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PERINATAL MORTALITY RISK FACTORS FOR PREGNANT WOMEN WITH HYPERTENSIVE DISORDERS

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ФАКТОРИ РИЗИКУ ПЕРИНАТАЛЬНОЇ СМЕРТНОСТІ ДЛЯ ВАГІТНИХ ЖІНОК З ГІПЕРТЕНЗИВНИМИ РОЗЛАДАМИ
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Ризик перинатальної захворюваності та смертності для вагітних жінок з підвищеним кров'яним тиском залежить від тяжкості прееклампсії, віку вагітної, рівня гомоцистеїну в крові, ступеня затримки внутрішньоутробного розвитку плода, кількості передчасних пологів і зростання стаціонарного рівня окиснення білка.

Метою дослідження було ідентифікувати і розглянути фактори ризику смерті новонароджених від вагітних жінок з гіпертензивними розладами.

Матеріали та методи дослідження. Вивчали перебіг вагітності, стан внутрішньоутробних плодів і новонароджених від 120 вагітних жінок з гіпертензивними розладами. Першу групу утворили вагітні жінки з помірною прееклампсією (n=30), що повідомили про неонатальну смертність (n=1). До групи порівняння увійшли вагітні жінки з хронічним підвищенням кров'яного тиску і м'якою прееклампсією, чиї діти вижили (n=60), контрольна група складалася зі здорових вагітних жінок (n=30).

Результати дослідження та їх обговорення. У досліджених групах виявлено істотну різницю між віком вагітних (p=0,019), станом їхнього здоров'я на початку вагітності (p<0,001), масою плодів (p<0,001), кількістю вагітностей (p=0,023), тривалістю латентного періоду (p<0,001), а також відмінність у стані дітей на першій (p<0,001) і п'ятій хвилинах (p<0,001) за шкалою Апгар. Фактори ризику були ідентифіковані за допомогою відповідної прогностичної моделі. Визначено три головні фактори смерті новонароджених у разі підвищеного кров'яного тиску: 1) вік матері; 2) гіпергомоцистеїнемія; 3) передчасні пологи; 4) збільшення стаціонарного рівня окиснення білка.

Висновки. Перинатальна смертність вагітних жінок з підвищеним кров'яним тиском залежить від гестаційного віку й маси ембріона. Були встановлені фактори ризику смерті новонароджених і дані, на які потрібно звернути увагу під час ведення вагітності та пологів у жінок з підвищеним кров'яним тиском (вік матері, умови, що потребують призначення гіпогомоцистеїнової терапії).

Ключові слова: фактори ризику, перинатальна смертність, ембріональний дистрес, гомоцистеїн, гіпертензивні розлади.

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The risk of perinatal morbidity and mortality for pregnant women with hypertension depends on the severity of preeclampsia, the age of pregnant women, the level of hyperhomocysteinemia, the incidence of delayed fetal development, the number of premature births and the increase of the rate of spontaneous oxidative modification of the protein.

The purpose of the research was to identify and investigate the risk factors for mortality of newborn from pregnant women with hypertensive disoders.
Materials and methods of research. It was studied the process of pregnancy, the condition of fetuses and newborns from 120 pregnant women with hypertensive disorders. The primary group consisted from pregnant women with moderate preeclampsia (n=30), who reported neonatal mortality (n=1). The comparison group consisted of pregnant women with chronic hypertension-grade I and mild preeclampsia, whose children survived after birth (n=60), control group was healthy pregnant women (n=30).
Results of the research and their discussion. It was found that in the researched groups there was a significant difference in maternal age (p=0.019), terms of gestation at birth (p<0.001), fetal weight at birth (p<0.001), number of pregnancies (p=0.023), duration of the latent phase (p<0.001), as well as the difference in the condition of children at birth at the first (p<0.001) and fifth minutes (p<0.001) on the Apgar scale. Risk factors were identified using an adequate logistic regression model. There are three main risk factors for newborns' mortality in case of hypertension disorders:1) mother's age (HS=1.25; 95% CI 1.04–1.51 per year); 2) hyperhomocysteinemia (VH 36.3; 95% CI 3; 4–386.7); 3) premature infant (VS 95; 95% CI 3–2900); 4) increased spontaneous oxidation of protein (HS 1.65; 95% CI 1.8–457.5).
Conclusions. Perinatal mortality of pregnant women with hypertension depends on gestational age and fetal weight at birth. The risk factors for newborns's mortality and the data that must be taken into account for management of pregnancy and childbirth for women with hypertension (maternal age, conditions requiring the appointment of hypohomocystein therapy).
Key words: risk factors, perinatal mortality, fetal distress, homocysteine, hypertensive disorders.

