Original Article

Evaluation Of Clinical Effectiveness Of Pathogenetically Oriented Therapy For Cervical Intraepithelial Neoplasia

Najmutdinova Dilbar Kamariddinovna

Tashkent Medical Academy Department of Obstetrics and Gynecology in Family Medicine
DOI: 10.47750/pnr.2022.13.S09.317

Abstract

Despite the widespread introduction of preventive measures, the development and implementation of new methods for the early diagnosis and treatment of cervical intraepithelial neoplasia is relevant. The average total effectiveness of the developed personalized therapy exceeds the traditional one by more than ≥51.8%. A comparative analysis of long-term results of treatment has convincingly demonstrated a higher clinical efficacy of pathogenetically substantiated therapy.

Keywords: cervical intraepithelial neoplasia, cervical cancer, human papillomavirus, cervical epithelium, colposcopic and cytological study.

Introduction. In the world, more than 570 thousand women worldwide fall ill with cervical cancer (CC) every year, which is 6.6% of the total structure of malignant tumors. It is the fourth most common form of cancer in women and causes more than 311,000 deaths per year [1,3,5] . Cervical intraepithelial neoplasia of three degrees is initiated by a persistent infection caused by high carcinogenic risk human papillomaviruses, preceding the development of cervical cancer for several years and even decades, which is a global problem in reproductive medicine [2,3,5,6]. Despite the widespread introduction of preventive measures, the development and implementation of new methods for the early diagnosis and treatment of cervical intraepithelial neoplasia (CIN) is relevant [4,6]. The search and implementation of sensitive specific markers for the diagnosis, risk of development, and an algorithm for the examination and treatment of neoplastic changes in the cervical epithelium are important for the prevention of oncological transformation of the cervical epithelium.

In the treatment of multifactorial pathology in currently and is widely used a new direction of predictive and personalized therapy, which, in addition to the analysis of the etiology and pathogenesis of the disease, the study of genetic polymorphisms that determine the key mechanisms of pathogenesis [3,5,7,8].

Purpose of the study. Conduct a clinical evaluation of new approaches to therapy cervical intraepithelial neoplasia based on a comprehensive clinical and genetic analysis diseases.

Material and Methods. 132 patients who were on outpatient treatment at the Women's Health Center Tashkent Medical Academy for cervical intraepithelial neoplasia (CIN). The age of the observed patients is from 18 to 45 years. (mean age 36.9±1.1 years). All surveyed were Uzbeks born and living in city of Tashkent (Uzbekistan). The diagnosis of CIN was established on the basis of colposcopic and cytological research.

The material for molecular genetic analysis was blood samples from the cubital vein, taken according to the manufacturer's instructions. For the analysis of gene polymorphisms, the allele-specific polymerase chain reaction (PCR) method was used in the mode real time. The study of CIN genetic markers was carried out on candidate genes related to genetically determined polymorbid pathology, including gynecological (endometriosis, cancer of the uterus and ovaries), affecting the processes of lipid metabolism and oxidative stress, the functioning of the intercellular cellular matrix and suppressor proteins tumor growth.

Patients of the 2 groups were comparable in frequency of genetic polymorphisms and clinical examination data. The 1st group, which was the main one, consisted of 67 patients who received traditional treatment, including local applications of 5.0 ml of Deflagin gel Aflucin R according to the scheme of drug use. At the same time to increase the cytoprotective effect, prevent and reduce viral invasion, suppress activity and replication HPV infection, stimulation of non-specific immunity, Panavir injections were prescribed according to the scheme. Simultaneously with conventional therapy, patients carried out pathogenetically oriented treatment with hormonal, enzyme and antioxidant preparations in agreement with internists. The control group included 65 patients who received local traditional treatment with Deflagin gel and Panavir injections.

Results and discussion. Prescribing personalized therapy cervical intraepithelial neoplasia was carried out on the basis of genetic testing . Prior to treatment, the comparison groups were homogeneous in terms of the frequency of complaints, the clinical condition of the cervix, the cytological characteristics of the cervical epithelium, the bacteriological assessment of the purity of the vagina, and the results of colposcopic examination.

The treatment had a positive effect on the clinical course of CIN in patients of both comparison groups: the number of complaints decreased, the clinical condition of the cervix improved, there was a tendency to normalize the cytomorphological state of the cervical epithelium and bacteriological purity of the vagina, there was a tendency to normalize the colposcopic picture.

It should be noted that a significantly more pronounced dynamics of the studied parameters was recorded in the main group of patients.

