DAILY MONITORING OF BLOOD PRESSURE INDICATORS IN PATIENTS WITH STAGE II HYPERTENSION IN ACCORDANCE WITH HYPOTENSIVE THERAPY

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Annotation: Arterial hypertension is a persistent increase in systolic blood pressure at rest (≥ 130 mmHg) and/or diastolic blood pressure (≥ 80 mmHg). An increase in blood pressure without a known cause (primary, essential hypertension) is the most common. Hypertension with an identified cause (secondary hypertension) is usually caused by primary aldosteronism. Sleep apnea, chronic kidney disease, obesity, or renal artery stenosis are other causes of secondary hypertension. Usually symptoms appear only with severe or prolonged course. The diagnosis is made on the basis of sphygmomanometry. Diagnostics allows you to determine the cause, assess organ damage, as well as identify other cardiovascular risk factors. Treatment includes lifestyle changes and medications, including diuretics, angiotensin converting enzyme (ACE) inhibitors, angiotensin II receptor blockers and calcium channel blockers.

Key words: arterial hypertension, ambulatory blood pressure monitoring, amlodipine, diurnal blood pressure variability, target organ damage, fixed combinations of antihypertensive drugs, antihypertensive therapy, perindopril.

Introduction.

Daily monitoring of blood pressure (DMBP) in conditions of normal human activity opens up additional diagnostic possibilities, allowing more accurate verification of the initial deviations in the circadian rhythm and blood pressure (BP), more accurately reflect the severity of hypertension and its prognosis. The most informative are the average values of blood pressure per day, day and night, maximum and minimum values of blood pressure in different periods of the day, indicators of "pressure load", variability of blood pressure, daily index (degree of nocturnal decrease in blood pressure), morning rise in blood pressure (magnitude and speed of morning rise in blood pressure). It is believed that the average values of systolic (SBP) and diastolic (DBP) blood pressure give an idea of the level of blood pressure in the patient, most accurately reflect the true level of hypertension and correlate more with the degree of damage to target organs in arterial hypertension (AH) than the results of the assessment of blood pressure in the clinic. There is a lot of evidence of the most important role of asymptomatic lesions of target organs in determining the risk of cardiovascular complications in patients with hypertension [1]. Any of the four markers of organ damage (microalbuminuria, increased pulse wave velocity, left ventricular hypertrophy and atherosclerotic plaques in the carotid arteries) is a predictor of death from cardiovascular diseases independent of SCORE stratification [2]. It is known that the risk increases with an increase in the number of affected target

organs [3]. In the study of Nedogoda S.V., Konradi A.O. et al. [4] it was also noted that the lower the percentage of decrease in blood pressure at night, the more pronounced left ventricular myocardial hypertrophy was in patients. A direct relationship between micro- and macroalbuminuria, left ventricular myocardial mass, left ventricular dysfunction, risk of cerebral complications, severity of retinopathy and average daily blood pressure values has been proven [5]. In 2010, the results of the ASCOTBPLA study on blood pressure variability appeared [6]. In this study, the effect of three types of blood pressure variability on the risk of stroke and myocardial infarction in patients with hypertension was analyzed – during the visit, daily and between visits [7]. The results indicate the role of SBP variability in DMBP as a predictor of stroke and myocardial infarction, although SBP variability during the day turned out to be less significant in prognostic terms than SBP variability between visits [7]. In international and Russian recommendations for the diagnosis and treatment of hypertension, risk stratification is currently based on the level of blood pressure, the presence of risk factors, target organ damage and associated clinical conditions. At the same time, more and more data indicate that not only cardiovascular risk, but also the effectiveness of antihypertensive therapy should be evaluated taking into account the variability of blood pressure and the daily index. In clinical practice, the use of antihypertensive drugs with a distinct positive effect on blood pressure variability may be most useful from the standpoint of organoprotection and prevention of complications [8]. However, the conducted studies do not clarify the contribution of hypotensive therapy to the development of target organ damage in patients with hypertension. The indicators of DMBP in patients with stage II hypertension have not been studied in detail, depending on the antihypertensive therapy received. Therefore, it is very important to assess the variability of blood pressure during the day in patients with stage II hypertension, depending on the components of the antihypertensive therapy received (angiotensin receptor blockers (ARBs) and diuretics or a combination of perindopril with amlodipine).

