



Uterine Myoma: Optimization of Management and Immunomodulating Therapy

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Abstract This article presents the results of studies of 37 women with uterine fibroids. Studies show the positive efficacy of T-life, used as an immunocorrective treatment for uterine fibroids.

Keywords: uterine fibroids, humoral immune response.

Introduction. Despite advances in conservative treatment, surgery remains the main method. As a result, uterine fibroids (UF) become the main cause of hysterectomy in many countries of the world (50-70% of cases) in diseases of the uterus [1,2,3,4,5,6], including women of reproductive age (24-26.8%) who have not had time to realize their reproductive function [7,8,9]. The problem of studying the etiopathogenesis of uterine fibroids and the factors determining it continues to be the focus of attention of domestic and foreign researchers. Despite the significant progress made in recent decades in this direction, the key provisions of the genesis and treatment of this disease still remain debatable and insufficiently studied [10,11,12,13].

It is relevant and promising to study the role of immune mechanisms in the pathogenesis of rapid tumor growth. The immune system controls the processes of regeneration, differentiation and growth of tissues (in particular the myometrium). The body has strict immunological control over the two main processes of cell vital activity - proliferation and apoptosis [14,15,16]. The main regulatory systems for proliferation and apoptosis are the endocrine and immune systems, the relationship between which has been proven. Estrogens suppress the reaction of T-lymphocytes to the action of phytohemagglutinin, reduce the activity of natural killers. The inhibitory effect of estradiol on the synthesis of T-helpers and the production of class M immunoglobulins has been proven. By reducing the activity of natural killers, the content of T-helpers, estrogens help to reduce the effectiveness of the body's antitumor defense, thereby causing progressive tumor growth [17,18,19,20].

It has been proven that the immune balance in patients with UF is disturbed towards an increase in the number of T-suppressors, which indicates the suppression of cellular immunity and a weakening of control over the process of cell proliferation [21,22,23,24].

Treatment of patients with uterine fibroids in reproductive age should begin as early as possible, immediately after diagnosis. Passive monitoring of patients (3-5 years or more) leads to the progression of the disease: the growth of myomatous nodes, the aggravation of pathological uterine bleeding, the formation of chronic iron deficiency anemia, endometrial hyperplastic processes, and systemic disorders in the body [25,26,27,28].

Conservative therapy of patients with uterine myoma is of great practical importance, as it is organ-preserving [29,30,31]. It provides for the impact on various links in the pathogenesis of uterine fibroids in order to inhibit growth and enhance the processes of atrophy in the fibroids, as well as reduce the severity of clinical symptoms [32,33,34]. As a result of conservative treatment, many

patients experience stabilization and reduction in the size of myomatous nodes, menstrual blood loss and pain syndrome [35,36]. Given the high medical and social significance, the problem of uterine fibroids requires further detailed study of the etiology, pathogenesis and methods of timely diagnosis and modern treatment [37,38,39].

The purpose of the study: Substantiation of the effectiveness of immunocorrective therapy in women with uterine myoma.

Material and methods. In connection with the foregoing, we present data from our own studies on the dynamics of some parameters of the immune system in women with uterine myoma during treatment with T-life.

We examined 55 women with uterine fibroids who applied to the gynecology department of the Bukhara Regional Perinatal Center for the period from January to June 2019. The main group consisted of 37 women with nodular forms of uterine fibroids. The control group consisted of 18 "virtually" healthy women of reproductive age. The patients' age ranged from 20 to 37 years and averaged 25.8 ± 2.3 years. During the examination, ultrasound scanning (transabdominal and transvaginal) was used, allowing to assess the initial size of the uterus, the size, location and structure of myomatous nodes.

The treatment was carried out with T-life (1 mg x 2 times a day i/m for 5 days, then every other day 1 mg x 2 times a day i/m for 20 days). The control group consisted of 18 practically healthy women of reproductive age.

The level of lymphocytes with an activation marker (CD25+, CD71+, CDHLADR+ and CD95+) in peripheral blood was studied by immunological study using monoclonal antibodies of the LT series. Statistical analysis of the obtained data was carried out using the methods of variation statistics. Differences were considered statistically significant at $P < 0.05$.

To assess the clinical efficacy of the drug with immunomodulatory activity, we formed a group of patients with newly diagnosed small interstitial MM. At the time of the examination, they did not need invasive methods of examination and treatment of the disease and were extremely interested in the preservation and speedy implementation of reproductive function.

