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ASSESSMENT OF VIRAL LOAD IN PATIENTS WITH HPV-ASSOCIATED CERVICITIS DURING THE COURSE OF COMPLEX TREATMENT

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The article presents information about examination and treatment of the 39 women with chronic cervicitis associated with papillomavirus infection (HPV). Inosine pranobex is a drug with immunostimulating and anti-inflammatory action. It was used in the complex treatment of the patients. Patients were given 3 courses of inosine pranobex in a daily dose of 3000 mg with an interval of 10 days. Efficacy of the therapy was evaluated on the basis of clinical data, PAP-test, colposcopy, PCR – determination of HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 types, as well as viral load of HPV before and after treatment. In 41.03±7.88% of patients who had a cytological picture of ASCUS, LSIL, HSIL, the concentration of HPV was clinically significant. Among the different types of HPV with high oncological risk, HPV types 16 and associations of different types of HPV prevailed in patients ($p<0.05$, $p_{;}<0.05$). As a result of the use inosine pranobex in the complex treatment the viral load decreased to a clinically insignificant virus concentration in 17.95% of women, and HPV elimination occurred in 74.36% of patients.
Key words: chronic cervicitis, human papillomavirus, viral load, inosine pranobex.
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Introduction

Chronic cervicitis comprises a significant part of all pelvic inflammatory diseases. Cervicitis is most commonly diagnosed in reproductive age (70%) and less commonly diagnosed in premenopausal period. As cervicitis is mostly asymptomatic in women and the potential patients do not ask for help, it is generally not possible to determine a certain incidence of the disease. Cervicitis is mostly diagnosed during routine controls or when women visit a gynecologist for other concerns. Chronic cervicitis may lead to infertility, pregnancy failure, preterm birth and intrauterine infection of the fetus (1-4).

Infectious component is one of the leading damaging factors playing a significant role in chronic cervicitis development. In most cases, multiple infection factors are detected in this pathology. The etiologic structure of cervicitis may constantly change. Sexually transmitted infections (STI), opportunistic microorganisms, viruses and their comorbidity cause chronic inflammative process in cervix (4,5).

The most common STI is papillomavirus infection (PVI). 86% of the women with chronic cervicitis are infected with human papillomavirus (HPV). Papillomavirus infection continues to be an urgent problem due to its high infectivity and the development of neoplastic processes in cervix. A characteristic feature of HPV is it can be eliminated on its

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own or after the treatment and it may cause recurrent chronic cervicitis, pre-cancerous diseases, and cervical cancer by staying too long in cervical epithelium (4,5).

It has been found that the viral load value is associated with the degree of cervical damage:

- Lg<3 – Virus exists but its amount is clinically insignificant.
- Lg 3 to 5 – Clinically significant viral load; possible oncopathology;
- Lg>5 – Critically high pathogen level in body; the risk of malignancy of neoplasm or dysplasia is extremely high [6,7].

The risk of cervical neoplasia associated with HPV is related to the fact that there is no efficient etiotropic treatment for this infection. According to many scholars, the treatment of this pathology should be intended for eliminating the cervical pathology associated with HPV. The scope of the therapeutic measures should contain the application of immunotropic medicines which activate the non-specific immunity, contributes to decrease in the viral load and elimination of HPV, as well as destructive methods [8, 9].

The purpose of the study is to evaluate the efficiency of inosine pranobex in patients with chronic cervicitis and high HPV viral load.

