

INNOVATIVE METHODS OF TREATMENT OF BACKGROUND AND PRECANCEROUS DISEASES OF THE CERVIX

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✓ Resume

Relevance. The article is devoted to the early diagnosis and treatment of background and precancerous diseases of the cervix is one of the important problems of gynecology, the ultimate goal of which is to reduce the incidence of cervical cancer.

Objective: To increase the effectiveness of the treatment of background and precancerous diseases of the cervix by photodynamic therapy.

Material and methods of the study: In accordance with the purpose and objectives of our study, 255 women with background and precancerous diseases of the cervix, who were in the gynecological departments of the regional perinatal center of the Bukhara region, were examined and treated for the period 2018 to 2020.

Conclusions: photodynamic therapy can be successfully used in the treatment of ectopia, leukoplakia, and endometriosis, dysplasia, not accompanied by pronounced deformation of the cervical tissue.

Key words: cervix, ectopia, leukoplakia, dysplasia, endometriosis, photodynamic therapy.

ИННОВАЦИОННЫЕ МЕТОДЫ ЛЕЧЕНИЯ ФОНОВЫХ И ПРЕДРАКОВЫХ ЗАБОЛЕВАНИЙ ШЕЙКИ МАТКИ

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✓ Резюме

Актуальность. Статья посвящена в раннюю диагностику и лечение фоновых и предраковых заболеваний шейки матки является одной из важных проблем гинекологии, конечной целью которой является снижение заболеваемости раком шейки матки.

Цель исследования: Повысить эффективность лечения фоновых и предраковых заболеваний шейки матки методом фотодинамической терапии.

Материал и методы исследования: В соответствии с целью и задачами нашего исследования за период 2018 по 2020 г.г. были обследованы и пролечены 255 женщины с фоновыми и предраковыми заболеваниями шейки матки, находившиеся в гинекологических отделениях областного перинатального центра Бухарской области.

Выводы: Фотодинамическая терапия успешно может применяться при лечении эктопии, лейкоплакии, эндометриоза, дисплазии, не сопровождающихся выраженной деформацией ткани шейки матки.

Ключевые слова: шейки матки, эктопия, лейкоплакия, дисплазия, эндометриоз, фотодинамическая терапия.

БАЧАДОН БЎЙНИ ФОН ВА РАК ОЛДИ КАСАЛЛИКЛАРИНИ ИННОВАЦИОН ДАВОЛАШ УСУЛЛАРИ

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✓ Резюме

Долзарблиги. Мақола гинекология муҳим муаммолардан бири бачадон саратони касаллини камайтириш учун, бачадон бўйни фон ва рак олди касалликлари эрта таъхислаш ва даволашга бағишланган.

Тадқиқотнинг мақсади. Фотодинамик даволаш орқали бачадон бўйни фон ва рак олди касалликлари даволаш самарадорлигини ошириш.

Материал ва усуллари. Тадқиқотимизнинг мақсад ва вазифаларига мувофиқ, 2018 йилдан 2020 йилгача бўлган давр мобайнида Бухоро вилояти вилоят перинатал марказининг гинекологик бўлимларида бачадон бўйни фон ва рак олди касалликлари билан оғриган 255 нафар аёл тиббий кўрикдан ўтказилди ва даволанди.

Хулосалар: Фотодинамик терапия бачадон тўқимасининг аниқ деформацияси билан бирга келмаган эктопия, лейкоплакия, эндометриоз, дисплазияни даволашда муваффақиятли қўлланилиши мумкин.

Калит сўзлар: бачадон бўйни, эктопия, лейкоплакия, дисплазия, эндометриоз, фотодинамик даво.

Relevance

The need to identify and treat background and precancerous diseases of the cervix is due to the high frequency of background and precancerous diseases of the cervix in the structure of gynecological pathology in young women, significantly impairing reproductive function, a significant degree of danger of malignant degeneration and insufficient effectiveness of existing treatment methods. It is known that the process of carcinogenesis is multistage and the preclinical existence of a tumor usually lasts for years. According to the WHO, the transition of cervical dysplasia to cancer in situ lasts about 3-8 years, another 10-15 years passes before the development of microinvasive cancer.

