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Clinical Experience in Management of Patients with Cervical Erosion and Ectopia

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Abstract

PURPOSE OF RESEARCH: The main objective of the study was to analyze the results of treatment of patients with cervical erosion and ectopia without surgical treatment.

MATERIALS AND METHODS: To this end, a complete clinical examination of women with cervical erosion and ectopia was carried out: A smear for oncocytology, PCR for HPV 16–18, herpes simplex virus, chlamydia, colposcopy extended, and bacteriological study to identify the vaginal microflora. As a result of examinations, 30% of women without specific symptoms and complaints were diagnosed with cervical ectopia and assigned to the first group (practically healthy women). About 68% of women were assigned to the second group – with cervical erosion, who need conservative treatment, 2% – to the third group – women with invasive cervical cancer, who were sent to the oncology center. About 82% of L-SIL developed against the background of infection with highly oncogenic types of HPV, most often HPV 16, with 30% of them infected with more than 1 type of HPV. To eliminate concomitant inflammation of the cervix and vagina, hexicon was used in this group. After the rehabilitation of the vagina and cervix, the next step was to connect the drug depantol.

RESULTS: The use of hexicon and depantol in the treatment of cervical erosion led to the regeneration of the defect of the cervical vaginal mucosa, bypassing the surgical treatment of cervical erosion.

THE NOVELTY OF THE RESEARCH: As a result of the treatment of uncomplicated ectopia, there was no need to apply a surgical method of treatment in connection with the healing of ectopia.

PRACTICAL APPLICATION OF THE STUDY: Such an approach to the treatment of women with cervical erosion among obstetrician-gynecologists would lead to the prevention of relapse and improve the quality of life of patients. After treating the cervix with solkovagin, healthy tissues begin to recover under these dead tissues, which in the process completely replace patients without scarring on the cervix.

Introduction

According to the clinical protocol of the ministry of health and social development of the Republic of Kazakhstan from 2015, cervical erosion (true erosion) is a disease of the cervix, in which there is a defect of the epithelium covering the vaginal part of the cervix, and ectopia (pseudoerosis) is a disease of the cervix, in which there is a shift of the boundaries of the high cylindrical epithelium of the endocervix beyond the outer throat to the vaginal part of the cervix. Cervical erosion is classified into inflammatory, traumatic, and trophic forms. Trophic form of cervical erosion occurs in the presence of cervical prolapse and prolapse. According to the WHO, the main cause of erosive lesions of the cervix as well as dysplasia and malignant tumors of the cervical epithelium is the human papilloma virus. The virus in this pathology is detected in almost 100% of cases [1]. More than 70% of cases of cervical cancer are associated with HPV types 16 and 18 [2], [3], [4], and therefore, women with confirmed papillomavirus lesions of the cervix (cervical erosion, dysplasia, leukoplakia, and cervical intraepithelial neoplasia of the cervix) should be examined annually by a gynecologist with colposcopy, cytological examination of cervical smears, virological, and immunological examination [5]. Lack of therapy or improper treatment of patients with papillomavirus infection (PVI) leads to the development of cervical erosion [6]. With further progression of the disease, malignancy of the erosive process (or the focus of infection, which visually may not appear in the form of erosion), and, consequently, the development of dysplasia and cervical cancer, is possible [7]. With the advent of modern methods of research on erosion, additional factors causing pathology have been identified. The causes of this pathological process: Genetic predisposition; an inflammatory process that causes a change in the composition, pH of cervical mucus, and vaginal microbiocenosis; exposure to pathogenic microorganisms that cause sexually transmitted diseases and urogenital inflammatory diseases; hormonal imbalance caused by age-related changes (puberty and menopause), menstrual