So, after treatment, only 4.5% of patients in the main group had various complaints against 21.5% in the control group (χ^2=8.559; P≤0.05); the corresponding frequencies of dysuric disorders were 5.9% versus 23.1% (χ^2=7.835; P≤0.05); the frequency of registration of itching and burning, respectively, 4.5% versus 15.4% (χ^2=4.421; P≤0.05);

Thus, after treatment, various discharges were found in 16.4% of patients of the main group versus 38.4% in the control group (χ^2 = 8.083; P≤0.05); including the frequency of mucous discharge after treatment was significantly higher in the main group, respectively, 29.9% vs. 13.9% (χ^2=5.095; P≤0.05); and the frequency of registration of pathological secretions of a milky and purulent nature is higher in the control group: 5.9% vs. 18.5% (χ^2=4.833; P≤0.05) and 7.5% vs. ; P≤0.05).

After treatment, the amount of discharge significantly decreased, while a significantly higher effect was also found in the main group. Thus, the proportion of patients with poor discharge in the main group after treatment was 4.5%, in the comparison group - 20.0 (χ^2=5.390; P≤0.05); the corresponding ratio of the frequency of registration of moderate secretions was 5.97% versus 18.5% (χ^2=4.833; P≤0.05). And abundant 4.5% versus 15.4% (χ^2=4.421; P≤0.05).

Any menstrual dysfunction after treatment persisted in 28.4% of patients in the main group versus 46.2% of patients in the comparison group (χ^2=3.963; P≤0.05); including painful menstruation occurred in 14.9% of patients of the main group versus 30.8% in the control group (χ^2=4.333; P≤0.05).

The treatment led to a significant improvement in the clinical condition of the cervix and vagina with significantly higher positive dynamics in the main group.

So, after treatment, the frequency of leukoplakia in the main group decreased to 13.4%; in the control group - up to 29.2% (χ^2=4.927; P≤0.05); the corresponding ratio of the incidence of cervical erosion was 14.9% versus 30.3% (χ^2 =4.717; P≤0.05); vaginitis - 8.9% versus 23.1% (χ^2=4.918; P≤0.05); cervicitis - 9.4% versus 38.5% (χ^2=4.927; P≤0.05); cicatricial deformity with ectropion - 26.9% versus 38.5% (χ^2=2.020; P≥0.05); cervical canal polyps after treatment were absent in both comparison groups; the frequency of combination of leukoplakia and cicatricial deformity after treatment in the comparison groups was 20.9% versus 38.5% (χ^2=4.891; P≤0.05); corresponding frequencies of detection of a combination of leukoplakia with cervicitis 7.5% versus 20.0% (χ^2=4.403; P≤0.05); and the frequency of combination of leukoplakia with vaginitis is 4.5% versus 18.5%, respectively (χ^2=6.405; P≤0.05).

The treatment led to the restoration of the cytomorphological state of the squamous epithelium of the cervix.

It should be noted that after treatment, cells assessed as LSIL and HSIL were absent in patients of both comparison groups. At the same time, in the overwhelming number of patients of the main group (61.2%), the cytomorphological state of the squamous epithelium of the cervix was assessed as NILM , the proportion of such patients in the control group was 27.7% (χ^2=14.980; P≤0.001); accordingly, the proportion of patients with the cytomorphological state of the squamous epithelium, assessed as ASC – US and ASC - H , was significantly lower in the main group, these ratios after treatment were 31.3% versus 50.8% and 7.5%, respectively (χ^2=5.150; P≤0.05) versus 21.5% (χ^2=5.305; P≤0.05) (Table 1).

Table 1. Comparative analysis (in%) of the cytomorphological state of the squamous epithelium (smears for oncocytology) of the cervix in the comparison groups before and after treatment

Cytological result	**Groups**		**x^2** **R**	**R**
	Main n=67	**Control n=65**		
Before treatment				
NILM	7/10.5	6/9.2	0.055 P=0.815	>0.05
ASC US	40/59.7	39/60.0	0.001 P=0.973	>0.05
ASC-H	19/28.4	19/29.2	0.003 P=0.956	>0.05
LSIL	1/1.5	1/1.5	0.001 P=0.983	>0.05
HSIL	-	-	-	-
Total	67/100.0	65/100.0		
After treatment				
NILM	41/61.2	18/27.7	14,980 P=0.001	<0.001
ASC US	21/31.3	33/50.8	5.150 P=0.024	<0.05
ASC-H	5/7.5	14/21.5	5.305 P=0.022	<0.05
LSIL	-	-		
HSIL	-	-		
Total	**67/100.0**	**65/100.0**		

The therapy carried out led to the restoration of the microbiological composition of the vaginal biotope, with a significantly more pronounced effect in the main group.

So, after treatment, 44.8% of the patients of the main group had vaginal normocenosis (N), the proportion of such patients after treatment in the control group was 18.5% (χ^2=10.179; P≤0.05); the corresponding ratios of I vaginal cleanliness in the comparison groups were 37.2% versus 21.5% (χ^2=3.944; P≤0.05); at the same time, the frequency of detection of II -th and III -th degrees, the purity of the vaginal biotope after treatment was significantly higher in the control group: 10.5% vs. 0% (χ^2=4.703; P≤0.05); it should be noted that III – IV degree of vaginal cleanliness after treatment was found only in 1 patient (1.5%) of the control group (χ^2=1.039; P≥0.05).

