Evaluation of Human Papillomavirus Elimination from Cervix Uteri by Infrared Laser Exposure

V. P. Dymkovets, V. V. Ezhov, A. A. Manykin, S. V. Belov, Yu. K. Danileiko*, V. V. Osiko, and V. A. Salyuk***

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Elimination of types 16 and 18 human papilloma virus from the surface of cervix uteri for secondary prevention of cervical cancer was evaluated. The method is protected by patent of invention of the Russian Federation. Infrared laser therapy of cervix uteri was carried out in patients with precancer diseases of cervix uteri at Department of Gynecology of Municipal Clinical Hospital No. 52 (Moscow). Papillomavirus infection was eliminated using a Russian diode laser (λ=1.06 μ, radiation power 10 W) with a collimating headpiece using carbon die at a distance of 10-12 cm from the exposed surface. The treatment resulted in a high percentage of elimination of types 16 and 18 oncogenic virus 4-6 weeks and during delayed periods after exposure.

Key Words: *papillomavirus infection; cervix uteri disease; infrared therapy*

Papillomavirus infection is a sexually transmitted infection. Human papillomavirus (HPV) infection of epithelial tissues of human organs initiates the formation on epithelial surface of cells with nuclei filled with mature HPV virions, which can be released from the epithelium and destroy normal cells. Human papillomavirus can cause severe diseases of infected organs, for example, condylomatosis and cancer, *e. g.* cancer of cervix uteri (CCU).

Cancer of cervix uteri remains a pressing problem of gynecology. Its incidence is continuously increasing and reaches about 30% of all gynecological diseases. In addition, the disease is now found in younger and younger women and virtually does not depend on the history of labor.

Cancer of cervix uteri is detected annually in 500,000 women all over the world. The relationship between CCU and high oncogenic risk in HPV patients has been proven. The most incident type of squamous cervical cancer is associated with HPV-16 and HPV-18. The targets of oncogenic activity of HPV are transformation and metaplasia foci and reserve cells, in other words, the interphase between the cylindrical and squamous epithelium of cervix uteri. Continuous and repeating mitotic activity in these zones promotes the development of HPV-associated precancerous and cancerous changes.

The methods used for the treatment of viral diseases of cervix uteri consist in destructive removal of the pathological tissue. However, treatment efficiency is sometimes doubtful, and hence, the development of new therapeutic methods for this disease is an important problem. We have carried out preliminary studies of laser therapy of viral disease of cervix uteri [1-3].

The aim of this study was the development of a highly effective method for the treatment of cervical disease associated with high oncogenic risk papillomavirus infection.

MATERIALS AND METHODS

Laser exposure was used at λ=1.06 μ in continuous mode with maximum radiation power of 10 W. Be-

Moscow Municipal Clinical Hospital No. 52; *A. M. Prokhorov Institute of Physics, Russian Academy of Sciences; **D. I. Ivanovsky Institute of Virology, Russian Academy of Medical Sciences, Moscow, Russia. ***Address for correspondence:*** an_manykin@mail.ru. A. A. Manykin

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TABLE 1. Presence of HPV-16 and HPV-18 before and after Therapy

HPV	Patients with HPV before treatment (*N*)	Cured patients (no HPV; *N*)	Treatment efficiency, %
Type 16	73	61	83.50±0.02
Type 18	35	18	51.4±0.01
Total	108	79	72.10±0.01

fore laser exposure, the vagina was treated by low frequency ultrasound (100 sec) through liquid medium (0.02% chlorohexidine solution) using the Gyneton-2 device. The operation was carried out with colposcopic control. In order to improve the radiation absorption, a thin layer of carbon stain (CS) was applied onto the surface of pathological exocervix. The CS applied onto biological tissue was then irradiated.

Reaction of laser radiation with CS results in rapid absorption of the radiation in the surface layer of the stain leading to an intense thermal effect (thermolaser destruction) of the sublying tissues with simultaneous cleansing thereof from CS. It is noteworthy that the destructive effect of thermolaser ceases if there is no SC on the epithelium.

The diameter of the laser spot released from a device with a special collimating headpiece was 0.5 cm at a distance of 10-12 cm from laser. This distance corresponded to the depth of cervix uteri location and hence, the operation on the ectocervix could be carried out without flexible light guide. A flexible monofiber light guide was used for exposure of the vaginal wall. The power density for biological tissues was 50 W/cm^2 in all cases.

The thickness of biological tissue destruction layer after a single 5-min exposure was 1-1.5 mm. The exposure was repeated, if necessary. The method was called "contrast thermal laser therapy" (CTLT).

RESULTS

The study was carried out at Gynecological Department of Clinical Hospital No. 52 in 2007-2010.

A total of 108 patients aged 19-62 (29.30±0.03) years infected with HPV-16 and HPV-18 were treated by CTLT. The diagnoses were as follows: ectopy with signs of chronic inflammation (58 women), leukoplakia (20 women), and signs of papillomavirus infection on intact surface of cervix uteri (30 patients).

