TREATMENT OF ARTERIAL HYPERTENSION IN PREGNANT WOMEN

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ABSTRACT

The purpose of this study was a comparative assessment of the effect of the selective beta-1 adrenoblocker metoprolol, clonidine and methyldopa on the hemodynamic parameters of the mother and the condition of the fetoplacental complex. 60 pregnant women with grade II hypertension and 20 healthy women were examined, compared they differ in age and gestation period. The patients were divided into 3 clinically equivalent groups, the first of which received metoprolol 50 mg 2 times a day as a hypotensive agent (with stabilization of the figures Blood pressure was switched to a maintenance dose of 25 mg / day), the second – clonidine at a dose of 0.075 mg 2-3 times a day, the third – methyldopa 250 mg 2 times a day. The effectiveness of treatment was assessed according to the data of echocardiography of the mother, additional plerometry of the fetal placental vessels, fetal cardiotocography, and the results of histological examination of the placentas. In the treatment of hypertension in pregnant women with hyperkinetic type of central hemodynamics , metoprolol was more effective than clonidine and methyldopa in reducing blood pressure, normalizing increased the indicators of the central hemodynamics of the mother, restored blood flow in the fetoplacental system, increased the reactivity of the fetal cardiovascular system. Clinical effects of clonidine have been noted in patients current with hypokinetic type of central hemodynamics, methyldopa – with eukinetic type of blood circulation preferences.

Antihypertensive therapy in pregnant women with hypertension should be differentiated and dependent the network depends on the type of central hemodynamics.

Key words: hypotensive therapy, pregnancy, central hemodynamics.

INTRODUCTION

The problem of treating hypertension in pregnant women was and remains relevant before the infusion Currently, despite the wide arsenal of antihypertensive drugs being used in modern clinical practice. The high medical and economic significance of this issue also lies in the fact that complications of arterial hypertension that occur during pregnancy occupy an important place in the structure of maternal and perinatal morbidity and mortality. According to WHO,

arterial hypertension is associated with 20 to 33% of cases of In the developed countries of the world, arterial hypertension is found in about 10% of pregnant women.

One of the most commonly used drugs for the drug therapy of hypertensive disease and symptomatic arterial hypertension are methyldopa and clonidine, which are It has been used clinically for many years in the treatment of arterial hypertension, including in pregnant women. In recent years , selective beta-adres have been successfully used for antihypertensive purposes generation II noblockers are metoprolol and generation III noblockers are nebivolol. However, in the available literature there are only a few works on their use in the tour drugs for the correction of blood pressure in pregnant women. Meanwhile, it is known that these drugs do not have a teratogenic effect and are not contraindicated in the II-III trimesters of gestation.

The purpose of our study was to conduct a comparative assessment of the clinical effectiveness of the treatment of hypertension in pregnant women with metoprolol, clonidine and methyldopa.

MATERIALS AND METHODS OF RESEARCH

To achieve this goal, a prospective and retrospective assessment of the course of pregnancy and childbirth in 60 pregnant women with stage II hypertension was carried out. For a comparative assessment of the indicators of functional research methods, 20 were examined there are 32 practically healthy pregnant women who are not gestating. The age of the subjects ranged from 32 to 42 years (on average – 36.5 years). The average pregnancy period at the beginning of treatment in women with arterial hypertension included in the examination, 33.5+1.5 weeks. The value of the average arterial pressure (BP) before treatment was 126.5+4.5mmHg, heart rate – 75.5+3.5 beats per minute. Informed consent for examination and treatment was obtained from all patients. All women with hypertension were divided into 3 clinically equivalent groups, the first of which was used as a hypotensive agent

the first group received metoprolol 50 mg 2 times a day (with stabilization of blood pressure values, they switched to a maintenance dose of 25 mg / day), the second – clonidine at a dose of 0.075 mg 2-3 times a day, the third – methyldopa 250mg 2 times a day. Prior to the start of treatment, all patients underwent an echocardiographic (EchoCG) examination using a Sequoia 512 ultrasound scanner from the company Akuson (USA) and combined daily monitoring of electrocardiogram (ECG) and blood pressure with the help of the company's Cardiotechnika 4000AD complex Inkart. Echocardiography assessed the ejection fraction (EF), systolic shortening (SU), shock (UO) and minute (MO) volumes, shock (UI) and systolic (SI) indices, the rate of circular shortening of myocardial fibers (Vcf), total peripheral vascular resistance (OPSS) and the type of central hemodynamics was established on the basis of the analysis of these indicators. During daily ECG monitoring, the features of the daily blood pressure profile (dippers, non dippers, night peakers), average SAD, DAD and SAD day and night, SNS SAD and DAD, average heart rate day and night, circadian index (CI), indicators of spectral (VLF, LF, HF) variability analysis were evaluated the