Table 1. Cytology results of female patients according to HPV viral load before treatment

HPV viral load with high oncological risk	Normal cytological table		ASCUS		LSIL		HSIL	
	abs.	%	abs.	%	abs.	%	abs.	%
Up to 3 Lg/10x5	6	15,38±5,78	8	20,51 ±6,47	9	23,08±6,75	0	
3-5 Lg/10x5	0		6	15,38±5,78	7	17,95±6,15	1	2,56±2,53
More than 5 Lg/10x5	0		0		0		2	5,13±3,53

Table 2. Colposcopic examination results of patients according to HPV viral load before treatment

HPV viral load with high oncological risk	Normal colposcopic table		1st degree Abnormal colposcopic table		2nd degree Abnormal colposcopic table		Other symptoms: condylomata, polyps, inflammation	
	abs.	%	abs.	%	abs.	%	abs.	%
Up to 3 Lg//10x5	2	5,13±3,53	8	20,51 ±6,47	2	5,13±3,53	3	7,69±4,27
3-5 Lg//10x5	0		15	38,46±8,52	7	17,95±6,1	0	
More than 5 Lg//10x5	0		0		2	5,13±3,53	0	

Materials and Methods

We performed a comprehensive examination and treatment in 39 women whose ages ranged from 18 to 35. All patients had chronic cervicitis associated with HPV type 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58 and 59. In addition to the first examination, we analyzed the clinical and laboratory data to evaluate the efficiency of the treatment.

Patients were examined with polymerase chain reaction (PCR) where the results are detected in real-time to determine the STIs as well as the co-existing opportunist microflora.

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Cytologic results were evaluated based on Papanicolaou classifying system (PAP test) associated with Bethesda classification. Changes related to mild, moderate and severe dysplasia in cervix correspond to the term of "Low-grade (LSIL) and high-grade (HSIL) squamous intraepithelial lesions".

HPV tying is determined by using PCR method. The viral load of HPV type 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58 and 59 were determined by using HPV Digene test which is a hybrid capture method.

The colposcopy is performed using Olympus 500 based on traditional methods. Colposcopic table was interpreted according to International Colposcopic Terms Classification, Rio de Janeiro (2011). This led the abnormal colposcopic patterns (mosaic, punctuation, asetoblastic epithelium, atypical veins) and other masses of the cervix (condylomata, polyps) to be detected.

The results of the study were subject to statistical transaction by measuring the arithmetic average (M), arithmetic average error (m) and the fiducial difference between indicators (p) considering the fiducial probability based on Student-Fisher test.

After the diagnosis is verified, the patients were treated with a complex treatment consisting of 3 stages. Phase I includes the antibiotic treatment of pathogen microflora co-existing with the 1st cure of Inosine pranobex while considering the etiology of the pathogen and its medicine tolerance. Phase II includes eliminating the pathological focus in cervix (radio wave treatment method on "Surgitron" device). Phase III, 2nd and 3rd cure inosine pranobex treatment was performed.

Inosine pranobex is a synthetic complex purine derivative having immunostimulatory activity and non-specific antiviral effects. Antiviral effect mechanism of Inosine pranobex is associated with the inhibition of viral RNA and dihydroperoxide synthetase enzyme which takes part in the replication of certain viruses; it increases the virus-suppressed synthesis of lymphocyte mRNA by suppressing the translation of viral RNA biosynthesis and viral proteins and increases the production of interferon- alpha and gamma having antiviral features by lymphocytes.

Therefore, the effect of inosine pranobex over the different parts of the immunological chain regains the immunity suppressed by viral infection and suppresses viral replication through a direct antiviral effect.

Inosine pranobex was applied to the patients as follows: 1000 mg three times a day for 10 days. Treatments consist of 3 cures at intervals of 10 days.

The efficiency of the treatment was evaluated through the analysis of clinical data, cytologic and colposcopic examination and qualitative analysis and determining the viral load of HPV with high oncological risk after treatment.

Results and Discussion

According to the results of the study, 84.62±5.78% of the patients complained about itchiness in external genital area and the burning sensation before treatment and 94.87±3.53% of women had genital discharge.

It was observed that six months after the treatment, the complaint of itchiness and burning continued in 7,69±4,27% of women and 10,26±4,86% of patients had genital discharge.

In the bacterioscopy examination, it was observed that the amount of leucocytes was at the rate of 87,18±5,35% in most of the patients before the treatment. After a six-month treatment, it was observed that there was an increase in the number of leucocyte in 5,13±3,53% of women during bacteriocopy.