In patients of both groups after treatment, normalization of the colposcopic picture was observed, which was significantly more significant in the main group. After treatment, there was no colposcopic picture in the main group, interpreted as “Stage II. Significant lesions” Only dense ABE was found in 1 (1.5%) patient of the main group against the number of those in the control group 3 (4.6%) (χ^2 = 0.373; P≥0.05); after treatment, in the control group, there were also 1 patient each with severe P, rapid onset of ABE, clear boundaries and elevation above the mucosa, in all cases the difference was insignificant (χ^2 = 1.039; P≥0.05). Thus, after treatment, the proportion of patients with stage II colposcopic changes in the main group was 1.5% versus 10.8% in the control group (χ^2=4.987; P≤0.05).

At the same time, after treatment, colposcopic changes, interpreted as “Stage I. Insignificant changes" already had 5 (7.5%) patients of the main group against 13 (20.0%) of the control group (χ^2 = 4.403; P≤0.05). Including: thin ABE was registered in 1.5% of patients of the main group against 3.1% (χ^2=0.373; P≥0.05) of the control group; tender M, respectively, 2.9% versus 4.6% (χ^2=0.241; P≥0.05); tender P - 1.5% versus 6.2% (χ^2=1.967; P≥0.05) and uneven geographical boundaries - 1.5% versus 6.2% (χ^2=1.967; P≥0.05).

It should be noted that after treatment, colposcopic changes, interpreted as "NILM. Norm" had 91.0% of patients of the main group, which significantly exceeded the corresponding prevalence of the control group, which was 69.2% (χ^2 = 9.916; P≤0.05). At the same time, the proportion of the colposcopic picture, designated as NILM in the main group, was 56.7% versus 30.8% in the control group (χ^2=9.017; P≤0.05); the corresponding prevalence of

stratified squamous epithelium was 16.4% versus 7.7% (χ^2=2.958; P≥0.05); cervical ectopia 10.5% versus 15.4% (χ^2=0.717; P≥0.05) and metaplastic epithelium 7.5% versus 15.4% (χ^2=2.056; P≥0.05).

Conclusions. The average total effectiveness of personalized therapy exceeds the traditional one by more than ≥51.8%. A comparative analysis of long-term results of treatment has convincingly demonstrated a higher clinical efficacy of pathogenetically substantiated therapy. At the same time, the duration of treatment relative to traditional therapy decreased by more than 37.4% (P≤0.05); the frequency of relapses within 12 months - by 60.0% (P≤0.01); and the duration of relapse therapy - by 35.4% (P≤0.05).

BIBLIOGRAPHY

1. Nazhmutdinova D.K., Yuldasheva D.Yu. The study frequencies of allelic variants and genotypes of RS 1042522 polymorphism of the TP53 gene in patients with intraepithelial neoplasia of the cervix // News dermatovenerol . and reprod . health. - 2015. - No. 2. – S. 98-99.
2. Noskova I.N., Artymuk N.V., Gulyaeva L.F. Polymorphism of CYP1A1, CYP1A2, CYP19 genes and SULT1A1 in women with early miscarriage // Fundament. and clinical medicine. - 2019. - V. 4, No. 4. – C. 47-57.
3. Chagay N.B., Mkrtumyan A.M. Methylation estrogen, obesity and breast cancer // Probl . endocrinol . - 2018. - T. 64, No. 4. – S. 244-251.
4. Ghebre RG, Grover S., Xu MJ Cervical cancer control in HIV-infected women: past, present and future // Gynecol. oncol. Rep. - 2017. - Vol. 21.-P. 101-108.
5. Kamilova , IA, Pakhomova , JE, & Nadjmutdinova , DK (2020). Analysis of the role of 1G/2G polymorphism in the MMP1 gene in the development and clinical course of cervical intraepithelial neoplasia. European Journal of Molecular and Clinical Medicine , 7 (2), 850-859.
6. Letra A., Silva RM, Garlet GP MMP1-1607 polymorphism increases the risk for periapical lesion development through the upregulation of MMP-1 expression in association with pro infammatory milieu elements // J. Appl. oral sci. - 2016. - Vol. 24, No. 4. - R. 366-375.
7. Moyer AM, de Andrade M., Weinshilboum RM et al. Influence of SULT1A1 genetic variation on age at menopause, estrogen levels, and response to hormone therapy in recently postmenopausal white women // Menopause. - 2016. - Vol. 23 (Is. 8). – P. 863-869.
8. Nazhmutdinova, D., Kamilova, I., & Shukurova, U. (2022). THE ROLE OF MOLECULAR GENETIC MARKERS IN THE CLINICAL COURSE OF CERVICAL INTRAEPITHELIAL NEOPLASIA. JOURNAL OF EDUCATION AND SCIENTIFIC MEDICINE , (2), 17-19. Retrieved from https://journals.tma.uz/index.php/jesm/article/view/262