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Review Article

Management of pregnant women from a high risk group with threat and premature labor. Prevention of intra-perinatal outcomes

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ABSTRACT:

Relevance of the research topic. The problem of preterm birth (PR) occupies one of the leading positions in terms of importance in modern obstetrics and neonatology, since they determine the level of perinatal and infant mortality and morbidity [59, 67, 68, 79]. Perinatal mortality among premature infants is much higher than among full-term infants. In 2015, complications of prematurity were the cause of death in 1 million cases [124]. Up to 70% of neonatal mortality and up to 75% of child mortality occur in premature babies [70].

Despite the close attention of scientists to this problem in recent years, the incidence of miscarriage remains high enough and does not tend to decrease [56].

In Russia, the incidence of preterm birth ranges from 7 to 12%, depending on the region.

Key words: women health, pregnancy, premature pregnancy, labor, gynecology, obstetrics

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The relevance of studying the problem of prematurity in Russia has increased significantly in recent years, which is associated with the introduction of new criteria for live birth (order of the Ministry of Health and Social Development of Russia No. 1687 dated December 27, 2011 "On medical criteria for birth, the form of a birth document and the procedure for issuing it"). According to this order, the termination of pregnancy from 22 weeks of gestation, and not from 28, as it was before, began to be attributed to premature birth [54]. At the same time, the share of premature births changed slightly and in 2013 amounted to 4.6% compared to 3.82% in 2010. However, over the same period, the number of disabled children increased from 519 to 568 thousand people against the background of a decrease in the indicators of general disability (13134 thousand and 13,082 thousand people in 2010 and 2013, respectively) [26]. This fact indicates a high the contribution of children born at a gestation period of 22-27 weeks 6 days to the structure of child disability against the background of a small number of births during these periods.

According to A.A. Gavrilova et al. (2018), the proportion of deeply premature babies is 5% of all premature babies and 1% of the total population of newborns [19].

In recent years, great strides have been made in modern obstetrics and neonatology, which makes it possible to nurture deeply premature newborns. The increase in the survival rate of children born with extremely low (ELBW) and very low birth weight (VLBW) has led to an increase in perinatal morbidity and childhood disability. So, according to data published in 2016, in the

Smolensk region, the survival rate of deeply premature babies increased from 59% in 2012 to 82.3% in 2015 [4]. Effective treatment and nursing are not a guarantee of the absence of severe childhood disability in the long term of the distant development of a deeply premature baby. The results of many studies on the quality of life of deeply premature infants indicate that the prognosis of long-term outcomes in this category is extremely unfavorable: no more than 10-25% of them do not have severe chronic pathology [19]. A large number of surviving premature infants develop neurological disorders in the early and late long-term periods [46].

Despite the relatively small proportion of children born before 28 weeks of age, their state of health is of particular concern [59].

The pathology of the central nervous system (CNS) dominates among the causes of early morbidity and disability [51].

Intraventricular hemorrhage (IVH), which is one of the causes of death and the development of a wide range of neurological disorders in childhood, is the most frequent and serious pathology of the central nervous system in premature infants [20].

According to N.V. Bashmakova (2014), disability due to neurological pathology among children born with EBMT is 32%. TO disabling neurological diseases include infantile cerebral palsy (cerebral palsy), blindness, deafness, mental retardation [9]. Among children with cerebral palsy, 50% had a birth weight of less than 1000 grams. 17% of children with severe visual impairment are born before 28 weeks of gestation [95].

The question of the influence of ante- and intranatal factors, medical support of pregnancy and methods of delivery on the neurological morbidity of deeply premature infants in the neonatal and long-term period of development remains insufficiently studied. And the available data on this topic is contradictory.

Thus, the priority direction of further research on the problem of preterm birth is not only the search for ways to reduce perinatal mortality among deeply premature infants, but also the reduction of neonatal and infant morbidity with a high risk of disability among this category of children.

