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PREECLAMPSIA AS A CONSEQUENCE OF SEVERE TOXEMIA

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Abstract: This article reflects maternal mortality rates according to WHO data, the Russian Federation, which show that preeclampsia remains a relevant problem in modern obstetrics worldwide and the reasons for early toxemia, which most often occurs in the first trimester and in some cases can continue until the third trimester of pregnancy. Based on the literature data, it can be said that with a diagnosis of early toxemia, manifested by vomiting and nausea in a pregnant woman, there is a risk of premature birth, neurological disorders, fetal asphyxia, esophageal rupture, retinal hemorrhage in the mother, as well as other complications.

Keywords: preeclampsia, eclampsia, pregnancy, maternal mortality, hypertension, pregnant women vomiting, toxemia.

1. Introduction

Preeclampsia is one of the most complex and important issues in scientific and practical obstetrics. This article reflects maternal mortality rates according to WHO data, the Russian Federation, which show that preeclampsia, remains a relevant problem in modern obstetrics worldwide. Also, the article discusses the reasons for early toxemia, which most often occurs in the first trimester and in some cases can continue until the third trimester of pregnancy. Based on the literature data, it can be said that with a diagnosis of early toxemia, manifested by vomiting and nausea in a pregnant woman, there is a risk of premature birth, neurological disorders, fetal asphyxia, esophageal rupture, retinal hemorrhage in the mother, as well as other complications.

The pathogenesis of early toxemia has many theories, such as the theory of the influence of chorionic gonadotropin or the mechanical theory of the development of pregnant vomiting, but none of them can fully explain all cases of the disease. In this case, it can be said that early toxemia is multifactorial.

Preeclampsia is a multisystem syndrome that reflects the inability of the maternal organism's adaptive mechanisms to adequately meet the needs of the developing fetus, manifested by elevated blood pressure and proteinuria.

Preeclampsia is one of the most complex and important issues in scientific and practical obstetrics. According to the WHO, preeclampsia is diagnosed in 28% of pregnant women, making up the majority of all hypertensive conditions during pregnancy. In high-income countries, maternal mortality from hypertensive disorders averages 20%. According to the analysis of the causes of maternal mortality in 2005, it was found that in half of the cases, the cause of death was severe pre-eclampsia (51.1%), with every second woman dying from a brain coma (50%), and every fourth woman dying from bleeding due to pre-eclampsia (22.7%).[1].

In the general population, hypertensive disorders occur in 11% of cases, with complications of varying severity during the gestational process in every third woman, of which almost every fourth woman has a severe form [2]. Preeclampsia is usually diagnosed in the presence of arterial hypertension and proteinuria after 20 weeks of pregnancy. Potentially life-threatening complications include premature placental abruption, disseminated intravascular coagulation (DIC), brain hemorrhage, liver failure, and acute kidney failure. Despite certain successes in the treatment and prevention of preeclampsia, it remains one of the main causes of maternal mortality,

perinatal morbidity, and mortality. Preeclampsia is a condition that occurs in pregnant women. It is characterized by high blood pressure and the presence of protein in the urine. In addition, patients with preeclampsia often experience swelling in the legs and arms. Preeclampsia usually occurs in the second half of pregnancy, towards the end of the second or in the third trimester, although it can also be detected earlier.

Toxicosis of pregnancy is a pathological condition that occurs in the first trimester of pregnancy and in some cases can continue until the third trimester [3]. In some cases, clinical symptoms may progress and then hyperemesis gravidarum develops, a severe form of early toxicosis that leads to fluid and electrolyte disturbances, muscle cramps, ketonuria and dehydration [4]. M.S. Fejzo et al. report that the incidence of early toxicosis of pregnancy is approximately 70%, and hyperemesis gravidarum - 0.3-10.8% [5]. This complication is more often diagnosed in India, Pakistan and New Zealand than in European countries. In Russia, according to statistics collected over the past 10 years, about 50-60% of pregnant women experience nausea and vomiting during pregnancy. At the same time, 1.5-2% of pregnant women are diagnosed with early severe toxicosis, complicated by dehydration and metabolic disorders [5, p. 57-58; 5]. Early toxicosis is one of the most common causes of hospitalization in pregnant women in the first trimester, which in rare cases can lead to maternal mortality [6].

The occurrence of early toxicosis in pregnant women is influenced by many factors: heredity, chronic diseases of the gastrointestinal tract, psychoneurological disorders, as well as the resulting hormonal imbalance. The main clinical manifestations of early toxicosis are nausea and vomiting, which are accompanied by changes in clinical and laboratory data [5, 7]. As for treatment, it will depend on the severity of the disease. Mild therapy will be based on diet; for moderate and severe severity, complex therapy and parenteral nutrition will be the basis. It should be noted that in relation to the treatment of patients with early toxicosis, the doctor may encounter some difficulties.

First, some women do not seek help from health care providers due to concerns about drug safety. Secondly, there are often situations when diseases of the gastrointestinal tract (cholecystitis, pancreatitis, hepatitis) are hidden under the guise of early toxicosis, which causes certain difficulties with diagnosis by an obstetrician-gynecologist. In the case of involving related specialists, the correct diagnosis is hampered by the popular belief that a pregnant woman is characterized by dysfunction of the gastrointestinal tract.

The result of such difficulties with adequate diagnosis is the progression of metabolic disorders, as a result of which mild toxicosis quickly turns into a moderate and then a severe form, often requiring termination of pregnancy [6, 8].

