



ACADEMICIA
**An International
Multidisciplinary
Research Journal**
(Double Blind Refereed & Peer Reviewed Journal)



DOI: **10.5958/2249-7137.2021.00881.8**

LASER PHOTODYNAMIC THERAPY IN THE TREATMENT OF CERVICAL PATHOLOGY

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ABSTRACT

Early diagnosis and treatment of background and precancerous diseases of the cervix is one of the important problems of gynecology, the ultimate goal of which is to reduce the incidence of cervical cancer. To date, many scientific papers have been devoted to the problem of treating cervical pathology and various methods of treating background and precancerous diseases of the cervix have been introduced. The most common methods are those based on the use of electro coagulation, cry destruction, and laser vaporization methods as a therapeutic effect. According to domestic and foreign authors, the therapeutic effect of the above-mentioned methods of treatment is 67-98. 7% [1, 2, 5]. However, each of these methods has its own indications, contraindications and a number of complications: exacerbation of chronic salpingoophoritis, bleeding, the occurrence of endometriosis, scarring of the cervix, cervical canal stenosis, violation of reproductive function [2, 4, 6, and 9]. In order to prevent cervical cancer, the treatment of background and precancerous diseases should be radical, but at the same time careful, while preserving the anatomical and functional fullness of the cervix, which largely determines the state of the reproductive system. In this regard, treatment methods are currently being developed that combine the optimal therapeutic effect in the absence of undesirable complications. One of the newest approaches to the treatment of cervical pathology is laser photodynamic therapy (LFTT). This method causes selective death of pathological cells, which is provided by the selectivity of the accumulation of the drug in the pathological tissue and local light supply. According to foreign sources, there are isolated cases of successful treatment of dysplasia and cervical cancer with the use of hematoporphyrin derivatives as a photosensitizer. In the sources available to us, no information was found about the use of LFTD in the treatment of background and precancerous diseases of the cervix, and the effectiveness of

the drug "0.05% solution of mytilene blue belonging to the group of phenothiazines (cationic azines)" in the use of LFTD in gynecology was not evaluated, which determined the purpose of our study.

KEYWORDS: *Revealed, Effectiveness, Precancerous, Concomitant.*

INTRODUCTION

PURPOSE OF THE STUDY

Improve the effectiveness of treatment of background and precancerous diseases of the cervix by innovative laser photodynamic therapy.

RESEARCH MATERIALS AND METHODS

In accordance with the purpose and objectives of our study, 112 women with background and precancerous diseases of the cervix, who were in the gynecological departments of the regional perinatal center of the Bukhara region, were examined and treated for the period 2017 to 2020. The age of the examined women ranged from 21 to 65 years (mean age 43.2 ± 0.3 years). The maximum number of patients (67%) was between the ages of 21 and 35 (mean age 32.2 ± 0.3 years). The following pathology of the cervix was revealed: ectopia - in 52 patients (46.4%), eroded ectropion - in 14 (15.5%), leukoplakia - in 21 (18.7 %), dysplasia of the I-II st. - in 7 (6.3%), endometriosis - in 12 (10.7%). The diagnosis of the disease was made in accordance with the International Statistical Classification of Diseases and Health Problems, 10-revision (ICD-10), adopted by WHO in 1995. To obtain a true understanding of the nature of the pathological process of the cervix, we conducted a comprehensive clinical, microbiological, colposcopic, cytological, and histological study. The clinical examination included a thorough analysis of the premorbid background, the study of complaints, transferred and concomitant extragenital and gynecological diseases, features of menstrual, sexual, and generative function. The state of the cardiovascular, respiratory, endocrine, urinary and digestive systems, and mammary glands was assessed. In the course of the work, a standard range of laboratory tests was used: a general blood test, a general urine test, blood for RW, HBs, HCv, and HIV. The gynecological status was determined on the basis of examination of the external genitalia, examination of the vagina and uterus with mirrors, and bimanual vaginal examination. Colposcopic examination was carried out with a colposcope "Som 52/42 KALTLICHT"(manufacturer Germany) with a resolution of 70 times magnification. Using colposcopic examination, we determined the size and shape of the cervix and external pharynx, the color and relief of the mucosa, the features of the vascular pattern, the boundaries of the flat and cylindrical epithelium, revealed the true area of ectocervix lesion, as well as signs of atypical transformation. Microbiological examination was carried out using bacterioscopic and bacteriological methods. Bacterioscopic examination made it possible to determine the affiliation of microorganisms to obligate-anaerobic species, lactobacilli, to assess the invasiveness of fungal flora, and to evaluate both the qualitative and quantitative composition of bacterial flora. The determination of specific pathogens in the mucus of the cervical canal was carried out by polymerase chain reaction (PCR). Cytological examination of smears-prints from the surface of the cervix and the cervical canal is one of the main methods for diagnosing precancerous and malignant diseases of the cervix. Cytological examination revealed the morphological features of

the cells, the relationship of individual cell groups, and the location of cell elements in the preparation. Much attention was paid to the detection of the nuclear-cytoplasmic index, the distribution of chromatin in cells, the increase in nucleoli, and the detection of mitotic division patterns. The results of the cytological examination were described according to the classification of Papanicolaou. Histological examination of cervical biopsies and scrapings of the cervical canal mucosa made it possible to make a final diagnosis. We interpreted the histological patterns in accordance with the classification of Ya. V. Bokhman (1989).

