.22363/2313-0245-2021-25-4-282-289

Introduction

A feature of the phenotypic course of arterial hypertension (AH), in addition to the presence or absence of the formation of metabolic syndrome. is the different dynamics of the nocturnal decrease in blood pressure (BP), which, according to the literature, is based on sympathicotonia at night in patients with AH [1, 2]. The degree of night decline is determined on the basis of the rate of night decrease in blood pressure, designated as the daily index (DI). In our work, a simpler gradation is applied in the form of the presence or absence of a nighttime decrease in blood pressure (DI≥10 % and DI≤10 %). Since all patients received adequate antihypertensive therapy that reached the target values, registration in both groups of load time in percentages for systolic BP and diastolic BP can be regarded as constancy in change, that is, as a state of hemodynamic allostasis. If the assumption is correct, then in addition to the load of time in % in the presence of hemodynamic allostasis, other integrative indicators of the cardiovascular system will be changed. The purpose of the study was to compare the data on the time load in% in patients with hypertension, depending on the night profile of blood pressure with the integrative indicators of the activity of the cardiovascular system in the form of the circadian index (CI), the structural point of BP (SPBP), the double product (DP). The relevance of the study is due to the fact that the existence of the organism in conditions of allostasis is the cause of its accelerated aging [3].

Materials and methods

The study included 72 patients who were treated and examined at the City Clinical Hospital No 13 in Moscow with the voluntary signing of an informed consent (WMA Declaration of Helsinki — Ethical Principles for Medical Research Involving Human Subjects, 2013). The study approved by the Ethics Committee of the Institute of Medicine, RUDN University (protocol code 10 and date of approval: 20.06.2019).

Exclusion criteria: metabolic syndrome and secondary forms of arterial hypertension, concomitant pathology that can change the nature of the course of arterial hypertension in patients. Inclusion criteria: the same second stage of the arterial hypertension. A feature of the course of hypertension, in addition to the presence or absence of the formation of metabolic syndrome, is the different dynamics of the night decrease in blood pressure. All patients underwent 24-hour arterial blood pressure monitoring (ABPM) daily blood pressure (BP) monitoring (TM-2430, AnD, Japan). Data ABPM were processed using the computer program EZDoctor 2.7. The degree of night decrease is determined on the basis of the rate of night decrease in blood pressure daily index (DI). In our work, a simpler gradation was applied in the form of the presence or absence of a nighttime decrease in blood pressure daily index (DI≥10 % and DI≤10 %). Using this criterion, 2 groups of patients were formed: 1 group (N = 32): patients with arterial hypertension with nocturnal decrease in blood pressure (non-dippers and night pickers 100 %); Group 2 (N = 40): patients

with arterial hypertension who had a nocturnal decrease in blood pressure (dippers and overdippers100 %). All patients with arterial hypertension received adequate therapy that reached the target values (mainly two groups of drugs were used). To analyze hemodynamic parameters, a control group (N= 15) aged 25 to 69 years was introduced into the study. The main indicators of the clinical and laboratory characteristics of the groups are presented in the Table 1.

Table 1
Clinical and laboratory features of the analyzed group of patients

	1	
Indicator	Group 1 (N=32)	Group 2 (N=40)
Age, years	58,25±4,05	59,5±3,03
Men,%	50	37,5
Women,%	50	62,5
BMI, kg/m2	26,65±0,39	26,85±0,4
WC, cm	91,7±1,33	91±1,15
Duration of hypertension, years	12,35±1,2	12,3±1,15
HbA1c, (6)%	6 %	5,7 %
Creatinine, (64–104) mmol/l	83,9±3,9	82,9±2,11
Urea, (3-9) mmol/l	6,25±0,5	5,95±0,42
MAU, (0,3) mg/l	0,6±0,01 0,5±0,002	
IRI (2-25) mkED/ml	26,65±0,39 26,85±0,4	
EF%	63,7±0,26	63,45±0,16

Note: BMI - body mass index, WC - waist circumference, MAU - microalbuminuria, IRI - immunoreactive insulin, EF - ejection fractions.

The exclusion of metabolic syndrome was carried out on the basis of an analysis of indicators: waist volume (WC), body mass index (BMI), glycated hemoglobin (HbA1c,%).