An important risk factor for the development of cerebrovascular insufficiency may not be the actual fact of an increase in blood pressure, but its instability and increased variability during the day [9]. In addition to blood pressure rises, episodes of hypotension are also a risk factor for the development of cerebral insufficiency [10]. Arterial hypotension, including at night, can be considered as a risk factor for a decrease in intellectual and mental functions [11]. In patients with hypertension with an excessive decrease in blood pressure at night, the risk of asymptomatic ischemic strokes increases [12]. The variability of blood pressure increases with age. High variability of BP correlates with the left ventricular myocardial mass index, plasma creatinine level and the degree of fundus changes, is associated with more frequent development of target organ damage and an increase in the frequency of cardiovascular complications in patients with hypertension [13]. Most cardiovascular complications develop in the morning. At this time, the maximum number of strokes,

cardiac arrhythmias, which can cause sudden death, is observed compared to other periods of the day. In the morning, physiological activation of the sympathoadrenal and renin-angiotensin-aldosterone systems occurs, leading to an increase in platelet aggregation ability, a decrease in fibrinolytic activity of blood, as well as an increase in vascular tone, including coronary and cerebral arteries. These physiological reactions, safe for a healthy person, acquire critical importance in patients with hypertension, provoking the development of cardiovascular complications. The magnitude and speed of the morning rise in blood pressure may depend on the characteristics of the daily profile of blood pressure. Patients with essential hypertension, especially in the early stages of the disease, are characterized by a large amount and speed of morning blood pressure rise compared to healthy individuals. J. D. Kobalava et al. it is noted that in persons with an excessive decrease in blood pressure at night, the morning rise is characterized by a greater magnitude and rate of pressure increase compared to patients with a normal daily index. In patients with an insufficient decrease in blood pressure during night sleep, a greater rate of increase in morning blood pressure was revealed compared to individuals with a normal daily index. It is of particular interest to study the dynamics of the rate of morning blood pressure rise in patients with stage II hypertension, depending on the hypotensive therapy received. Thus, blood pressure monitoring more fully reflects the level of hemodynamic load on the cardiovascular system and correlates more closely with the severity of its remodeling than office blood pressure. At the same time, in the development of remodeling, not only the blood pressure level is important, but its daily profile and variability. Therefore, the purpose of this study was to study in detail the indicators of DMBP in patients with stage III AG depending on the received hypotensive therapy.

Materials and methods.

The case-control observational study was performed in accordance with the standards of good clinical practice and principles. All patients, prior to the general clinical examination and daily blood pressure monitoring (DMBP), gave written informed consent to the use of the results of their studies for scientific purposes. The study included patients with previously diagnosed stage II hypertension who underwent additional examination due to the presence of complaints of episodes of increased blood pressure against the background of hypotensive therapy. The criterion for inclusion in the study was the presence of the results of daily monitoring

Blood pressure performed during the last month, and the presence of left ventricular hypertrophy according to EchoCG data, that is, the left ventricular myocardial mass index (LVMI) is more than 110 g/m2 in men and more than 89 g/m2 in women. The exclusion criteria were patients with symptomatic hypertension. 60 patients with stage II hypertension were examined (men – 30, women – 24). All the examined were outpatient patients and were under the supervision of district therapists and general practitioners in the outpatient department of the SFRNCEMP with a diagnosis of "arterial hypertension of stage II". The diagnosis of "arterial

hypertension of stage II" was established in patients on the basis of anamnesis and additional research methods (echocardiography, assessment of the fundus, functional state of the kidneys). According to the social status of the examined group of patients were employees (70%), workers of industrial enterprises and agriculture (30%). All patients received planned combined hypotensive therapy (ARB and diuretic, at an average dose of 50 mg and 12.5 mg) according to the recommendations for the management of patients with hypertension (2022), the average level of systolic blood pressure (SBP) in their office measurement was 133.4 ± 14.1 mm Hg, diastolic blood pressure (DBP) – 89.1 ±6.8 mm Hg. Due to the fact that the target blood pressure level was not reached, all patients underwent DMBP. The same patients, due to the fact that the results of the DMBP had changes in the indicators of the daily profile, antihypertensive therapy (perindopril with amlodipine) was adjusted at an average dose of 5/5 mg per day, which the patients received for 3 months. After 3 months of therapy, according to office measurements, the average level of SBP was 119.2 ± 7.4 mm Hg, the average level of DBP was 70.1 ± 5.8 mm Hg. After 3 months, they underwent DMBP. In this paper, an attempt was made to analyze the possibilities of antihypertensive therapy (ARBs and diuretics) at the stage of inclusion in the study and 3 months after the correction of therapy and its replacement with combined therapy with perindopril and amlodipine (fixed combination of Prestance, Servier) according to daily blood pressure monitoring. In addition to the general clinical examination, all patients at the stage of inclusion in the study and 3 months after the change of antihypertensive therapy were monitored daily blood pressure (BP-3400 monitor) in a discrete mode and lasted at least 24 hours. The intervals between blood pressure measurements were 30 minutes during the day and 60 minutes at night. Conducting the study in an outpatient setting allowed the use of fixed time periods of sleep (from 23 to 7 hours) and wakefulness (from 7 to 23 hours). The monitor cuff was placed on the middle third of the shoulder. Before the start of the study, verification measurements of blood pressure were carried out in an auscultative way using a conventional tonometer, and then by means of an installed monitor; if the latter demonstrated significant and stable differences between the measured values from the standard (by more than 5 mm Hg. article), they were taken into account when interpreting the results of the study as a systematic error. The patient was instructed about the need to keep a self-observation diary, in which he should enter data on episodes of physical and emotional activity. At the end of the study, the data were processed according to a special program. Mathematical data processing allowed us to obtain a number of the above indicators used in the practical evaluation of daily blood pressure monitoring data. According to the DMBP data, the following indicators were calculated: average systolic blood pressure during the day (SBPd, mmHg. average diastolic blood pressure during the day (DBP d, mmHg), SBP at night (SBP n, mmHg), DBP at night (DBP n, mmHg). In addition, the variability of SBP and DBP was determined during the daytime (VAR SBP d, VAR DBP d, mmHg) and at night (VAR SBP