heart rhythm. To assess the condition of the fetus and diagnose placental insufficiency, an ultrasound examination with fetometry for ap was performed ACUSON Combined Sonography 128/xp (USA) with convexic (3.5 MHz) and transvaginal (7.5MHz) sensors operating in real time there is no time. Ultrasound Dopplerometry with determination of systolic diastolic ratio (SDO) was performed on the same device with a convexic sensor. The reactivity of the fetal cardiovascular system was assessed by recording cardiotocograms on the Sonicard Team Fetal Monitor Oxford device Instrument. When decrypting a record CTG was used to evaluate the reactivity of the fetal cardiovascular system, proposed by W. Fischer, where 8 or more points are the reactivity of the fetal cardiovascular system within the burrows we; 6 7 points – slight reactivity disorder; 4 5 points – severe impairment; 3 or less points– terminal fetal condition.

After 3 weeks from the start of antihypertensive therapy, repeated echocardiographic examination and control daily blood pressure monitoring were performed and an assessment of the condition of the fetoplacental complex.

During the entire period of taking the drugs, dynamic clinical and laboratory examination of pregnant women was carried out in accordance with the existing

industry standards. After delivery , the fetal condition was assessed according to the V.Apgar scale and a histological examination of the placentas was performed.

Statistical processing of the received data is performed using software Microsoft Office 2003 Professional for Windows XP on an Intel Pentium 4 computer. When conducting a variation The Student's criterion was used for the analysis. The differences were considered significant at a significance level of $p<0.05$.

THE RESULTS AND THEIR DISCUSSION

Depending on the type of central hemodynamics, patients with elevated blood pressure were distributed as follows: hyperkinetic type CGD – 36 people (60%), eukinetic type CGD – 15 (25%), hypokinetic type CGD – 9 (15%). The hyperkinetic type of CGD was characterized by increased figures of ejection fraction (EF), systolic shortening (SS), time of systolic shortening of myocardial fibers (TSMF), shock volume (SV), minute volume (MV), shock index (ShI) and systolic index (SI), indicators of general peripheral sosu resistance dov (OPSS) are significantly reduced. With the eukinetic type, PV, SU, Vcf, UO, MO, UI and SI correspond to they corresponded to the average values and practically did not

differ from the indicators of healthy pregnant women, it was upgraded. In the hypokinetic type– the indicators of PV, SU corresponded to the lower limit of the norm; the indices of the pumping function of the left ventricle (UO, MO, UI and SI) were reduced, the OPSS was slightly increased. In all patients with arterial hypertension, the study of heart rate variability showed the actual power of the spectrum (tP) has been reduced, the frequency VLF was high and reached 68-71%, wave ratio LF and HF

indicated pronounced sympathies and inhibition of parasympathetic influence. Comparative analysis showed that blood pressure values normalized more quickly in the group of women who received metoprolol, while hypotensive effect of using a selective beta blocker was more stable than with clonidine and methyldopa. A week after the start of treatment, the SAD index was 103.3 ± 2.3 mmHg, in pregnant women patients taking metoprolol, 113.5 ± 2.5 mmHg. – during treatment with clonidine and 105.5 ± 2.5 mmHg. –when using methyldopa. Repeated daily monitoring of blood pressure, echocardiography and ECG revealed an ambiguous direction of action of the drugs. Normalization of echocardiogram parameters was noted in patients with metoprolol therapy For example, the values of blood pressure, and in the case of a control study of heart rate variability, an increase in the total power of the spectrum and a decrease in the value of the nLF/nHF ratio. It should be especially noted that in the treatment of metoprolol, the patients with arterial hypertension and hyperkinetic the transition to the eukinetic type of blood circulation and a decrease in the values of total peripheral vascular resistance were noted by the type of central hemodynamics. The most significant positive differences in echocardiographic parameters when using clonidine were revealed in hypokinetic type of blood circulation: SI and UI

increased, and OPSS decreased. Methyldopa According to the data we obtained, it had an effect only in the group of women with the eukinetic type of CGD: the values of average blood pressure and heart rate decreased without change so far