Thus, early diagnosis and treatment of background and precancerous diseases of the cervix is one of the important problems of gynecology, the ultimate goal of which is to reduce the incidence of cervical cancer. To date, a lot of scientific works have been devoted to the problem of treating cervical pathology, and various methods of treating background and precancerous diseases of the cervix have been introduced. The most common are methods based on the use of electrocoagulation, cryodestruction, and vaporization lasers as a therapeutic effect. According to domestic and foreign authors, the therapeutic effect of the above treatment methods is 67-98.7%.

However, each of these methods has its own indications, contraindications and a number of

oophoritis, bleeding, the occurrence of endometriosis, cicatricial changes in the cervix, stenosis of the cervical canal, impaired reproductive function. In pursuit of the goal of preventing cervical cancer, the treatment of background and precancerous diseases should be radical, but at the same time careful, while maintaining the anatomical and functional usefulness of the cervix, which largely determines the state of the reproductive system.

In this regard, methods of treatment are currently being developed that combine the optimal therapeutic effect in the absence of unwanted complications. One of the newest approaches to the treatment of cervical pathology is photodynamic therapy (PDT). This method causes selective death of pathological cells, which is ensured by the selectivity of drug accumulation in the pathological tissue and local light supply. According to foreign sources, isolated cases of successful treatment of dysplasia and cervical cancer with the use of hematoporphyrin derivatives as a photosensitizer are known.

In the sources available to us, no information was found on PDT in the treatment of background and precancerous diseases of the cervix, and the effectiveness of the drug "Photoditazin" in PDT was not sufficiently evaluated, which determined the purpose of our study.

Objective of the study: To increase the efficiency of treatment of background and precancerous diseases of the cervix uteri by the method of innovative photodynamic therapy.

Material and methods

In accordance with the goal and objectives of our study for the period 2017-2020. 255 women with background and precancerous diseases of the cervix, who were in the gynecological departments of the regional perinatal center of the Bukhara region, were examined and treated. The age of the examined women varied from 21 to 65 years (mean age 43.2 ± 0.3 years).

The maximum number of patients (67%) was between 21 and 35 years old (mean age 32.2 ± 0.3 years). The following pathology of the cervix was revealed: ectopia - in 52 patients (20.4%), eroded ectropion - in 14 (5.5%), leukoplakia - in 21 (8.2%), grade I-II dysplasia - in 11 (4.3%), endometriosis - in 13 (5.1%). The diagnosis of the disease was made in accordance with the International Statistical Classification of Diseases and Problems Related to Health, 10 - revision (ICD-10), adopted by WHO in 1995. To get a true idea of the nature of the pathological process of the cervix, we carried out a comprehensive clinical, microbiological, colposcopic, cytological, histological examination.

The clinical examination included a thorough analysis of the premorbid background, the study of complaints, past and concomitant extragenital and gynecological diseases, the characteristics of the menstrual, sexual, generative function. The state of the cardiovascular, respiratory, endocrine, urinary and digestive systems, mammary glands was assessed. In the process of work, a standard range of laboratory tests was used: general blood test, general urinalysis, blood for RW, HBs, HCV, HIV. The gynecological status was determined on the basis of examination of the external genital organs, examination of the vagina and uterus using mirrors, and bimanual vaginal examination.

Colposcopic examination was carried out with a Leisegang colposcope with a resolution of 15 times magnification. With the help of colposcopic examination, we determined the size, shape of the cervix and external os, the color and relief of the mucosa, the features of the vascular pattern, the boundaries of the squamous and cylindrical epithelium, revealed the true lesion area of the ectocervix, as well as signs of atypical transformation. Microbiological research was carried out using a bacterioscopic and bacteriological method.

Bacterioscopic examination made it possible to determine the belonging of microorganisms to obligate-anaerobic species, lactobacilli, to assess the invasiveness of the fungal flora, and to assess both the qualitative and quantitative composition of the bacterial flora. The determination of specific pathogens in the mucus of the cervical canal was carried out by the method of polymerase chain reaction (PCR). Cytological examination of smears - prints from the surface of the cervix and cervical canal is one of the main methods for diagnosing precancerous and malignant diseases of the cervix.

