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Features of Cytokine Status of Pregnant Women with Chronic Pyelonephritis, Depending on the Placenta Morphological Characteristics

ABSTRACT

It has been shown that for an objective appraisal of the impact of active influence of chronic pyelonephritis on the feto-placental complex is possible in determining the constituents of pro- and anti-inflammatory cytokines. The results of this research on cytokine status give an evidence of the unstabilized nature of the immune system in women with CP. In spite of the complete clinical and laboratory remission of the disease, contributions to the development of gestational complications were due to the lack of pregravidal training and early prevention of placental insufficiency. It has been established that, despite the absence of specific features in the placenta of women with chronic pyelonephritis that highlighted to the compensatory and sub-compensatory changes against the backdrop of dystrophic, microcirculatory and other disorders, reflecting not only the provision of the required conditions for the existence of the fetus, but as well as the degree of destructive lesions and severe shift in immunological equilibrium.

Keywords: chronic pyelonephritis, cytokines, placental insufficiency, pregravid preparation.

INTRODUCTION

Chronic pyelonephritis (CP) is one of the most common kidney diseases, especially among the female population of reproductive period.

The correlation between chronic infectious and inflammatory diseases of the urinary tract with local and systemic immunity damages proves the results of the previous studies. However, the detailed nature of the immune-pathological reactions remains unknown. It is obvious that the immune response of the mother is formed in accordance with the need to limit and eliminate an infectious process, along with pre-gestational immunological restructuring on one hand and implementation of genetically determined program of childbearing on the other hand.

A disorder of thin inter-systemic correlations at CP was implemented due to the inadequacy in the production of humoral and cellular immune factors. Moreover, the functional activity of immune-competent cells varies depending on the severity of the inflammatory process. The available data and difference in the versions of cytokine imbalance in pregnant women with CP are rare and this makes it almost impossible to create a complex representation

for further course of study during pregnancy and the outcome of the disease. Taking into account, the negative impact of CP on a fully formed feto-placental complex, the risk of preeclampsia and premature birth, anemia, placental failure, chronic fetal hypoxia and the delay in intrauterine development is very important for the clarification of cause-effect relationships that serve grounds in the birth of unhealthy children. Early detection of groups with high risk of developing gestational complications can lead to the possibility of their timely correction, which is extremely important taken into account the likelihood of developing placental insufficiency (PI), which is not depended on the course of CP.

Thus, detecting the regulation within the intercellular communication, mediated system cytokines in women with CP will help clarify the current status of their immune system, the severity of the disorder and further, this will help us get an idea of pathogenesis of the obstetrical complications. Cytokines based on their biological effect are divided into pro-inflammatory regulators of immune response (IL-1, IL-2, IL-6, IL-12, TNF-a), and those involved in the formation of the inflammatory response and as well as offer a protective effect (IL-4, IL-10, IL-13, INF-g, pg / ml). Management of cytokine balance seems to be a new direction of impact in pregravidal training, in connection with what has been delivered.

Aim of our research: to study the dynamics of cytokine status in pregnant women with HP and different morphological characteristics of the placenta.

MATERIALS AND METHODS

In accordance with the purpose of our scientific work, 120 pregnant women were examined. 30 of them - with normal pregnancy (control group). The group consisted of women between the ages of 20 to 32 years (average age -26. 1 ± 1.2 yrs).

Criteria for exclusion were: the absence of chronic infectious and inflammatory diseases in exacerbation stage, diseases associated with impaired immune surveillance (neoplastic processes, allergic, immunoproliferative and autoimmune diseases).

With the aim of studying and assessing the prognostic significance of the immune status in the pregnant women and its variability based on morphological characteristics of the placenta, 90 women with chronic pyelonephritis in the clinical and laboratory remission stage (duration of disease ranged from 3 to 7 years) were examined. The women were between the ages of 22 to 37 years (mean age – 26.7 ± 1.8 yrs).

The grouping was performed based on the morphological characteristics of the placenta and the types of PI:

1. Compensatory - with the appropriate degree of maturity of the villi in gestational age, normal vessel lumen, hyperplasia and hypertrophy of the terminal villi.

2. Subcompensatory - with a maturity mismatch villi of the gestational period, architectural destructions of the villous tree, anemia, arteriolar narrowing and dilatation of the veins, small foci of hemorrhage and thrombosis in the inter-villous space, infarction and pseudo-infarcts

3. Destructive lesions in the placenta - due to inflammatory infiltration, foci of productive inflammation are localized on the basement membrane of the placenta and circulatory disorders, severe dystrophic changes and impaired maturation of the villous tree.

Group I (n = 32) included pregnant women with pregravidal training and prophylaxis of PN in the early stages of pregnancy.