The obtained data of ABPM were processed using a linear analysis according to the developed methodology, the following indicators were calculated: average blood pressure and heart rate, BP time load as a percentage of increased blood pressure. The possibility of using an average value (M±m) is due to the fact that hemodynamic parameters are the subject of regulation of cardio-vascular functional system (CVS). In the paper are also studied the parameters that allow to

assess the integrative features of the regulation of the cardiovascular system. These are: circadian indices CI (CI=day BP/night BP for SBP, DBP) and structural blood pressure point (SPBP (DBP/SBP) — indirectly reflecting the conditions of tissue perfusion)), double product (DP (DP = $HR \times SBP/100$)) indirectly reflects the need for myocardium in oxygen (gradation of need in oxygen: 75 or less — above average, 76—89 — average, 90 or higher — below average). All data were analyzed for statistically significant differences at 5 % significance level using the nonparametric Mann-Whitney U-test and the Fisher angular transform for percentage shares. The use of non-parametric criteria does not allow determining the power of the study. Homogeneity of the groups when comparing hemodynamic indicators was estimated on the basis of the coefficient of variation of the indicator (standard deviation/ average value of the indicator): with its value less than 0,3; the group is regarded as homogeneous. For the analysis of the BP time load, the dynamics of the SPBP, the DP, a variance analysis was used with the determination of the median indicator and a quartile assessment of the range of oscillations (25—75 %), as well as the determination of the minimum and maximum indicator.

Results and discussion

In the comparative analysis of the daily dynamics of blood pressure, obtained on the basis of the analysis of ABPM according to the linear analysis, first of all, it should be noted that the groups were homogeneous in hemodynamic indicators (blood pressure and heart rate): the coefficient of variation did not exceed 30 % (Table 2), which allows for further comparison of groups.

The groups had gender differences, but no differences were established for the rest of the indicators (Table 1). Metabolic syndrome was excluded on the basis of HbA1c,%, BMI, WC. Levels of creatinine, urea and microalbuminuria (Uria) made it possible to exclude hidden forms of secondary hypertension and complications of hypertension in the form of nephrosclerosis. The level of FV in % allows to exclude in both groups the presence of HF and its effect on hemodynamic parameters.

Table 2
Comparative analysis of the dynamics of hemodynamic parameters

Indicator	Control (N=15)	Group 1 (N=32)	Group 2 (N=40)
Average daily SBP, mmHg	120±1,87	139,6±2,2*	134,0±1,47
Average daily DBP, mmHg	76,2±1,55	79,5±2,19	78,15±1,17
Average daily HR, b/m	76,2±1,80	76,08±2,7	70,45±1,16
Daily CV for SBP	0,06	0,09	0,06
Daily CV for DBP	0,08	0,15	0,09
Daily CV for HR	0,09	0,2	0,1
SBP circadian index,%	1,18±0,04	1±0,01*	1,2± 0,03 •
DBP circadian index,%	1,2±0,02	1,02± 0,02*	1,2± 0,02•
HR circadian index%	1,18±0,01	1,15± 0,02	1,2± 0,02
Time index of the SBP,%	22,9±3,21	60,9±5,71*	57,8± 3,9*
Time index of the DBP,%	18,4±2,78	42,7± 5,8*	38,4± 2,91*

Note: $p \le 0.05$ — the reliability of the difference with the control group; CV- coefficient of variation; $p \le 0.05$ — the reliability of the difference between groups.

Data of the Table 2 demonstrate the presence of a clinical effect from the ongoing antihypertensive therapy on average per day — the average values of SBP were significantly increased only in 1 group of patients compared with the control group. There were no differences between the groups on hemodynamic indicators. However, an analysis of the time load factor in% for SBP and DBP indicates the presence of hemodynamic load on the cardiovascular system for both groups. A decrease in CI (Table 1) indicates that the changed profile of nocturnal blood pressure is one

of the causes of this load. In this regard, a dispersion analysis of the time load in% for SBP for both groups of patients with hypertension (Fig.1, 2) separately for day and night was carried out in order to establish the effect of these changes on integrative hemodynamic indicators. SBP was used, since this load was higher in terms of its values compared to DBP.