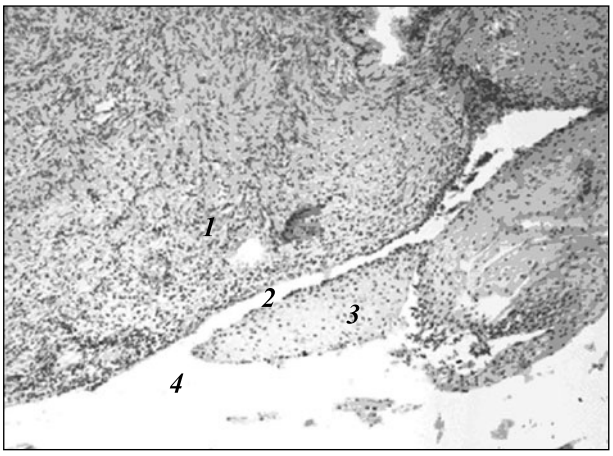

Fig. 1. Histology of the cervical cavity after a session of CTLT in patient K. (42 years) with leukoplakia. The criteria for evaluating treatment efficiency were the absence of HPV in DNA-PCR smears and cytological verification of cell normalization in the cervical multilamellar squamous epithelium. Rupture of the epithelium from the basal membrane (directly after exposure): *1*) stroma; *2*) basal membrane; *3*) multilamellar squamous epithelium; *4*) site of epithelium rupture from cervical surface.

Standard examinations carried out in all women included extensive colposcopy, complete bacterioscopic and bacteriological studies of vaginal smears, DNA PCR for latent infection, cytological and histological studies. If pathogenic flora was detected, appropriate drug therapy was carried out before CTLT.

The results of CTLT are summed up in Tables 1 and 2. The studies were carried out before laser therapy and 4-6 weeks after it. An obvious trend to elimination of HPV was seen. The concentration of HPV-16 on the surface of cervix uteri after therapy

TABLE 2. Efficiency of HPV Elimination from Cervical Surface

Disease	Before therapy (with HPV; *N*)	After therapy (no HPV; *N*)	Treatment efficiency, %
Ectopy	58	37	63.80±0.01
Leukoplakia	20	17	85
HPV without morphological abnormalities of cervix uteri	30	25	83.30±0.02

was 30% lower than of HPV-18 (Table 1). The results of papillomavirus elimination from cervix uteri surface after laser therapy of different diseases are presented in Table 2. Virus elimination was more effective in women with leukoplakia and without pathological changes on cervix uteri.

Histological studies of the cervical surface in patients with HPV-16-associated leukoplakia showed that the squamous and metaplastic epithelium was completely detached from the basal membrane after therapy; normal squamous epithelium was restored and HPV was eliminated (Fig. 1).

Hence, CTLT resulted in a significant elimination of HPV-16 and -18 with the probability of 83.5 and 51.4%, respectively. The effect was confirmed after 4-6 weeks and later.

The proposed method for HPV-16 and -18 elimination is a promising method for prevention of CCR development.

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REFERENCES

1. V. V. Ezhov, A. M. Torchinov, A. V. Geinits, *et al.*, *Lazer Med.*, **12**, No. 3, 15-17 (2008).
2. V. V. Ezhov, A. M. Torchinov, A. A. Manykin, *et al.*, *Vopr. Ginekol. Akush. Perinatol.*, **8**, No. 1, 42-44 (2009).
3. V. V. Ezhov, A. M. Torchinov, and A. A. Manykin, *Ibid.*, **7**, No. 3, 40-43 (2008).
4. *Low Intense and High Energy Laser Exposure in Obstetrics and Gynecology*, Ed. M. I. Kovalyov [in Russian], Moscow (2000), pp. 1-168.
5. M. I. Kovalyov and E. V. Rokhlina, *Lazer. Med.*, **14**, No. 2, 36-38 (2010).
6. V. I. Kulakov, J. Paavonen, and V. N. Prilepskaya, *Prevention of Cancer of Cervix Uteri. Manual for Physicians* [in Russian], Moscow (2007), pp. 6-15.
7. A. A. Manykin, *Medical Virology*, Ed. D. K. Lvov [in Russian], Moscow (2008), pp. 269-276.
8. A. A. Manykin, *Ibid.*, pp. 436-440.
9. V. V. Ezhov, A. M. Torchinov, V. I. Firchenko, *et al.*, *Patent of the Russian Federation No. 2330630. A Method for Surgical Treatment of Underlying and Precancer Diseases of Cervix Uteri*, Registration 10.08.2008 (priority of 13.12.2006).
10. V. N. Prilepskaya, *Diseases of Cervix Uteri, Vagina, and Vulva* [in Russian], Moscow (2005), pp. 7-65.
11. V. N. Prilepskaya and M. N. Kostava, *Rus. Med. Zh.*, **17**, No. 1, 16-19 (2009).
12. S. L. Sergeeva and T. I. Starodubova, *Practical Gynecology* [in Russian], Moscow, Kursk (2006), pp. 115-162.
13. A. M. Torchinov, A. V. Geinits, V. V. Ezhov, and G. A. Varev, *Vopr. Ginekol. Akush. Perinatol.*, **7**, No. 3, 40-42 (2008).
14. A. Z. Khashukoeva, A. M. Torchinov, S. L. Rekhviashvili, and V. V. Ezhov, *Lazer. Med.*, **8**, No. 3, 152-153 (2004).