

**EFFECTIVENESS OF ANTIHYPERTENSIVE THERAPY IN PREGNANT WOMEN**

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ABSTRACT

Arterial hypertension in pregnant women - The criteria for diagnosing arterial hypertension in pregnant women are an increase in systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg. Elevated blood pressure should be confirmed with two measurements using a mercury sphygmomanometer (V tone is used to register diastolic blood pressure) in a sitting position or an aneroid device. It is possible to measure blood pressure lying on the left side. Only validated tonometers and devices for outpatient monitoring should be used. The results of outpatient blood pressure monitoring make it possible to predict outcomes more accurately than the office measurement of blood pressure. Gestational hypertension, accompanied and not accompanied by proteinuria, is an increase in blood pressure associated with pregnancy itself. Complicates the course of pregnancy in 6-7% of cases. Preeclampsia is a pregnancy-specific syndrome that develops at 21 weeks gestation. and more and is characterized by de novo arterial hypertension in combination with proteinuria ≥ 0.3 g/day. Preeclampsia is a systemic disease that causes changes in the body of both mother and fetus. Edema is no longer considered a diagnostic criterion today, since their frequency in the normal course of pregnancy reaches 60%. In general, preeclampsia complicates the course of pregnancy in 5-7% of cases, but its frequency increases to 25% in women with arterial hypertension before pregnancy. Preeclampsia is more common during the first pregnancy, multiple pregnancies, bladder drift and diabetes mellitus. Preeclampsia is gestational hypertension, which is accompanied by proteinuria (≥ 0.3 g / day in daily urine or ≥ 30 mg /mmol of creatinine in a single portion of urine). Gestational hypertension develops from 21 weeks of gestation and in most cases passes within 42 days after delivery. It leads to deterioration of organ perfusion. It is combined with placental insufficiency, which often leads to a deterioration in fetal growth. Additionally, preeclampsia is one of the most common causes of prematurity. Its share in the structure of the causes of the birth of children with very low body weight (less than 1500 g) is 25%, and in the structure of the causes of premature birth – 50%. Severe preeclampsia is the cause of intracranial hemorrhages and acute renal failure, which together account for up to 90% of the causes of all deaths in pregnancy with preeclampsia.

Keywords: Hypertension in pregnant women, gestational hypertension, morphofunctional parameters of the heart, central α_2 -agonists, β -blockers, calcium antagonists.



INTRODUCTION

Arterial hypertension (AH) is currently one of the most common forms of pathology during pregnancy. According to WHO, it is associated with 20-33% of maternal deaths. In Uzbekistan, hypertension occurs in 5-30% of pregnant women and, recently, there has been a tendency to increase this indicator. The development of hypertension during pregnancy can lead to detachment of the normally located placenta, cause the development of severe forms of gestosis, impaired cerebral circulation and retinal detachment.

The increase in the frequency of hypertension during pregnancy is due to an increase in the number of women with diabetes, obesity, cardiovascular diseases and the age of pregnant women (over 40 years).

Despite significant progress in the treatment of hypertension in recent years, approaches to hypotensive therapy of pregnant women have not changed. This is due to the negative effect of most drugs on the fetus, which requires adhering to the principle of "proven efficacy and proven safety" when choosing a drug. There is practically no information about the safety and efficacy of most new drugs for the treatment of hypertension in pregnant women. The main drugs prescribed for the treatment of hypertension during pregnancy are central α_2 -agonists, beta-blockers, calcium antagonists.

In this regard, there is a need to conduct a study on the pharmacotherapy of hypertension in pregnant women using non-toxic and non-affecting fetal development.

The purpose of the study. To compare the effect of antihypertensive drugs of different groups on the course of hypertension and pregnancy outcomes.

MATERIALS AND METHODS

We examined 89 pregnant women aged 18-45 with moderate and severe arterial hypertension, registered for pregnancy in the I, II, III trimesters.

All patients underwent a generally accepted clinical examination, as well as a standard laboratory diagnostic examination of the mother and fetus for a first-level medical and preventive institution. In addition, a comprehensive assessment of the state of the cardiovascular system of patients - SMAD, EchoCG and a study of the quality of life (QOL) was carried out in dynamics.

