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THE SUCCESSFUL CLINICAL CASE OF A SEVERE ARTERIAL HYPERTENSION MANAGEMENT DURING PRECONCEPTION AND PREGNANCY

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Abstract:

A timely diagnosis and rational management of arterial hypertension (AH) in pregnancy are of the great importance among the practicing doctors. According to the World Health Organization (WHO), different types of hypertension in pregnancy took the 2nd place in maternal mortality structure in 2014 causing at least 76 thousand of maternal and 500 thousand of fetal deaths annually [3, 11]. Over the past decade, the 4th place of mortality rate in fetus is caused by hypertension and its complications. The maximum rate of fetal mortality was indicated at women 35 years of age or older. Perinatal mortality rates and the frequency of preterm births (10–12%) in AH patients prevail greatly over the corresponding values in relatively healthy pregnant women. AH increases the risk of the premature detachment of a normally positioned placenta, can cause cerebral circulation disorder, retinal detachment, pre-eclampsia, eclampsia, massive coagulopathic bleeding, placental insufficiency, and, in severe cases, asphyxia and fetal death [5,6]. The long-term prognosis for such patients is also unfavorable: the frequency of obesity, coronary heart disease, diabetes mellitus and stroke increases; and children born to such mothers suffer from metabolic, cardiovascular and hormonal diseases.

A limited number of antihypertensive medications meet the safety criterion for the fetus and, thus, could be used in pregnancy. In case of monotherapy failure, combination therapy is administered to the patient.

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INTRODUCTION:

Arterial hypertension in pregnancy is a national medical problem. General practitioners, cardiologists and obstetricians-gynecologists face it in their daily activities. Hypertensive conditions in pregnancy result in pathologies in women and in fetus causing disabilities of the latter [9]. Hypertensive disorders and pre-eclampsia are indicated by the World Health Organization as acute problems, which annually possess the leading positions in maternal mortality [9, 11]. Despite the great amount of studies in this area, hypertension in pregnancy remains one of the most important unsolved medical problems. Small vessels dysfunction leads to dysregulation of blood pressure (BP) and microcirculation in body tissues. Another important point is that gestational hypertension can often cause the pathology development in mother and in fetus resulting in a child's disability [11, 14]. It is noted that in infants of mothers with pre-eclampsia (PE) or hypertensive disorders not only a perinatal morbidity increases, but also mental and physical development suffers.

Arterial hypertension in pregnant women is characterized by elevated blood pressure, the main criterion of which are systolic BP levels ≥ 140 mmHg and/or diastolic BP ≥ 90 mmHg. [1]. According to the International Federation of Gynecology and Obstetrics (FIGO, 2016), AH is registered in 5–10% of pregnant women [8], while in the Russian Federation the rates are higher - 7–30%. There are the following clinical AH types in pregnancy: 1) AH existing prior pregnancy - chronic AH (CAH) or hypertensive disease (HD) also known as symptomatic hypertension; 2) gestational arterial hypertension (GAH); 3) CAH, complicated by PE; 4) PE / eclampsia. A woman with AH who is planning a pregnancy must have a careful preconception care provided, which includes the administration of an adequate basic therapy and safe medications prescription. It is recommended [2] to hospitalize a patient with hypertension three times during the pregnancy course. The first hospitalization should be arranged before the 12th week of the pregnancy in order to make a decision of the pregnancy continuation or abortion (when indicated). The second hospitalization is recommended on 28^{th}–32^{d} week, when a patient is carefully examined, administered therapy is adjusted and placental insufficiency is treated. The third hospitalization happens when preparing a woman for a childbirth, 2-3 weeks before the delivery.