Clinically, vomiting in pregnant women can occur in mild, moderate, and severe degrees of severity, and in the latter case, a so-called vicious circle often forms, which includes severe electrolyte disturbances, neurological disorders, and alkalosis. Treatment of mild vomiting in pregnant women is carried out on an outpatient basis, while moderate and severe cases are treated in a hospital.

2. Risk factors

Pre-eclampsia/eclampsia during a previous pregnancy, family history of pre-eclampsia, multiple pregnancies, and in severe cases of pre-eclampsia: severe hypertension + proteinuria, hypertension of any severity + proteinuria + one of the following symptoms - severe headache, visual disturbances, epigastric pain and/or nausea, vomiting, seizure readiness, generalized edema, oliguria (less than 30 ml/hour or less than 50 ml of urine in 24 hours), tenderness on palpation of

the liver, platelet count below 100x10^9 g/L, elevated levels of liver enzymes, HELLP syndrome [3].

It is known that early toxicosis in pregnant women is characterized by the presence of predisposing factors. These include somatic diseases of a woman before pregnancy, for example, chronic diseases of the gastrointestinal tract and liver, dysfunction of the thyroid gland, asthenic syndrome and neuropsychiatric diseases, young age of the pregnant woman, trophoblastic disease, or hydatidiform mole, multiple pregnancy, bronchial asthma, diabetes mellitus. diabetes, etc.

According to T.Kh. Rakhmanova et al., there is information that a number of patients' mothers and sisters had symptoms of early toxicosis during pregnancy. The percentage of such women with a family history is 28 and 19%, respectively. Also, if a woman experienced nausea and vomiting in her first pregnancy, the likelihood that she will have a relapse is high compared to those pregnant women who did not experience these symptoms [5, 16].

In the general population of pregnant women, the frequency of preeclampsia is 5-10%, and eclampsia is 0.05%. In the global structure of maternal mortality, the share of preeclampsia is 12-15%, and in developing countries this figure reaches 30%.

In developed countries, the indicators of maternal and perinatal mortality related to preeclampsia are an order of magnitude lower than in developing countries, which indicates the manageability of complicated forms of preeclampsia and the possibility of effectively influencing the outcome with a systematic approach to this problem [4].

According to Russian authors, this pathology remains one of the main causes of maternal mortality and accounts for about 20% of all cases of maternal deaths in the Russian Federation. In Moscow, maternal mortality from various forms of preeclampsia and their complications ranks first among all causes of maternal mortality, ranging from 17 to 28% per year, i.e. The share of preeclampsia turned out to be slightly higher than in Russia as a whole. Currently, due to the improvement of treatment methods, obstetric tactics, the emergence of new methods of intensive care and resuscitation, the life expectancy of postpartum women suffering from preeclampsia (90% of women lived more than 72 hours after childbirth) and eclampsia (more than 72 hours after convulsions) has increased significantly. 54%) compared with rapid deaths in the 70s (51.0% of women died in the first 24 hours after an eclamptic seizure) [5,6,8].

In Russia, as in other countries, the incidence of preeclampsia is increasing. According to industry statistics from the Ministry of Health and Social Development of the Russian Federation, the national average incidence of preeclampsia in pregnant women is:

1998 - 18.5%; 2000 - 22.2%; 2006 - 21.6%. Preeclampsia, as a direct cause of death, ranks third in the structure of maternal mortality and amounts to 12-15%; with severe preeclampsia and its critical forms, maternal mortality rates are 20-25%. Perinatal mortality in preeclampsia ranges from 10.0 to 30.0%, perinatal morbidity in them is 463-780%. Preeclampsia is one of the main causes leading to the development of placental insufficiency, the frequency of which ranges from 26.8% to 37.2% [6]. Preeclampsia is also dangerous in the postpartum period and is equally dangerous for the life of mother and child. With preeclampsia, the functions of vital organs are disrupted: kidneys, brain, liver, lungs, which often leads to the development of multiple organ failure. The consequences of preeclampsia manifest themselves not only in the early postpartum period, but also in subsequent years of a woman's life, and above all this concerns the functions of the brain.

Preeclampsia requires close attention. Of the total number of deaths from preeclampsia, 96.8% of women died after childbirth [4,7]. To predict long-term postpartum complications in women who have suffered preeclampsia, indicators of central and cerebral hemodynamics are used, obtained using the method of integral body rheography and rheoencephalographic study of cerebral blood flow. A number of authors have proposed using "quality of life" for such an assessment; in

particular, S.V. Govorov and G.Ya. Klimenko (2007) carried out such an assessment using the Russian version of the international program Medical Outcomes Study Short Form (SF-36). An objective integrative assessment of the violation of the functional-adaptive status of the body of postpartum women is carried out in the postpartum period due to preeclampsia. This was made possible through the use of a cardiorespiratory synchrony test. This test shows the possibility of predicting the development of postpartum complications in postpartum women who have had preeclampsia in order to prevent these complications. Currently, none of the methods for predicting preeclampsia can be recommended as a universal screening test to determine the risk of preeclampsia, because there are 40 theories of the etiology and pathogenesis of preeclampsia [7,8]. According to modern ideas about preeclampsia, the leading role in the pathogenesis of hypertensive disorders is assigned to damage to the prostaglandin system, which has a pronounced pressor and depressor effect on the vascular wall. It is known that platelet aggregation in the vascular bed is under the regulatory influence of a number of inhibitors and activators of this process. An important role in the regulation of functional activity belongs to prostacyclins, an imbalance of which can become one of the causes of disturbances in central and peripheral hemodynamics, which leads to hypovolemia, impaired microcirculation, increased blood pressure and multiple organ failure [8].