The study of blood pressure was carried out according to the standard protocol of 24-hour monitoring. Before the study, significant physical activity and the intake of products containing caffeine were excluded. The patients independently kept a "Diary of daily blood pressure monitoring" during the day.

Echocardiography was performed according to the standard procedure on a Siemens ultrasound scanner before prescribing the drug and after a course of antihypertensive therapy.

Dopplerometry of uteroplacental and fetal blood flow was performed according to the standard procedure, three times: at 16-18 weeks and at the screening time for ultrasound examination (22-24 and 36 weeks of pregnancy).

Each patient twice (after determining the inclusion criteria and after a course of antihypertensive therapy) filled out a widespread multidimensional European Quality of Life questionnaire (Euro Quality of Life, 1993), which allows assessing such areas of health as



mobility, self-care, household activity, pain/discomfort, anxiety/depression, as well as giving a general ("global") assessment of QOL related to health.

All patients were divided into 4 groups:

The first group included 26 pregnant women who received methyldopa monotherapy at a daily dose of 500-2000 mg in three to four doses.

The second group included 31 patients who received nifedipine therapy at a daily dose of 20-40 mg in three or four doses.

The third group included 23 pregnant women who received bisoprolol 2.5-5 mg per day at one time.

The fourth group consisted of 9 pregnant women who demonstrated low compliance with the constant use of antihypertensive drugs at the beginning of the second stage.

Patients of different groups were comparable in age, duration and severity of clinical manifestations of hypertension. Evaluation of the effectiveness of treatment was carried out comprehensively taking into account the general condition, indicators of daily rhythm and daily profile of blood pressure, quality of life and the effect of drugs on uterine-fetal blood flow.

RESEARCH RESULTS AND THEIR DISCUSSION

During a comprehensive examination of pregnant women with hypertension, the following forms were identified: chronic hypertension (which occurred before pregnancy) in 58 pregnant women (65.2%), gestational hypertension - in 31 people (34.8%), while preeclampsia/eclampsia on the background of chronic hypertension developed in 8 (9%) pregnant women, and on the background of gestational AG – u 3 (3.4%). In addition, pregnant women with moderate hypertension (SAD 140-159 mmHg and/or DAD 90-109 mmHg) were 78 (87.6%), and with severe hypertension (SAD > 160 and/or DAD > 110 mmHg) – 11 (12.4%). All pregnant women with hypertension had 24-hour blood pressure monitoring before the start of therapy. According to the SMAD, arterial hypertension was confirmed in all 89 (100%) patients. The SMAD data by groups are presented in Table 1.

Table 1 Indicators of daily monitoring of blood pressure in pregnant women with hypertension before the start of therapy

SMAD indicator	Group 1 n=26	Group 2 n=31	Group 3 n=23	Group 4 n=9
SBP(24), mmHg.	141,5±2,1	146,7±5,5	142,1±5,9	145,3±9,1
SBP(D), mmHg.	155,3±2,0	159,5±5,2	154,9±5,7	156,7±7,8
SBP(N), mmHg.	132,7±3,9	130,4±9,6	134,6±9,6	138,7±11,1
SBP(24), mmHg.	97,4±5,3	91,4±9,6	99,8±4,7	91,7±4,8
SBP(D), mmHg.	100,8±6,1	104,1±9,3	105,6±10,0	103,7±3,3
SBP(N), mmHg.	80,1±3,9	85,3±11,3	81,6±9,2	85,3±9,1

Repeated daily monitoring of blood pressure was carried out in all study groups at 36-40 weeks of pregnancy (after a continuous course of therapy with antihypertensive drugs). The



effectiveness of lowering blood pressure on average per day, during daytime and night hours was analyzed (Table 2).

When analyzing the indicators of SMAD, a comparable effect was noted in terms of the degree of decrease in SAD and DAD from the baseline level in groups 1, 2. and 3. In group 4, there was no decrease in SAD and DAD, which is explained by the low adherence of patients to treatment.

When analyzing the echocardiographic examination parameters, the intergroup differences turned out to be unreliable, however, in all groups, including the group of pregnant women who did not receive systematic antihypertensive therapy, there was no deterioration in central hemodynamics, systolic and diastolic function.