The degree of elaboration of the topic. In the modern literature, there is evidence that among the risk factors for neurological pathology, in particular intraventricular hemorrhage (IVH), in a full-term newborn, maternal somatic diseases, complicated pregnancy, and rapid labor are of particular importance [39, 44]. It is also known that with a decrease in the body weight of the newborn and gestational age, the risk of developing IVH increases [51]. However, to date, there are no systematized data on the place of maternal factors in the development of IVH against the background of deep prematurity.

Previous foreign and domestic studies have demonstrated a positive result of antenatal steroid use against the background of tocolytic therapy for a premature baby [93, 112, 143, 148, 155, 165]. It is also known that magnesium therapy helps to reduce the incidence of neurological pathology in premature infants [25, 67].

The use of micronized progesterone in patients with a cervical length less than 25 mm according to echography or a history of preterm labor is an effective and cost-effective measure for the prevention of preterm labor [63, 72, 96, 98, 103, 104, 105, 107, 109, 110, 116, 125, 129, 132, 135, 140, 141, 145, 161, 164]. However, in the available literature there is no information on the possible effect of this drug on the frequency and severity of cerebral pathology in children born deeply premature.

Worldwide, there has been no decrease in the incidence of preterm birth, including very early and early births, despite a fairly wide range of measures used to prevent and treat prematurity. This indicates the need for further search for ways to prolong pregnancy and improve outcomes for the newborn.

Researchers' close attention is drawn to the problem of choosing the method of delivery in very early delivery (ERP) and early preterm birth (ERP). This is due to the possible influence of this factor on neonatal outcomes on the one hand [9, 22, 30, 41, 43, 57, 68], on the other hand, a high risk of severe obstetric complications in the near and distant future with abdominal delivery [65, 120]. However, in modern obstetrics there is no consensus about the advantage of any method of delivery in relation to the prognosis for a deeply premature baby.

Objective of the study: to reduce adverse outcomes of very early and early preterm births for mother and child by choosing optimal obstetric tactics.

The results of our study have proved for the first time that micronized progesterone improves the prognosis for the development of neurological diseases in a deeply premature baby both in the neonatal and in the long-term period of development. The use of this drug in a complex of drug therapy for threatening RRP and RRP helps to reduce the frequency and severity of cerebral pathology in children born at 22-30 weeks 6 days.

In our study, we obtained data indicating the absence of a reliable effect of the mode of delivery on the frequency and severity of cerebral pathology in premature infants with EBMT and VLBW in the near and distant period of development.

The theoretical and practical significance of the work. Based on the study of the somatic and obstetric-gynecological anamnesis, as well as complications of the course of this pregnancy in mothers whose children had pathology of the central nervous system in the neonatal period and / or in the long-term period of development, significant risk factors for this

pathology in deeply premature infants have been identified. This knowledge allows us to recommend the necessary preventive measures among patients at high risk of undermaturity.