irregularities, the appearance of the first menstruation before 12 years, taking hormonal drugs, pregnancy; chemical effects of hygiene products, spermicides (lubricants), and vaginal suppository substances; and mechanical injuries arising from the use of barrier contraceptives, rough sex, diagnostic manipulations, abortions, and difficult births. Aggravating factors include frequent changes in sexual partners; early onset of sexual activity; bad habits; more than 3 births; stress; increased libido; irregular or non-satisfying sex life; and the presence of genital infections. Erosion can be associated with work with chemicals, the presence of chronic pathologies that are not related to the reproductive system. Modern medicine has revealed another important factor causing cervical erosion – immunological. A decrease in the barrier function of the cervix and the entire body increases the risk of introducing an infectious agent and erosion. Systematization of clinical trial data has established that the most common causes of erosion are inflammation of the cervix and vagina in 67.7% [8]. Ectopia of the cervix is classified according to etiopathogenesis: Wrona (the impact of the high hormone levels of the mother's body) and priobreteniya (during pubertal period, there has been a rapid growth of the muscular structure of the cervix with a lag of proliferative process in the stratified squamous epithelium). The clinical course: uncomplicated form; complicated form (combined with cervicitis, vaginitis. On histological structure: Glandular (follicular – many glandular moves; papillary (papillary – a growth of stroma; epidemiology (healing sections of the columnar epithelium replaced by stratified squamous in the result of metaplasia of the reserve cells or "Napoletana" cells of the squamous epithelium from the periphery to the zone of ectopia.

Ectopia is not considered as a disease and even as a risk factor for a disease, respectively, such a condition needs only to be observed and regular cytological monitoring performed. Despite the fact that ectopia is a normal physiological process and does not need treatment, there are several arguments in favor of treating this condition. The most famous is the fact that chronic cervicitis (CC) against the background of CE ectopia serves as a powerful cofactor for the persistence of HPV and the occurrence of intraepithelial lesions [9]. Ectopy of the cervix often has a complicated character, in particular, this condition is often supplemented by an inflammatory process. In the area of the transformation zone against the background of prolonged inflammation, various changes can occur that lead to the appearance of unpleasant symptoms (including pain), are characterized by the appearance of foci of dysplasia, and disrupt reproductive function (we are talking about the cervical factor of infertility).

Summarizing the clinical experience, it is got to admit that nowadays, the main problems are the untimely and poor-quality diagnosis of cervical pathology, the lack of accurate schemes, and unambiguous recommendations for deciding on medical tactics, as well as the lack of patient adherence to treatment, which led us to the search for tactics for women with cervical erosion.

Materials and Methods

I have accumulated experience in the management of gynecological patients with cervical pathology, which were divided by age groups and pathologies. Of 100 patients, 30% were under the age of 30 years, from 30 to 40 years – 50%, and over 40 years – 20%. When collecting a history of life, three patients indicated the beginning of sexual intercourse with 15 years, one patient admitted that sexual intercourse began with 12 years, 10 patients work in shifts at the field, constantly use barrier methods of contraception 52 women, and primary dysmenorrhea was in 20 women. A complete clinical examination of women was conducted: A smear for oncocytology, PCR for HPV 16-18, herpes simplex virus 2, chlamydia, colposcopy extended, and bacteriological study to identify the vaginal microflora. Cytological examination of the smear was carried out by the method of Papanicolaou (PAP test) after the treatment of colpitis [10]. Before taking a smear on oncocytology, all women were warned about abstinence from sexual life 2 days before the procedure; a few days before oncocytology, it is not recommended to use tampons, vaginal creams, and douching. Interpretation of the smear was carried out on the scale of Bethesda [11]. The main sections of the classification – The Bethesda System (TBS) developed in 1998, the most recent changes to whichwere made in 2001, include lesions of the squamousand glandular epithelium. Low-grade squamous intraepithelial lesions include changes associated with PVI and mild dysplasia (CIN 1), and high-grade mild dysplasia (CIN 2), severe dysplasia (CIN 3), and intraepithelial cancer (Table 1).

