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Changes of cytokine profile in the blood of pregnant women with anemia

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ABSTRACT

The aim of this study was to investigate the level of serum cytokines in different periods of pregnancy associated with anemia. 85 pregnant patients with anemia were examined. 46 of them were in their first pregnancy (1st group), and 39 (2nd group) patients were in their second or further pregnancy period. The comparison group consisted of 19 pregnant women without anemia. The level of hemoglobin and serum iron were determined by using colorimetric method, as well as the level of cytokines IL-2, IL-6, IL-8 and IL-10 were determined using an enzyme-linked immunosorbent assay method. The results showed a significant decrease in hemoglobin and serum iron level in the blood of pregnant women with anemia, significant increase in proinflammatory ytokines, such as IL-2 and IL-8, and a significant decrease in IL-10 compared with pregnant women without anemia were also detected. The most pronounced changes in the cytokine profile were observed in the third trimester and during second or futher pregnancy, which is caused by the progression of anemia.

1. Introduction

In practical obstetrics, the problem of iron deficiency anemia (IDA) in pregnant women and puerperal remains very relevant. Worldwide, the frequency of anemia in pregnant women ranges from 25% to 50%, in developing countries - from 35% to 75%, in developed countries is 18%-20% [1], [2]. The average rate of anemia in the Russian Federation reaches 32% [3]. In residents of the Central Asian republics, pregnancy in most cases proceeds against the background of IDA. Thus, the prevalence of IDA among women of reproductive age has decreased in the last 12 years from 60% (1996) to 33.5% (2008) in Uzbekistan [4]. It is well known that anemia aggravates pregnancy and childbirth, due to iron deficiency and chronic hypoxia, which negatively affect the mother's body, contribute to the development of preeclampsia, miscarriage, weakness of labor, premature detachment of a normally located placenta, bleeding in the postpartum period, postpartum septic diseases, perinatal, complications [5], [6] Based on the analysis of literature data [6] indicate that a violation of the course of gestation occurs as a result of the fact that with severe anemia there is no transformation of the spiral arteries, their smooth muscle layer is preserved, but does not disappear, as is the case with normal pregnancy. The result is increased fetal hypoxia - fetoplacental insufficiency, since not expanding spiral arteries are not able to provide the growing demand for blood supply. It is these

pathological processes that underlie the established relationship between anemia and miscarriage, premature detachment of a normally located placenta. In addition, these changes can increase the risk of preeclampsia, bleeding during childbirth, weak labor, postpartum septic complications [7– 10]. Anemia causes circulatory and tissue hypoxia, characterized by a deficiency of protein, iron and other essential trace elements. These factors are the pathogenetic basis for the development of preeclampsia. The frequency of development of hypertensive states in IDA reaches 32-45%.11 The combination of preeclampsia with anemia is a real threat to the life of the mother and newborn. Among women who died of preeclampsia, IDA was observed in 85.3%, the frequency of preeclampsia increases with decreasing hemoglobin (HB) levels: for example, it was 11.1% with hemoglobin <70g/l, 14.5% with hemoglobin <60g/l and 30.0% at its level <50g/l [12].

2. Methods

To clarify the role of immunological disorders in IDA in the genesis of preeclampsia, we conducted immunological studies by method of random sampling in 96 women in the third trimester of gestation. The inclusion criteria were: pregnancy in the third trimester; hypochromic microcytic anemia: Hb level less than 110g/l; absence or appearance of signs of mild preeclapsia; 18 to 42years of age; the informed consent. Exclusion criteria were: other types of anaemia, blood disease; heavy endocrinopathy; heart and vascular diseases; lesions of other organs and systems (chronic renal, hepatic failure); acute infections (AIDS, viral hepatitis, etc.).

3. Discussion

The placenta produces a large number of hormones and acts as an immunological barrier, synthesizing immunosuppressive factors, which creates immunologically privileged conditions for the development of the fetus. Activation of pro-inflammatory cytokines occurs with progesterone deficiency. Under the influence of proinflammatory cytokines, primary placental insufficiency is formed. Placental dysfunction, in particular, increased apoptosis plays a role in the pathogenesis of the formation of preeclampsia [23– 25] while Fas-mediated apoptosis may be involved in creating conditions for abnormal placentation leading to preeclampsia.26 Preeclampsia is associated with systemic inflammation and damage to trophoblast invasion into the decidual uterine membrane. Macrophage infiltration is involved in damage to trophoblast invasion, leading to the development of preeclampsia. We believe that preeclampsia could be associated with an increase in decidual dendritic cell infiltration and that IL-1β increases the production of dendritic cell-mediated chemokinesis. It has been suggested that dendritic cells may play a decisive role in the pathogenesis of preeclampsia [17], [27].

4. Conclusions

Thus, our data on the imbalance of the cytokine status at the systemic level indicate a malfunctioning immune response of the mother to the antigens of the ovum against the background of rearrangement of the endocrine system and iron deficiency anemia, which is one of the main causes of preeclampsia. High activation of pro-inflammatory cytokines at the site of attachment of the placenta can be considered a threat of allograft rejection, clinically manifested by premature placental abruption / preterm delivery, the most common complications of preeclampsia.

5. References

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