3. Etiology and pathogenesis

Scientists have not yet come to a consensus on why early toxicosis of pregnant women occurs. There are many theories, in particular, hormonal, neurogenic, immunological, cortico-visceral, reflex, but, undoubtedly, the pathogenesis of toxicosis may have several causes simultaneously [9]. Currently, there is a widespread theory about the influence of the fertilized egg on the mother's body, which is associated with the introduction of chorionic villi into the uterine wall and irritation of the autonomic receptors of the endometrium [10]. Further, along the afferent fibers, the impulse reaches the subcortical structures of the brain, where the reticular formation is located, as well as the center for regulating breathing. However, excitation affects not only the above-mentioned structures, but also the vomiting center, chemoreceptor trigger zone, salivary, vasomotor centers and olfactory nuclei, therefore, clinics such as hypercapnia, hypersalivation, vomiting, nausea, perversion of smell, spasm of peripheral vessels, tachycardia can be observed [10].

The hormonal theory of the development of vomiting in pregnancy is based on the presumed influence of human chorionic gonadotropin (hCG), the production of placental prostaglandin E2 and the development of nausea and vomiting in pregnant women [11].

In addition, it was found that with an increase in human chorionic gonadotropin in the first trimester, a parallel increase in thyroid hormones and estradiol occurs, and since the structure of hCG contains an element similar to the glycoprotein of thyroid-stimulating hormone (TSH), then, accordingly, with an increase in the concentration of chorionic hormone human gonadotropin increases the concentration of TSH, hyperthyroidism occurs, which clinically can also be manifested by nausea and vomiting [7, 12].

When considering the pathogenesis from the neuroendocrine system, one can see that the water-salt balance, protein, fat and carbohydrate metabolism are disturbed, which lead to the body activating glycogen reserves and increasing the breakdown of proteins and carbohydrates. The anaerobic breakdown of glucose and amino acids increases due to disruption of tissue respiration, the anaerobic decomposition of ketogenic amino acids increases - as a result, under-oxidized products of fat metabolism - ketones - remain and ultimately the development of ketoacidosis occurs. All of the above processes lead to dehydration of the body, and then to dystrophic changes

in the organs and tissues of the pregnant woman [10]. The mechanical theory of vomiting during pregnancy cannot be ruled out. It is known that the uterus, which increases in size, begins to compress the overlying organs of the gastrointestinal tract. For example, the stomach, gradually moving into a vertical position and moving upward, reduces its tone, increases intragastric
The pressure and gastrointestinal angle moves anteriorly, which leads to reflux of contents into the esophagus. This theory applies more to pregnant women in later stages. In the pathogenesis of vomiting, a change in taste sensations and an increase in the appetite of a pregnant woman cannot be excluded, which can also lead to nausea and vomiting [13].
A study was conducted by the University of Britain, the results of which revealed that the etiology of the development of clinical manifestations of early toxicosis is based "on the boundary of the development of interaction between the mother and the ovum" [14]. M. Bustos et. aL. It is reported that 88% of women had human chorionic gonadotropin levels that increased within 10 days of ovulation, and 67% of women reported symptoms within 20 days of ovulation, suggesting that the onset of clinical symptoms actually occurs earlier than with 6th week pregnancy [15].
One of the reasons for the development of early toxicosis, according to I.S. Lipatova et al., is an increase in the level of markers of a nonspecific inflammatory reaction. This occurs because the primary immune response is activated to changes in the structure of the decidua as the fertilized egg implants. C-reactive protein and anti-inflammatory cytokines increase, and activation of the coagulation potential of the blood and vascular endothelium begins. The content of D-dimer, fibronectin, and leptin increases, platelet aggregation increases, and at the same time there is a decrease in the level of platelets and placental growth factor. Moreover, the more pronounced the deviations of markers of gestational maladjustment from the norm, the brighter the clinical picture of toxicosis [15]. Another theory for the development of vomiting during pregnancy, which was developed at the Birjand University of Medical Sciences, is an increase in the level of visfatin activity. Visfatin is one of the hormones of adipose tissue. It is synthesized from visceral fat and also has insulin-mimetic activity, which is also expressed there. However, it has been noted that insulin-mimetic effects may involve the placenta and fetal membrane.
Visfatin, like other adiposenes, plays a role in the development of obesity, insulin resistance and gestational diabetes. A study was conducted at the University of Iran, which found that fluctuations in visfatin levels do not depend on weight gain per se, but depend on the rate of maternal weight gain during pregnancy. A reduced level of visfatin was also noted in the second and third trimesters relative to the first and an indirect relationship between vomiting of pregnancy and visfatin, but there is a disagreement in the conclusions with the studies of A. Skvarca et. aL. and N. Rezvan et. aL., which showed a high level of visfatin in the second and third trimesters, compared to the first. Thus, these conclusions cannot be called fundamental [16].
There is also evidence that nausea and vomiting in pregnancy can be genetically inherited. Thus, S. Oraz et al. refer to the research of University of California professor M. Feizo, who, together with his colleagues, revealed the existence of 2 loci, one of which contains the bOP15 gene on the 19th chromosome, and the other on the 4th chromosome - gene !SRBR7. At high levels of these genes, the development of nausea and vomiting in pregnant women is observed, and biP15 increases in the first and second trimesters of pregnancy [13].
Also, with preeclampsia, placental perfusion is impaired (stage 1) and due to insufficient remodeling of the spiral arteries supplying the intervillous space, factors arise that lead to clinical manifestations of preeclampsia (stage 2). This hypothesis is based on compelling evidence of increased concentrations of biomarkers of oxidative stress and decreased concentrations of antioxidants such as vitamins C and E in the serum and tissues of women with established preeclampsia. Antioxidants play an important role in maintaining cellular function in normal pregnancy and act by inhibiting peroxidation, thereby protecting enzymes and proteins. Results

