
LIFE SCIENCES

**EVALUATION OF BLOOD PRESSURE VARIABILITY
IN CHRONIC HYPERTENSION IN PREGNANT
WOMEN**

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Abstract: The risk of developing gestational and perinatal complications increases with arterial hypertension, while inadequate blood pressure control on the one hand is accompanied by an increase in the number of adverse outcomes for both mother and fetus. The presented study aimed at studying the specific features of blood pressure variability in pregnant women arterial hypertension and evaluation of the effectiveness of antihypertensive therapy on the parameters of BP variability, pregnant women with chronic arterial hypertension of pregnant women. It was revealed that in patients with chronic arterial hypertension during pregnancy, the level and variability of blood pressure were elevated. Disruptions in circadian rhythm of blood pressure, decrease in night-time decrease in blood pressure, increase in general peripheral vascular resistance from the first weeks of pregnancy, increase the mass of the left ventricular myocardium and its concentric remodeling by the beginning of the third trimester, which is a predictor of preeclampsia. It was revealed that Amlodipine restores the diurnal blood pressure profile by 2.7% ($p = 0.05$) more efficiently than nifedipine, does not increase the variability of blood pressure, does not violate the daily rhythm of blood pressure, does not reduce the weight of newborns and does not adversely affect hemodynamic parameters.

Keywords: blood pressure, chronic arterial hypertension, pregnancy, variability, target organ damage, cardiovascular complications.

Currently, hypertension has come to the first among the causes of death in pregnant women. Treatment of this disease in pregnant women is rather difficult, since the doctor deals simultaneously with two patients - a mother and a child, whose interests do not always coincide. Hypertension during pregnancy is a common cause of maternal and perinatal morbidity and mortality. It is observed in 5-15% of cases of gestation [4-6].

Over the past 10-15 years, the frequency of hypertension in pregnant women in developed countries has increased by almost a third. In about 30% of cases, hypertension develops before the onset of pregnancy (chronic hypertension), in 70% during gestation (gestational hypertension and preeclampsia-eclampsia) [6]. Preeclampsia occurs in the United States with a frequency of 1 case per 1000 delivers [5]. In women with preeclampsia and eclampsia, the risk of severe complications (rupture of the placenta, thrombocytopenia, disseminated intravascular coagulation, pulmonary edema, and aspiration pneumonia) increases 3-25 times [5]. The physiological characteristics of the cardiovascular system, depending on the developing pregnancy, sometimes create a situation where it is difficult to distinguish between physiological and pathological changes [7]. After detecting hypertension in a pregnant woman, the patient should be examined to clarify the origin of the hypertensive syndrome, determine the severity of hypertension, identify associated organ disorders, including the state of the target organs, placenta and fetus.

Blood pressure variability (BP) is a fluctuation of blood pressure that exceeds the limits of physiological values. Daily blood pressure monitoring (DBPM) in the context of normal human activity opens up additional diagnostic capabilities, allowing you to more accurately verify the initial deviations in the daily rhythm and BP, more accurately reflect the severity of hypertension and its prognosis in terms of cardiovascular complications. ABPM provides important information about the state of the mechanisms of cardiovascular regulation, in particular, allows you to determine the circadian rhythm of blood pressure, night hypotension and hypertension, the dynamics of blood pressure over time and the uniformity of the antihypertensive effect of drugs [1, 2, 3].

When analyzing the data obtained in the ABPM, the most informative are the average values of blood pressure per day, day and night, the maximum and minimum values of blood pressure at different periods of the day, indicators of "pressure load", blood pressure variability, daily index (degree of night BP decrease), morning rise in blood pressure (magnitude and speed of morning rise in blood pressure). It is believed that the mean values of systolic (SBP) and diastolic (DBP) blood pressure give an idea of the level of blood pressure in a patient, most accurately reflect the true level of hypertension and more correlate with the degree of target organ damage (TOD) in arterial hypertension (AH), than the results of the assessment of blood pressure in the clinic. In addition to the average values of blood pressure, important indicators affecting the prognosis are systolic variability (VSBP) and diastolic (VDBP) blood pressure and the daily index of SBP and DBP and the characteristics of the morning pressure rise. In a series of studies, it was shown that increased blood pressure variability is an important and independent factor in PTO and a high risk of cardiovascular events [2, 3].

It is known that high blood pressure variability depends largely on the degree of decrease in blood pressure at night, the magnitude and speed of morning blood pressure rise, which, in turn, contributes to the development of endothelial dysfunction, which can lead to atherogenesis [4]. Endothelial disorders and increased vascular tone affect blood pressure and its variability. Patients with a high variability of blood pressure, as a rule, are individuals with abnormal neurohumoral activity, especially with increased activity of the sympathetic nervous system, as it increases vascular tone, especially in the morning hours, which leads to an increased risk of CC. Among such patients, pregnant women with hypertension take a special place. There are not enough studies devoted to studying the dynamics of various indices of the diurnal blood pressure profile, its relationship with the structural and functional state of the myocardium, peripheral vessels and metabolic abnormalities in pregnant women with hypertension, some are contradictory. Due to the high risk of CVD in patients who had increased blood pressure during pregnancy, there are concerns about the lack of standard therapy, which was the reason for conducting this study.