n, VAR DBP n, mmHg), the degree of nocturnal decline of SBP and DBP (SNS SBP and SNS DBP, %), the rate of morning rise of SBP, DBP (SOUP GARDEN, SOUP DBP, mmHg / hour), as well as time indices GARDEN, DBP (IV GARDEN, IV DBP, %), area indices given GARDEN and DBP (IPP GARDEN, IPP DBP). The time index indicates in what percentage of the total duration of monitoring (or in what percentage of measurements) blood pressure was higher than normal. The conditional gradation of the norm for daytime is 140/90, and for night – 120/80 mm Hg. This indicator has a high prognostic value and can be used both for the diagnosis of hypertension and for evaluating the effectiveness of drug therapy. The area index shows for what time over a 24 —hour period the patient has increased blood pressure. Variability was assessed in the daytime and at night according to the standard deviation of SBP and DBP (VAR SBP and VAR DBP, mmHg). The variability of SBP exceeding 14 mmHg during the day and/or 15 mmHg at night was considered to be increased, DAP — 14 and 13 mmHg, respectively. The rate of morning rise in blood pressure was calculated between 4 and 10 o'clock in the morning. Based on the assessment of the daily index (SI), the types of daily blood pressure curves were distinguished: dippers – patients with sufficient nocturnal decrease in blood pressure (SI from 10 to 20%), non-dippers — patients with insufficient nocturnal decrease in blood pressure (SI from 0 to 10%), over-dippers – patients with excessive nocturnal decrease in blood pressure (SI more than 22%), night-peakers are patients whose blood pressure is higher at night than during the day (SI less than 0%).

Results.

The age of the examined AH patients ranged from 35 to 75 years, two thirds of them were women. 36 (60%) patients were overweight, 20 (33.3%) were obese, up to morbid. 40% had type II diabetes mellitus. Hypertension was diagnosed from 1 to 20 years ago, all patients received combined antihypertensive therapy, which included angiotensin II receptor blockers and a diuretic. At the stage of receiving combination therapy (perindopril and amlodipine), 4 patients dropped out of the study (2 due to refusal of therapy, 2 did not perform daily blood pressure monitoring). In patients with hypertension receiving ARB and diuretic, despite the antihypertensive therapy, there was systolic hypertension of the 1st degree during the day and at night and there was a statistically significant increase in VAR SBP d, VAR SBP n and VAR DBP n in comparison with the group of patients receiving a combination of perindopril and amlodipine for 3 months.

Initially, in the group of patients receiving a combination of ARBs and diuretics, a statistically significant (ANOVA, p=0.038) smaller proportion of people with preserved normal circadian rhythm (dippers) was observed with a simultaneously larger number of patients with impaired circadian rhythm of blood pressure. Moreover, the structure of the pathological profile was dominated by patients with insufficient nocturnal decrease in blood pressure (non-dippers). In addition, the proportion of night-peaker

among people on ARB and diuretic therapy was 2 times higher than among patients 3 months after the appointment of perindopril and amlodipine.

Discussion.