from a randomized controlled trial showed that vitamin C and E supplementation were associated with a significant reduction in maternal concentrations of biomarkers for preeclampsia (plasminogen activator inhibitor [PAI]-1-to-PAI-2 ratio), with a 54% reduction in risk preeclampsia was also a 37% reduction in the risk of placental abruption was found [1,5,9].

4. Diagnostic criteria and differential diagnostics

Pregnant women suffering from CAH, in particular hypertension, have a more favorable prognosis compared to patients whose pregnancy was complicated by preeclampsia. Chronic increase in blood pressure, which does not lead to damage to target organs, with stable blood pressure values, as a rule, has a significantly less negative impact on the condition of the pregnant woman and the fetus than preeclampsia. According to most authors, in this case, the severity and stage of headache will have a major impact on the course of pregnancy and childbirth

For differential diagnosis of various forms of hypertension, including essential hypertension, it is necessary to use: a detailed history taking (family history, patient history, professional history); physical and obstetric examination; clinical and laboratory examination (clinical blood test, biochemical blood test, coagulogram, acid-base balance, general urine test, urine test according to Nechiporenko and Zimnitsky, daily protein loss, kidney ultrasound); prenatal examination (ultrasound, Doppler, cardiotocography); 24-hour blood pressure monitoring; determination of central hemodynamic parameters using tetrapolar bioimpedansometry and rheography; consultations with a therapist and ophthalmologist (Table 5). The most common somatic pathology characterized by increased blood pressure in pregnant women is hypertension.
Vomiting of pregnant women should be differentiated from other pathological conditions. For example, esophageal vomiting can be observed with tumor processes in the esophagus, achalasia cardia, and esophagospasm. This type of vomiting occurs when the passage of food into the stomach is disrupted. Another option is gastric vomiting. Causes may include gastritis and peptic ulcer. The causes of pancreatic vomiting are acute and chronic pancreatitis, as well as pancreatic cancer. This type of vomiting, as a rule, is indomitable, does not bring relief and occurs along with epigastric pain in the projection of the pancreas. There is biliary vomiting with pathology of the biliary tract and stenotic vomiting with stenosis of the pylorus and duodenum. With biliary vomiting, the color of the vomit will be yellow-green; with stenotic vomiting, the color of the vomit will be brown, with an unpleasant putrid odor. They also produce fecal vomiting, which occurs when there is a significant narrowing of the intestinal lumen or when the innervation of the blood supply and intestinal motility is impaired.
In this regard, differential diagnostic methods are necessary. You should start by carefully collecting medical history, assessing the duration of symptoms, the time of onset of nausea and vomiting, the relationship of vomiting with food intake, pain, as well as assessing the volume, consistency, smell and color, the presence of food debris, the presence of pathological impurities in the vomit. During an objective examination, it is necessary to pay attention to the presence of fever, yellowness of the skin, asthenia, and pain on palpation of the abdomen. If necessary, perform instrumental diagnostics: ultrasound examination of the abdominal organs, fibroesophagogastroduodenoscopy, electrocardiography, blood pressure measurement, as well as clinical and laboratory studies [12].
Diagnostic criteria for early toxicosis are largely based on the determination of clinical and laboratory data. Laboratory tests usually include a general blood and urine test, hematocrit determination, a biochemical blood test, including bilirubin, residual nitrogen, urea, potassium, sodium, magnesium, chlorides, total protein, protein fractions, transaminases, glucose, acidity

levels. alkaline balance. It is advisable to determine the presence and level of acetone, urobilin, and protein in urine. In a patient with a severe form of toxicosis, a blood test can determine increased levels of hemoglobin, red blood cells and protein, and the true degree of dehydration must be determined by the level of hematocrit. When its value is above 40%, we can speak of severe dehydration [15].

5. Clinical manifestations

Preeclampsia may be asymptomatic or cause swelling or sudden, excessive weight gain (>5 pounds [2.27 kg] per week). Local swelling, such as of the face or hands (the patient's ring no longer fits on the finger), is more common than generalized swelling. Petechiae and other signs of bleeding disorders may appear. Eclampsia manifests itself with generalized (tonic-clonic) seizures. Preeclampsia with severe symptoms can cause organ damage; these signs may include

Strong headache

- Visual impairment
- Confusion
- Hyperreflexia
- Pain in the epigastrium or right upper quadrant of the abdomen (reflecting liver ischemia or distension of its capsule)
- Nausea and/or vomiting
- Dyspnea (indicative of pulmonary edema, acute respiratory distress syndrome [ARDS], or cardiac dysfunction due to increased afterload)