The analysis of the presented figures 1, 2, 3, 4 allows us to confirm the earlier assumption about the effect of the load time in% for SBP in the first group of the study on the value of the CI (it was reduced compared with the control group of Table 2). The time load in% for SBP in the second group of patients occurs both at night and during the day at a comparable level. The obtained results indicate that the assessment of the average daily values of blood pressure is not always an adequate method of analysis. When selecting adequate therapy, it is advisable to conduct an independent analysis of day and night blood pressure values, regardless of the type of night decrease in blood pressure. This is due to the fact that with arterial hypertension there are ultradian rhythms in the regulation of the activity of the cardiovascular system. They reflect a violation of electrolyte metabolism in hypertension [4, 5].

The conducted dispersion analysis of DP indicators (Fig. 3) allows us to talk about the same decrease in the level of metabolic processes in the myocardium in both groups of patients, regardless of the formation of the load during the day (day — night).

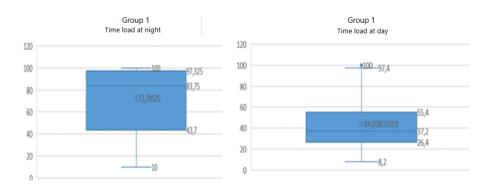


Fig. 1. Data of dispersion analysis on the SBP time load in patients of group 1

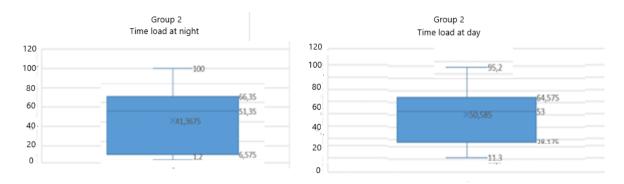


Fig. 2. Data of dispersion analysis on the SBP time load in patients of group 2

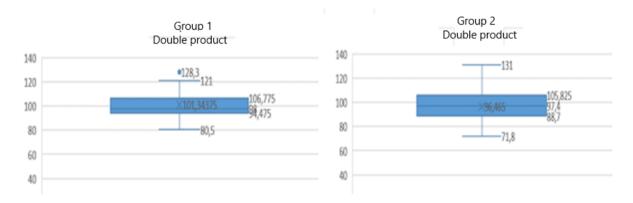


Fig. 3. Variance analysis indicators for DP

Thus, the altered myocardial metabolism rate is a common indicator for patients with hypertension without metabolic syndrome compared with the control group (90.29±1.39 versus 75.2±2.25 in the control group). Dispersion analysis of SPBP indicates a possible common mechanism for the formation of a decrease in cellular metabolism in patients of both groups. This is a

change in the conditions of perfusion. It should be noted that the value of the SPBP «leaves» for the characteristic for the control group value of the SPBP, close to the golden ratio (control 0.62, golden ratio 0.618).

Thus, the analysis of the results of the study suggests that violations of the cardiovascular system of patients with arterial hypertension without metabolic

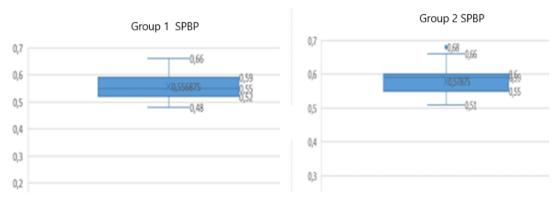


Fig. 4. Variance analysis indicators for SPBPs

syndrome occur at different levels of regulation and allows us to regard this condition not as homeostasis, but as allostasis [4—9]. For the first time, B.S. McEwen and P. Sterling reported on the existence of allostasis in psychoemotional [10—12]. In the future, the concept of biomarkers in allostasis, including hemodynamic, as a reflection of the effects of stress on the body was developed [13—16]. The absence of metabolic syndrome in patients with arterial hypertension in this study allows us to associate the identified changes in the regulation of the cardiovascular system with indicators characterizing the features of hemodynamics in patients with hypertension, and not with other biomarkers of allostasis. This is a change in the nocturnal profile of blood pressure, leading to a decrease in CI, as well as a change in the conditions of perfusion (SPBP) and myocardial metabolism (DP). The basis of these changes is the formation, including the time load in % for SBP and DBP on the basis of altered neurohumoral regulation of the cardiovascular system with the formation of sympathicotonia at night (group 1), a change in the activity of renin-angiotensin proteins — aldosterone system (group 2). This allows us to consider this state of hemodynamics in arterial hypertension without metabolic syndrome as a state of hemodynamic allostasis, despite the ongoing antihypertensive therapy.