Thus, in patients with stage II arterial hypertension who received planned hypotensive therapy (ARB and diuretic), the daily blood pressure profile was characterized by an increase in SBP and DBP during the day, which was combined with a violation of the circadian rhythm due to an insufficient decrease in blood pressure at night and a rapid morning rise in blood pressure. An increase in the hypertensive load on the target organs was recorded both during the day and at night, which was combined with the dynamics of blood pressure variability indicators. In the group of patients who received timely correction of hypotensive therapy, there was a significant improvement in hemodynamic parameters: the daily blood pressure targets were achieved, there was a significant decrease in variability during the day, the rate of morning blood pressure rise, and the proportion of patients with a normal daily blood pressure profile increased. Taking into account changes in the circadian rhythm of blood pressure, such indicators as blood pressure variability, when choosing an antihypertensive drug, one should not forget about the special position of Ca-blockers, which are leaders in controlling blood pressure variability during monotherapy and the only group that reduces blood pressure variability when added to a combination. In the ASCOT study, a more significant decrease in intravisit blood pressure variability was demonstrated when using a combination of perindopril with amlodipine, and further studies with the appointment of combination therapy with perindopril and amlodipine demonstrated a decrease in intervisit blood pressure variability. The appointment of any antihypertensive drug for a doctor is not only a reduction in blood pressure, which can be measured in millimeters, but also saving lives and improving the quality of life for the patient and his loved ones. The data obtained coincide with the results of long-term follow-up of patients participating in clinical trials. Thus, in the ASCOT-Legacy study, in which patients receiving antihypertensive therapy with a combination of amlodipine / perindopril had a long-term positive effect, affecting a reduction in mortality (by 21%) and stroke (by 29%), even 11 years after discontinuation of therapy. It can be assumed that taking amlodipine / perindopril for 5 years created a "safety margin" of the body for many years. These ASCOT-Legacy studies emphasize the importance of reducing blood pressure variability and have demonstrated a significant reduction in the risk of atrial fibrillation, which leads to a decrease in the number of strokes and coronary events [6].

Conclusion.

In order to achieve the target level of blood pressure within the framework of dispensary observation for district therapists and general practitioners, it is advisable to assess in detail the circadian rhythm of blood pressure, the variability of blood pressure during the day, the rate of morning rise in blood pressure in patients with stage II hypertension, especially at the stage of selection of hypotensive therapy. The

use of a combination of perindopril with amlodipine allows patients with stage II hypertension to reach the target range of blood pressure during the day, reduce the variability of blood pressure and normalize the rate of morning rise in blood pressure

REFERENCES:

1. Kamberi LS, Bedri Bakalli A, Muhamet Budima N, Budima NM, et al. Pleiotropic and Lipid-lowering Effects of Statins in Hypertension. *Mater Sociomed.* 2012;**24**(2):84–86.
2. Kamberi LS, Bedri Bakalli A, Muhamet Budima N, Budima NM, et al. Pleiotropic and Lipid-lowering Effects of Statins in Hypertension. *Mater Sociomed.* 2012;**24**(2):84–86.
3. Ritz E, Menne J, HallerH H. Prevalence of microalbuminuria in type 2 diabetes: lessons learned from the ROADMAP study. *Nephrol Dial Transplant.* 2012;**27**(Suppl 4):28–30.
4. Muntner P, Carey RM, Gidding S, et al. Potential US Population Impact of the 2017 ACC/AHA High Blood Pressure Guideline. Circulation 2018; 137:109.
5. Yoon SS, Gu Q, Nwankwo T, et al. Trends in blood pressure among adults with hypertension: United States, 2003 to 2012. Hypertension 2015; 65:54.
6. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension 2018; 71:e13.
7. Williams B, Mancia G, Spiering W, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension. Eur Heart J 2018; 39:3021.
8. Flack JM, Calhoun D. The ACC/AHA and ESC/ESH Hypertension Guidelines: Contrasting Versions of Idiosyncratic Excellence. Am J Hypertens 2019; 32:705.
9. Wald DS, Morris JK, Wald NJ. Randomized Polypill crossover trial in people aged 50 and over. PLoS One 2012; 7:e41297.
10. Chow CK, Atkins ER, Hillis GS, et al. Initial treatment with a single pill containing quadruple combination of quarter doses of blood pressure medicines versus standard dose monotherapy in patients with hypertension (QUARTET): a phase 3, randomised, double-blind, active-controlled trial. Lancet 2021; 398:1043.
11. Yusuf S, Joseph P, Dans A, et al. Polypill with or without Aspirin in Persons without Cardiovascular Disease. N Engl J Med 2021; 384:216.
12. Egan BM, Bandyopadhyay D, Shaftman SR, et al. Initial monotherapy and combination therapy and hypertension control the first year. Hypertension 2012; 59:1124.

13. Mourad JJ, Waeber B, Zannad F, et al. Comparison of different therapeutic strategies in hypertension: a low-dose combination of perindopril/indapamide versus a sequential monotherapy or a stepped-care approach. J Hypertens 2004; 22:2379.

14. MacDonald TM, Williams B, Webb DJ, et al. Combination Therapy Is Superior to Sequential Monotherapy for the Initial Treatment of Hypertension: A Double-Blind Randomized Controlled Trial. J Am Heart Assoc 2017; 6.