Cytological examination revealed the morphological characteristics of cells, the relationship of individual cell groups, the location of cellular elements in the preparation. Much attention was paid to the identification of the nuclear-cytoplasmic index, the distribution of chromatin in cells, an increase in the nucleoli, and the detection of figures of mitotic division. We described the results of the cytological examination according to the Papanicolaou classification. Histological examination of biopsies of the cervix and scrapings of the mucous membrane of the cervical canal made it possible to make a final diagnosis. We interpreted the histological pictures in accordance with the classification of Ya.V. Bohman (1989).

Preoperative preparation was carried out for all women with a detected genital tract infection and included etiotropic, immunomodulatory therapy, followed by the appointment of eubiotics to normalize the vaginal microbiocenosis. The treatment was carried out in the first phase of the menstrual cycle. PDT did not require anesthesia. The PDT session was carried out 2 hours after the application of the FS "Photoditazin" 0.5% in the form of a gel to the pathological zone of the ectocervix. A semiconductor laser device "ALT-Vostok-03" was used as a source of laser radiation.

The output wavelength was 662 nm in continuous mode for 10 - 20 minutes (depending on the affected area), the output power was -1 W, the energy density was 80 - 250 J / cm². Assessing the process of cervical epithelization, we took into account the presence of complications during manipulation, the nature of the scab, the period of its rejection, the timing of regeneration, the dynamics of the results of cytological and bacteriological studies, as well as the presence of complications in the early (4 - 10 weeks) and late (6 - 9 months) terms of treatment.

Result and discussion

Anamnesis analysis, clinical picture of cervical pathology, the effectiveness of diagnostic methods, immediate and long-term results of treatment carried out in 105 patients with background and precancerous diseases of the cervix, made it possible to obtain data on the causes of the development and features of the course of background and precancerous diseases of the cervix, the nature of reparative processes after PDT in comparison with the diathermy surgical method of treatment, to develop methods and indications for PDT.

Basically, the nature of the complaints presented by the patients: leucorrhoea (39.8%), burning sensation in the vagina (12.6%), pulling pains in the lower abdomen (21.9%), itching (7.6%) was associated with concomitant infectious inflammatory diseases of the vagina, cervix and uterine appendages. The study of the somatic history showed a fairly high percentage of infectious diseases, especially those suffered during the formation of menstrual function (29.2%) and the presence of chronic foci of endogenous infection in 41.1%, which, possibly, is an indicator of immunosuppressive conditions that reduce the body's resistance to infections and contributing to the chronicity of infectious and inflammatory diseases of the external and internal genital organs.

According to a number of authors, in women with menstrual irregularities, cervical pathology is more common than in the population. We have identified various menstrual irregularities: algomenorrhea (17.9%), oligomenorrhea (10.7%), hyperpolymenorrhea (6.9%), metrorrhagia (2.8%), which may indicate hormonal imbalance as a provoking factor of development pathology of the cervix. It was found that the risk factors in the development of cervical pathology are unprotected sex, numerous partners, early onset of sexual activity. Analysis of the use of contraceptive methods by patients revealed that 37 (35.2%) patients did not use any methods of contraception.

Hormonal contraception was used by 10 (9.5%) women, 31 (29.5%) used a condom, 5 (4.7%) - spermicides, 19 (18.1%) - interrupted intercourse. The rare use of barrier methods of contraception in the surveyed women contributed to the infection of the genital tract and the development of cervical pathology. When studying the reproductive function, we found that the patients had 255 pregnancies, of which 199 had births and 56 had abortions. The first pregnancy ended in abortion in 21.9% of women. Ruptures of the cervix during labor were detected in 31.1% of patients. The analysis of reproductive function testifies to the great role of postpartum and

after abortion traumatization of the cervix in the development of cervical pathology.

The high level of concomitant gynecological pathology draws attention to itself: a history of colpitis was detected in 54% of cases; chronic inflammation of the uterine appendages was found in 29.3% of patients, and 15.8% of them repeatedly underwent inpatient treatment for exacerbation of the inflammatory process; in 58.5% of cases, various hormone-dependent diseases were identified (uterine fibroids, hyperplastic processes of the endometrium, menstrual irregularities).

Thus, the analysis of anamnestic data revealed extragenital, behavioral and genital risk factors for the development of cervical pathology, which create not only the background for the development of background and precancerous diseases of the cervix, but also cause the development of background and precancerous diseases of the cervix.