The main drugs for a planned therapy in pregnant women with hypertension are [1]: methyldopa (B-safety level) as the first-line drug, nifedipine with a slow drug release (the level of evidence is C) as the first- and/or the second-line drug, metoprolol succinate (C) – as a drug of choice among β-blockers – could be used starting from the 12^{th} week of the pregnancy. Along with the above-mentioned drugs, a lot of experience has been gained in the use of amlodipine (C), verapamil (C), bisoprolol (C), nebivolol (C), which is reflected in a number of reviews and recommendations on the management of pregnant women [4]. Pindolol (B) and labetalol (B) are also administered in a range of countries. In some situations, the other drugs are used: clonidine (C), indapamide (B), hydrochlorothiazide (C) and others [8]. In case monotherapy failure, combination therapy is administered. A rational combination is a calcium antagonist (most commonly used long-acting nifedipine) + β-blocker [1].

The reserved drugs should not be prescribed for AH treatment in pregnancy unless the administration of the main drugs is ineffective or associated with drugs intolerance. The choice of medication is a subject to medical commission, a clinical pharmacologist or a specialist in safe pharmacotherapy during pregnancy approval [2]. The original drugs are of much preference due to the safety reasons.

RESEARCH RESULTS:

Twenty-four years old patient K. of a normosthenic physique with a severe (3^{d} stage) arterial hypertension has been managed for several years in Belgorod regional clinics, after being hospitalized and carefully examined in 2015. It should be noted that the patient was not diagnosed with the secondary hypertension while being observed at the place of residence. The long-lasting and ineffective attempts of making a diagnosis and to administering a proper treatment significantly influenced the patient's attitude toward the doctor and the institute of medicine itself. Eventually, she turned to the Regional Center of Safe Medication during Pregnancy and Breastfeeding ("BelTIS") in order to have an antihypertensive therapy administered.

During the first appointment in June 2016, the patient indicated the episodes of the elevated SBP to 180-220 mm Hg (habitual blood pressure - 140/90 mmHg). That time she administered perindopril irregularly ("Prestarium") with a positive effect resulting in BP decrease to 180/140 mmHg. In terms of the preconception care, it was recommended to withdraw perindopril and to administer nifedipine-retard ("Adalat", "Corinfar"). Due to the arisen side effects (tachycardia, hypotension), the patient withdrawn the

drug by herself, and at the next visit (visit-2) it was decided to administer another calcium antagonist – amlodipine (metoprolol was suggested as an alternative option). Ten days after the prescription of the original amlodipine ("Norvask") at a dose of 5.0 mg [7], the patient did not have any complaints, indicating the improvement of general well-being and a decrease in the blood pressure to 160/90 mmHg (visit-3). However, a month later (visit-4), it turned out that the patient reduced the dosage of amlodipine by half due to swelling legs. As a result, the BP began to rise again and during the next appointment totaled 170/95 mmHg. Therefore, a combination therapy was administered (Fig. 1).

