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PREDICTING THE RISK OF DEVELOPING CERVICAL INTRAEPITHELIAL NEOPLASIA ASSOCIATED WITH HUMAN PAPILLOMAVIRUS INFECTION

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✓ ***Resume***

A cytological sign of HPV lesions of the cervix in women of any age is koilocytosis. The koilocyte count decreases depending on the patient's age and the severity of the disease. The highest koilocyte counts are detected in adolescence and in patients infected with low-oncogenic types of the virus.

Keywords: cervix, human papillomavirus, intraepithelial neoplasia.

ПРОГНОЗИРОВАНИЕ РИСКА РАЗВИТИЯ ЦЕРВИКАЛЬНЫХ ИНТРАЭПИТЕЛИАЛЬНЫХ НЕОПЛАЗИЙ, АССОЦИИРОВАННЫХ С ПАПИЛЛОМАВИРУСНОЙ ИНФЕКЦИЕЙ

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✓ ***Резюме***

Цитологическим признаком ВПЧ-поражений шейки матки у женщин любого возраста является койлоцитоз, количество койлоцитов уменьшается в зависимости от возраста пациенток и тяжести процесса. Наибольшее количество койлоцитов выявляется в подростковом возрасте и у пациенток инфицированных низко онкогенными типами вируса.

Кючевые слова: шейка матки, вирус папилломы человека, внутри эпителиальная неоплазия.

INSON PAPILLOMAVIRUSI INFEKTSIYASI BILAN BOG'LIQ INTRAEPITELIAL NEOPLAZIYASINI RIVOJLANISH XAVFINI BASHORAT QILISH

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✓ ***Rezyume***

Har qanday yoshdagi ayollarda bachadon bo'yni HPV lezyonlarining sitologik belgisi koilotsitozdir. Koilotsitlar soni bemorning yoshiga va kasallikning og'irligiga qarab kamayadi. Eng yuqori koilotsitlar soni o'smirlik davrida va virusning past onkogen turlari bilan kasallangan bemorlarda aniqlanadi.

Kalit so'zlar: bachadon bo'yni, inson papillomavirusi, intraepitelial neoplaziya.

Relevance

Oncopathology of the female reproductive system, and cervical cancer in particular, is not only a medical but also a socio-demographic problem [1,3,5,7,9]. The viral etiology of cervical cancer has been confirmed by a number of studies by Russian and foreign researchers [2,4,6,8,10]. The key etiological factor is considered to be the human papillomavirus. Therefore, an important step in the prevention of malignant neoplasms of the cervix is the early diagnosis and effective treatment of cervical lesions caused by the human papillomavirus [2,11,12,14,15]. The relevance of this problem is determined, first of all, by the

fact that there is no single algorithm for the diagnosis and treatment of HPV lesions of the cervix, which leads to disease progression and the development of squamous cell intraepithelial lesions and cervical cancer. The presence of a large number of clinical, subclinical, and latent forms of this pathology determines the need for timely diagnosis and treatment in patients of any age. Risk factors and triggers in the pathogenesis of HPV lesions, cervical intraepithelial neoplasia (CIN), and squamous cell lesions are also generally recognized. These include immunological changes in the cellular and humoral immune systems, smoking, early onset of sexual activity, high sexual activity, failure to use barrier contraception, a high infection index, and concomitant STIs [4,13,16,18].

Diagnosis of cervical lesions associated with the human papillomavirus, despite numerous developments in diagnostic programs, still presents certain difficulties. Modern diagnostic algorithms include advanced colposcopy, Pap smear screening (PAP smear testing of cervical lesions), pathomorphological markers of HPV, and molecular biological methods (PCR) [1,19,20,21]. There is no generally accepted diagnostic and treatment protocol for detecting this pathology at any age. Some studies have found that up to 55-75% of adolescents are infected with HPV, with HPV lesions of the cervix often associated with genital warts [1,22].

A number of reproductive disorders associated with cervical infection with the human papillomavirus have been identified [18]. In perimenopausal women, due to hormonal changes, altered homeostasis, and impaired apoptosis, HPV lesions of the cervix typically persist longer and are more often associated with intraepithelial neoplasia.

