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CONTENTS OF MCP-1 AND VEGF-A IN PRIMARY INFERTILITY IN INFERTILE WOMEN AND MEN OF UZBEK NATIONALITY

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ABSTRACT

Purpose

To study the levels of chemokine and growth factor in blood serum in men and women with primary infertility.

Material and Methods

Blood serum of 48 women and 54 men aged 22 to 45 years with a diagnosis of primary infertility. The control group consisted of 32 fertile men and 30 women of the same age who are married and have 2 or more children. The concentration of MCP-1, VEGF-A in blood serum was determined by enzyme-linked immunosorbent assay using test systems of Vector-Best JSC (Novosibirsk, Russia).

Results

In individuals with primary infertility, an imbalance of the studied cytokines is observed - an increased level of MCP-1 and VEGF-A.

Keywords: infertility, men, cytokines, women, immunity.

RELEVANCE

The immune system plays an important role in human reproduction. Intercellular signaling in the immune system is carried out by direct contact interaction of cells or with the help of mediators of intercellular interactions. When studying the differentiation of immunocompetent and hematopoietic cells, as well as the mechanisms of intercellular interaction that form the immune response, a large and diverse group of soluble mediators of a protein nature was discovered - intermediary molecules ("coupling proteins") involved in intercellular signaling - cytokines [1].

Cytokines have traditionally been the subject of special attention from researchers involved in reproductive immunology. A wide range of biological effects of cytokines includes direct participation in the regulation of reproductive processes in general [7]. Cytokines of various families are integrated into a multilevel system of regulation of the development of gametogenesis processes and the functioning of the reproductive system in both men and women [6,8].

The aim of this study was to study the levels of chemokine (MCP-1) and growth factor (VEGF-A) in blood serum in men and women with primary infertility.

MATERIALS AND METHODS

The present study included 48 women and 54 men aged 22 to 45 years diagnosed with primary infertility. The average age of infertile women was 28.3±0.72 years, the average age of infertile men was 33.4±0.9 years. According to the goal, all examined were divided into 3 groups: the 1st group included 32 infertile women (ICD-10: N97.8 (other forms of female infertility)), the 2nd group consisted of 38 infertile men (ICD-10: N46 (varicocele; idiopathic oligo-, astheno- and azoospermia)) and the 3rd group included 18 pairs of infertile couples with idiopathic infertility (ICD-10: N97.8-9 (other forms of female infertility; female infertility unspecified), N46 (varicocele; idiopathic oligo-, astheno- and azoospermia)). 32 fertile men and 30 fertile women of the same age who are married and have 2 or more children made up the control group.

Immunological studies in the examined men and women were carried out in the laboratory of reproduction immunology of the Institute of Immunology and Human Genomics of the Academy of Sciences of the Republic of Uzbekistan. The concentration of monocytic chemotactic protein-1 (MCP-1) and vascular endothelial growth factor-A (VEGF-A) in blood serum was determined by enzyme-linked immunosorbent assay using test systems of Vector-Best JSC (Novosibirsk, Russia), in in accordance with the manufacturer's recommendations.

Quantitative evaluation of the results was carried out by constructing a calibration curve, reflecting the dependence of optical density on concentration for a standard antigen and allowing comparison of the studied samples with it.

Statistical processing of the obtained data was carried out using the computer program Statistica 6.0. The significance of differences in the mean values (P) of the compared indicators was assessed by Student's t-test (t).

RESULTS AND ITS DISCUSSION

A comparative analysis of the cytokine profile in all infertile couples revealed significant multidirectional values of the studied mediators of the immune response. The results obtained are shown in table 1.

Table 1. Level of cytokines (pg/ml) in examined women and men, M±m

	Fertile women (n=30)	I- Group (n=32)	Fertile men (n=32)	II- Group (n=38)	III- Group (n=36)
MCP-1	171,1±7,07	374,2±10,5*	163,2±3,1	406,2±18,4*	353,1±10,2*
VEGF-A	66,5±2,3	209,3±7,3*	65,4±1,4	237,9±11,4*	215,8±9,5*

Note. * Values are significant in relation to the control group (p<0,05 - 0,001)

As is known, chemokines (chemotactic cytokines) are a superfamily of small secreted proteins that function as intercellular messengers to control the migration and activation of leukocytes involved in inflammatory reactions and immunity. In addition, chemokines are important mediators in many pathological processes [2,8].

Monocytic chemotactic protein-1 (MCP-1), also known as monocyte chemotactic and activating factor (MCAF) was characterized as a monocyte-specific chemoattractant, but was later shown to interact with both T-lymphocytes and NK cells [3,4].

In our study, the serum concentration of MCP-1 reached its maximum values in the group of individuals with male infertility. Thus, the level of the studied chemokine in the group with male infertility was 406.2±18.44 pg/ml ($P<0.01$), while in the control group of fertile men, the average value was 163.2±3.1 pg/ml. In the group with female infertility 374.2±10.52 pg/ml ($P<0.05$), and in the group of infertile couples it was 353.1±10.23 pg/ml ($P<0.05$) versus 171, 1±7.07 pg/ml. The increased level in the group of infertile men in our study is also consistent with the work of a number of authors [9,10], where changes were found in the seminiferous tubules in men with impaired spermatogenesis, which corresponds to the diagnosis of infertile men (azoospermia, asthenozoospermia) in this sample.

According to the literature data, the normal functioning of tissues depends on the regular delivery of oxygen by the blood vessels. Angiogenesis is the process of formation of new blood vessels from an already existing vascular system. It plays an important role in development, normal tissue growth, wound healing, the reproductive cycle in women (development of the placenta, ovulation, corpus luteum) and also plays a major role in various diseases [5].

Vascular endothelial growth factor (VEGF) is a powerful angiogenic factor produced by various tissues of the reproductive tract, a key regulator of physiological and pathological angiogenesis. VEGF is the main modulator of growth, remodeling and vascular permeability in the endometrium, decidua and trophoblast. In addition Moreover, VEGF stimulates endothelial cell proliferation, promotes cell migration, and inhibits apoptosis [6].

All the examined groups significantly differed in the serum level of VEGF-A, which exceeded the control values. Thus, a comparative analysis of the content of this growth factor found that in the group of infertile women, the synthesis was increased 3.1 times ($P<0.01$), in the group of men with infertility 3.6 times (group II - 237.9±11, 4 pg/ml) ($P<0.001$) compared with the indicators of the control group of men (65.4±1.4 pg/ml), and in the group of couples with idiopathic infertility by 3.2 times ($P<0.01$) (with mean values of group I - 209.3±7.3 pg/ml, group III - 215.8±9.5 pg/ml versus control - 66.5±2.3 pg/ml). The results obtained indicate the likelihood of pathological growth processes in the reproductive system, both in men and women, which allows us to consider it as an unfavorable predictor.

Thus, our results indicate the important role of the analyzed immunological parameters, using the example of cytokine status as a marker involved in the development of primary infertility, both female and male genesis, which can be further studied and used to clarify immune mechanisms. infertility.

CONCLUSION

1. A pronounced hypercytokinemia was established, which indicates a direct connection between the cytokine status and disorders in the reproductive system.

2. An increase in the level of MCP-1, VEGF-A in the blood serum indicates a pronounced inflammatory reaction in the body in the general group of men and women with primary infertility.

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