

Endometrial hyperplasia as a consequence of mixed urogenital infections

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ABSTRACT

Aim: Investigation of hyperproliferative diseases of the female genital organs as a consequence of mixed urogenital infections.

Materials and Methods: The study included 56 women of reproductive age who experienced discomfort in the external genital area in the form of excessive vaginal discharge and/or unpleasant odour of the discharge, itching in the external genital area (main group). The control group consisted of 30 somatically and gynaecologically healthy patients.

Results: The following complaints were noted in mixed infections: increased amount of vaginal discharge (28 women / 50% of the main group), unpleasant odour of discharge (19 women / 34%), less frequently - itching (10 women / 18%), burning (11 women / 20%), pain during intercourse (8 women / 14%), digestive tract disorders - bloating and irregular bowel movements (13 women / 23%). Two or more complaints were noted in 29 patients (52% of the main group). The microscopy revealed a small number or complete absence of lactobacilli, abundant polymorphic gram-negative and gram-positive bacillus and coccusmicroflora, and the presence of 'key cells'.

Conclusions: Taking into account the information described above, it can be noted that mixed urogenital infections affect the pathogenesis of endometrial hyperplastic processes.

KEY WORDS: urogenital infections, microbiota, inflammatory diseases of pelvic organs, hyperplastic processes

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INTRODUCTION

The inflammatory processes of female genital organs make up 55-70% of cases in the structure of all gynaecological diseases, 40-50% of which are vaginal infections. In spite of a considerable amount of scientific research and the latest antibacterial drugs, there is no tendency for the inflammatory diseases to decrease.

The vaginal microbiome is a dynamic system that can change periodically under the influence of endogenous physiological factors (age, phase of the menstrual cycle, etc.). These changes are usually temporary and do not affect a woman's health [1]. Many exogenous factors also have a significant impact on the state of the vaginal microbiome. These include poor hygiene and frequent douching, smoking and other unhealthy habits, psycho-emotional stress, the use of antibiotics, hormones, contraceptives, immunosuppressants, cytostatics and radiotherapy.

Over the recent years social and behavioral factors have negatively impacted the women's genital organs. This has resulted in a decrease in immune defense

against infections and has enabled the diseases to spread [2, 3]. Chronic alcoholism, drug addiction, low living standards (insufficient and irrational nutrition), and ongoing stressful situations are examples of social factors [4, 5]. The behavioral factors include the early onset of sexual life, a great number of sexual contacts and sexual partners, unconventional forms of sexual contact (orogenital, anal), sexual relations during menstruation etc.

The pathogenetic mechanisms of proliferative diseases of the reproductive system are unclear. Since the 1990s, the leading role in the development of hyperplastic processes has been attributed to increased oestrogen concentration - absolute or relative hyperoestrogenism and imbalance of oestrogenhydroxymetabolites [6-8].

In the last few decades in Ukraine, as in most countries of the world, there has been an increase in the incidence of hormone-dependent tumours, especially endometrial hyperplastic processes (EHP). According to both domestic and foreign authors, they represent

a multifaceted problem of theoretical and clinical medicine and hold one of the leading places in the structure of gynecological pathology. Their frequency ranges from 14% to 83% [6, 7]. The relevance of the problem is determined by the possibility of HPE degeneration into endometrial cancer. Numerous studies confirm the likelihood of developing oncological processes in the setting of HPE, which is possible in 4-67.2% of patients. This pathology is also of interest due to the tendency to a long and recurrent course, the absence of specific, pathognomonic symptoms, the complexity of differential diagnosis, and the difficulty of individualising treatment [7].

AIM

Investigation of hyperproliferative diseases of the female genital organs as a consequence of mixed urogenital infections.

MATERIALS AND METHODS

The study included 56 women of reproductive age who experienced discomfort in the external genital area in the form of excessive vaginal discharge and/or unpleasant odour of the discharge, itching in the external genital area (main group). The control group consisted of 30 somatically and gynaecologically healthy patients.

The contingent of the examined women did not differ greatly in terms of age, general and obstetric and gynaecological history. Comparisons were made based on the principles of selecting patients with the same nosologies and somatic background.