Table 2 Indicators of daily monitoring of blood pressure in pregnant women with hypertension against the background of hypotensive therapy

SMAD indicator	Group 1 n=26	Group 2 n=31	Group 3 n=23	Group 4 n=9
SBP(24), mmHg.	122,3±2,3	121,8±5,3	120,1±4,9	148,1±8,9
SBP(D), mmHg.	125,3±2,1	123,4±4,8	121,7±5,3	157,4±7,5
SBP(N), mmHg.	111,4±3,3	110,4±8,9	109,3±7,6	138,4±10,1
SBP(24), mmHg.	81,4±4,9	80,4±9,3	78,7±4,2	97,7±4,5
SBP(D), mmHg.	87,6±5,7	85,9±8,6	85,5±9,4	104,8±3,6
SBP(N), mmHg.	72,3±3,5	72,1±10,3	71,7±8,2	91,1±9,4

Echodopplerometry of uterine arteries and fetal umbilical cord arteries revealed no pathological blood flow curves in groups 1, 2 and 3; in the group of low-compliance patients, pathological blood flow in the utero-placental pool was detected in two cases during pregnancy of 32 and 36 weeks, which was accompanied by the development of eclampsia in one case and fetal intrauterine hypoxia in the other. Both pregnant women were hospitalized in an obstetric hospital, where they were later delivered by caesarean section due to the ineffectiveness of the therapy.

Table 3 Complications and outcomes of pregnancy in the examined women

Complications and outcomes	Group 1 n=26	Group 2 n=31	Group 3 n=23	Group 4 n=9
Full-term pregnancy	21/80,8 %	25/80,6 %	18/78,2 %	5/55,6 %
Premature birth	5/19,2 %	6/19,4 %	5/21,8 %	4/44,4 %
Preeclampsia of I – II degree	9/34,6 %	13/41,9 %	8/34,8 %	8/88,9 %
Severe preeclampsia	1/3,8 %	1/3,2 %	-	3/33,3 %
Eclampsia	-	-	-	1/11,1 %



QOL indicators are independent criteria for evaluating the effectiveness of treatment and an important addition to general clinical and functional research methods.

The quality of life study conducted at the first stage showed that all pregnant women included in the study groups have changes in physical, psychological and social well-being. The assessment of various aspects of the quality of life was carried out independently by each pregnant woman in points. The value of QL indicators obtained as a result of summation before treatment was compared with QL indicators after treatment (36-40 weeks of gestation) in each group. An 18% improvement in the quality of life was noted. In a comparative analysis of QOL indicators, the greatest differences were found between the Bisoprolol group and the Methyldopa and Nifedipine groups, which is due to the greater adherence of patients to treatment in the first case, due to the frequency of use of the drug (once a day).

The largest number of timely deliveries was observed in the first three groups – 80%, in the fourth group – 55.6%. Preeclampsia of I-II severity complicated the course of pregnancy in all groups, eclampsia was registered in 1 (11.1%) case in the fourth group (Table 3).

Newborns in all groups were born alive. No cases of fetal hypotrophy were observed in groups 1, 2 and 3. All children were born with a score of 8-9 points on the Apgar scale. When evaluating newborns in group 4, attention is drawn to the development of fetal hypotrophy in 4 (44.4%) cases and the tendency to decrease Apgar scores in childbirth.

CONCLUSIONS

1. All the studied drugs (methyldopa, nifedipine, bisoprolol) contributed to the improvement of SMAD indicators in groups 1, 2 and 3. Hypotensive effects in terms of SAD and DAD were comparable.
2. The use of antihypertensive drugs led to an improvement in utero-placental blood flow in groups 1, 2 and 3, compared with group 4, in which pathological curves of utero-placental blood flow were traced.
3. Taking antihypertensive drugs in groups 1, 2 and 3 prevented the development of fetal hypotrophy and contributed to the birth of newborns with higher Apgar scores compared to group 4.
4. According to the results of a comparative assessment of the effect of drugs on quality of life indicators, the best indicators were observed in the 3 group receiving bisoprolol, which is associated with the frequency of taking the drug.

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