Preoperative preparation was carried out for all women with a detected infection of the genital tract and included etiotropic, immunomodulatory therapy followed by the appointment of eubiotics to normalize the vaginal microbiocenosis. The treatment was carried out in the first phase of the menstrual cycle. Performing PDT did not require anesthesia. The PDT session was performed 2 hours after applying the Photoditazin 0.5% gel to the pathological area of the ectocervix.

As a source of laser radiation, a semiconductor laser device "ALT-Vostok-03" corresponding to the technical specifications TSh 64-15302652-002:2010 was used. Manufacturer "NAF" LLC (Republic of Uzbekistan) with the following technical characteristics: supply voltage-110-220 V, 50 Hz, 10 W; radiation range-660-670 nm; average total radiation power in the output; plane of the emitting terminal-1.0 W; area of the output hole of the emitting terminal-4 cm²; pulse frequency-24±10% Hz; modulation frequency-1.2±10% Hz. The output wavelength was 662 nm in continuous mode for 10 to 20 minutes (depending on the affected area), the output power was 1 W, and the energy density was 80 to 250 J/cm². Evaluating the process of cervical epithelization, we took into account the presence of complications during manipulation, the nature of the scab, the period of its rejection, the timing of regeneration, the dynamics of the results of cytological and bacteriological studies, as well as the presence of complications in the early (4-12 weeks) and late (6-12 months) treatment periods.

RESEARCH RESULTS AND DISCUSSION

Analysis of anamnesis, clinical picture of cervical pathology, effectiveness of diagnostic methods, immediate and long-term results of treatment performed in 135 patients with background and precancerous diseases of the cervix, allowed us to obtain data on the causes and features of the course of background and precancerous diseases of the cervix, the nature of reparative processes after PDT in comparison with diathermosurgical treatment, to develop methods and indications for PDT.

The analysis of anamnestic data revealed extra-genital, behavioral and genital risk factors for the development of cervical pathology, which create not only a background for the development of background and precancerous diseases of the cervix, but also cause the development of background and precancerous diseases of the cervix.

Our laboratory and instrumental examination allowed us to obtain data on the causes of background and precancerous diseases of the cervix, the features of their course, to identify the true size and study the structure of the pathological process. Colposcopic examination of the majority of patients (71.3%) revealed the presence of areas of cylindrical epithelium on the surface of the ectocervix.

Cylindrical epithelial cells were found in smears-prints from the surface of the cervix. Cytological studies conducted by us have shown low information content in the detection of leukoplakia.

Important colposcopic signs of precancerous diseases of the cervix are certain markers, which can be used to judge the high probability of dysplasia of the multilayer squamous epithelium. As a rule, their appearance is associated with an increase in the concentration of DNA in cells (acetobelium epithelium) or the formation of atypical vascularization. The atypical transformation zone was detected in 31.5% of patients and was mainly associated with the presence of inflammatory changes in the cervix, leukoplakia, and dysplasia. The results of our study confirmed the high informative value of colposcopy in the diagnosis of background and precancerous diseases of the cervix. Many researchers have proven the role of infectious agents in the development of background and precancerous diseases of the cervix [1, 3, 6, 7]. In this regard, we pay great attention to the identification of infectious agents by bacterioscopic, bacteriological examination and diagnosis by PCR. Bacterioscopic examination revealed the 2nd and 3rd degrees of vaginal purity in the majority of patients (46.9 % and 37.8%, respectively), and the 1st and IV degrees of vaginal purity were less common (5.8% and 6.9%, respectively).

Thus, among 21 patients with colposcopic signs of leukoplakia, 8 did not have cytological signs characteristic of leukoplakia. The cytogram of inflammation was noted in 39.9% of patients. Cytological signs of dysplasia against the background of ectopia, leukoplakia and concomitant inflammation were detected in 18.2% of patients. After a course of anti-inflammatory and antibacterial therapy, these patients underwent a cervical biopsy followed by histological examination, which confirmed the presence of dysplasia in 9.2% of patients with colposcopic ectopia and leukoplakia in combination with an atypical transformation zone.

Dysplasia of the I-II degree was detected in 7 patients, of which 1 - against the background of chronic cervicitis and ectopia, 4-against the background of ectopia in combination with viral lesions, 1-in combination with leukoplakia and viral lesions of the squamous epithelium, 1-with leukoplakia and concomitant chronic inflammation of the cervix.

Histological examination was performed in 25 patients with abnormal colposcopic pattern and cytological confirmed dysplasia, which allowed to make a final diagnosis.