The microbiocenosis of the urogenital tract was assessed by real-time PCR using the Femoflor-16 test system. As for the additional examination of hormonal status, the day of the menstrual cycle (MC) and preparation for the tests were taken into account. On the 3-5 day of the menstrual cycle, estradiol, NOMA index, and prolactin were additionally examined. On the 21-22 day of the MC - prolactin, progesterone, estradiol. Material: venous blood, testing method: immunochemical with electrochemiluminescent detection (ECLIA), analyser and test system: Cobas 6000/ Cobas 8000, Roche Diagnostics (Switzerland). Ultrasound examination of the pelvic organs was performed on the 7-8 and the 21-22 days of MC.

RESULTS

The following complaints were noted in mixed infections: increased amount of vaginal discharge (28 women / 50% of the main group), unpleasant odour of discharge (19 women / 34%), less frequently - itching (10 women / 18%), burning

(11 women / 20%), pain during intercourse (8 women / 14%), digestive tract disorders - bloating and irregular bowel movements (13 women / 23%). Two or more complaints were noted in 29 patients (52% of the main group). The microscopy revealed a small number or complete absence of lactobacilli, abundant polymorphic gram-negative and gram-positive bacillus and coccus microflora, and the presence of 'key cells'. The number of leukocytes was variable and often did not correspond to the severity of vaginal dysbiosis.

In the majority of patients (84%), the PCR examination revealed severe vaginal dysbiosis. The disruption of the vaginal microbiome was characterised by a significant predominance of aerobic and anaerobic opportunistic microorganisms with a significant decrease (80%) and in some cases (4%) a complete absence of lactobacilli. Moderate dysbiosis was diagnosed in 9 (16%) of the women in the main group. Among the facultative anaerobic microorganisms, the most commonly detected were *Enterobacterium* spp. Obligat anaerobic microorganisms were mostly represented by the groups *Gardnerellavaginalis* / *Prevotellabivia* / *Porphyromonas* spp., *Lactobacterium* spp. / *Clostridium* spp. and *Atopobium* vaginae.

Before coming to the clinic, 20 (36%) patients were receiving antibiotic therapy for extragenital pathology; 12 (21%) were being monitored for infertility; 6 (11%) women were preparing for assisted reproductive technologies. The average age of patients was 27.8 ± 6.4 years. Treatment for mixed urogenital infections in the history was noted in 26 (46%) women, and recurrent disease (2-4 relapses per year) was diagnosed in 11 (20%) patients.

Detection was based on complaints and the nature of vaginal discharge, as well as the use of laboratory methods, according to current understanding of the clinical diagnosis of mixed urogenital infections. Normal human flora is a set of microbiocenoses that occupy numerous ecological niches on the skin and mucous membranes in places of contact of the human body with the environment. The microbiocenosis is a highly sensitive indicator that responds with quantitative and qualitative changes to any disturbances in the external and internal environment. A change in the number of a particular species of microorganisms in a habitat or the appearance of bacteria that are not typical for a given habitat is a signal of adaptive or irreversible changes in the relevant link of the microecological system [1].

Lactobacilli of various types are an important component of the vaginal microflora, with a normal content of $1 \times 10^7 - 10^9$ CFU/ml. Lactobacilli, in turn, produce lactic acid, which acidifies the vaginal environment (normal pH is 3.8-4.5), as well as a number of microbicidal factors and hydrogen peroxide (H_2O_2), which inhibit the growth of many microorganisms [2, 5].

The microorganisms that can cause inflammatory diseases of the genital organs are mainly sexually transmitted mi-

icrobial-protozoan-viral associations, characterized by new properties, specific clinical features and are not pathological components of individual infectious components. They can persist in a human body lifelong, leading to periodic exacerbation of adnexitis, cervicitis, vaginitis, bartholinitis, cystitis, etc., which result in infertility [8].

The study included women with minimal or no lactobacilli with polymorphic gram-negative and gram-positive bacillus and coccus flora. A microbiological examination of vaginal discharge was performed before treatment.

The following pattern was observed when examining the hormonal status of the above mentioned groups: in patients of the main group, the level of estradiol was elevated - 256.0 pg/ml; the NOMA index was also observed in the range of 3.2-3.5 (increased) in 50% of patients of the main group; prolactin level - 10.2-18.0 ng/ml (normal). All these examinations were performed in the first phase of MC (on day 3-5). As for the patients in the control group, these indicators were within the normal range. During the studies in phase II of MC (on day 21-22): prolactin levels in patients of the main group were slightly elevated - in the range of 25.4-27.9 ng/ml, in patients of the control group they remained within the normal range (8.8-16.7 ng/ml); progesterone levels - 0.8-1.1 ng/ml (reduced) in patients of the main group and 4.6-19.2 ng/ml (normal) in patients of the control group; estradiol levels were similarly elevated as in phase I of MC - 360.2 pg/ml in patients of the main group, compared to the control group, where they were normal (within 130.4-183.5 pg/ml).

