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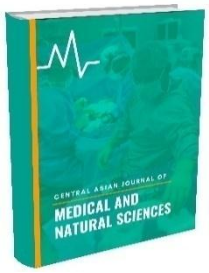

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Premature Water Discharge The Role of Vitamin D

1. **Isroilova Guljannat Pardabaevna**
2. **Narzullayeva Dilnoza**
3. **Narzullayeva Xafiza**

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[1,] Assistant of the Department of Obstetrics and Gynecology.

[2,] kl. Ordinator of Medical Institute

[3] Assistant of Medical Institute Samarkand State Medical Institute, Samarkand Uzbekistan

Abstract: The role of vitamin D as a potential modulator of immune responses during pregnancy was first reported over 50 years ago, but the specific mechanisms for fulfilling this role have only recently received due attention. Already in the first weeks of pregnancy, the trophoblast simultaneously synthesizes and responds to the action of vitamin D, which locally implements an anti-inflammatory function and simultaneously stimulates the growth of decidual tissue necessary for normal pregnancy.

Key words: Vitamin D, pregnancy, fetus, placenta, newborn.

Introduction

Currently, there is more and more data on the pleiotropic effect of vitamin D, including those related to its effect on the body of a pregnant woman and the fetus. At the same time, it was found that a sufficient level of vitamin D is necessary throughout pregnancy, starting from the moment of implantation and the formation of the placenta. Vitamin D plays an important role in the adequate functioning of the mother-placenta-fetus system, and also has a positive effect on embryogenesis, the course of intra- and postnatal periods.

Calcidiol ($25(OH)D_3$) is involved in the development and formation of a child's place - the placenta. The placenta begins to form on the 4th week. pregnancy. From that time on, vitamin D of a pregnant woman enters the fetus and largely determines the development of the bone and immune systems, and then other organs and systems. The concentration of calcitriol ($1.25\ (OH)_2D_3$) by 12 weeks. pregnancy increases by 2-3 times, which is associated with an increase in the production of a metabolite in the kidneys of a pregnant woman, as well as in the trophoblast, decidual tissue and placenta. In the decidual tissue and the outer cell layer of the blastocyst, when the *CYP27B1* gene (encodes 1α-hydroxylase) is expressed, $1,25(OH)_2D_3$ is formed, the maximum production of which was noted in the I–II trimesters of pregnancy.

Historically, the placenta was one of the first extrarenal tissues capable of synthesizing $1,25(OH)_2D_3$, but only calcidiol ($25(OH)D_3$) crosses the placental barrier and supplies the fetus. In early pregnancy, vitamin D stimulates the expression of the *HOXA10* and *HOXA11* genes, which ensures decidual transformation of the endometrium, control of the mother's immune response (regulation of the ratio of

cytokines), stimulates the hormonal function of the placenta, and provides the antimicrobial effect of the trophoblast and placenta.

During pregnancy, vitamin D receptors (VDRs) and enzymes that regulate metabolism are expressed in the placenta and uterine decidua, indicating a critical immunomodulation point at the mother-fetus interface. The level of vitamin D-binding protein in the blood increases during pregnancy from 46% to 103%.

In the fetal body, $25(OH)D_3$ is converted to the active form - $1,25(OH)_2D_3$, which, interacting with VDR in organs and tissues, implements the classic effects of vitamin D.

Vitamin D receptors (VDRs) are present in most of the cells of the body; in many tissues there is the enzyme 1α-hydroxylase, which is necessary for the synthesis of the active form of the D-hormone - $1,25(OH)_2D_3$. There is evidence that $1,25(OH)_2D_3$ coordinates the transcription and function of genes associated with trophoblast invasion, implantation, and angiogenesis. The level of $1,25(OH)_2D_3$ in the fetus and cord blood is lower than in adults and significantly lower than in the mother's blood. During the first days of life, in response to a decrease in calcium levels and an increase in the concentration of parathyroid hormone in the blood of newborns, the synthesis of $1,25(OH)_2D_3$ is activated, which, apparently, is associated with the need to activate calcium absorption in the intestine immediately after birth.

The effect of vitamin D on the fetus and early child development

Since the fetus undergoes physiological changes during pregnancy associated with rapid growth, vitamin D and its metabolites influence the realization of the genetic characteristics of the developing fetus and minimize the risk of adverse pregnancy outcomes. At the same time, it was found that vitamin D deficiency in pregnant women is not only associated with an increased risk of preterm birth, high rates of neonatal morbidity and mortality, but also adversely affects the postnatal development of children, especially when the level of vitamin D in the mother's blood serum is less than 50 nmol / l (<20 ng/ml). Thus, it was found that the administration of vitamin D to pregnant women at a dose of 2400 IU/day significantly improved bone mineralization in preschool children compared to those whose mothers received standard supplements (400 IU/day).

Insufficient intake of calcidiol in the fetal body can lead to metabolic changes, prematurity, delayed formation of brain structures, physical development, hypocalcemic convulsions, hyperbilirubinemia, an increase in the incidence of necrotizing enterocolitis and bronchopulmonary dysplasia, as well as increase the risk of lower respiratory tract infections and sepsis. At the same time, in recent years, more and more research is related to the study of the role of vitamin D deficiency in the development of infections in children and newborns. It has been established that one of the properties of calcidiol is its ability to stimulate the formation of antimicrobial peptides (*β2*-defensins and cathelicidins), which have a pronounced bactericidal activity. Thus, vitamin D deficiency is a significant factor in reducing the level of antimicrobial peptides, which is accompanied by an increased risk of sepsis in newborns.

Given the high basal expression of *CYP27B1* and *VDR* in placental trophoblastic cells, it is suggested that the anti-inflammatory effects of vitamin D may be particularly important in this organ as well. Vitamin D metabolites determine the formation of surfactant and the development of lung tissue. Deficiency of vitamin D and its metabolites increases the need for oxygenation in neonates, especially preterm infants, and is considered a risk factor for respiratory distress syndrome and respiratory tract infections.

By now, the impact of vitamin D deficiency on the development of the central nervous system is well known. It has been proven that with a deficiency of $25(OH)_2D_3$ in the antenatal and early postnatal periods, delayed speech development, fainting, epilepsy, and a number of demyelinating diseases may

occur. In addition, it has been shown that preschool children with attention deficit hyperactivity disorder at birth had low levels of $25(OH)D_3$ in the cord blood compared to newborns without this pathology.

The level of $25(OH)D_3$ in the cord blood of a child is 50-80% of its level in the mother's blood serum ($p=0.001$), regardless of the gestational age. And since $25(OH)D_3$ deficiency is widespread among pregnant women, this explains the large number of newborns with vitamin D deficiency, newborns, is vitamin D supplementation during pregnancy.

Conclusion

Thus, vitamin D deficiency is a public health problem worldwide. Due to the multifaceted regulatory effect (on immunity, on biochemical and cellular processes), vitamin D is an extremely significant factor determining the favorable course of pregnancy, as well as adequate intrauterine and postnatal development of the child. In this regard, the prevention of insufficient supply of vitamin D in pregnant and newborn children should become an obligatory component in the preventive work not only of pediatricians and neonatologists, but also of obstetricians and gynecologists.

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