Introduction

Hypertensive disorders not only frequently complicate the process of pregnancy and childbirth, but are also a leading risk factor in the development of complications of the perinatal period of newborns and mother's mortality. The current problem of predicting pregnancy complications in pregnant women with hypertensive disorders is not completely solved until today.

Major complications to the fetus during preeclampsia and hypertension of pregnant associated with prematurity and placental insufficiency. Chronic placental dysfunction and violation of utero-placental blood flow develops fetal distress, which leads to intrauterine growth retardation, recorded low birth weight for the gestational age (asymmetric and symmetric shape retardation) [1; 2].

Mother's complications of hypertensive disorders depend on obstetric and gynecological history. The incidence of fetal distress with increasing obstetric and gynecological pathology and proportionally increases to 5–13.5% by 100 births [3; 4].

The consequences of suffering fetal distress in newborns is hypoxic-ischemic lesions of the CNS, the consequences of the birth of premature infants is respiratory disorders, convulsions and cerebral palsy in the future. Among these infants recorded a high percentage of perinatal mortality and morbidity [5]. Thus newborns from those who were born with extreme body mass and early gestational age have unfavorable long-term consequences associated with defects in the nervous system, auditory and visual analyzers, respiratory organs, as well as disorders of the development of the psyche and training. The aforementioned diseases lead to a significant increase of childhood morbidity and disability. Perinatal mortality in cases of hypertensive disorders increases from 6,3 to 18–20‰ (according to some authors).

Hypertensive disorders cause placental dysfunction, chronic hypoxia and fetal growth retardation, defection in protein metabolism, circulatory and respiratory system of pregnant women. Pregnancy and childbirth often (from 15 to 29.7%) are complicated by premature deliveries due to the increase in severity of pre-eclampsia, the birth of morphologically immature preterm infants, which eventually lead to such dangerous disorders as respiratory failure, RDS syndrome, and hypoxical, ischemical damages of the central nervous system [6; 7].

We fixed changes in the exchange of homocysteine and the activity of enzymes in the group of pregnant women with hypertension, it was significantly higher, associated with the increasing tension of metabolic processes and functional condition of the liver.

After analysis of the indicators of spontaneous oxidative modification of the protein, it was established that its activation in case of pregnant women with preeclampsia, in particular with moderate preeclampsia. Comparing the metalcatalysational oxidative modification of the protein, a significant difference (decrease) was found in pregnant women with preeclampsia [10; 11]. Particularly significant changes were found at a wavelength of 356 nm, that is in the ultraviolet region. These indices proved the presence of oxidative stress, changes in the structural and functional organization of protein, accumulation in the body of pregnant women with hypertensive disorders of low molecular weight protein degradation products, which provide a toxic effect at all organs and systems of pregnant women [8; 9].

Consequently, such a pattern of detected changes in the activity of enzymes may indicate that at preeclampsia of pregnant women there is an increase in the activity of these enzymes, moreover there is a directly proportional dependence [12; 13].

The purpose of this research was to identify and study the conditions of newborns after delivery and there risk factors of mortality from mothers with hypertensive disorders during pregnancy.

Materials and Methods

The frequency of development of fetal distress in pregnant women with hypertension was studied according to the data of VCCMH № 2, VRCH named by M. I. Pirogov, VRCPH with the participation of the Department of Obstetrics and Gynecology № 2 of VNMU named after M. I. Pirogov. Under the observation were pregnant women at term gestation from 32 to 37 weeks in age from 20 to 39 years old. Pregnant women were monitored and gave birth in the maternity ward of the Pirogov Regional Clinical Hospital. Among them were 90 women with hypertensive disorders: 30 pregnant women with mild preeclampsia, 30 women with preeclampsia pregnant moderate severity, 30 pregnant women with chronic hypertension I severity, and 30 healthy pregnant women (control group). It was investigated 120 birth stories and developmental maps for newborns. In the comparison group (60), preterm births took a part from the total number of general in the study period. The term of pregnancy at the time of the pivotal resolution in the comparison group was from 31 to 41 full weeks. Childbirth histories, birth control cards and neonatal development maps were analyzed.

Details of anamnesis, gynecological, obstetric, extragenital complications were studied. Clinical, laboratory (including molecular-genetic) methods were used, thorough physical examination, collection of reproductive and somatic medical history, assessment of the course of pregnancy complications analysis of the mother and fetus, the consequences of childbirth and newborn state in the early neonatal period. All pregnant women were conducted a comprehensive clinical and laboratory examination. Pregnant women were examined related professionals.