Objective: to study the features of blood pressure variability in pregnant women with chronic arterial hypertension and to evaluate the effectiveness of antihypertensive therapy on the parameters of blood pressure variability.

Materials and research methods. Pregnant women with chronic arterial hypertension in pregnant women (HPW) were under observation - 61 patients aged from 18 to 42 years, cf. age 28 ± 5.6 years. The study was conducted on an outpatient basis, monitoring the condition of the patients was carried out in conjunction with obstetrician-gynecologists. None of the patients with CAH have undergone continuous antihypertensive therapy, and 28% of women used different antihypertensive drugs on a regular basis.

In patients with CAH, that is, with an increase in blood pressure before the 20th week of pregnancy, registered before pregnancy and continuing 6-12 weeks after delivery, with a high probability of developing hypertension and other cardiovascular complications. At the end of I, in II (20-22 week) and III (30-32 week) trimesters, pregnant women underwent clinical and laboratory studies, Smad, echocardiography (EchoCG). The outcomes of pregnancy and childbirth were analyzed, the observation was carried out within 6-12 weeks after delivery. Smad in pregnant women was performed on an outpatient basis at 10-11, 32-33 weeks of gestation, blood pressure was measured in standard mode at intervals of 15 minutes during the day, at night - 30 minutes. Calculated average per day, day and night numbers of systolic and diastolic blood pressure. The degree of nightly decrease in blood pressure, or daily index (DI), was determined as the ratio of the difference between day and night blood pressure to day blood pressure, expressed in%. To characterize the variability of blood pressure used the standard deviation rate (Std) systolic

and diastolic blood pressure. The temporal hypertonic index (HI), or pressure load, was calculated for the daily systolic and diastolic blood pressure in percent, and the intervisit (weekly), intravisit (at each visit) blood pressure variability was also estimated.

Biometric analysis was carried out using the STATISTICS-6 package and Microsoft Excel capabilities. The average sample values of quantitative traits are given in the text as $M+SE$, where M is the sample mean, SE is the standard error of the mean. In all statistical analysis procedures, the critical significance level p was taken to be $p = 0.05$.

Results and its discussion. When assessing the variability of blood pressure, it turned out that the majority of patients in the study group not only did not control the clinical blood pressure, but they had an adverse daily blood pressure index. The most serious violations were noted in relation to a decrease in ABP during night hours, 27% of pregnant women included in the study had a normal (optimal) degree of nightly decline in BP (dipper), while 13% of patients had anormal indicator of the daily DBP index. Patients with an insufficient degree of nocturnal decrease in DBP (non dipper) were 30%. A sustained increase in night, night peaker was observed in 10% of patients, but was not detected in relation to DBP. Patients with a high degree of nighttime decline in SBP and dad (over dipper) were approximately the same amount. Thus, at the time of inclusion in the study, the patients had not only uncontrolled clinical blood pressure, but also blood pressure at night, especially the MAP. As is well known, persistent high SBP in the night and early morning hours is a risk factor for PTO, especially left ventricular hypertrophy, impaired renal function and development of MTR. In this regard, there is a serious question about the need for antihypertensive therapy for pregnant women (subject to term) with various forms of hypertension to prevent further complications for both the mother and the fetus.

The dynamics of the indices of the daily profile of blood pressure during uncomplicated pregnancy in patients with CAHP showed an increased level of blood pressure and its variability throughout the gestational period. The dynamics of the daily blood pressure profile in patients with CAHP by the end of pregnancy showed an increase in blood pressure of approximately 7-8 / 4-5 mm Hg, the blood pressure drop was reduced by 4/4% day-night.

The development of preeclampsia in pregnant women in patients with CAH was associated with a decrease in day-night pressure drop and an increase in blood pressure variability. Each of these factors is involved in the formation of target organ damage and increases the risk of cardiovascular complications in patients with hypertension [1, 3, 4]. Reducing the difference in day and night blood pressure ($CI < 10\%$) in the second trimester in all pregnant women (with initially normal blood pressure and

CAG) increased the risk of developing PE by 2.1 times ($P = 0.001$). The combination of two factors - diastolic blood pressure, diurnal > 60 mm Hg. + SI $< 10\%$ - increased the risk of PE development by 7.4 times ($P = 0.0005$). The relative risk of developing PE in pregnant women with CAG with CI $< 10\%$ increased fourfold in the first trimester ($P = 0.01$). There is no doubt that for the early diagnosis of PE in pregnant women with CAH, a comprehensive (clinical, laboratory and instrumental) approach should be used, in which the indices of the daily blood pressure profile in the first half of pregnancy can be crucial.

