Changes in Local Immunity Factors in Women with Pre-Existing Cervical Disease and Benign Ovarian Tumors

Nazar Matviykiv

Abstract
The objective of the research was to study the indices of local immunity in relation to the hormonal state of the body in women with benign ovarian tumors and pre-existing cervical diseases.

Materials and methods. The concentration of major gonadotropic and steroid hormones during the female ovarian and menstrual cycle, as well as individual local immunity factors of proinflammatory cytokines and secretory immunoglobulin A was studied in 40 patients with benign ovarian tumors and pre-existing cervical diseases.

Results and discussion. In the second phase of the ovarian and menstrual cycle, a significant reduction (by 3.0 times) in the concentration of progesterone and relative hypoestrogenism (by 1.5 times as compared to the control data) were found. Anovulation was observed in 40.00% of cases and corpus luteum deficiency syndrome was diagnosed in 62.5% of women. The assessment of secretory immunoglobulin A concentration allowed us to note (along with the hypersecretion of proinflammatory cytokines) an increase in this marker in half of the examined women in the presence of chronic cervicitis and vaginitis, candidiasis and viral lesion - along with the activation of proinflammatory cytokine depression of secretory immunoglobulin A synthesis as compared to the control data.

Conclusions. Local immunity changes in women with benign ovarian tumors and pre-existing cervical diseases are accompanied by abnormalities of the hormonal profile and the association of maladaptive changes in the system of local immunity manifested by fluctuations in the level of secretory immunoglobulin A during the secretory phase of the menstrual cycle and an increase in proinflammatory cytokine synthesis. The results of the conducted study allowed us to note a significant increase in the concentration of secretory immunoglobulin A along with the activation of proinflammatory cytokine synthesis in most women with benign ovarian tumors and pre-existing cervical diseases which confirms the development of acute inflammatory reactions on the background of the existing hormonal imbalance. In patients with pre-cancerous cervical diseases, there was a tendency toward depression of secretory immunoglobulin A synthesis, a significant inhibition of local immunity, especially typical for cervical intraepithelial neoplasia on the background of human papillomavirus infection. All the aforementioned data confirm the formation of secondary immunodeficiency in this category of patients.

Keywords
pre-existing cervical diseases; benign ovarian tumors; local immunity indices; hormonal imbalance

Ivano-Frankivsk National Medical University, Ivano-Frankivsk, Ukraine
Corresponding author: nazario04@ukr.net

Problem statement and analysis of the recent research
Immunodeficiency in female patients with dishormonal diseases affects the clinical course and treatment outcomes being one of the leading causes of the process exacerbation. Persistent changes in the immune system lead to the formation of immune deficiency, which results in the chronization of inflammatory changes and relapses [2, 3, 5].

Proceeding from the mentioned above, under modern conditions of patients with impaired ovarian function management, prophylaxis and formation of groups at probable risk of relapse, early diagnosis with complex assessment of the immune status, phased treatment with adequate targeted immunocorrection, as well as the restoration of the ovarian and menstrual cycle become more significant [1, 6]. Since the system of local immunity is the first line of defense against various pathogens, local antimicrobial barrier dysfunction contributes to the development, distribution and chronization of the infectious process, as well as the initiation of proliferative changes in cervical epithelium and the vaginal part of the cervix [2, 5, 7]. Abnormal gonadotropin and sex hormone synthesis as well as changes in hormonal concentration of the vaginal epithelium as a target organ in women with benign ovarian tumors and pre-existing cervical diseases were the basis of our study. The directions of our research included the study of vaginal microbiota and local immunity indicators, since the state of these systems is directly related to hormonal homeostasis of the body and a target organ – the vaginal mucosa [1, 2, 4, 5].
The objective of the research was to study the level of individual indicators of local immunity as markers of evaluating the mechanisms of immune defense in relation to hormonal homeostasis in women with benign ovarian tumors and pre-existing cervical diseases.

1. Materials and methods

According to the objective of our research, we studied the state of hormonal homeostasis based on the evaluation of the levels of steroid hormones (estradiol (E2), progesterone (Pg) and testosterone) and protein hormones (luteinizing hormone (LH), follicitropin and prolactin) in the blood serum of 40 women with benign ovarian tumors and pre-existing cervical diseases in comparison with the control group (20 healthy women). All the patients were examined in the first (the 5th – 7th days) and the second (the 21st – 23rd days) phase of the menstrual cycle using the enzyme-linked immunosorbent assay (ELISA). The assessment of the concentration of secretory immunoglobulin A (Ig A) and individual indicators of cytokine profile (interleukin-1 (IL-1), interleukin-6 (IL-6), tumor necrosis factor (TNF)) in the cervical mucus of female patients with benign ovarian tumors and pre-existing cervical diseases was carried out using the standard methods as well as the ELISA. The obtained data were statistically processed using the method of variational mathematical statistics.