The clinical manifestations of early toxicosis are based on a functional disorder of embryo-placental interaction. There is inadequate functioning of the endothelial system and the platelet component of hemostasis, as well as programmed death of lymphocytes as a result of activation of the placental immunopathological reaction.
Currently, the following criteria for early toxicosis are applied (table) [10, 15].
According to the table above, early toxicosis has three degrees of severity: mild, moderate and severe. Criteria such as the frequency of vomiting during the day, heart rate, systolic blood pressure, body weight loss over 7 days, the presence of fever, assessment of jaundice of the sclera and skin, assessment of dry skin, stool frequency, diuresis and severity are taken into account. ketonuria.
Mild vomiting is characterized by a relatively satisfactory condition and slight apathy. The frequency of vomiting approximately 3-5 times a day is accompanied by a feeling of nausea. Despite vomiting, critical weight loss does not occur; weight loss is no more than 5% of the initial body weight. At the same time, hemodynamic parameters, diuresis, and morphological composition of the blood remain normal in most pregnant women. Mild vomiting does not require hospital treatment. However, in 10-15% of women, there is an increase in the clinical manifestations of early toxicosis and a transition to the second stage - moderate vomiting. This degree is characterized by an increase in nausea and vomiting up to 10 times a day, metabolic disorders and the development of ketoacidosis. Vomiting is accompanied by hypersalivation, progression of dehydration and a decrease in body weight to 6-10% of the original. There is dryness and yellowness of the skin, low-grade fever, and decreased diuresis. Anemia is observed in clinical laboratory blood parameters

mild, metabolic acidosis. Moderate vomiting requires hospital treatment and usually has a favorable outcome. If the situation worsens, severe vomiting may develop, which is characterized by severe intoxication of the body and, as a consequence, the development of dystrophic changes. The frequency of vomiting is 11 times a day or more. A sharp decrease in body weight, over 10% of the original. There is a deterioration in the general condition, adynamia, dryness and sagging skin, a decrease in subcutaneous fat, and the smell of acetone is noted when breathing. Body temperature can rise to 38 °C. When examining laboratory parameters, an increase in residual nitrogen, urea, and bilirubin in the blood is noted. In the general blood test - an increase in hematocrit and leukocytes. At the same time, albumin, potassium and chlorides decrease. Protein, casts, urobilin, leukocytes and red blood cells can be detected in the urine. The reaction of urine to acetone is sharply positive.

Signs of a threatening condition are a sharp and rapid increase in weakness, adynamia, delirium, tachycardia, hypotension, yellowness of the skin and sclera, a decrease in diuresis to 300 ml or less per day, hyperbilirubinemia (with values from 100 μmol/l), an increase in the level of residual nitrogen , urea, proteinuria, cylindruria. If a threatening condition is suspected, emergency termination of pregnancy should be considered [10].

6. Complications

Although there is not enough data on the long-term effects of vomiting gravidarum on the fetus, A.J. Smith et al. in 2021, they began to lean towards the opinion that there are no cognitive impairments in the offspring [9]. However, cases of placental abruption, neurological complications, premature birth, fetal growth restriction and other pathological processes cannot be excluded. It has also been noted that Hyperemesis gravidarum may subsequently reduce insulin sensitivity in children, but another study found that early pregnancy weight loss of more than 5 kg had no negative effect on the child's blood sugar, lipids and body mass index. up to 5-6 years [19].

There is also a downside to the development of early toxicosis in pregnant women. Women suffering from metabolic syndrome (MS) experience nausea and vomiting during pregnancy more often than women who do not suffer from MS. Moreover, against the background of metabolic syndrome with associated early toxicosis, the percentage of complications in childbirth is quite high and amounts to 46.7%. Abnormalities of labor are also observed. The effect on the fetus of such a combined disease is also negative: in women with MS complicated by toxicosis, children were born with asphyxia more often than in those patients who do not suffer from metabolic disorders and toxicosis [2].

One of the serious complications is dehydration due to uncontrollable vomiting. This leads to the electrolyte balance being disturbed, hypokalemia, hypomagnesemia, metabolic alkalosis developing, and a decrease in thiamine levels. It is assumed that such changes lead to antenatal fetal death. Yu.K. Husak et al. in their study analyzed 147 birth histories that resulted in a dead fetus: 89.6% were complicated by early toxicosis and other clinical manifestations of placental dysfunction [11].

Metabolic alkalosis, in turn, threatens with the development of depression and hallucinations, and in severe cases of the disease, these symptoms are observed quite often - 47 and 48%, respectively. Magnesium deficiency leads to muscle cramps, insomnia, tinnitus, and dizziness. There is also a study, the results of which suggest that pregnant women who are without physical activity for a long time, with frequent alcohol consumption and with a history of gastrointestinal diseases are at risk for a longer and more severe course of toxicosis in pregnant women [7, 16].

According to the results of the study, it was revealed that pregnant women with dyspeptic disorder were more likely to be at risk of miscarriage, placental insufficiency, and had a high tendency to

urinary tract infections and anemia. It was noted that the incidence of preeclampsia and premature birth does not depend on disorders of the gastrointestinal system, however, according to another study, it was found that with vomiting of pregnancy that developed in the second trimester, preeclampsia is observed 2 times more often, and the risk of placental abruption increases 3 times [7,12]. V. KeskinkiLiç in his article mentions that hyperemesis gravidarum has been identified as a transient risk factor for pulmonary embolism (PE) [13].

Early toxicosis can be complicated by termination of pregnancy. The question of termination of pregnancy will arise in the event of an increase in symptom complexes, the development of excessive vomiting of pregnant women and the appearance of signs of a threatening condition.