The classical methods of mathematical statistics were used to process the results of clinical and laboratory researches, analyze them and identify system interrelations, and also to assess the reliability. It was assumed that the normal distribution law is inherent for the investigated sample indices. The reliability of the difference in compared groups was determined using Student's criterion. The results were considered to be reliable if the coefficient of reliability was less than or equal to 0.05.

Results of the Research and Their Discussion

Clinical characteristics of pregnant women: the first phase of our research included studying the peculiarities of pregnancy, childbirth and the postpartum period and reproductive history of pregnant women admitted to hospital with preeclampsia different severity and varying degree of hypertension during 2009–2010.

The analysis made it possible to determine the population frequency of hypertensive disorders, which was 15.24% among pregnant women in a retrospective study. The age of the examined women varied from 17 to 41 years, and in all groups the majority of pregnancies were from 21 to 25 years old (49.5%). In case of pregnant women with hypertension, the frequency of somatic pathology per a woman is almost twice as much as the corresponding index in the control group. It was found that in the studied groups there was a significant difference in maternal age ($p=0.019$), terms of gestation at birth ($p<0.001$), fetal weight at birth ($p<0.001$), ($p<0.001$), number of pregnancies ($p=0.023$), as well as the difference in the condition of children at birth at the first ($p<0.001$) and fifth minutes ($p<0.001$) on the Apgar scale. It should be noted that in case of pregnant women the control group of benign illnesses of the uterus corpus, hyperplastic processes of the endometrium were not observed, and in the anamnesis of pregnant women with polyhydramnios they occurred, and the total difference was significant ($p<0.05$). The frequency of extragenital pathology among pregnant women with hypertension is 1.6 times higher than in case of pregnant women in the control group and was respectively 1.06 and 0.65 per a woman. Cardiovascular pathology (4.8%) is statistically significant ($p<0.05$) in case of pregnant women with hypertension, among which the vegetative vascular dystonia for the hypertonic and cardiac type is at the first place. Microcirculation disturbances also occur in the "mother-placenta-fetus" system, which leads to disorders of the secretory and resorptive function of the membranes and trophic function of the placenta. The kidney disease in case of pregnant women with hypertension was 2.9% ($p<0.05$), the gastrointestinal tract was 2.6% ($p<0.01$), sinusitis — 1.6% ($p<0.05$). Extragenital pathology is considered as a significant risk factor for the development of obstetric complications, especially highlighting its importance in recent years. It is clear that in case of such an unfavorable somatic and genital background the frequency of complications of pregnancy was quite high. Thus, at the first half of pregnancy the most frequent one were acute respiratory viral infections — 7.1% ($p<0.05$) and colpitis — 2.4% ($p<0.05$). Early gestosis were also common in pregnant women with hypertension (15%), but there was no significant difference with the control group. And such complication of pregnancy, as the threat of interruption in the control group, was even significantly more frequent ($p<0.05$) than in women with hypertensive disorders. In contrast to the first half of the pregnancy after 20 weeks of gestation, various complications were observed significantly more often. In case of pregnant women with hypertension placental dysfunction (according to ultrasound screening) was found in 67.6%, anemia of pregnant women — 7.3%, colpitis — 7.2%, the risk of abortion — 31.6%, and in the control group these indicators respectively were: (PN) 8.5, the threat of abortion — 48.1 and colpitis 2.2%. In the structure of the

complications of the second half of pregnancy in case of women with hypertension, a significant percentage belongs to such pathologies as hypoplasia of the placenta (26.5%), fetal distress (17.0%). Such complications as measles, sore throat, pneumonia, acute bartolinitis, istmico-cervical insufficiency and placenta previa were not observed in the studied groups. Fetal growth retardation, unstable fetal position ($p<0.01$) were diagnosed more frequently in the control group in case of pregnant women with hypertension. Preterm labor, the threat of premature birth. ($p<0.05$). The high frequency of complications of pregnancy has led to a greater frequency of surgical interventions during labor. Such surgical interventions as manual revision of the walls of the uterus and manual removal of the litter were performed only in a group of pregnant women with hypertension disorders. Caesarean section was carried out in the control group of the ruminal implant in the uterus, whereas in the group of pregnant women with hypertension, the cesarean section was performed due to the progression of the severity of late gestosis, fetal distress, and FVFR. In case of 1 pregnant woman of the second group (2.0%), due to the hypotension of the uterus, there was an early postpartum bleeding, which was not observed in the gestational age of the control group ($p>0.05$), which led to the operation of the supravaginal extirpation of the uterus. Anomalies of labor in the II group of pregnant women with hypertension were recorded in 6.2% ($p<0.001$), in the control group they were 2.5% ($p<0.05$). Premature detachment of a normally located placenta, failure of the cord and small parts of the fetus were not observed in both groups. During the examination of pregnant women for the presence of genital infections, it was found that association of microorganisms during pregnancy in case of women with hypertension and the polyhydramnios is quite frequent in contrast to the control group. Thus, in 12.4% of pregnant women with hypertension, associations of two microorganisms were identified, 5.0% of polyhydramniosis and 4% of three or more microorganisms. During the research, we found a violation of utero-placental and a little less violation of fetal-placental blood flow, as well as metabolic disorders in case of pregnant women with hypertension. The same disorder is also typical for placental dysfunction. In case of detection fetal distress during the examination of pregnant women with hypertensive disorders, we prescribed Actovegin 5.0 ml per 400 ml of physical solution 1 time per day intravenously, alternating with Tivortin 100 ml per day, for a course of 5 infusions. During assessing of the condition of newborns at the 5th minute of life on the Apgar scale, we found that 78.1% of newborns in the group of pregnant women with hypertension had satisfactory condition, and 93.4% in the control group.