As a result of the study, the optimal obstetric tactics were determined for threatening and incipient ORPR and RDM. It has been established that none of the methods of delivery has advantages in terms of the prognosis of severe cerebral pathology in a child born deeply premature. The problem of premature birth today is quite acute in almost all countries of the world. The prevalence of pre-term births in Africa and East Asia reaches 18%, but their proportion is high in developed countries as well. For example, in the United States, despite significant investments in health care, preterm births account for 12% of live births, which is much higher than in other developed countries (this is probably also due to the high quality of statistics in the United States) [75]. In Russia, the incidence of preterm birth ranges from 7 to 12%, depending on the region [14]. According to Rosstat (2017), the frequency of pre-term births in Russia in 2014-2016. was 4.4%, and the share of premature babies in the total number of live births was 5.8%. Over the past decade, the number of preterm births has not only not decreased, but tends to increase worldwide [113, 174]. The relevance of studying the problem of prematurity in Russia has increased significantly in recent years, which is associated with the beginning of the order of the Ministry of Health and Social Development of Russia No. 1687 dated December 27, 2011 "On medical criteria for birth, the form of a birth document and the procedure for issuing it." According to this order, the termination of pregnancy from 22 weeks of gestation began to be attributed to premature birth. At the same time, the share of premature births changed slightly and in 2013 amounted to 4.6% compared to 3.82% in 2010. However, over the same period, the number of disabled children increased from 519 to 568 thousand people against the background of a decrease in the indicators of general disability (13134 thousand and 13,082 thousand people in 2010 and 2013, respectively) [26]. This fact testifies to the high contribution of children born at 22-27 weeks 6 days to the structure of child disability against the background of a small number of births during these periods. Premature birth is a syndrome that can be caused by a variety of etiological factors, such as an infectious and inflammatory process, uterine hyperextension, immune and endocrine factors, structural abnormalities of the cervix, thrombophilia of various origins. In 70-80% of cases, it is not possible to reliably establish the cause of premature birth [28, 75]. A fairly large number of studies have been devoted to the study of the causes of premature birth. It is known that risk factors for preterm birth are low socioeconomic status, young age and age over 35, disorder in family life, bad habits, history of reproductive losses, infections of the urinary and reproductive systems, severe extragenital diseases, multiple pregnancy, pregnancy as a result of auxiliary reproductive technologies (ART) [8, 33, 73].

In recent years, there has been evidence of a causal relationship between bacterial vaginosis and preterm labor [21, 52, 66, 78]. Some authors note that most often there is a combination of several causes of undermaturity [38]. Currently, more and more attention of specialists is attracted by issues of prevention of premature birth. To date, the generally recognized preventive measures of prematurity are the limitation of intrauterine manipulations and the limitation of the number of transferred embryos during ART [72]. A special place among the measures for the prevention of early termination of pregnancy is occupied by pre-conceptional preparation, which contributes not only to a decrease in the incidence of PR, but also to the improvement of the health of premature infants [61]. To determine the degree of risk of perinatal complications in Russia, the scale proposed by V.E. Radzinsky (2011). According to this scale, the degree of perinatal risk is determined in all pregnant women, taking into account the individual characteristics of the somatic and obstetric-gynecological history, as well as the characteristics of the course of pregnancy.

Prescribing progesterone drugs to patients with a cervical length of less than 25 mm or a history of preterm labor, as well as the imposition of a cerclage thread, are referred to as secondary prevention of prematurity during pregnancy [63, 72, 125, 104, 129, 146, 161]. Progesterone is known to be critical in maintaining pregnancy. It exhibits biological effects in the myometrium, chorioamniotic membranes, and the cervix [126, 158, 173]. Decreased progesterone activity plays a key role in remodeling (“maturation”) of the cervix [122, 133, 176, 177, 176]. In turn, the removal of the action of progesterone is the trigger mechanism for the onset of labor [126]. The results of many studies confirm that the use of vaginal progesterone is an effective and cost-effective measure for the prevention of early birth in pregnant women with a "short" cervix and a history of premature birth [96, 98, 103, 105, 107, 109, 110, 116, 123, 132, 135, 136, 140, 141, 144, 145, 164]. Patients with a "short" cervix are recommended to prescribe 200 mg of vaginal progesterone (micronized progesterone) daily. In patients with a history of preterm labor, both vaginal progesterone and oral (dydrogestron) and intramuscular (17-hydroxyprogesterone caproate) can be used [102, 104, 125, 129, 146, 161].