Indications for termination of pregnancy include: lack of effect from the therapy, uncontrollable vomiting, dehydration, progressive decrease in body weight of more than 10% of the original, jaundice of the skin and sclera, progressive ketonuria, severe tachycardia (with a heart rate of more than 100-120 beats per minute), adynamia, increasing apathy, delirium or euphoric state, hyperbilirubinemia (critical value 100 μmol/l) [10, 13].

7. Treatment

The basic drug in the treatment of preeclampsia and eclampsia is magnesium sulfate, administered at a concentration of 25%, the initial dose is 4 grams of dry matter over 10-15 minutes IV, slowly, then a maintenance dose of 1-2 g/hour is administered. Routine use of magnesium sulfate for the treatment of preeclampsia has been shown to have a significant impact on maternal mortality rates. Magnesium therapy should be carried out continuously at any stage of pregnancy, during childbirth and the postpartum period. Despite this, the use of magnesium sulfate is not a definitive treatment for severe preeclampsia. Delivery is the only effective treatment for severe preeclampsia [4;9]. In this aspect, the correct assessment of clinical symptoms and justified, rational intensive drug therapy in critical conditions is one of the criteria for favorable outcomes during pregnancy and childbirth. Improving the methods and principles of treatment is possible only on the basis of developing the principles of intensive therapy, monitoring the treatment process using monitoring of small hemodynamic profiles (BP, HR, CVP, CO, OPSS). With preeclampsia of varying severity, unjustified drug therapy is the cause of increased perinatal and maternal morbidity and mortality.

Treatment of early toxicosis is carried out depending on the severity and extent of the clinical picture. Approaches to the treatment of early toxicosis are usually divided into medicinal and non-medicinal. Non-drug therapy includes psychotherapy, homeopathy, and acupuncture. Regarding psychotherapy, it is known that there is a rational method that is aimed at reducing the negative and false ideas of a pregnant woman regarding her health. According to the Royal College of Obstetricians and Gynecologists "The Management of Nausea and Vomiting of Pregnancy and Hyperemesis Gravidarum", acupuncture for pregnant women is safe [1, 15]. Efferent methods of treatment are also used - plasmapheresis. Plasmapheresis is a universal and fairly effective detoxification procedure that is used for moderate to severe vomiting during pregnancy. When plasma pheresis was included in therapy for early toxicosis, there was a complete cessation of vomiting, improvement in general condition, return of appetite, and improvement in laboratory parameters [16]. A.K. Blbulyan et al. and E.G. Alekseeva et al. in their studies also came to the conclusion that plasmapheresis helps normalize organ and systemic blood flow and is a fairly effective method of alternative treatment for vomiting in pregnant women [7, 8].

The goal of drug treatment is to restore metabolism and water-salt metabolism. Diet therapy is recommended for all pregnant women, which should be based on easily digestible food. Food should be taken reclining, chilled, in small portions. The break between doses should be no more than 2-3 hours. All pregnant women suffering from nausea and vomiting are prescribed vitamin B6 - pyridoxine in a dosage of 10-25 mg [3, 10, 9]. In foreign clinical guidelines, doxylamine is considered the main drug in the treatment of vomiting during pregnancy1. Vitamin B1 - thiamine is also used to prevent Wernicke encephalopathy [9]. However, another source provides information that according to studies conducted in 2004, 34% of women did not use drugs, in particular vitamin B6, and 26% used a lower dosage, arguing for a subjective lack of confidence in the safe effect of the drug on fruit [10].

Treatment of mild vomiting during pregnancy is carried out on an outpatient basis and therapy will consist of symptom relief. So, according to the research of L.F. Mozheiko et al., it is advisable to prescribe a homeopathic medicine based on ginger root. Ginger root is a safe, non-toxic and quite effective means of symptomatic treatment of nausea and vomiting in pregnant women [10, 11, 12]. According to the results of studies conducted in 2014, the positive effect of aromatherapy with peppermint and lavender oils on pregnant women suffering from nausea and vomiting was established [30, 33, p. 241-244].

Treatment of vomiting during pregnancy of moderate and severe severity is carried out in a hospital. It is recommended to place the patient in a separate room for maximum comfort and reduction of stress. Enteral or parenteral therapy is prescribed, aimed at blocking the gag reflex by influencing the neurotransmitters of the medulla oblongata. These drugs include M-anticholinergic blockers (atropine), dopamine receptor blockers (haloperidol, thiethylperazine), direct dopamine antagonists (metoclopramide) and drugs that block serotonin receptors (ondansetron). It is worth noting that the drug ondansetron needs additional research to exclude a negative effect on the fetus [3,14]. According to the instructions for the drug, it is contraindicated for oral use in the first trimester of pregnancy. In case of severe vomiting, it is necessary to prevent the progression of dehydration and correct the water-salt balance. For this purpose, rehydration therapy is prescribed - the introduction of crystalloids. Massive infusion therapy is carried out in a volume of up to 6 liters of NaCL 0.9%.

Drugs such as Trisol, Chlosol, Ringer's solution (3 liters in the first 12 hours) are used. In combination with rehydration, parenteral nutrition is carried out with a solution of glucose together with insulin, amino acids and fat emulsion. The total energy value should be at least 1500 kcal per day. In addition to infusion therapy, pyridoxine hydrochloride 50-150 mg, thiamine 50-150 mg, riboflavin, ascorbic acid, Actovegin, essential phospholipids are prescribed. If blood protein decreases below 5 g/l, 200-400 ml of a 5-10% solution of albumin or other colloids is infused. With an adequate response to therapy, an increase in hematocrit and diuresis occurs. According to the data found, it is possible to use drugs that indirectly inhibit the formation of renin and aldosterone, and drugs that reduce the production of potassium and aldosterone [7, 15].