Given the high incidence of human papillomavirus infection, especially in young women, and the lack of clear treatment approaches, studying the characteristics of human papillomavirus lesions of the cervix at different ages and identifying these characteristics will improve the diagnosis and treatment of this pathology.

Purpose of the study: To improve the effectiveness of diagnosis, treatment, and prevention of human papillomavirus lesions of the cervix in adolescent, reproductive, and perimenopausal women.

Materials and method

The study included 335 patients with confirmed human papillomavirus cervical lesions. The patients were divided by age as follows: 17 adolescents, 217 women of reproductive age, and 101 perimenopausal patients. To study the incidence of HPV lesions of the cervix in adolescent, reproductive, and perimenopausal patients, the following approaches and research areas were used: Assessing the incidence of HPV lesions among patients based on visits to medical facilities and data from preventive examinations. Analyzing the detection rate of HPV lesions of the cervix based on data from extended colposcopy, cytological, pathological, and PCR studies. Studying endogenous and exogenous risk factors for the development of HPV lesions. Assessing the incidence of concomitant sexually transmitted diseases based on testing using PCR, ELISA, and IF. Studying indicators of systemic and local immunity, as well as the levels of endogenous IL-1 and TNF in the serum of patients. A comparison of the efficacy of high-intensity laser vaporization and local cytokine therapy for treating HPV lesions. A study of HPV carriage in sexual partners was conducted using PCR testing for human papillomavirus. In addition to standard clinical techniques and methods, specialized methods were used.

Morphological examination was performed using a standard methodology. Smears for cytological examination were collected using an Ayre spatula, Volkmann spoons, and endobranch blades. Biopsies were taken using conchotomes and disposable scalpels. The sample preparation technique was routine. Cytological findings were evaluated using the Papanicolaou classification, CIN, and the Bethesda classification system. Criteria for papillomavirus infection included the presence of koilocytic atypia in the cytological and morphological material, as well as acanthosis, parakeratosis, hyperkeratosis, and varying degrees of cervical intraepithelial neoplasia.

STI diagnosis and HPV testing were performed using polymerase chain reaction, while herpes simplex virus types I and II (HSV) and cytomegalovirus (CMV) were detected using enzyme-linked immunosorbent assay.

Result and discussions

The percentage of HPV lesions in cervical pathology was high (36.3%). The highest proportion of HPV lesions in cervical pathologies was observed among adolescents (56.3%), while the lowest was among perimenopausal women (21.2%) ($p < 0.05$). The study results do not significantly differ from published data (1998).

Of 335 patients examined using extended colposcopy, we identified 321 patients with abnormal epithelium detected on the cervix, who constituted a risk group. In the study, before the introduction of the molecular biological method (PCR in 2019), the criterion for HPV cervical lesions was morphological

confirmation of the diagnosis; since 2019, this has been PCR testing and morphological examination. Thus, 335 patients of various ages were included in the study. Depending on the age composition, they were divided into 3 groups: Group I - 17 teenage girls, Group II - 217 patients of reproductive age and Group III - 101 patients in perimenopause.

Our analysis of risk factors for the development of papillomavirus lesions of the cervix among the patients included in our study, compared with women without HPV lesions, showed that the leading ones are: low level of sexual culture, which is expressed in unsatisfactory social status; early onset of sexual life; high sexual activity; frequent change of sexual partners; smoking; history of sexually transmitted infections. It was found that 54.7% of adolescents, 35.6% of patients of reproductive age and 28.7% of perimenopausal women came from working-class families. 48% of adolescents, 31% of patients of reproductive age and 15.8% in perimenopause smoked. In general, 43.6% of adolescents, 54.2% of patients of reproductive age and only 21% of perimenopausal patients had low social status. Age and menstrual function characteristics were consistent with those in the general population across all age groups. The average age of adolescent girls was 16.4±0.1 years, with only 1.7% of adolescents under 14 years of age. The average age of patients during the reproductive years was 25.4±0.2 years, and during perimenopause, 49.4±0.1 years.