Signs of leukoplakia in the form of acanthosis, hyperkeratosis, parakeratosis, without atypia were found in 16 patients. Of these, chronic cervicitis was detected in 7 patients. The presence of ectopia on the background of chronic cervicitis was revealed in 9 patients. Of these, 3 had a viral lesion of the squamous epithelium.

To conduct an objective comparative study, depending on the treatment methods used, the patients were divided into two groups, group I included 82 patients with background and precancerous diseases of the cervix at the age of 21 to 55 years (average age 36.32 ± 0.3 years), who underwent PDT.

The comparison group (group II) consisted of 30 patients with background cervical diseases aged 21 to 65 (mean age 44.2 ± 0.3 years), who were treated with diathermosurgical (DH) treatment. Depending on the method of DH treatment, this group was randomly divided into two subgroups: group 1 included 15 patients who underwent diathermocoagulation, group II consisted of 15 patients who underwent diathermoconidation. In both groups, the duration of

epithelization after various methods of exposure was evaluated, the beginning, end, and total duration of epithelization were evaluated. As can be seen from the data presented in Figure 1, the epithelization time was significantly shorter in the group of patients who underwent PDT (26.5 ± 2.7 days), whereas after DH treatment, the average time for completion of epithelization was 41.5 ± 0.9 days ($p < 0.001$).

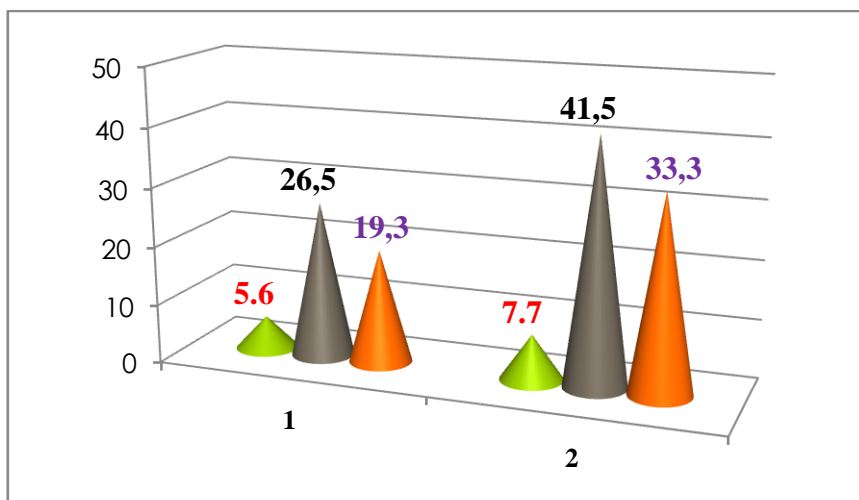


Chart 1. Dynamics of the process of epithelialization of the cervical mucosa in various types of treatment (1-FTD, 2-DH (conization and coagulation)).

It was found that the duration of epithelization of the cervical mucosa in the main group was almost 15 days shorter than in women after DH (26.5 ± 2.7 and 41.3 ± 0.9 days, respectively).

We have shown that PDT is characterized by shorter epithelialization times compared to the DH method. At the same time, when comparing the two methods of DH treatment, it can be seen that the beginning and end of epithelization occur significantly later in conization than in coagulation ($p < 0.05$), and the total duration of the epithelization process was almost the same ($p > 0.1$).

The analysis of the immediate results of treatment showed that the frequency of complications significantly depends on the type of treatment used: Thus, in 4.1% of patients of the main group, postoperative complications were presented in the form of incomplete epithelization. At the same time, patients after DH treatment had a significantly high rate of postoperative complications: 88.8% of patients were concerned about pain in the lower abdomen ($p < 0.01$), 5.1%-bleeding ($p < 0.05$), 8.2%-exacerbation of chronic salpingitis ($p < 0.5$), 28.2%-colpitis ($p < 0.001$), 22.3%-incomplete epithelialization ($p < 0.001$). A comparison of both methods of DH treatment showed that the frequency of such postoperative complications as exacerbation of chronic salpingoophoritis ($p < 0.1$), pain ($p < 0.001$), bleeding ($p < 0.1$) after diathermoconization was significantly higher than after diathermocoagulation.

It is known that after DH intervention, a deep necrosis zone is formed on the cervix, accompanied by pronounced leukocyte infiltration in the wound surface [2,3,5,7,8]. In this regard, along with clinical observations, we conducted bacterioscopic and cytological studies in dynamics 12 and 30 days after treatment.

We found that in patients after PDT, the cytogram of inflammation after 12 and 30 days was detected in 7.1% and 1.2% of patients, respectively, while the cytogram of inflammation after DH treatment after 12 days was detected in 55% of cases, and after 30 days it was preserved in 25% of patients ($p < 0.001$).

Similar results were found when analyzing the results of bacterioscopy taken 12 and 30 days after PDT and DH treatment ($p < 0.001$).

Thus, the results of our observation showed the inexpediency of using diathermocoagulation in the treatment of extensive, long-existing pathology of the cervix, especially in nulliparous women due to the high percentage of side effects that violate the reproductive function.

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