The duration of the disease in them did not exceed 3 years; in most women, fibroids were detected for the first time; and by the time of treatment in 75% of patients, the size of the uterus did not exceed 5-6 weeks of pregnancy. More than half of the patients in this group did not present any complaints characteristic of this disease. Only with active collection, anamnesis, 20% of women indicated the presence of long, heavy menstruation and 22.5% noted painful menstruation. According to A.L. Tikhomirov and D.M. Lubnina (2005), these patients had "clinically insignificant" uterine myoma. The main reason for visiting a doctor was a violation of reproductive function in the form of reproductive losses: (miscarriage, perinatal death of a child) and infertility. In a significant part of the patients, laboratory examination revealed markers of exacerbation of a viral infection (71.4%), which required the appointment of antiviral and / or antibiotic therapy, depending on the infection identified by clinical and laboratory data.

Treatment was carried out on an outpatient basis. During treatment with T-life, no adverse reactions were noted.

Research results

The study was conducted before treatment and one month after its completion.

Table 1.

Effect of treatment with T-life on the level of activation lymphocytes, (M \pm m)

Index, %	Control group, n=18	Women with UF before treatment, n=37	Women with UF after treatment, n=22

CD25+	18,7 ± 0,7	38,5 ± 1,0*	20,6 ± 0,8 **
CD71+	22,8 ± 0,9	36,3 ± 1,1*	24,2 ± 0,8**
CD HLA DR+	24,6 ± 0,8	34,9 ± 1,2*	26,4 ± 0,9**
CD38+	14,5 ± 0,7	17,3 ± 0,8	14,1 ± 0,6
CD95+	25,3 ± 1,0	18,6 ± 0,8*	22,3 ± 0,7**

Note: * Values are significant in relation to the control group ** Values are significant in relation to the group before treatment (P<0.05 - 0.001).

As can be seen from the data presented, in women with UF, an increase in the level of early activation lymphocytes was observed. Thus, the level of CD25+ cells was 2 times higher than the control values (P<0.001), and the number of CD71+ lymphocytes was 1.6 times higher than the control values (P<0.05).

It is known that increased expression of CD71 and HLADR molecules on the cell surface occurs at different stages of lymphocyte activation (Yarilin A.A., 2009). The CD71 molecule is a receptor for transferrin and is expressed on proliferating lymphocytes that have entered the initial phases of the cell cycle. HLADR molecules begin to be expressed on the cell membrane of already fully differentiated cells and are markers of the very late stages of lymphocyte activation. The CD38 molecule is expressed at various stages of the cell cycle. First, this molecule appears on the surface membrane of lymphocytes at the earliest stages of differentiation, being a marker of immature cells.

Then, at the intermediate stages of maturation, the cells lose it, but on mature, fully differentiated lymphocytes, they begin to be expressed again. So in our studies, women with UF showed an increase in the expression of CD38 molecules on the surface of lymphocytes compared with the control group. Apparently, the appearance of a pool of immature lymphocytes in the systemic circulation reflects a violation of the processes of maturation and differentiation of cells of the immune system, which, in turn, can lead to suppression of immune surveillance and the development of rapid tumor growth.

Assessment of cell readiness for apoptosis based on the determination of the level of expression and CD95 molecules showed that in women with UF the level of lymphocytes with the CD95 molecule was significantly reduced (P<0.05).

A month after treatment with T-life, the results of the studies showed that there was a positive trend. The normalization of the studied indicators of the activation process was noted. The clinical effect of the use of the drug T-life in women with small UF was the absence of growth of existing and the formation of new myoma nodes during the year of observation.

Conclusions:

1. The results of our studies have shown the inadmissibility of managing women of reproductive age with small uterine fibroids and minimal clinical manifestations, since this disease is very often combined with active forms of a viral infection that acts as a trigger for rapid tumor growth. When this clinical situation is identified, the appointment of antiviral therapy and drugs with immunomodulatory effects is indicated.

2. A month after treatment with T-life, normalization of the studied indicators of the activation process was noted. The clinical effect of the use of the drug T-life in women with small UF was the absence of growth of existing and the formation of new myoma nodes during the year of observation.

3. The data obtained make it possible to determine the prognosis of the course of uterine myoma in women, which leads to an improvement in the quality of life of patients and an increase in the effectiveness of ongoing therapeutic measures.

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