Amino-test was positive in 74,36±6,99% of the patients before the treatment and after the treatment, no amino-test positivity is detected.

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During STI screening: in 20 (51,28±8,00%) patients, *Ureaplasma urealyticum*; in 6 (15,38±5,78%) patients, *Mycoplasma hominis*; in 7 (17,95±6,24%) patients, *Chlamydia trachomatis*; in 8 (20,51±6,47%) patients, cytomegalovirus infection was detected.

Associations of microorganisms were detected in 28.20±7.21% of patients. Most of the patients had serious vaginal dybiosis at the rate of 82,05±6,15% before the treatment.

Before the treatment, the cytologic examination results were as follows: 15.38±5.78% had normal cytologic table, ASCUS was diagnosed at 35.9±7.68%, LSIL at 41,03±7,88%, HSIL at 7,69±4,27%

Cytogram was in conformity with ASCUS, LSIL and HSIL in 41,03±7,88% of the patients with significant HPV viral load.

After the 6th month of the treatment, the cytological table was normal in 92,31±4,27% of the patients and ASCUS in 7,69±4,27% of the patients. Data is presented in Table 1.

Table 3: Incidence of different HPV types in patients before treatment

HPV type	n=39		
	abs	**%**	**degree of reliability**
16	9	23,08±6,75	p<0,05
18	5	12,82±5,35	
31	2	5,13±3,53	
33	2	5,13±3,53	
35	1	2,56±2,53	
39	1	2,56±2,53	
45	1	2,56±2,53	
51	3	7,69±4,27	
52	2	5,13±3,53	
56	2	5,13±3,53	
58	1	2,56±2,53	
59	1	2,56±2,53	
Association of different types of HPV	9	23,08±6,75	p<0,05

Note: p – significant difference of value between the groups of HPV type 16 and type 31, 33, 35, 39, 45, 52, 56, 58, 59; p, - significant difference of value between the associations of HPV and HPV type 31,33, 35, 39, 45, 52, 56, 58, 59.

During the colposcopy performed before the treatment, normal colposcopical table was detected in 2 patients (5.13±3.53%). Abnormal colposcopical table was detected in 34 women (87,18±5,35%) and stage I lesion was detected in 23 of them (58,97±7,88%), stage II lesion was detected in 11 of them (28,21±7,21%), condyloma was detected in 1 one of them (2,56±2,53%) and cervical polype was detected in 2 of them (5,13±3,53%). In the 61,54±7,79% of the patients with abnormal colposcopic table consisting of Stage I and II lesions, there was clinically significant HPV viral loads. Six months after the beginning of the treatment, colposcopical table was normal in 35 women (89,74±4,86%), and inflammation findings were detected in 4 patients (10,26±4,86%) during colposcopy. Data is presented in Table 2.

The frequency of different types of HPV is presented in Table 3. The association of HPV type 16 and different types of HPV were significantly more common in our study ($p<0.05$, $p_1<0.05$).

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Before the treatment, there was a clinically significant HPV viral load in 24 patients (61,54±7,79%). 6 months after the beginning of the treatment, the virus was completely eliminated in 29 patients (74,36±6,99%), HPV viral load reached a clinically insignificant concentration in 7 patients (17,95±6,15%), HPV concentration maintained in a clinically significant level in 2 patients (5,13±3,53%).

Our data shows the efficiency of a comprehensive approach in the treatment of chronic cervicitis associated with HPV.

Using Inosine pranobex having immunostimulator effect and non-specific antiviral activity helps to reduce the viral load of HPV and eliminate it in 74,36% of the patients after a six-month treatment.

Our data shows the efficiency of using Inosine pranobex in women with chronic cervicitis associated with HPV with high oncological risk and the combined treatment.

Therefore, inosine pranobex and adequate immunotherapy support HPV elimination in 93,02% of the patients.

The long experience of using inosine pranobex shows promising results enabling the high elimination of HPV. Using this medicine leads us to conclude that it is suggested to include this immunomodulator in the scheme of traditional treatment methods for the cervical pathology associated with HPV. In addition, more research is to be done regarding the efficiency of this method based on evidence-based medicine (9,10).