Table 1: The scale of Bethesda

PAP test	The Bethesda scale	Conclusion
Class 1	NIL (malignancy not observed)	The absence of pathological disorders smear, cytological normal cervical structure
Class 2	ASC-US (atypical cells of unknown origin)	Revealed changes of unclear genesis. The main cause is the inflammatory process. Depending on the nature of the rebirth, an assumption about the pathogen is made. Requires clarification of the diagnosis and further examination
	LSIL (low-grade lesions)	Minor signs of atypia. The dysplasia is mild, koilocytes, and signs of HPV infection
	ASC-H (atypical elements not related to HSIL)	There are single brushstroke transformations like HSIL, but they are not enough to go to the lower gradation
Class 3	HSIL (lesions of high degree of malignancy)	Precancerous conditions of the cervix – moderate and severe dysplasia
Class 4	HSIL suspected malignant transformation	Cancer *in situ*
Class 5	Invasive cancer	Invasive cancer

The study of blood on HPV 16-18, chlamydia, and HSV Type I was carried out by PCR. All women were trained for PCR testing for HPV:

1. Do not visit the toilet 2–3 h before the tests. Urine does not have an antiseptic effect, but the jet will wash off the surface of the urethral mucosa of pathogens. Because of this, a false-negative result of the study is possible
2. Do not take antibiotics 1 month before the test
3. Do not wash or douche the day before the test
4. PCR analysis should be taken before menstruation or 3 days after its end
5. For 3 days, it is necessary to prevent sexual acts.

The sample for PCR on HPV, chlamydia, and HSV Type II was taken from women from the cervical canal. We used a combined method of PCR in diagnosis of HPV, which comprises the qualitative detection of 16th type of HPV with genotyping. The interpretation of the analysis was given in three variants: No HPV DNA was detected, i.e., no HPV DNA was removed; human papillomavirus type 16 was detected, i.e., in addition to HPV type 16, there are other HPV genotypes; type 16 papillomavirus was detected indicating the presence of only HPV type 16. The next stage of the examination was an extended colposcopy. Colposcopy of the cervix helps to identify vascular changes in the mucosa, accurately diagnose diseases such as endometriosis, ectopia, erythroplakia, dysplasia, and leukoplakia, to study in detail the nature and stage of erosion or other lesions. It is possible to identify oncological pathologies – malignant neoplasms in the early stages of development using colposcopy. For more informative diagnostic procedures, our women were recommended: At least 2 days before the procedure to abandon sexual intercourse; during the week before the examination, do not make douches, do not use special means for intimate hygiene; refrain from using contraceptive creams, preparations in the form of vaginal candles or sprays. Colposcopic pictures were divided into two groups: Normal (30%) and abnormal (70%). The normal patterns were multilayer flat epithelium (atrophic, mature), ectopia and ectropion, metaplastic epithelium. In women under 30 years in the body, there are physiological changes: Cylindrical epithelium “screwed” into the internal pharynx and replaced by a multilayer flat epithelium [12]. An abnormal paintings include the presence of acetabular epithelium with mosaic and/or punctuation, a leukoplakia, a true erosion of the cervix, atypical and brittle blood vessels, necrosis, and necrotizing ulcers.

A bacteriological study to identify the vaginal microflora was carried out by sowing the test material on nutrient media to identify and identify the pure culture of the pathogen before menstruation or in the 1st day after menstruation. During menstruation, the smear was not taken. For a more informative analysis of our patients, it was recommended: 2–3 days before the analysis, the woman should not affect the microflora of the vagina and cervix through douching and the use of vaginal and oral tablets, candles, ointments, 1–2 days before taking a smear, the woman should observe sexual rest, in the evening before the test, and the patient needs to wash and perform hygienic procedures for the care of the external genitals without the use of intimate hygiene. Before the procedure of taking a smear, you can wash only with warm water. A woman should try not to empty the bladder directly for 2–3 h before taking the material for bacteriological examination. In normal picture in the planting is dominated by *Lactobacilli*, conditionally pathogenic microorganisms do not exist or are identified in a small number – less than 104. In bacterial vaginosis, an increase in quantity of opportunistic microorganisms was detected, as well as the growth of *Lactobacilli* sharply reduced or absent. During inoculation were detected anaerobic microorganisms such as *Gardnerella vaginalis*, *Mycoplasma hominis*, and *Mobiluncus* spp. and in isolated cases - *Bacteroides* spp., *peptostreptococci*. When *Candida,* the candidiasis on the background of reducing the number of *Lactobacilli* is observed the growth of *Candida* spp. over 104. In this pathology, microscopy of material shall be deemed pseudomycelia mushroom. Non-specific bacterial vulvovaginitis is characterized by the growth of one or more opportunistic microorganisms in a diagnostically significant titer with a decrease in the number or absence of lactobacilli in sowing.