Conclusion

- 1. Hemodynamics in arterial hypertension without metabolic syndrome exists within the framework of hemodynamic allostasis, which forms a BP time load (in %) in patients of groups 1 and 2.
- 2. The study of night and day dynamics of the SBP time load (in %) in patients of groups 1 and 2 allows us to conclude that in group 1 the pressure load is higher at night, which is associated with changes in the CI for blood pressure. The SBP time load (in %) is significantly higher compared to the control group in the second group, but exists more evenly during the day.
- 3. Reflection of the allostatic load on hemodynamics is change of values of DP and of SPBP compared with the control group. These changes are not associated with the peculiarities of the nocturnal blood

pressure profile in patients with hypertension without metabolic syndrome.

References/ Библиографический список

1. Shlyakhto EV, Conrady AO. Causes and consequences of sympathetic overactivity in hypertension. "Arterial'naya Gipertenziya" ("Arterial Hypertension"). 2003;9(3):81—88. https://doi.org/10.18705/1607-419X-2003-9-3-81-88 (In Russian)

[Шляхто Е.В., Конради А.О. Причины и последствия активации симпатической нервной системы при артериальной гипертензии // Артериальная гипертензия. 2003. Т. 9. № 3. С. 81—88. https://doi.org/10.18705/1607-419X-2003-9-3-81-88]

2. Tsfasman AZ, Alpaev DV, Karetskaya TD. Diurnal profile of arterial pressure during sleep deprivation in patients with hypertensive disease receiving antihypertensive therapy. *Klin Med (Mosk)*. 2012;90(7):34—7. PMID: 2301997 (In Russian)

[Цфасман А.З., Алпаев Д.В., Карецкая Т.Д. Суточный профиль артериального давления при депривации сна у больных гипертонической болезнью на фоне артериальной гипертензии // Клиническая медицина. 2012. Т. 90. № 7. С. 34—7. PMID: 2301997.]

3. Altman DSh, Davydova EV, Kochetkova NG, Zurochka AV. Growth of biological markers of aging and allostasis in veterans of the Afghan war conflict with early forms of chronic brain ischemia. *ESC Heart Fail*. 2020;7(6):3487—96. doi: 10.1002/ehf2.13002. (In Russian)

[Альтман Д.Ш., Давыдова Е.В., Кочеткова Н.Г., Зурочка А.В. Темпы биологического старения и маркеры аллостаза у ветеранов афганского конфликта с ранними формами хронической ишемии мозга. Acta Biomedica Scientifica. 2012. Т. 3. № 2. С. 15—18. doi: 10.1002/ehf2.13002.]

4. Zotova TY, Blagonravov ML, Lapaev NN, Denisova AP. Hemodinamic allostasis of pregnant women against the background of preeclampsia. *Bulletin of Experimental Biology and Medicine*. 2018;165(4):440—444. https://doi.org/10.1007/s10517-018-4189-4 (In Russian).

[Зотова Т.Ю., Благонравов М.Л., Лапаев Н.Н., Денисова А.П. Состояние гемодинамического аллостаза на фоне преэклампсии у беременных. Бюллетень экспериментальной биологии и медицины. 2018. Т. 165. \mathbb{N} 4. С. 428—433.]

5. Baryshnikova GA, Chorbinskaya SA, Stepanova II. Electrolyte Imbalance and its Role in the Development of Cardiovascular Diseases. *Effective Pharmacotherapy*. 2019;14:54—60. doi: 10.33978/2307-3586-2019-15-20-54-60. (In Russian)

[Барышникова Г.А., Чорбинская С.А., Степанова И.И. Дисбаланс электролитов и его роль в развитии сердечно-сосудистых заболевания. Эффективная фармакотерапия. 2019. Т. 15. № 20. С. 56—63.]