One of the risk factors and manifestations of human papillomavirus infection is its localization on the external genitalia. In our study, HPV infection of the external genitalia was detected in 67.5% of cases, primarily as genital warts and associated with low-risk HPV. In reproductive age, vulvar lesions occurred in 44.5% of cases, primarily as vestibular papillomatosis and genital warts, associated with low- and mid-risk HPV. Perimenopausal patients were characterized by single HPV lesions of the external genitalia (15.6%) and they were associated with HPV types 16 and/or 18 ($p < 0.05$).

Analyzing the anamnestic data, we found that 70.3% of patients across all age groups had experienced sexually transmitted infections. The most common infections were vaginal candidiasis and bacterial vaginosis, which, according to the WHO, are the most common sexually transmitted diseases worldwide.

Mycoplasmosis, genital herpes, gonorrhea, syphilis, and human papillomavirus infection were less common, consistent with data from several researchers (1997).

Analyzing the duration of illness, we found that the shortest duration of illness was in adolescent patients (12.4±0.1 months), for patients of reproductive age, the duration was 3.5±0.2 years, and the longest was in perimenopausal patients – 5.7±0.3 years ($p<0.05$). It's possible that older women had cervical HPV infection for much longer, but due to the imperfections of diagnostic programs more than 5 years ago, diagnosing HPV lesions of the cervix was difficult. We were able to estimate the duration of the disease based on anamnestic data and by analyzing patient records. Determining the duration of HPV lesions of the cervix is, in our opinion, important given the development of widespread lesions over a long period of persistent HPV infection (Ka, 2021). To verify the diagnosis, STI tests (using polymerase chain reaction), bacteriological and bacterioscopic examinations, extended colposcopy, cytological examination of cervical smears and scrapings from the cervical canal, histological examination of targeted cervical biopsies, and HPV type determination using PCR were performed. In other words, methods proposed by modern authors as screening methods for the diagnosis of HPV lesions (2019) were used. A comprehensive microbiological examination of the vaginal contents in patients with HPV lesions of the cervix revealed signs of microecological disturbances, manifested by bacterial vaginosis (26.4%), candidiasis (11.5%), and nonspecific vaginitis (32.2%). Moreover, they were more common among adolescents and perimenopausal patients compared to the reproductive age group. Thus, among adolescents, BV was present in 29.1%, and in perimenopause in 27.7%, which is significantly more common than in the reproductive period (17.1%).

This can be explained by the fact that in adolescents, due to their young age and the large number of physiological ectopias, the processes of disruption of vaginal biotope parameters are more pronounced, whereas in perimenopausal patients, all changes occur due to mucosal atrophy associated with hormonal deficiency.

In reproductive-age patients, colposcopic signs of abnormal epithelium were observed both within the area of squamous cell metaplasia (23.6%) and beyond (76.4%). In this age group, widespread pathological processes were detected (23.1%), but their number was insignificant. Based on data from foreign authors (2012) on high apoptotic activity at this age, even with HPV infection with high-risk oncological viruses, in our study, only 17.8% of reproductive-age patients had signs of leukoplakia.

Thus, HPV lesions of the cervix have both age-related characteristics and differences in colposcopic appearance depending on the type of human papillomavirus. This is important for practical healthcare and makes extended colposcopy the method of choice for screening cervical pathologies and squamous intraepithelial lesions in particular.

Conclusion

Human papillomavirus lesions of the cervix are a subclinical form of human papillomavirus infection and occur in 37% of gynecological patients. The prevalence of HPV lesions, colposcopic findings, and morphological and immunological changes depend on the patient's age and HPV type.

2. Characteristic features of the course of HPV lesions of the cervix in adolescents include the absence of widespread lesions, a combination of abnormal epithelium on colposcopic examination with ectopia, and a high frequency of HPV lesions and cervical cysts combined. Morphologically, koilocytoatypia predominates over signs of CIN, and cervical infection with a high-risk oncological virus is observed.

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