

## Therapeutic Tactics in Patients with Cervical Intraepithelial Neoplasia of the Cervix

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**Abstract:** This development of a phased diagnosis and treatment of cervical pathology in women of reproductive age are discussed in this article. Advanced video colposcopy is an informative diagnostic method, which is allowed to include it in the mandatory stage of diagnosis of cervical diseases. At present, screening of examination for cervical pathology was developed, diagnostic methods are being improved, including cytological ones (examination of smears from endo and exocervix, liquid cytology, video fluorescence colposcopy).

**Keywords:** cervix, reproductive system, background diseases, human papillomavirus, CIN I-II degree, video colposcopy.

### Introduction

The cervix, due to its structural and functional features, occupies a special place in the reproductive system. Despite modern advances in the diagnosis and treatment of diseases of the cervix, its pathology continues to be a major problem.

Of particular relevance are cervical diseases in women of reproductive age. This is due to the increased incidence of cervical cancer at this age, especially before the age of 29 [1,2,3,18]. The number of patients with cervical cancer under the age of 30 has increased more than 2 times in recent years [1,2,3,6,13]. In the structure of causes of death in women under 30 years of age, cervical cancer is 8.5% [3,6,14]. The high incidence of neoplastic processes of the cervix is explained by the increasing prevalence of papillomavirus infection and the clinical activation of herpes and cytomegalovirus infections [5,7,12]. HPV infection (human papillomavirus) and other sexually transmitted infections increases the risk of dysplasia by 10 times [1,2,3,4,5,18]. The high incidence of neoplastic processes of the cervix is explained by the increasing prevalence of papillomavirus infection and the clinical activation of herpes and cytomegalovirus infections [5,7,12]. HPV infection (human papillomavirus) and other sexually transmitted infections increases the risk of dysplasia by 10 times [1,2,3,4,5,18]. According to the WHO, about 500,000 new cervical cancers are diagnosed annually. A significant increase in morbidity and mortality has been noted in recent years in many developing countries, including the countries of the former

Soviet Union [3,4,6,8,9]. A high mortality rate is associated with insufficient or ineffective preventive measures and late diagnosis. This is provided that cervical cancer is one of the few diseases for which screening is simple and affordable [1,2,15,16]. The incidence of cervical pathology as a whole reaches 30% in the population and increases with concomitant gynecological pathology. Despite the fact that the methods for diagnosing pathological conditions of the cervix are well known and are considered as screening methods, however, in practice they are not used enough, inconsistently, their interpretation is often unclear and often erroneous [7,10,14].

The absence in our country of a unified approach to the classification and clinical assessment of pathological conditions of the cervix, and, consequently, the tactics of managing patients, gives rise to a number of difficulties and discrepancies among practitioners, prompting them either to unjustified radicalism or to prolonged unjustified conservatism [11,13, 17]. In this regard, the purpose of the study was to develop a step-by-step diagnosis and therapy of cervical pathology in women of reproductive age.

To solve this goal, the following tasks were set:

1. To analyze the frequency, causes, clinical picture and risk factors of cervical diseases in women of reproductive age.
2. To determine the value of extended colposcopy with targeted biopsy / taking smears for cytology in the differential diagnosis of cervical pathology. Based on the results of an in-depth study, including hormonal examination, justify the implementation of appropriate methods of treating cervical pathology in patients of reproductive age

### **Material and methods of research**

Retrospective evaluation of 100 outpatient charts of patients with background and precancerous cervical diseases was performed to examine regional risk factors for this pathology. Of the 100, there were 70 women with background cervical diseases, of whom 55 had cervical ectopia (subgroup Ia), 15 had cervical polyps (subgroup Ic), and subgroups were identified according to the nosological forms of the ICD X revision. Group II included patients with cervical I-II degree CIN. For grade III CIN, the women were treated by an oncogynecologist because of their borderline condition with intraepithelial carcinoma. Also, a comprehensive prospective study and treatment were conducted in 100 women of reproductive age, including 70 women with background (group 1) and 30 (group 2) with precancerous cervix diseases. The comparison group consisted of 15 women of the same age group without gynecological diseases.