Since with early toxicosis pathogenetic disorders occur, in particular: degenerative processes of the liver as a result of dehydration and increased catabolic reactions, disturbances in the functional state of the nervous system, as well as symptomatic disorders - nervous excitability, which can lead to insomnia, disturbances in vascular tone and tendency to tachycardia, it is appropriate to prescribe a magnesium drug with orotic acid [8, 14]. According to the instructions for the drug magnesium orotate, the indications for prescribing this drug include: increased irritability, minor sleep disturbances, rapid heartbeat, increased fatigue and other symptoms. However, the instructions also note that it is necessary to use this drug with caution and according to indications during pregnancy and lactation, since at this time the need for magnesium increases, and its

excessive amount can lead to serious complications, including miscarriage, therefore, magnesium orotate should be prescribed if the potential benefit outweighs the possible risk to the fetus.

Treatment of patients with early toxicosis continues until complete recovery. If there is no effect on the therapy, a threatening condition may develop, which requires consideration of termination of pregnancy, since with prolongation, irreversible complications may develop, such as rhabdomyolysis, esophageal rupture, venous thrombosis, retinal hemorrhage, pneumothorax, kidney damage, encephalopathy and death [7, 15].

Maternal and perinatal morbidity and mortality are also influenced by the method of delivery for preeclampsia. Since preeclampsia is common in preterm pregnant women, the rate of cesarean section is estimated to be high. Vaginal delivery is preferable to operative delivery. According to the literature, cesarean section rates are 70% or more for preterm pregnancies because many obstetrician-gynecologists prefer to perform cesarean section in these patients, even if the fetal condition allows vaginal delivery. However, it has not yet been proven that cesarean section improves neonatal outcome and maternal mortality. Conversely, observational studies suggest that vaginal delivery may be better in the long term for preterm infants, also offering maternal benefits with fewer complications, shorter hospital stays with lower complication rates, and shorter hospital stays. In addition, the incidence of neonatal cerebral palsy remains the same [2,4].

At the present stage, vaginal delivery for severe preeclampsia is becoming an alternative to surgical delivery. Several methods are used to induce labor, depending on the degree of maturity of the cervix. When the cervix is immature, hydrophilic dilators (kelp) and prostaglandins (PG) are used to ripen it. Particular interest in prostaglandins is determined by their ability to stimulate the contractile activity of the myometrium at any stage of pregnancy. Cervical ripening with the use of prostaglandins increases the likelihood of successful induction of labor and achieving delivery within 12-24 hours. In recent years, the use of the synthetic drug misoprostol (PGE) has been intensively studied to accelerate cervical ripening and induce labor, including in women with severe preeclampsia. In addition, preparation with misoprostol reduces the need for oxytocin infusion to enhance uterine activity, and the number of deliveries by cesarean section is reduced. When using misoprostol, there is some concern that it can provoke excessive contractile activity of the uterus. However, perinatal outcomes were not significantly different [1,5].

Another important problem in preeclampsia is determining the indications for emergency delivery and the gestational age at which complications for children will be minimal. In this regard, the opinions of scientists are divided. Some scientists advocate the tactics of early delivery to avoid maternal complications (eclampsia, placental abruption, HELLP syndrome, cerebral hemorrhage, acute renal failure, and others) [8]. Other scientists advocate the tactics of prolonging pregnancy in order to avoid complications from the fetus associated with its immaturity (respiratory distress syndrome, cerebral hemorrhage, necrotizing enterocolitis, and others). As practice shows, therapy carried out by obstetricians is effective in 80 - 100% of patients. But it is precisely 10–20% of patients resistant to conventional therapy that account for the majority of severe complications.

Delaying delivery until the degree of fetal maturity increases creates a risk to the life of both mother and fetus [5].

According to various authors, the incidence of preeclampsia ranges from 7% to 16%. Preeclampsia develops in 6-12% of healthy pregnant women, 20-40% in pregnant women with extragenital pathology. According to WHO, preeclampsia occupies one of the first places in the structure of maternal mortality, being the cause of premature birth, premature abruption of a normally located placenta, the development of fetoplacental insufficiency, intrauterine growth retardation, and the birth of low birth weight children. According to various authors, preeclampsia as a cause of perinatal mortality ranks 1st - 2nd. Perinatal losses in preeclampsia are 4 times higher than in the group of healthy women. Among children born alive to mothers with

preeclampsia, every fourth child is delayed in physical development. Despite numerous studies devoted to the problem preeclampsia, many issues of the etiology, pathogenesis and genetics of this pregnancy complication remain controversial. None of the hypotheses
the occurrence of preeclampsia does not answer all questions related to this complication of pregnancy [4,6,8]. Thus, among the many problems associated with preeclampsia and eclampsia, the problem of diagnosis, prognosis and assessment of severity occupies one of the most important places and is of great importance for both obstetricians-gynecologists and anesthesiologists-resuscitators. Reducing perinatal and maternal morbidity and mortality remains the main goal of obstetricians and gynecologists. Its solution is impossible without reliable methods for predicting the course of pregnancy and the condition of newborns, which involve the timely use of therapeutic and preventive measures to eliminate adverse outcomes of pregnancy and childbirth. In this regard, it should be recognized that it is urgent to search for new prognostic and diagnostic criteria for the unfavorable course of pregnancy and childbirth, which will allow timely identification of a group at increased risk of perinatal complications in order to prevent or reduce the severity of such complications [1].
To reduce maternal mortality from preeclampsia and eclampsia, it is necessary to: take into account and identify risk factors for the development of preeclampsia, ensure proper monitoring of pregnant women at risk for preeclampsia, comply with the diagnostic criteria for preeclampsia when making a diagnosis, adhere to the principles of regionalization for preeclampsia, strict implementation of protocols when conducting magnesium and infusion therapy, compliance with delivery standards for preeclampsia and eclampsia, clinical examination of women with extragenital diseases, their rehabilitation and treatment, integration of perinatal centers with multidisciplinary hospitals [4].