Group II (n = 58) consisted of patients, in whom the said strategy did not yield any results, among them 34 women were in sub compensatory type of PI. 24 - with destructive changes in the placenta. In the presence of pregravid training, changes in the placenta were described as compensatory. Cytokine concentration in serum was determined in an immunological complex Stat-Fax 2100 with the help of enzyme immunoassay system test (LLC "cytokine" St. Petersburg), in accordance with the manufacturer's instructions. Sampling of plasma and the Study of cytokines (IL-1β, IL-8, TNF-a, IL-10, IFN-γ, IL-10) was performed in 22-24 weeks of examinees' pregnancy.

Morphometric and the morphological study of the placenta was conducted in a standardized scheme (A.P. Milovanov, 1999), which included macroscopic analysis, incised material and histological study in three phases.

Mathematical processing of the obtained results was carried out by methods description and a parametrical statistics on a personal computer with the aid of the program «Statistics 7.0».

RESULTS AND DISCUSSION

In studying the cytokine status in pregnant women with CP, differences in the level of the studied parameters were detected, depending on the morphological characteristics of placenta and type of PI. IL-1β - multifunctional cytokine with a broad spectrum effect plays a key role in the development and regulation of non-specific and specific defense of the immune system, the immediate release of which is regarded as a response or defense reaction of the organism to the action of pathogenic factors. Significant differences in the content of inducers of protein synthesis during the acute phase IL-1β were determined in the control group (21.8 ± 1.12). In the absence of pregravid training: in sub-compensatory type of PI its level seemed to have increase

by 1.8 times (38.4 ± 2.4) (p <0.05), destructive changes in the placenta - 2.4 times (52.8 ± 3.6) (p <0.05).

The content of IL-8 - cofactor of the acute phase reaction during the inflammation significantly exceeded the rate of healthy pregnant women (42.4 ± 3.86) in the absence of pregravid training in women with CP: in the group with sub-compensatory PI – one and half (62.2 ± 3.5) (P <0.05), with destructive changes in the placenta (74.7 ± 3.3) (p <0.05) - 1.8 times.

According to the canons of the immune regulation of TNF-a, which has the ability to stimulate the production of other pro-inflammatory cytokines - IL-1, IL-6 and to activate humoral and cellular immune responses with the tendency of bringing about hypercoagulability and hemodynamic impairments, to provide non-specific cytotoxic effect as an integral marker of inflammation. Its level in the group with HP, where no pregravid training was practiced, has shown substantial increase as compared to the healthy pregnant women (12,2 ± 0,6): in sub-compensatory - 2.6 times (31.6 ± 2.5) (p <0.05), in severe PI conjugated with the presence of inflammatory changes in the placenta - 3.8 times (46.8 ± 2.3) (p <0.05).

Index of IL-10 in women with PI confirmed with the help of morphological study of the placenta was elevated as compared to that of healthy pregnant women (7.86 ± 0.8) (p <0.05). It turned out that sub-compensatory PI level of this cytokine amounted to 18.3 ± 1.4 (p <0.05), whilst destructive changes in the placenta was – 32.6 ± 2.8 (p <0.05). The distributions of IFN-γ, one of the potent inducers of cellular immune system and cytotoxicity in groups of women with CP turned out to be identical, with an increase of 2.7 times (43.8 ± 2.4) (p <0.05) and 4 times (68.4 ± 4.3) (p <0.05) in different PI – sub-compensatory and destructive changes in the placenta.

Study of the level of IL-4 enabled us to establish a significant increase in the development of sub-compensatory PI (9.4 ± 0.08) (p <0.05), and 3.2 ± 0.02 (p <0.05) – with changes of an inflammatory nature in the placenta, indicating low resistance of the body of pregnant women with foci of chronic infectious and inflammatory diseases.

A number of pro-inflammatory cytokine levels in the group of women with CP who received pregravid training and course on preventive measures of PN were almost identical with those of healthy pregnant women, except for a slight increase in the level of IL-1β.

Thus, the destruction of an adequate restructuring of cytokine balance may serve the cause of various complications of the gestational process – PI. Prematurely, increase in the activity of pro-inflammatory cytokines and shift of the immunological equilibrium towards Th-1

type in pregnant women with CP, significant indications of chronic stress adaption of the immune system prevailed in the absence of a comprehensive pregravidal training and prophylaxis of PI.

Prolonged existence of the foci of chronic infectious and inflammatory process that was initiated before pregnancy and sustainable to maladaptive state, characterizes the complexity of the pathogenic abnormalities in the "mother-placenta-fetus". Severe immunosuppression at the system level has a negative impact on the morpho-functional characteristics of the feto-placental complex and the outcomes of pregnancy and childbirth respectively. Consequently, the implementation of pregravidal training and prevention of PN(diet rich in protein and polyunsaturated fatty acids; stabilized the lipid-protein bi-layered cells (Essentiale, vitamin E / amount of tocopherols), correcting micro-biocenosis of the genital tract, improved cellular metabolism and utero-placental blood flow (aktovegin, Trental)) in the early stages of pregnancy helped retain the balance of producing pro- and anti-inflammatory cytokines and a significant degree of compensation in women with CP and high risk of recurrent disease course and gestational complications.

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