### **Results of the study and discussion**

The mean age of the patients in the study groups was  $25.1 \pm 0.2$  years and  $29.4 \pm 0.2$  years, respectively. Of the 100 patients included in the retrospective study, 42 (52.5%) patients in Group 1 were housewives, 28 (35%) were students, and 10 (12.5%) were office workers by social status. 20 (25%) patients in Group I had oncological diseases in their family tree, 7 (35%) in Group II. Patients with precancerous diseases in the family tree had CC, ovarian and breast cancer more often than background diseases. Of the extragenital pathology, chronic anemia (41.3%) and Urinary tract infection (UTI) (26.3%) prevailed. It was noted that chronic tonsillitis was more frequently (35%) diagnosed in patients with CIN of I-II degree. Characteristically, the patients with background cervical diseases were twice as likely to use hormonal contraception, which was recommended in every 5 cases to regulate menstrual function.

The frequency of gynecological diseases in the anamnesis of background and precancerous diseases was similar; retention ovarian cysts were more common in the background, uterine myoma and adenomyosis in the precancerous ones, which indicates the role of endocrine factor in the occurrence of this pathology. Cervical diseases in the anamnesis were reported more by patients with cervical leukoplakia than by those with ectopia and polyp. The number of births in the anamnesis of patients with background and precancerous cervical diseases did not practically differ. Medical abortions were twice as frequent in patients with background diseases.

Other factors, including infectious ones, were likely to have played a role in the development of background and precancerous cervical diseases. The microscopic picture of vaginitis with a large number of leukocytes was almost twice as frequent in the patients of the second group. Vaginal dysbiosis was detected more frequently in background cervical diseases and vaginitis in precancerous ones. Based on the retrospective analysis, the following risk factors for the development of background and precancerous cervical diseases were specified: oncopathological heredity, spontaneous miscarriages, uterine myoma and adenomyosis, STI, cervical scar deformities, STI. The problem of cervical pathology and the role of STI in its development is not in doubt, so in our work we did not set the task of determining the type of STI pathogen.

In a prospective study we traced serum hormone content in patients with cervical diseases depending on the phase of the menstrual cycle. In our studies, serum FSH content in women without gynecological diseases and with background cervical diseases corresponded to menstrual cycle phases. In the group of women with grade I-II CIN, the absence of a pre-ovulatory FSH peak was detected.

The dynamics of LH levels in women with background cervical diseases and grade I-II CIN corresponded to the phases of the menstrual cycle, but the preovulatory peak was lower than that in women without gynecological diseases. The detected decrease in serum FSH and LH in the pre-ovulatory period indicates the impaired neuroendocrine regulation, which may be one of the pathogenetic mechanisms in the development of this pathology. This postulate is confirmed by NMF in the patients we examined. The serum E2 content in patients with background cervical diseases did not differ significantly in menstrual cycle phases from that in gynecologically healthy women. The serum P content in the blood serum of the women with the background and precancerous cervix diseases in the luteal phase of the cycle was twice as low as in the gynecologically healthy women. Therefore, the role of sex steroid hormones is important in the development of cervical pathology and is the basis for the improvement of conservative treatment methods, including the use of hormonal drugs of systemic and local effects.

Currently, screening examination for cervical pathology is developed, diagnostic methods, including cytological (endo- and exocervical smears, liquid cytology, videofluorescence colposcopy), are being improved.

We used extended videocolposcopy to diagnose cervical pathology and evaluate the effectiveness during treatment. Normal videocolposcopic picture in the form of CE and ST in the subgroups of patients with background cervical diseases was found in 100% of cases and in 40.0% of patients with precancerous diseases. Abnormal colposcopic signs in patients with CIN of I-II degree in the form of puncturation, mosaicism were 1.5 times more frequent than in those with background cervical diseases, iodine-negative, ABE - 1.7 times, atypical vessels - 10 times more frequent respectively. The frequency of different colposcopic findings of inflammation in patients with background and precancerous cervical diseases did not differ. Final verification of the diagnosis was based on the results of histological examination of biopsy material.