8. Conclusions

The association between severe toxicosis and preeclampsia in pregnancy highlights the importance of early recognition and effective management of these conditions. Further research and development of effective prevention and management strategies are key to improving pregnancy outcomes in women at increased risk of developing these complications.

Literature

1. H. Critchley, A. Poston, J. Walker, Pre-eclampsia, RCOG Press, London: 2003. - P. 189-207
2. Alanis MC, Johnson DD. Early initiation of severe preeclampsia induction of labor is versus elected cesarean delivery and newborn//American Journal of Obstetrics and Gynecology 2008. - 199 (3). - 262. - e1-262. - e6.
3. Протоколы МЗ РК № 262 от 04 мая 2011г.
4. Бикташева Х.М. и др. Преэклампсия в системе «мать-плацента-плод»// Материалы научно-практической конференции, Алматы-Актау: 2010 г.
5. Абрамченко В.В. Ф.Д. Каримова. Современные аспекты охраны репродуктивного здоровья населения//Материалы V юбилейной научно-практической конференции, - Нижневартовск: 2001. - С. 111-118.
6. Абрамченко В.В., Н.П. Шабалов. Клиническая перинатология.//Петрозаводск: Интелтек. - 2004. - 424 с.
7. Айламазян Э.К. Акушерство: учебник для медицинских вузов. 4-е изд., переработанное // СПб.: СпецЛит. - 2005. - 527 с.

8. Айламазян Э. К. Неотложная помощь при экстремальных состояниях в акушерской практике.// 3-е изд. СПб.: 2002. - С. 426-432.
9. Аккер Л.В., Варшавский Б.Я., и др. Показатели оксидантного и антиоксидантного статуса у беременных с гестозом// Акушерство и гинекология, 2000. - № 4. - С. 17-20.
10. Morning Sickness: Nausea and Vomiting of Pregnancy, May 2020. Available at: https://www.acog. org/womens-health/faqs/morning-sickness-nausea-and-vomiting-of-pregnancy.
11. Shehmar M., Maclean M.A., Nelson-Piercy C., Gadsby R., O'Hara M.
The Management of Nausea and Vomiting of Pregnancy and Hyperemesis Gravidarum Green-top Guideline No. 69. Royal College of Obstetricians and Gynaecologists; 2016. Available at: https://www.rcog.org.uk/globalassets/ documents/guidelines/green-top-guidelines/gtg69-hyperemesis.pdf.
12. Garcia Saborio O.E., Hines B.K., Wesselman J. Safe Management of Nausea and Vomiting During Pregnancy in the Emergency Department. Adv Emerg Nurs J. 2019;41(4):336-347. https//doi.org/10.1097/tme.0000000000000258.
13. Fejzo M.S., Trovik J., Grooten IJ., Sridharan K., Roseboom TJ., Vikanes A.
et al. Nausea and vomiting of pregnancy and hyperemesis gravidarum. Nat Rev Dis Primers. 2019;5(1):62. https://doi.org/10.1038/s41572-019-0110-3.
14. Павлова К.С. Токсикоз первой половины беременности. Физиотерапевтическая коррекция. В: Мечниковские чтения - 2020: материалы 93-й Всероссийской научно-практической студенческой конференции с международным участием. Санкт-Петербург. 29-30 апреля, 2020 г. СПб.: Северо-Западный государственный медицинский университет имени И.И. Мечникова; 2020. Режим доступа: https://elibrary.ru/item.asp?id=42961395&. Pavlova K.S. Toxicosis of the first half of pregnancy. Physiotherapy correction. In: Mechnikov Readings - 2020: Materials of the 93rd All-Russian Scientific and Practical Student Conference with international participation. St Petersburg. April 29-30, 2020. St Petersburg: I.I. Mechnikov Northwestern State Medical University; 2020. (In Russ.) Available at: https://elibrary.ru/item.asp?id=42961395&.
15. Рахманова Т.Х., Исенова С.Ш., Святова ПС., Эгле М. Современный взгляд на вопрос этиологии чрезмерной рвоты беременных. Вестник Казахского национального медицинского университета. 2020;(3):7-12. Режим доступа: https://elibrary.ru/item.asp?id=44838706. Rakhmanova T.Kh., Isenova S.Sh., Svyatova G.S., Egle M. Modern view on
the etiology of excessive vomiting of pregnant women. Vestnik KazNMU. 2020;(3):7-12. (In Russ.) Available at: https//elibrary.ru/item.asp?id=44838706.
16. Boelig R.C., Barton SJ., Saccone G., Kelly AJ., Edwards SJ., Berghella V. Interventions for treating hyperemesis gravidarum: a Cochrane systematic review and meta-analysis. J Matern Fetal Neonatal Med. 2018;31(18): 2492-2505. https://doi.org/10.1080/14767058.2017.1342805.