Some authors in their studies indicate that when the cervix is shortened, the application of a circlage suture does not have any advantages over the use of vaginal progesterone [105]. However, according to M.I. Bazina

et al. (2014), the appointment of progesterone does not affect the likelihood of a very early preterm birth, since the termination of pregnancy at 22-27 weeks is mainly due to medical indications on the part of the mother or fetus. At the same time, the authors point to the important role of vaginal micronized progesterone in the term for singleton pregnancy [5]. Progesterone receptors are present not only in the reproductive system, but also in the central and peripheral nervous system [91, 158, 173]. The physiological effects of progesterone in the nervous tissue are manifested in the form of a decrease in postischemic cellular edema and maintenance of the integrity of the blood-brain barrier [106]. In addition, this steroid hormone inhibits postischemic apoptosis and activates the release of growth factors. It also reduces the expression of proinflammatory cytokines (interleukin-1, interleukin-6, tumor necrosis factor-alpha), which suppresses postischemic inflammation [177]. The administration of progesterone leads to the release of markers of synaptogenesis [106]. In the third trimester of pregnancy, the concentration of progesterone in the woman's blood serum increases 100 times from the initial level [175]. In case of premature birth, the child leaves this environment "enriched" with progesterone, which probably cannot but affect the state of his nervous tissue.

Thus, the attention of scientists around the world is focused on the prevention of premature birth and prolongation of pregnancy using progesterone therapy. While the effect of progesterone on the likelihood of developing severe cerebral pathology in a premature baby is not well understood. One of the undoubted ways to reduce the incidence of neonatal morbidity associated with profound prematurity is steroid prophylaxis in the antenatal period [59].

The use of antenatal tocolysis allows gaining time for the full course of prophylaxis of fetal respiratory distress syndrome (RDS) with glucocorticosteroids. Beta-adrenomimetics, oxytocin receptor blockers, and calcium channel blockers have a tocolytic effect that allows delaying preterm labor by relaxing the myometrium [115]. The goal of acute tocolysis is to prolong pregnancy by 48 hours for the implementation of glucocorticoid prophylaxis of respiratory distress of the fetus and transportation of a pregnant woman to a medical institution of the appropriate level [121]. Currently, it is generally accepted that it is inexpedient to prolong tocolysis to three or more days to reduce unfavorable perinatal outcomes [72, 172]. The absence of a decrease in the frequency of preterm birth worldwide, despite a fairly wide range of measures used to prevent prematurity, indicates the need to further search for ways to prolong pregnancy and improve the outcomes of preterm birth for the mother and newborn. Magnesium sulfate has also been used as a tocolytic for a long time. The results of recent studies have shown that the use of magnesia therapy helps to reduce the incidence of cerebral palsy and disorders of large motor functions in children born deeply premature, which is associated with its neuroprotective effect [84, 99]. In 2013, Russian researchers published data that the use of magnesia therapy in pregnant women does not lead to hypermagnesemia in the fetus, which contributes to the development of muscle hypotension and suppression of the function of the parathyroid glands in the neonatal period [37]. Premature birth and prematurity is not only a medical, but also a social and economic problem for the state. The high incidence of disabling diseases among premature babies is associated with high costs of nursing, rehabilitation and social adaptation of such members of society. In 2013, out of 10 children born in the world, more than one child was born prematurely, which amounted to more than 15 million newborns [174].

As a rule, the majority of preterm births (about 70%) occur at 34-36 weeks of gestation (the first degree of prematurity of newborns). However, children born before 31 weeks are much more likely to require high-tech medical care [7]. In the United States, $ 26 billion is spent annually on nursing premature babies, not counting the costs that the government may incur if the premature baby is left disabled [75]. Currently, there is no single approach to solving urgent problems related to pregnancy miscarriage, which is confirmed by the data presented in the book edited by prof. G. Karpa “Habitual pregnancy loss. The reasons. Contraversion. Treatment". It presents opposing views on some aspects of preterm birth. In particular, some authors, on the basis of qualitative studies, assert the significant role of the use of progesterone in order to maintain pregnancy, while others consider this preventive measure inappropriate [94].

CONCLUSION

Thus, the rate of preterm birth, which remains at a constant level, despite a large number of studies in this area, indicates the insufficient effectiveness of modern measures to prevent prematurity. The high mortality and morbidity with the risk of disability in children born deeply premature confirms the need for further search for ways to prolong pregnancy, as well as optimal approaches to drug support of pregnancy and delivery in case of premature birth.

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