indicators of cardiac output and volume. In the functional assessment of the fetoplacental complex in pregnant women treated with metoprolol, the subcompensated form of placental insufficiency was less common than with the use of clonidine (2 times) and methyldopa (1.6 times) (7, 14 and 11 people, respectively). Clinical manifestations of placental insufficiency in group 1 patients were chronic intrauterine fetal hypoxia (cardiotogram score 6-7 points, fetal respiratory movements during ultrasound examination). Manifestations chronic placental insufficiency in the 2nd clinical group were more diverse: in 9women – chronic intrauterine fetal hypoxia; in 3 women – an asymmetric form of fetal growth retardation of the I degree; in 2 patients, a combination of intrauterine hypoxia and an asymmetric form of fetal development delay of the I II degree was revealed. In the 3rd group of pregnant women, in 8 cases there was chronic intrauterine fetal hypoxia; in 2 x – combination of intrauterine hypoxia and an asymmetric form of fetal development delay of the first degree; in 1 m – an asymmetric form of fetal development delay of the first degree. When assessing umbilical placental blood flow with a normative Dopplerometric indicator the LMS for the gestation period of 32-34 weeks was considered 2.52, for 35-37 weeks – 2.4 [8]. Initial values the SDR in the umbilical cord arteries in pregnant women with hypertension was 2.9±0.9, which is a witness there was a marked violation of placental fetal blood flow. Against the background of normalization of

blood pressure when taking metoprolol, a decrease in blood pressure to 2.5±0.19 ($p<0.05$) was recorded in the examined patients during repeated examination at 35-36 weeks of gestation. In pregnant women, according to after receiving clonidine and methyldopa, the values of SDO did not significantly differ from the baseline values and amounted to 2.7±0.09 ($p>0.05$) and 2.6±0.11 ($p>0.05$), respectively.

Stabilization of blood pressure by relative normotonia in pregnant women of the 1st clinical group and normalization of blood flow in the system "mother placenta fetus" naturally led to a significant improvement in the reactivity of the cardiovascular system of their fetuses. The average cumulative assessment of cardiotocogram parameters in patients treated with metoprolol was 7.4+0.3 points against 5.2+0.2 points before treatment ($p<0.05$), against the background of treatment with clonidine – 6.2±0.3 points ($p<0.05$), methyldopa – 6.8±0.2 points ($p<0.05$). Normalization of hemodynamic parameters and relatively satisfactory condition of the fetoplacental complex in patients of the 1st and groups 3led to the fact that the average delivery time when using metoprolol was 37.6±0.5 weeks, methyldopa was 37.3±0.6 weeks versus 35.8±0.7 weeks in women receiving clonidine($p<0.05$). The average weight and length of fetuses in the 1st group of pregnant women were 2976±265 g and 49.4±1.7 cm, in the 2nd – 2505 ±156 g and 43.5±1.5 cm, in the 3rd – 2668 ±215 g and 46.7 ± 1.8 cm, respectively. The average score of children on the Apgar scale at the 1st minute of life was 7.4±0.4

points in mothers of the 1st clinical group, 5.8±0.3 points in the 2nd and 6.8±0.3 points in the 3rd clinical group ($p<0.05$). Histological studies of placentas revealed

that in all patients of the 1st group there was a relative chronic placental insufficiency, the morphological signs of which were: stasis of a large number of maternal erythrocytes, the presence of groups of closely related villi with collapsed

fetal capillaries (compensated angio matosis of terminal villi), narrowing of the interstitial space containing single maternal erythrocytes (the so-called non -functional zones) against the background of moderately pronounced compensatory adaptive processes (some increase in placental mass, an increase in the number of

small-caliber terminal villi and syncytial nodules). There were no dystrophic changes in the placenta in this clinical group. In 5 women who received clonidine, and in 3 – methyldopa, and gave birth to children with intrauterine delay development, focal involutively detected dystrophic changes in the stroma and epithelium of the with fibrinoid deposition in the intervillous space with calcareous encrustation, the presence of focal pseudoinfarcts due to impaired blood circulation

inflammation in the intervillous space; focal necrosis of syncytiotrophoblast; stasis of a large number of male erythrocytes. A large number of immature villi were noted, as well as thrombosis of the interstitial space, which is a sign of pronounced

circulatory disorders in the placenta.

CONCLUSIONS

1. Before prescribing antihypertensive drugs to pregnant women with arterial hypertension, the type of central hemodynamics should be determined.

2. When choosing drugs for hypotensive therapy for pregnant women with arterial hypertension, it is necessary to adhere to a differentiated approach and take into account the advantages of the selective beta–1 adrenoblocker metoprolol in hyperkinetic type of central hemodynamics, clonidine in hypokinetic, methyldopa in eukinetic about the type of blood circulation.

3. Selective beta-blockers metoprolol, unlike beta blockers atenolol and propranolola does not cause violations of uteroplacental perfusion and, therefore, does not have a negative effect on the fetoplacental complex, which is confirmed by ultrasound dopplerometry of placental fetal blood flow, cardio tokography and the results of histological examination of the placenta.

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