The efficacy of dilated videocolposcopy in our studies for background cervical diseases was 96.9% and for precancerous ones - 89.6%. Complex examination of patients with background diseases of the cervix, CIN of I-II degree, carried out taking into account pathogenetic links of their development, allowed us to determine an individual treatment plan. We determined the volume of treatment and method of action on the pathological process of the cervix uteri on the basis of medical history, parity of birth, presence of cervical scarring, detected STIs, serum hormone levels, extended video-colposcopy, cytological and histological examination. The treatment was carried out in two stages. Stage I included etiotropic therapy depending on the STI detected.

Stage II treatment included destructive methods of cervical exposure. The choice of

method was determined taking into account the age, parity of delivery, size of the pathological process, its location, and previously used methods of destructive action. The treatment effectiveness criteria were: special gynecological examination, extended cervical video colposcopy, bacterioscopy of the contents of the cervical canal, vagina, and urethra, cytological examination of the endocervical, exocervical, and transitional zone epitheliums. At the first follow-up examination after 2 months, the rate of early recurrence in women with background and precancerous cervical diseases was 6.7%. The cause of relapse in 100% of cases was exacerbation of STI (sexually transmitted infections) that occurred after destructive treatment. The lower relapse rate in patients with cervical scarring indicates the effectiveness of the combined method. Treatment efficacy after 6 months was 100%

### **Conclusions**

1. The stepwise diagnosis of cervical diseases in women of reproductive age begins with a thorough anamnesis. The heritability of oncopathology in background cervical diseases in women of reproductive age is 83% and in precancerous diseases 83.3%. Spontaneous miscarriages, uterine myoma, and adenomyosis in the anamnesis are more common in precancerous cervical diseases, medical abortions - in background ones.

2. Expanded videocolposcopy is an informative diagnostic method, which makes it a mandatory step in the diagnosis of cervical diseases. Normal videocolposcopic signs were revealed 1.5 times more frequently in background cervical diseases; they were noted in 100% of cases. The signs of precancerous diseases were punctuated, mosaic (63.3%) and atypical vessels (33.3%).

3. Hormonal examination is the next stage of diagnostic procedures. The serum FSH and EH contents in women of reproductive age with background cervical diseases do not differ from those in women without gynecological diseases, LH - lower on the 14th day of the menstrual cycle, P - on the 21st; with precancerous diseases the FSH and LH decrease on the 14th, P - on the 21st day of the menstrual cycle.

4. Treatment of background and precancerous cervical diseases in women of reproductive age includes etiotropic therapy (depending on the infectious agent isolated), immunomodulatory and systemic or topical gestagens (if indicated). The second stage shows chemical destruction by Solkovagin or CD (cryodestruction) RX (radiofrequency surgery) or a combined method that allows to restore the anatomical structure of the cervix.

5. The frequency of early recurrences of background and precancerous cervical diseases is associated with an exacerbation of the infection. Late recurrences were not observed in 100%.

Based on the findings, the following measures are recommended:

In women of reproductive age, the examination and treatment of background and precancerous cervical diseases should be performed in three stages:

Stage I (primary examination) includes: history, general clinical, special gynecological, bacterioscopic and cytological examinations, simple colposcopy.

Stage II (in-depth examination), which is performed if cervical pathology is detected at the 1st stage, includes: extended video colposcopy and additional examination depending on colposcopic signs. For abnormal signs and different results, the examination for STI, RW, HIV, HBS-antigen, determination of serum Hg and P, blood tests for oncomarkers, pelvic ultrasound, hysteroscopy and cervicoscopy (if needed), targeted cytology, cervical biopsy with cytological and histological examination.

Stage III (complex treatment) includes conservative treatment:

etiologic, immunomodulatory therapy, gestagens of systemic or local influence (as indicated) and surgical treatment. The method of choice is KD, (cryodestruction) RX or a combined method including sequential application of KD, RX and repeated KD.



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