Findings

1. In the examination of patients with chronic cervicitis associated with HPV with high oncological risk, cytogram was in conformity with ASCUS, LSIL and HSIL in 41,03±7,88% of the patients with clinically significant viral load.
2. The relation between HPV type 16 and different types of HPV with a high risk of oncology was significantly more common ($p<0.05$, $p1<0.05$).
3. The abnormal colposcopic table corresponding to lesion level I and II were accompanied by clinically significant HPV viral load with high risk in 61,54±7,79% of the patients.
4. Inosine pranobex decreased the viral load to clinically insignificant values at 17,95±6,15% and eliminated HPV at 74,36%.

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References

1. Прилепская В.Н., Новикова Е.П. Возможности раннего лечения и профилактики папилломавирусной инфекции. Гинекология. 2013; 15 (1): 94–7. / Prilepskaya V.N., , Novikova E.P. Possibilities of early treatment and prophylaxis of papillomavirus infection. Gynecology. 2013; 15 (1): 94–7. [in Russian]
2. Gaspar J et al. Sociodemografic and clinical factors of women with HIV. Rev Lat Am Enfermagem 2015; 23 (1): 74–81.
3. Madeddu G et al. HPV infection in HPV-positive females: the need for cervical cancer screening including HPV-DNA defection despite successful HAART. Eur Rev Med Pfarmacol Sci 2014; 18 (8): 1277–85.
4. Пестрикова Т.Ю., Юрасова Е.А.. Бутко Т.М. Перинатальные по- тери. Резервы снижения. М.: Литтера, 2008. / Pestrikova T.Iu., Iurasova E.A.. Butko T.M. Perinatal'nye poteri. Rezervy snizheniia. M.: Littera, 2008. [in Russian]
5. Радзинский В.Е., Ордиянц И.М., Буянова Н.В., Побединская О.С. Тактика ведения пациенток с заболеваниями шейки матки при персистирующей ВПЧ-инфекции: возможности комбинированного лечения. Гинекология. 2014; 16 (6): 12–5. / Radzinsky V.E., Ordiyants I.M., Buyanova N.V., Pobedinskaya O.S. Clinical management
of patients with diseases of the cervix with persistent HPV infection: the possibility of combined treatment. Gynecology. 2014; 16 (6):12–5. [in Russian]
6. Dalstein V, Bory J, Graesslin O et al. Human papillomavirus testing for primary cervical cancer screening. Basel: Karger, 2006; p. 103–19.
7. Luhn P, Wentzensen N, Walker J et al. The role of co-factors in the progression from human papillomavirys infection to cervical cancer. Gynecol Oncol 2013; 128 (2): 265–70.
8. Пестрикова Т.Ю., Юрасова Е.А., Юрасов И.В. Медикаментозная терапия в практике акушера-гинеколога. М.: Литтерра, 2011. / Pestrikova T.Iu., Iurasova E.A., Iurasov I.V. Medikamentoznaia terapiia v praktike akushera-ginekologa. M. Litterra, 2011. [in Russian]
9. Пестрикова Т.Ю., Панфилова Ю.О. Прегравидарная подготовка женщин с хроническим цервицитом, ассоциированным с папилломавирусной инфекцией. Consilium Medicum. 2016; 18 (6): 35–7. / Pestrikova T.Yu., Panfilova Yu.O. Pregravid training for women with chronic cervicitis associated with HPV infection. Consilium Medicum. 2016; 18 (6): 35–7. [in Russian].
10. Пестрикова Т.Ю., Пушкарь В.А. Оценка эффективности комплексной терапии патологии шейки матки, ассоциированной с палилломовирусной инфекцией. Гинекология. 2015; 17 (4):50–3. / Pestrikova T.Yu., Pushkar V.A. Evaluation of comprehensive treatment of cervical pathology associated with HPV. Gynecology. 2015; 17 (4): 50–3. [in Russian]