2. Results and discussion

Genital examination was carried out during the initial visit and the entire course of treatment. Almost all women included in the study were diagnosed with human papillomavirus (HPV) infection (32.5%), cytomegalovirus (CMV) (15.0%), chlamydia and ureaplasma (17.5%), mycoplasma and other medical conditions caused by infectious factors in various combinations. The abnormalities in vaginal microbiocenosis were accompanied by a decrease in the amount of lactobacilli and bifidobacteria.

The results of LH study on the 5th - 7th days of the menstrual cycle in this category of patients were significantly higher as compared to healthy women - by 36.02% (p>0.05). The LH/ follicle-stimulating hormone (FSH) ratio was 1.1 in the control group and 1.9 in the group of women with benign ovarian tumors and pre-existing cervical diseases indicating significantly impaired production of gonadotrophins in this category of patients in the first phase of the ovarian and menstrual cycle already. The E2/Pg ratio was 1.6 times lower than that in the control group indirectly indicating hormonal imbalance in the first phase of the ovarian and menstrual cycle already. In females with benign ovarian tumors and pre-existing cervical diseases, there was observed a trend towards increased concentration of prolactin to (3864.82±22.20) mMOg/L vs. (238.64±19.22) mMOg/L, which exceeded the data of the control group by 1.6 times (p<0.05). Testosterone levels exceeded the control values by 1.5 times. The obtained results indicated underlying moderate hyperprolactinemia and hyperandrogenemia in this category of patients.

The most significant (p<0.05) changes in the concentration of gonadotropic and sex hormones were observed in 67.5% of women with benign ovarian tumors and pre-existing cervical diseases in the second phase of the ovarian and menstrual cycle. LH concentration increased significantly - by 2.4 times; FSH concentration increased by 1.4 times; the LH/FSH ratio increased by 1.6 times (p<0.05). At the same time, on the 21st - 23rd days of the ovarian and menstrual cycle, an increase in E2 concentration (by 1.5 times, p<0.05) with a significant decrease in Pg concentration (by 3.0 times, p<0.05) and a tendency to increase the concentration of prolactin and testosterone were observed.

The ovulatory cycles were noted in 24 (60.00%) women with benign ovarian tumors and pre-existing cervical diseases, among them, 15 (62.5%) women developed corpus luteum deficiency syndrome; anovulation was detected in 16 (40.00%) women: in 7 (43.75%) cases, it occurred on the background of hypostrogenism, in 9 (56.25%) cases - on the background of hypoestrogenism.

The analysis of secretory Ig A concentration in the mucosa of healthy patients revealed that its average level was (52.18±2.2) mg/l. In 21 (52.5%) patients with benign ovarian tumors and pre-existing cervical diseases, the average secretory Ig A level was 32.43% higher than that in the control group (p<0.05); the maximum secretory Ig A levels (up to 80.28±2.08 mg/l) were observed in 13 (32.5%) patients indicating the highest degree of the intensity of local immunity response and a high degree of infection contamination in this category of women. In 19 (47.5%) patients, low secretory Ig A levels were seen. The concentration of secretory Ig A in the cervical mucus as one of the indicators of local immunity is characterized by variability and depends, to a certain extent, on age, the phase of the menstrual cycle and the form of inflammatory damage to the reproductive tract [1, 2, 7]. Elevated levels of interleukin 1 beta (IL-1β) (by 2.4 times), IL-6 (by 4 times), TNF (by 6 times), especially in recurrent cervical diseases, were detected. It should be noted that long-term chronic inflammatory diseases were accompanied by a depression of secretory Ig A synthesis, the indicators of which were 1.5 times lower than those in the control group when diagnosing cervicitis and vaginitis associated with viral infection, candidiasis, and ureaplasmosis that indicated the inhibition of local immunity. In patients with pre-cancerous cervical diseases, there was a tendency toward depression of secretory Ig A synthesis, a significant inhibition of local immunity, especially typical for cervical intraepithelial neoplasia (CIN) on the background of HPV infection.