Results

According to the results of oncocytology, Grade 1 smear was not in any woman. Moderate-to-severe dysplasia was detected in 20 patients. Suspected malignancy of the cervix was 10 patients. Invasive cancer was detected in three women. Low-grade squamous cell intraepithelial lesions were detected in 67% of patients, and high-grade lesions were detected in 23% of patients. Detection of DNA *Chlamydia trachomatis* and HSV Type II PCR indicates infection with chlamydia, HSV, which was 80%, the remaining 20% was found only HSV Type II. The frequency of abnormal colposcopic patterns was found in 70% of cases. Bacteriological examination of the vaginal flora showed a predominance of specific colpitis (65%) among our subjects over non-specific (35%). The normal pattern of sowing on the vaginal microflora was not a single case. In surveys, 30% of women without showing specific symptoms and complaints were diagnosed with pseudo and assigned to the first group (healthy women). About 68% of women were assigned to the second group – with cervical pathology, who need conservative treatment, 2% – to the third group – women with invasive cervical cancer, who were sent to the oncology center. About 82% of L-SIL developed against the background of infection with highly oncogenic types of HPV, most often HPV 16, with 30% of them infected

with more than 1 type of HPV. In the early stages of its development, L-SIL is a reversible disease, most women may regress within the next 3 years [13]. CIN 1 is most often a manifestation of a productive viral infection, has low malignant potential, and rarely requires treatment. The risk of CIN 2 or more severe changes is low at around 28%. This group of women was recommended conservative treatment and control of cytological smear 1 time in 6 months and HPV DNA once a year. At 3 times negative results, standard screening is performed. The first and second groups of women were used treatment regimen tested by clinical experience. The initial phase of treatment of ectopia accompanied with elimination of the concomitant inflammation of the cervix and vagina, then there was the incentive of manipulating regeneration of the epithelium of the cervix, and the last stage was the removal of pathologically altered tissue, i.e. the surgical technique, only the combination of ectopia of the cervix with CIN 1–2° and the deformation of the cervix, according to clinical protocols [14]. To eliminate concomitant inflammation of the cervix and vagina, hexicon was used in this group. Because the active substance chlorhexidine bigluconate, which is part of it is an antiseptic drug that is active against protozoa, Gram-positive and Gram-negative bacteria, including such pathogens as *Neisseria gonorrhoeae* (gonorrhea pathogen), *Chlamydia* spp. (the causative agent of trachomatis), *Ureaplasma* spp. (causative agent of ureaplasm), *Treponema pallidum* (causative agent of syphilis), *Trichomonas vaginalis* (causative agent of trichomoniasis), *G. vaginalis* (causative agent of gardnerellosis, bacterial vaginosis), and *Bacteroides fragilis*, and does not violate the functional activity of lactobacilli, i.e., is a universal drug. Hexicon was used for 1 suppository at night for 10 days. After sanitation of the vagina and cervix, the next step was the preparation of depantol, which includes dexpanthenol, which stimulates the regeneration of mucous membranes, normalizes cellular metabolism, accelerates mitosis, and increases the strength of collagen fibers. Depantol was prescribed at 1 suppository * 2 times for 10 days. Against the background of this treatment, out of 68 patients, 54 patients (79.4%) normalized the vaginal flora by smear on the degree of vaginal purity and colposcopic picture. The remaining 14 patients were transferred to the 3rd stage of treatment – surgical. Of the surgical methods of treatment, the cervix was treated with solkovagin (71.4%), because when using this drug, only pathological tissues die off without damaging healthy tissue, which favorably affects women of childbearing age for further pregnancy planning. After the treatment of the cervix with solkovagin, the drug depantol was again prescribed for the rapid healing of the cervix at 1 suppository * 2 times for 10 days. Two weeks after cervical treatment, a control colposcopy was performed in which pathological changes were not detected. Subsequently, this group was registered for 1 year. For 1 year, they underwent colposcopy and passed a smear for oncocytology. The remaining patients underwent radio wave treatment (29.6%). In the absence of cervical erosion recurrence, patients were removed from the cervical pathology register.

