

# МЕДИЦИНСКИЕ НАУКИ

## CAUSAL FACTORS OF CERVICAL INTRAEPITHELIAL NEOPLASIA DEVELOPMENT

*Andreeva Natalia Anatolyevna*

*Candidate of Medical Sciences, Associate Professor of the  
Department of Obstetrics and Gynecology, Saransk*

*Nemova Natalya Alekseevna*

*6th year student of Ogarev Mordovia State University, Medical Institute*

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## ПРИЧИННЫЕ ФАКТОРЫ РАЗВИТИЯ ШЕЙНОЙ ИНТРАЭПИТЕЛЬНОЙ НЕОПЛАЗИИ

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*Андреева Наталья Анатольевна*

*Кандидат медицинских наук, доцент*

*Кафедра акушерства и гинекологии, Саранск*

*Немова Наталья Алексеевна*

*Студент 6 курса Мордовского государственного университета им. Огарева,  
Медицинский институт*

### ABSTRACT

The article analyzes the causal factors of the cervical intraepithelial neoplasia of I and II degrees development, which is the leading pathogenetic link in the cervical cancer development. The relevance of the immunomodulators with antiviral activity use to CIN I and CIN II patients is evaluated.

**Keywords:** Papilloma Viral Infection, Cervical Intraepithelial Neoplasia, human papilloma virus, colposcopy, koilocytosis, biopsy, polymerase chain reaction, immunomodulators.

Cervical intraepithelial neoplasia is a pathological condition in which there is a epithelial cell differentiation violation, the development of atypia in them as a result of proliferation of cambial elements and a histo-structure violation.

According to WHO, CIN- is a change in which part of the epithelium is replaced by cells, with varying degrees of atypia and loss of stratification and polarity, but the stroma remains unchanged during this process. Depending on the intensity of cell proliferation, the severity of cellular and structural atypia, there are CIN I, CIN II, CIN III.

Cervical intraepithelial neoplasia is regarded as a precancerous cervical disease. Cervical cancer steadily occupies a leading position in the structure of obstetrics and gynecology. In the world ranking it is on the 4th place among the most common types of women cancer. From 2014 to 2017 according to Russian experts, 175 427 new cases of cervical cancer were registered. A rather impressive fact is that, on average, 275,000 women in the world die from cervical cancer every year, 17 Russian women die every day from this pathology. The average age of morbidity is 35.3 years, however, there has recently been an alarming trend, cervical cancer is diagnosed in reproductive age young women, at the age of 27 +/- 1.5 years [2].

More than 80% of LSIL and 100% of HSIL are associated with high oncogenic HPV infection. The most common type found in both lesions is 16,18,31,33rd HPV. The rate of progression in each case is different.

In order to HPV starts oncological cell proliferation, a number of predictor factors and cascade reactions in the cells themselves are required. It is worth noting that not every woman's virus can provoke the appearance of cervical intraepithelial neoplasia. As a rule, from the time of HPV infection or its activation and ending with the appearance of CIN and Cain situ, it takes about 1.5 to 5 years.

Based on the foregoing, the purpose of our study is to study the predisposing factors in the development of cervical intraepithelial neoplasia, the development of an algorithm for stepwise significant diagnostic schemes and principles of therapy for women with CIN I and CIN II.

**Materials and methods:** We examined 71 patients of reproductive age with CIN I, II according to oncocytological examination.

The patients included in the examination groups were of the age from 19 to 55 years, and the middle age was 27 +/- 2.5 years. According to our observations, 35% of the women who applied, the cervical pathology was visualized in the form of ectopia, leukoplakia and the cervix nabot cysts.

All patients underwent cytological examination, the conclusion of which was confirmation of CIN I, II. In this regard, the patients were divided into 2 groups: women with CIN I were observed in the 1st group, patients with CIN II were assigned to the 2nd group.

We found that the peak of HPV infection occurred at a young age (19-27 years), which was 54%. This indicator includes young women, i.e. the most sexually active part of the population, 47% of them were single and had a frequent change of sexual partners.

Regarding contraceptive history, we were only interested in the barrier method of contraception, only 27% of the women surveyed used a barrier method using a condom, 25.3% of the patients used the hormonal contraceptive method, and 47.7% did not have contraceptive alertness during sexual intercourse.