Indicators of the level of clinical blood pressure in the studied groups were significantly elevated. In 55.7% of patients with CAH, the level of clinical BP corresponded to grade I AH, in 23.1% of grade II AH, in 21.2% of AH III grade. Average daily blood pressure levels in the CAH groups were elevated compared with the group without the burdened gestational history, i.e. the presence of increased blood pressure during previous pregnancies. A decrease in day / night pressure drop (SI $< 10\%$, non-dipper) was observed more often in the CAH group than in GAG patients (36.6% versus 12%, $P = 0.03$), and only in one woman in the comparison group. The decrease in the daily rhythm of blood pressure is associated with the damage to target organs in hypertension and indicates a more severe course of the disease [4,7] and an increase in the activity of the sympathetic nervous system [3]. Increased pressure drop (SI $> 20\%$, i.e. over-dipper) was also often observed in the studied groups: in 33% of cases of the CAG group.

The study of the clinical effects of antihypertensive drugs for CAG in pregnant women was performed in four groups: I - amlodipine 10 mg / day (from 28 to 34 weeks of gestation), prolonged form, II - nifedipine 10 mg (only with increased blood pressure), short-acting, III - metoprolol 50 mg / days in comparison with group (IV) patients who received metoprolol SR 23.75 mg / day. The level of office BP at 22-24 weeks of pregnancy before the start of therapy in groups I, II, III and IV was $154.5 \pm 2.2 / 89.9 \pm 1.0$ mm Hg. Art., $149.7 \pm 2.1 / 90.9 \pm 1.6$ mm Hg. Art., $149.9 \pm 2.0 / 91.3 \pm 1.4$ mm Hg. Art. and $154.4 \pm 1.9 / 90.4 \pm 1.1$ mm Hg. Art., respectively, and not significantly different.

The average daily blood pressure in all groups did not differ significantly. The effectiveness of the treatment was evaluated on the basis of indicators of office BP, as well as according to the SMAD. The criterion of effectiveness was considered a reduction in the level of clinical blood pressure below 140/90 mm Hg. The data of average daily blood pressure values were compared with blood pressure indicators in the comparison groups at the same time of pregnancy. When patients were re-examined at 32-34 weeks, the level of the average per day BP in the groups was not statistically significantly different. The diurnal rhythm of blood pressure in all observation

groups was preserved and was not statistically significantly changed during the observation period, which can be attributed to both the short observation period and the presence of a persistent increase in blood pressure in CAG.

The use of amlodipine had a positive effect on the variability of blood pressure, an undesirable effect of short-range nifedipine is its ability to increase the variability of blood pressure, in this group significantly increased rates of blood pressure variability were noted. Preeclampsia in late pregnancy developed in 10-24% of women participating in the study, in the amlodipine group to a lesser extent, most rarely in the metoprolol SR group.

Everyone has patients taking amlodipine, the pregnancy ended in urgent delivery, the observation dynamics showed the lowest incidence of postpartum complications. In the groups with metoprolol therapy (both short-term and long-acting), there were patients who required cesarean section or had preterm labor complicated by postpartum hemorrhage and accompanied by hypoxia of the fetus. So, among the studied drugs that had the same antihypertensive effect in pregnant women with CAH, the benefits of amlodipine were revealed - the ability to maintain a normal daily rhythm of blood pressure, not to increase the variability, to positively influence the state of the mother, not to cause metabolic abnormalities in the mother and not to reduce fetal weight. In patients taking nifedipine, there was a tendency towards the most favorable course of pregnancy and labor, but in 49% of cases it was accompanied by a reflex tachycardia in the mother with a paradoxical decrease in the number of heart contractions in the fetus to 95.5 ± 5.3 beats / min in the fetus.

Thus, even with a short hypertensive history in pregnant women, an increase in pulse pressure during the day is determined, especially in daytime and with increased blood pressure variability, which is a predictor of pregnancy and childbirth complications.

In patients with CAH during pregnancy, the level and variability of blood pressure were increased, the mass of the left ventricular myocardium was increased.

A predictor of PE in pregnant women with initially normal levels of blood pressure and in patients with CAH are: disruption of the circadian rhythm of blood pressure with a decrease in night-time blood pressure reduction, an increase in total peripheral vascular resistance from the first weeks of pregnancy, an increase in the mass of the left ventricular myocardium and its concentric remodeling by the beginning of the third trimester. Disruption of the circadian rhythm of blood pressure (CI <10%) is associated with an increase in the risk of developing PE in women with initially normal levels of blood pressure by 3.3 times, in pregnant women with CAH - 4 times.

Amlodipine, nifedipine and metoprolol in pregnant women with CAH have the same antihypertensive effect and do not have a significant adverse effect on metabolic parameters. Amlodipine restores the daily blood pressure profile by 2.7% ($p = 0.05$) more efficiently than nifedipine, does not increase the variability of blood pressure, does not violate the daily rhythm of blood pressure, does not reduce the weight of newborns and does not adversely affect hemodynamic parameters.

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