Discussion

Ectopia occurs in approximately 40% of women and is recognized as the norm. In Europe and America, such a feature of the structure of the neck is not considered a pathology that requires additional tests and constant monitoring by a gynecologist. In October 2019, Dutch scientists (Radboud Institute for Molecular Life Sciences) came to the conclusion that there was often prescribed excessive treatment for women with not very favorable colposcopy in the country [15]. The main causes of cervical erosion in our case were: Early sexual intercourse, immunodeficiency, hormonal imbalance, frequent changes in sexual partners (the vaginal microflora changes due to this), bacterial and viral infection, inflammatory processes of the cervix, traumatic injuries in severe childbirth, abortion, inept douching, medical manipulations, and various genital infections (*Trichomonas*, *Gonococcus*, chlamydia, and especially human papillomavirus). Uncomplicated ectopia took place on its own after the treatment for colpitis and genital infection. Surgical treatment with solkovagin was used as the next stage of treatment after the rehabilitation of chronic foci of infection. The procedure is gentle, scars on the cervix, and its deformities after this type of cauterization is not formed. Due to the fact that the cylindrical epithelium is susceptible to the effects of solkovagin, and the stratified squamous epithelium is not, treatment of cervical erosion with solkovagin in many cases has positive results. Healthy tissues of the stratified squamous epithelium are not damaged, and pathologically changed tissue sites die. Under these dead tissues, healthy tissues begin to recover, which in the process completely replace the diseased. Another advantage of this method is the absence of cicatricial changes in the cervix. However, in recent years, the radio wave method of eliminating cervical erosion has become more and more popular - the only non-contact method of treatment. Excision of pathologically changed sections of the epithelium by this method completely eliminates the destruction of the structure of soft tissues in this area. The complete safety of the procedure is guaranteed by the fact that the generated radio signals cause local dehydration of cellular elements in the pathological focus without affecting the surrounding tissue. Since during the use of the radio knife, instantaneous coagulation of the wound surface is observed, the removal of the deformed section of the epithelial layer occurs 1.5 times faster compared to other surgical methods. The patient also significantly reduced the recovery period after this treatment procedure. The disadvantages of the radio

wave treatment method are practically absent. Of the relative disadvantages, slow healing in the presence of infectious genital diseases can be noted. All our patients not only received anti-inflammatory therapy but also received treatment together with a sexual partner and under the control of a bacteriological study, which is not always done in reality and this leads to relapse of cervical erosion. This is especially true for sexually transmitted infections (chlamydia, gonorrhea, ureaplasmosis, and trichomoniasis). Other causes of relapse may include incorrect establishment of the etiology of the disease or an incomplete course of treatment. In our case, there was not a single case of recurrence of cervical erosion.

Conclusion

The use of hexicon and depantol in the complex of anti-inflammatory treatment of cervical erosion leads to the regeneration of a cervical vaginal mucosa defect, bypassing surgical methods for treating cervical erosion in uncomplicated ectopia, and in case of dysplasia and CC, it contributes to the rapid healing of the wound surface after destructive intervention.

Extensive experience in the study of complications of diathermocoagulation, indicating a large traumatic nature of this method and the risk of many complications. In light of current data, this method, especially with the use of old equipment, is unacceptable for the treatment of benign diseases of the cervix [16]. Thus, at the present stage, the anti-inflammatory method of treating cervical erosion, especially together with the sexual partner, should pay special attention to reduce surgical methods of treating cervical erosion, prevent relapse of cervical erosion, as well as the safe course of the recovery post-operative period during surgical interventions.

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