The laboratory and instrumental examination carried out by us made it possible to obtain data on the causes of the development of background and precancerous diseases of the cervix, the peculiarities of their course, to reveal the true dimensions and to study the structure of the pathological process.

Colposcopic examination in the majority of patients (71.3%) revealed the presence of sections of columnar epithelium on the surface of the ectocervix. Colposcopic signs of leukoplakia were detected in 21.4% of patients, endometriosis - in 5.8%. The normal transformation zone was observed in 65.6% of patients. Important colposcopic signs of precancerous diseases of the cervix are certain markers, which can be used to judge the high probability of dysplasia of stratified squamous epithelium. As a rule, their appearance is associated with an increase in the concentration of DNA in cells (aceto-white epithelium) or the formation of atypical vascularization.

The atypical transformation zone was found in 31.5% of patients and was mainly associated with the presence of inflammatory changes in the cervix, leukoplakia, and dysplasia. The results of our study confirmed the high information content of colposcopy in the diagnosis of background and precancerous diseases of the cervix. Many researchers have proven the role of infectious agents in the development of background and precancerous diseases of the cervix [1,3]. In this regard, we paid great attention to the identification of infectious agents using bacterioscopic, bacteriological research and diagnostics by PCR.

At bacterioscopic examination, the majority of patients showed the 2nd and 3rd degrees of vaginal cleanliness (46.9% and 37.8%, respectively), less often the 1st and IVth degrees of vaginal

cleanliness (5.8% and 6, 9% respectively). According to the bacteriological study, *Staphylococcus epidermidis* (27.2%), *Staphylococcus saprophyticus* (31.1%), *Staphylococcus aureus* (24.4%), *Candida albicans* (22.1%), *Bacteroides* (22.4 %), *Escherichia coli* (18.2%), *Peptostreptococcus* (16.2%), *Enterococcus* (11.7%). Moreover, in 82.4% of cases, a mixed infection was detected.

The data of microbiological studies revealed a sharp decrease in the frequency of isolation of the main obligate representatives of the microbiocenosis of the vagina and cervix - lacto- and bifidobacteria, which contributes to the growth of opportunistic microorganisms. When examining the mucus of the cervical canal, various pathogens were found: *Gardnerella vaginalis* in 21.6% of patients, *Ureaplasma urealiticum* in 17.6%, *Mycoplasma hominis* in 11.8%, *Candida albicans* in 11.8%, *Chlamidia trachomatis* in 7, 8%, *Trichomonas vaginalis* - in 5.9%. The presence of mixed infection was found in almost every third patient.

Recently, a number of researchers have paid great attention to the herpes simplex virus (serotype II) and human papillomaviruses, especially types with a high oncogenic risk (types 16 and 18), in the development of precancer and cervical cancer. The human papilloma virus was detected by us in 12.8% of patients, of which HPV 6.11, 40 types were found in 6.9% of patients with ectopia and leukoplakia of the cervix. HPV of high oncogenic risk was detected in 5.9% of patients with grade I-II dysplasia, confirmed by cytological and histological examination. All patients with identified

papillomavirus infection had no clinical symptoms of infection.

The cytological method is one of the main ones in the diagnosis of diseases of the cervix. A number of authors point to the coincidence of cytological findings with the results of morphological studies of the cervix in 79.2% -93.4% of cases [2,5]. Cytological examination of the exo- and endocervix in 18.6% of cases did not reveal any pathology. In 66.7% of patients, cytological examination revealed cells of columnar epithelium in smears - prints from the surface of the cervix. Cytological studies carried out by us have shown low information content in the detection of leukoplakia.

So, among 23 patients with colposcopic signs of leukoplakia, 8 did not find cytological signs characteristic of leukoplakia. The cytogram of inflammation was observed in 41.2% of patients. Cytological signs of dysplasia against the background of ectopia, leukoplakia and concomitant inflammation were detected in 14.7% of patients. After a course of anti-inflammatory and antibiotic therapy, these patients underwent a biopsy of the cervix with subsequent histological examination, which confirmed the presence of dysplasia in 8.8% of patients with a colposcopic picture of ectopia and leukoplakia in combination with an atypical transformation zone.

Conclusion

Thus, photodynamic therapy can be successfully used in the treatment of ectopia, leukoplakia, endometriosis, dysplasia, which are not accompanied by severe deformation of the cervical tissue.

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