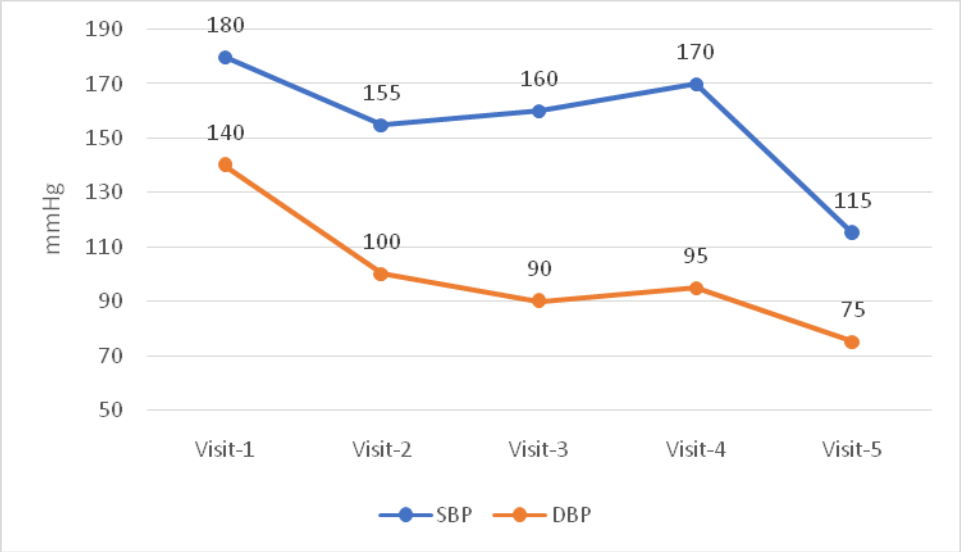

Fig. 1. The dynamics of the blood pressure during the treatment course

In order to choose an adequate pharmacotherapy in the preconception period, therapist planned to compare the efficiency of two antihypertensive therapy regimens: the first one – amlodipine 2.5 mg once a day + methyldopa ("Dopegit") 0.25 3 times a day – for 1-1.5 weeks, the second regimen for 1-1.5 weeks – amlodipine 2.5 mg once a day + bisoprolol ("Concor") 2.5 mg once a day. The efficiency of the regimens was compared (visit-5) (Fig. 2), and the second regimen was administered for the patient management – amlodipine 2.5 mg once a day + bisoprolol 2.5 mg once a day + magnesium lactate + pyridoxine 0.47/0.005 - 6 tablets a day. Over the next 6 months (visits 6 and 7), following the therapist recommendations, the patient indicated the improvement of the general well-being and the blood pressure leveling in the range of 110-120/70-80 mmHg.

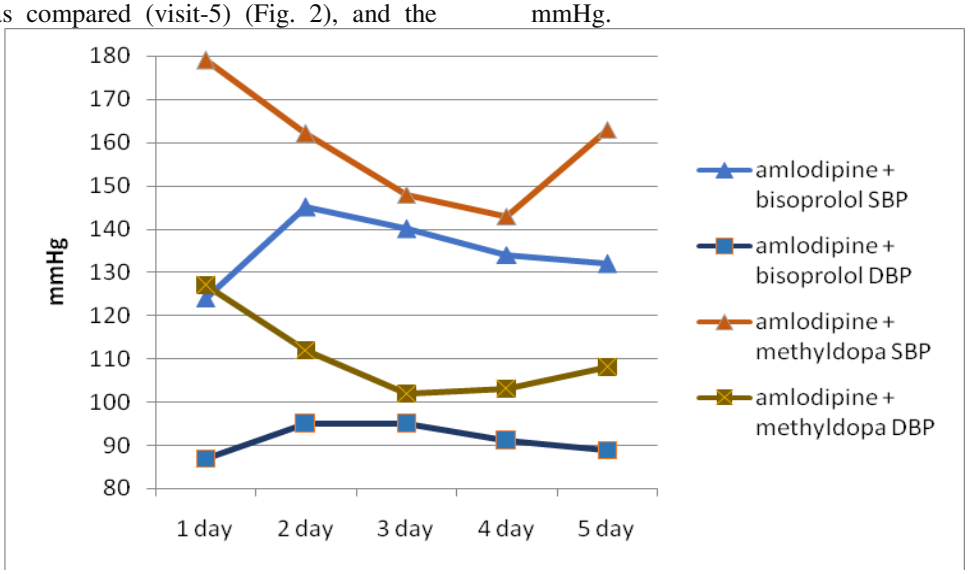

Fig. 2. The comparison of the efficiency of AH therapy regimens depending on the level of the maximum BP

The next appointment (visit-7) was on the 6th week of the pregnancy in March 2017. After becoming pregnant the combination of drugs was not changed (the average level of the BP during periodic appointments was 116/81 mmHg) and was administered during the whole pregnancy course (visits 8-10) (fig. 3). On the 31st-32d weeks of the pregnancy the patient indicated hypotension resulting in adjusting the bisoprolol dosage to 1,25 mg a day. After that, the BP normalized till the end of the pregnancy.