- 6. Buckwalter JG, Castellani B, McEwen B, Karlamangla AS, Rizzo AA, John B. Allostatic load as a complex clinical construct: a case-based computational modeling approach. *Complexity*. 2016; S1:291—306. https://doi.org/10.1002/cplx.21743.
- 7. Atkov OYu, Gorokhova SG. Determination of allostatic load dynamics in the assessment of adaptation in temporary workers in the Arctic. *Russian Journal of Occupational Health and Industrial Ecology*.

2019;59(9): 547—54. doi: 10.31089/1026-9428-2019-59-9-547-548 (In Russian)

[Атыков О.Ю., Горохова С.Г. Определение динамики аллостатической нагрузки при оценке адаптации у временно работающих в условиях Арктики. Медицина труда и промышленная экология. 2019. № 9. С. 547—548. doi: 10.31089/1026-9428-2019-59-9-547-548]

8. Merkulov YuA., Pyatkov AA., Gorokhova SG., Merkulova DM., Atkov OYu. Disturbances of Autonomic Regulation of Cardiovascular System at Different Working Regimes with Night Shifts. *Kardiologiia*. 2020;60(9):62—67. https://doi.org/10.18087/cardio.2020.9.n113 (In Russian)

[Меркулов Ю.А., Пятков А.А., Горохова С.Г., Меркулова Д.М., Атьков О.Ю. Нарушение вегетативной регуляции сердечно-сосудистой системы при разных режимах работы с ночными сменами. Кардиология. 2020;60(9):62—67. https://doi.org/10.18087/cardio.2020.9.n113]

- 9. Mocayar Marón FJ, Ferder L, Saraví FD, Manucha W. Hypertension linked to allostatic load: from psychosocial stress to inflammation and mitochondrial dysfunction. *Stress*. 2019;22(2):169—181. doi: 10.1080/10253890.2018.1542683.
- 10. McEwen BS. Central effects of stress hormones in health and disease: understanding the protective and damaging effects of stress

and stress mediators. *Eur J Pharmacol*. 2008;583(2—3):174—185. doi: 10.1016/j.ejphar.2007.11.071.

- 11. Sterling P. Allostasis: A model of predictive regulation. *Physiology & Behavior*. 2012;106: 5—15. doi: 10.1016/j.physbeh.2011.06.004.
- 12. Clark MS, Bond MJ, Hecker JR Environmental stress, psychological stress and allostatic load. *Psychol Health Med*. 2007;12(1):18—30. doi:10.1080/13548500500429338.
- 13. Romero LM, Dickens MJ, Cyr NE. The Reactive Scope Model a new model integrating homeostasis, allostasis, and stress. *Horm Behav.* 2009;55(3):375—89. doi: 10.1016/j.yhbeh.2008.12.009.
- 14. Juster RP, McEwen BS, Lupien SJ. Allostatic load biomarkers of chronic stress and impact on health and cognition. *Neurosci Biobehav Rev.* 2010;35(1):2—16. doi: 10.1016/j.neubiorev.2009.10.002.
- 15. McEwen BS. Central effects of stress hormones in health and disease: Understanding the protective and damaging effects of stress and stress mediators. *Eur J Pharmacol*. 2008;583(2—3):174—85. doi: 10.1016/j.ejphar.2007.11.071.
- 16. Schulkin J, Sterling P. Allostasis: A Brain-Centered, Predictive Mode of Physiological Regulation. *Trends Neurosci*. 2019;42(10):740—752. doi: 10.1016/j.tins.2019.07.010.