According to the results of evaluation of the biophysical profile of the fetus, it was found that in a group of pregnant women with hypertension, a satisfactory condition of the fetus was observed in 88%, which is 28% less than in the control group of pregnant women. In case of pregnant women with hypertension, the development of late gestosis, namely, preeclampsia, was typical during the period of pregnancy 24–25 weeks, the severity of gestosis increased to 32–34 weeks of gestation (in 7 pregnant women — moderate (35.0%), in 4 (20.0%) — severe. Compensatory-adapt mechanisms have the boundary tension, which does not allow to provide their realization for the adequate flow of pregnancy and fetal development, the risk of complications for the fetus and the newborn increases.

In case of moderate or severe pre-eclampsia, we recommend evaluating of the biophysical profile of the fetus (BPF), in case of normal assessment of the BPF, a complex reassessment is possible after 10 days and 1 day. In case of result 4–6 points — reassessment of the BPF and blood flow of the FPC in 24 hours, in case of result 0–2 points — to solve the question in the interests of the fetus and mother.

Women with the risk of hypertension should have pregravidary training and dynamic monitoring. Pregravidary preparation involves planning of the pregnancy, sanation of chronic source of infections, assessment of the somatic and genetic health of the spouses, prevention of acute infection diseases, the appointment of folic acid by 1 g to 24 weeks of gestation, calcium, iodine and polyunsaturated fatty acids. In case of such women it is necessary to carry out sanitary and educational about the formation of a healthy lifestyle: elimination of hypodynamia, bad habits and work with the computer, rational nutrition. Due to the high frequency of fetal distress in case of pregnant women with hypertension, it is necessary to carry out BPF control with further, if it's necessary, treatment. Pregnant from high-risk groups must be hospitalized in 34–35 weeks prior to the obstetric hospital for a comprehensive assessment of the functional condition of the fetoplacental complex, prenatal care and the choice of delivery method. Compliance with the above-mentioned preventive measures in case of pregnant women with risk for the development of hypertensive disorders and proper management of pregnant women with this pathology will make it possible to reduce perinatal morbidity and mortality, raise the reproductive health of the population.

Conclusions

1. Pregnant women with hypertensive disorders are at increased level of perinatal pathology, including fetal distress, fetal retardation. The severity of the condition and the development of serious complications in newborns correlates with the severity of preeclampsia and related extragenital mothers.

2. The main complications of obstetrical and gynecological history in pregnant women with hypertensive disorders marked increase in the frequen-

cy of preterm birth, fetal abnormality (distress and retardation, hypoxic-ischemic neonatal CNS), increase frequency cesarean section in women.

3. Much of newborns from mothers with hypertensive disorders requiring further treatment and care of newborns in the Department of Pathology at the regional children's hospital.

4. The risk factors for the occurrence of hypertensive disorders are: burdened obstetric and gynecological, somatic anamnesis and complications of the current pregnancy (aggravation of extragenital pathology, placental dysfunction, placental hypoplasia, perinatal infections), leading to disturbances of the compensatory potential of the placenta, an increase in the percentage of DFD, anomalies of maternity, fetal distress during childbirth and surgical interventions.

5. Women with risk of hypertension should be trained at the stage of pregnancy planning. During pregnancy, they require further careful monitoring, which involves monitoring of the dynamics of blood pressure, protein in the urine, abdominal cavity, and the height of the abdomen, the fetus, indications of medical genetic counseling and additional ultrasound examination. During the childbirth it is necessary to carry out stench, to prevent abnormalities of contractile activity of the uterus, and also to prevent distress of the fetus in a timely manner.

Ключові слова: фактори ризику, перинатальна смертність, ембріональний дистрес, гомоцистеїн, гіпертензивні розлади.

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