The pregnancy course was accompanied by hydramnion (the amniotic fluid index is 22.4) and a thin placenta of 16 mm on 20th week term (II ultrasound screening). No infections were spotted during the infectious screening. The metabolic therapy was prescribed to improve an uteroplacental blood current. Acetylsalicylic acid in a dose of 75 mg a day was administered up to the 36th week of the pregnancy for the prevention of pre-eclampsia and eclampsia [3].

On the 36th week of the pregnancy, during the next visit to "BelTIS" (the 10th visit), a phone consultation regarding management tactics was held by Natalia A. Chukhareva – an employee of the Department of therapeutic pathologies in pregnant of FSBI "National Medical Research Center of Obstetrics, Gynecology and Perinatology named after V.I. Kulakov". As a result, it was decided to manage the patient without hospitalization till the childbirth with a regular BP monitoring and urine analysis. Also, it was recommended to continue the ongoing antihypertensive treatment regimen during the prenatal, patrimonial and postpartum periods. This pregnancy was successful and in November 2017 a full-term baby was born on the 40th gestational week. The disappointing fact is that the doctors of the postpartum department, without consulting with the clinical pharmacologists who prescribed treatment to the patient during the preconception period and the pregnancy, made an irrational decision about the artificial feeding, motivating that with an unsafe hypotensive therapy administered to the mother.

During the phone consultation in April 2018 the patient admitted the satisfactory well-being with a stable normotension supported by a combination therapy (amlodipine 2.5 mg + bisoprolol 2.5 mg).

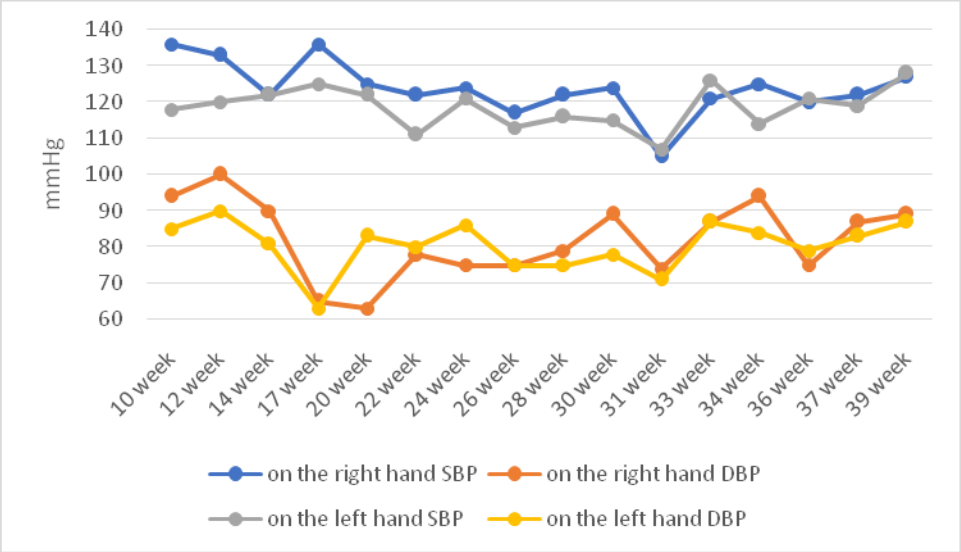

Fig. 3. The dynamics of the patient's blood pressure during the pregnancy.

CONCLUSIONS:

The rational arterial hypertension therapy in pregnancy is a necessary but complicated issue, since it requires considering drugs' influence on the mother and the fetus. Despite an initial severe course of such extragenital disease as arterial hypertension (arterial hypertension of the 3d stage), correctly administered pharmacological therapy during the preconception period and throughout the pregnancy makes it possible to ensure a successful result –

delivering of a healthy, full-term baby. It also helps avoiding such complications of the second half of the pregnancy as: pre-eclampsia, eclampsia, detachment of a normally positioned placenta.

It is necessary to improve the level of knowledge and the level of collaboration of the adjacent specialists in similar complicated and specific clinical situations.

Conflicts of interest

The authors have no conflict of interest to declare.

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