Нагрузка временем артериального давления у пациентов с артериальной гипертензией без метаболического синдрома

Т.Ю. Зотова , А.А. Луканина , М.Л. Благонравов

Российский университет дружбы народов, г. Москва, Российская Федерация ⊠ zotovat@mail.ru

Аннотация. Актуальность. Изучение суточной динамики артериального давления при артериальной гипертонии как на основе суточного индекса, так и на основе временной нагрузки является актуальной задачей, поскольку эти показатели в литературе связывают со стабильными изменениями нейрогуморальной регуляции сердечно-сосудистой системы при артериальной гипертензии. Целью исследования явилось сопоставление данных временной нагрузки у пациентов с артериальной гипертензией в зависимости от профиля ночного артериального давления с интегративными показателями активности сердечно-сосудистой системы в виде циркадного индекса, структурной точки артериального давления, двойного произведения. *Материалы и методы*. В исследование включены 72 пациента, которые проходили лечение в Городской клинической больнице № 13 г. Москвы и подписали добровольное согласие на участие в исследовании и обработку персональных данных. Критерии включения: артериальная гипертензия. Критерии исключения: метаболический синдром, вторичные формы артериальной гипертензии и сопутствующая патология. В зависимости от суточного индекса (DI≥10 % и DI≤10 %) пациенты были разделены на 2 группы: 1 группа (N=32) — пациенты с артериальной гипертензией без ночного снижения артериального давления (не дипперы и найт-пикеры 100 %); 2-я группа (N=40) — пациенты с артериальной гипертензией, у которых в ночное время наблюдалось снижение артериального давления (дипперы и овердипперы 100 %). У всех пациентов и членов контрольной группы (N=15) проводился ежедневный мониторинг артериального давления (24-часовой мониторинг артериального давления). Данные были обработаны статистически с определением 5 % уровня значимости различий (р≤0,05) (критерий Стьюдента). При сравнительном анализе интегративных показателей днем и ночью применялся дисперсионный анализ. Результаты и обсуждение. В результате исследования было установлено, что значения циркадного индекса артериального давления меняются

в зависимости от типа ночного снижения артериального давления и временной нагрузки артериального давления, в то время как суточный индекс и структурная точка артериального давления остаются неизменными, что отражает гемодинамический аллостаз при артериальной гипертензи, существующий в обеих группах. Выводы. Отражением аллостатической нагрузки на гемодинамику является изменение значений двойного произведения и структурной точки артериального давления по сравнению с контрольной группой. Эти изменения не связаны с особенностями ночного профиля артериального давления у пациентов с артериальной гипертензией без метаболического синдрома.

Ключевые слова: артериальная гипертензия, АГ без метаболического синдрома, профиль артериального давления, аллостаз, циркадный индекс артериального давления

Вклад авторов. Все авторы внесли свой вклад в это исследование: концептуализация, методология — Т.З.; программное обеспечение, анализ, исследование — А.Л.; контроль — М.В.; написание, подготовка черновика рукописи — Т.З., написание и редактирование — М.Б., Т.З.; управление проектом и привлечение финансирования — М.В. Все авторы прочитали и согласились с представленной версией рукописи.

Информация о конфликте интересов. Авторы заявляют об отсутствии конфликта интересов.

Поступила 07.08.2021. Принята 25.10.2021

Для цитирования: *Zotova T. Yu., Lukanina A.A., Blagonravov M.L.* Blood pressure time load formation in patients with arterial hypertension without metabolic syndrome // Вестник Российского университета дружбы народов. Серия: Медицина. 2021. Т. 25. № 4. С. 282—289. doi: 10.22363/2313-0245-2021-25-4-282-289

Corresponding author: Tatjana Yu. Zotova — MD, professor of the V.A. Frolov Chair of General Pathology and Pathophysiology, Medical Institute, Peoples' Friendship University of Russia, Moscow, 117198, ul. Miklukho-Maklaya, 8, Moscow, Russian Federation. E-mail: zotovat@mail.ru

Zotova T. Yu. ORCID 0000-0002-8415-5506 Lukanina A.A. ORCID 0000-0002-7486-9257

Blagonravov M.L. ORCID 0000-0001-7838-0486

Ответственный за переписку: Зотова Татьяна Юрьевна— д.м.н., профессор кафедры общей патологии и патофизиологии имени В.А. Фролова Медицинского института Российского университета дружбы народов, Российский университет дружбы народов, Российская Федерация, 117198, Москва, ул. Миклухо-Маклая 8. E-mail: zotovat@mail.ru

Зотова Т.Ю. SPIN-код: 5430-4259; ORCID 0000 0002 8415-5506

Луканина A.A. ORCID 0000 0002074869257

Благонравов М.Л. SPIN-код: 1050-0527; ORCID 0000-0001-7838-0486