Anamnesis of the sexual function of the examined women was as follows: 44.3% of the women had an early onset of sexual activity, which corresponded to 15.5 +/- 1.5 years, 43% of the patients had their first sexual contact at 19-21, 16.7% of the examined noted the late onset of sexual activity - 25.5- 30 years.

Evaluating the history of the patient's menstrual function we got to know that: 66.4% of them had a regular menstrual cycle, 25.3% took combined oral contraceptives, both for the purpose of contraception and for the regulation of the menstrual cycle, and 8.3% of the women surveyed did not have regularity cycle from 35 to 90 days - it can be considered as a hormonal trigger mechanism in the development of cervical pathology.

An analysis of reproductive performance showed that 55% of the women had a history of both childbirth and abortion; 26.7% of patients had one or more abortions by the method of instrumental curettage, 18.3% of patients did not have childbirth and abortions in history.

At the second stage, a comparative analysis of laboratory and instrumental parameters in the both groups was performed. Laboratory studies revealed in the 1st group in 82% of observations the I-II degree of purity of the vaginal contents and in 12% of examinations the presence of key cells, mobiluncus, leptotrix. In 18% of studies, smears for purity of vaginal contents corresponded to III-IV degrees of purity and the content of *Candida* fungi and microorganisms that play a key role in the development of bacterial vaginosis. In the 2nd group, patients with the presence of III-IV degree of purity and the presence of pathogenic microflora in smears in its various dissociation prevailed, which accounted for 79.8%, and only 20.2% of cases had no reason to prescribe etiotropic therapy.

Extended colposcopy in both groups showed an unsatisfactory colposcopic pattern, and in the 2nd group in 19.4% of cases we found leukoplakia.

For the purpose of differential diagnostics, a sample with acetic acid was carried out. Both in the first and in the second group in 25.5% and in 19.7% of observations, respectively, we identified a negative vasoconstrictive reaction, which should not be observed in the norm.

During the Schiller test, in 64% of the observations, in both groups, the affected areas of the ectocervix were stained as a whitish point - "semolina", "snowstorm zones", which indirectly indicates viral damage to the epithelium. The patients from the second group (79.3%) had the iodine-negative test.

When conducting a cytological study of patients in both groups, the pattern of proliferation of stratified squamous epithelium prevailed. In 76.3%, signs of papillomavirus lesion of the cervical epithelium were the presence of koilocytosis in cells in combination with dyskeratosis, signs of inflammation, CIN I- for the first group and CIN II for the second group. This was an indisputable fact for a biopsy of the cervix in the second group.

In order to identify the virus, PCR was performed - diagnostics of material from the cervical canal and urethra. In the first and second group of patients, the presence of high-risk human papillomavirus was detected in 34.4% and 56.2% of cases, respectively. HPV of low oncogenic risk was detected in 23.5% and 37.7% of cases, both in the first and in the second groups. In 17.5% of the research identified - *Cl. Trachomatis*, in 11.4% - *Mycoplasma urealiticum*.

The choice of treatment tactics depended on the results of the examination, the nature and localization of human papillomavirus lesions.

All patients received combination therapy, which included antiviral and immunomodulatory therapy in combination with symptomatic therapy. The results of the therapy were evaluated not earlier than in 3-4 months.

The effectiveness of the combined treatment in group 1 was 86%, in 2 - 56%, according to the results of the control cytological study. In 44% of women of the 2nd group, CIN II degree was confirmed 3 months after the treatment.

During PCR diagnostics, after treatment of high-risk HPV in the 1st group, it was detected in 29.8% and low oncogenic risk in 20.5%. In the 2nd group of HPV, low oncogenic risk was detected in 18.2%, and high oncogenic risk in 24.8%

Conclusions: 1. Prolonged infection of HPV, especially its highly oncogenic types, the use of combined oral contraceptives for a long period of time, the onset of early sexual life, the presence of mixed infections, hormonal imbalance, the presence of bad habits, namely smoking, can cause the development of cervical intraepithelial neoplasia and cervical cancer.

2. In the presence of CIN I, II, especially those associated with HPV, it is necessary to apply a wide range of diagnostic methods. Which includes: clinical and visual method, advanced colposcopy, cytology, PCR diagnosis, cervical biopsy according to indications.

3. Adequate immunomodulating therapy with immunomodulators with antiviral activity, symptomatic therapy contributes to the elimination of virions and CIN I regression, and when CIN II is combined with destructive-surgical therapy, the effectiveness of treatment is increased.

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