The composition of the urogenital microbiota of a healthy woman may have characteristics depending on the phase of the menstrual cycle and age [5, 6]. The optimal number and species composition of lactobacilli ensures the acidity of the vaginal secretion within 4-4.5, the formation of a barrier to the fixation of opportunistic and pathogenic flora to vaginal epithelial cells and participates in a number of immune mechanisms [5, 7]. The composition of the microbiome is strongly correlated with the state of the vaginal mucosa which depends primarily on the levels of sex hormones, in particular estrogens. The latter stimulate the proliferation of stratified squamous epithelium and the production of glycogen in surface cells, which is a substrate for the vital activity of lactobacilli [5, 8]. Due to the influence of estrogen, the mucosal plug of the cervical canal is saturated with bactericidal enzymes and is able to act as a barrier, a kind of filter that prevents the spread of pathogenic pathogens (specific or nonspecific infection) to the upper parts of the urogenital tract and the generalisation of the inflammatory process. Progesterone slows down the maturation of the stratified squamous epithelium. It causes cytolysis and desquamation of stratified squamous epithelium with the release of glycogen into the vaginal lumen. Under the influence of cellular enzymes sugars, maltose and glucose

are formed from glycogen, which is a nutrient medium for lactic acid bacteria (lactobacilli).

During the pelvic ultrasound examination on days 7-8 and 21-22 of the MC, the following pattern was observed: the endometrial level in phase I was 10-11 mm in patients of the main group, and in phase II, its thickening was also observed (up to 16-17 mm). We interpreted this as a discrepancy with the phase of the menstrual cycle - endometrial hyperplasia.

DISCUSSION

According to the data available in the literature, 20-55% of women suffering from vaginal dysbiosis are also diagnosed with intestinal dysbiosis, which indicates a single dysbiotic process in the body with a dominant display in the genital or digestive system [1, 2]. The main representatives of the obligate vaginal microflora found in women of reproductive age are lactobacilli, which play a leading role in maintaining normal vaginal biocenosis due to high competition and antagonism to most pathogenic and opportunistic bacteria. Lactobacilli metabolise glycogen into glucose and eventually into lactic acid, which maintains the acidic reaction of the vaginal contents (pH 3.8-4.4), which is necessary for the growth of lactobacilli.

The restoration of an adequate state of the genital tract microenvironment in women with mixed infections is based on the creation of an optimal pH level for the dominant influence of normal representatives of this biotope. The predominance of natural bacterial protective agents will not only restore the colonization resistance of the vaginal biotope, but will also reduce the frequency of recurrence of vaginal microcenosis disorders.

Lactobacilli of various types are an important component of the vaginal microflora, with a normal content of 1×10^7 - 10^9 CFU/ml. Lactobacilli, in turn, produce lactic acid, which acidifies the vaginal environment (normal pH is 3.8-4.5), as well as a number of microbicidal factors and hydrogen peroxide (H₂O₂), which inhibit the growth of many microorganisms [2, 5].

The microorganisms that can cause inflammatory diseases of the genital organs are mainly sexually transmitted microbial-protozoan-viral associations, characterized by new properties, specific clinical features and are not pathological components of individual infectious components. They can persist in a human body lifelong, leading to periodic exacerbation of adnexitis, cervicitis, vaginitis, bartholinitis, cystitis, etc., which result in infertility [8].


CONCLUSIONS

Taking into account the information described above, it can be noted that mixed urogenital infections affect the pathogenesis of endometrial hyperplas-

tic processes. The concept of vaginal biocenosis is currently in the focus of attention of many scientists and doctors. The functioning and coordinated interaction of all parts of the microecosystem is ensured by the immune and endocrine systems. It reflects their functional state and depends on factors of both

the internal and external environment. A disruption in one of these links invariably leads to disruption of the vaginal microenvironment which can further lead to the development of inflammatory processes in the genital tract, which in turn can lead to hyperplastic processes in the endometrium.

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CONFLICT OF INTEREST










The Authors declare no conflict of interest

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