Considering previously collected data, where the parallel between the incidence of vaginal dysbiosis and the state of local immunity has been drawn [1, 6], we tend to think that in 32.5% of patients with benign ovarian tumors and pre-existing cervical diseases, the endocrine system was responsible for a significant increase in the concentration of secretory Ig A...
which can be considered as an indirect indicator of the physiological adaptation of local defense mechanisms and a peculiar marker of changes in the regulation of adaptation processes. Therefore, in routine practice, it is reasonable to carry out standard methods of examination as well as to evaluate the levels of proinflammatory cytokines and secretory Ig A simultaneously. It significantly increases the understanding of tissue changes and the status of local homeostasis, metabolic and proliferative mechanisms substantiating the choice of therapeutic technologies and prediction of treatment outcomes, as well as the rehabilitation period.

3. Conclusions
The obtained results indicated that local immunity changes in women with benign ovarian tumors and pre-existing cervical diseases are accompanied by abnormalities of the hormonal profile and the association of maladaptive change in the system of local immunity, manifested by fluctuations in the level of secretory Ig A during the secretory phase of the menstrual cycle and an increase in proinflammatory cytokine synthesis. The results of the conducted study allowed us to note a significant increase in the concentration of secretory Ig A along with the activation of proinflammatory cytokine synthesis in most women with benign ovarian tumors and pre-existing cervical diseases which confirms the development of acute inflammatory reactions caused by an infectious factor on the background of the existing hormonal imbalance. In patients with pre-cancerous cervical diseases, there was a tendency toward depression of secretory Ig A synthesis, a significant inhibition of local immunity, especially typical for CIN on the background of HPV infection. All the aforementioned data confirm the formation of secondary immunodeficiency in this category of patients.

4. Prospects for further research
The study of the effect of hormonal imbalance on changes in the indices of local defense factors of urinary tract mucosa is promising.

References

[1] Voznesenskaya NV, Kozhemyatova IV, Trubnikov VS. Sekretsiya S1gA v tservikalnoy slizi u zhenshchin s zabol'evaniyami sheyki matki. Materialy 44-y mezhrregionalnoy nauchno-prakticheskoy konferentsii "Razvitiye sistemy zdravookhraneniya i aspekty zdorovogo obraza zhizni"; 2009; Ulianovsk; 2009;84.

[2] Voznesenskaya NV, Kozhemyatova IV, Albutova ML. Diagnosticheskaya znachimost metoda izucheniya morfoloogii tservikalnoy slizi dlya otsenki urovnya gormonal'nyh nasyshhennosti v dinamike mestrenualnogo tsikla. Materialy Vserossiyskoy konferentsiyi "Innovatsionnye tekhnologii ranney diagnostiki i lecheniya v meditsinskom praktike"; 2009; Ulianovsk; 2009;84-89.

[3] Vorobiova LI. Stan ta problemy onkohinekolohii v Ukraini. Zbirnyk naukovykh prats asotsiatsii akusher-hinekolohiv Ukrainy. Kyiv: Intermed. 2006;110-114.

[4] Grigoryan OR, Uzhegova ZhA, Andreyeva EN. Rol endogennykh polovykh steroidov v geneze predrakovikh zabol'evaniy i raka sheyki matki pri endokrinopatiyakh. Problemy endokrinologiyi. 2007;53(2):15-19.

[5] Zhuk SI, Nochvina YeA. Sostav mikroflory kishechnika i vlagalishchcha u zhenshchin rannego reproduktivnogo vozrasta na fone disgormonalnykh rasstroystv. Zbirnyk naukovykh prats asotsiatsii akusher-hinekolohiv Ukrainy. Kyiv: Intermed. 2006;273-276.

[6] Kulakov VI, Gataulina RG, Sukhikh GT. Izmeneniya reproduktivnoy sistemy i ikh korrektsiya u zhenshchin s dobrokachestvennymi opukholami i opukholevidnymi obra-zovaniyami yaichnikov. Moscow: Triada-Kh. 2005;256.

[7] Trubnikova LI, Voznesenskaya NV, Kozhemyatova IV. Sekretsiya S1gA v tservikalnoy slizi u zhenshchin s fonovymi zabol'evaniyami sheyki matki. Meditsinskij almanakh. Akusherstvo i ginekologiya. N.-Novgorod. 2009;4(9):134.

Received: 24 July 2017
Revised: 29 Sept 2017
Accepted: 29 Sept 2017