THE AZERBAIJAN REPUBLIC

In the right of manuscript

ABSTRACT

of the dissertation for the degree of Doctor of Philosophy

IMPROVING OF DIAGNOSTIC AND TREATMENT OF BENIGN CERVICAL DISEASES

Specialty: 3215.01- Obstetrics and gynaecology

Field of science: Medicine

Applicant: **Nigar Bayramali Majidova**

Baku -2024

The dissertation has been conducted at the PC Scientific Research Institute of Obstetrics and Gynaecology.

Scientific supervisor: Doctor of science in Medicine, Professor **Jamila Fazil Gurbanova**

Official opponents: Doctor of Science in Medicine, Professor **Hicran Firudin Bagirova**

Doctor of Science in Medicine, Professor **Leyla Musa Rzaguliyeva**

Doctor of Science in Medicine, Professor **İslam Sharif Mahalov**

Dissertation Council ED 2.06 of Supreme Attestation Commission under the President of the Republic of Azerbaijan operating at Azerbaijan Medical University

Chairman of the Dissertation Council:
Doctor of Science in Medicine, Professor
Fariz Hidayat Jamalov

Scientific secretary of the Dissertation Council:
Doctor of Science in Medicine, Professor
Eldar Allahverdi Aliyev

Chairman of the scientific seminar:
Doctor of Science in Medicine, Professor
Saadat Hasan Sultanova

İMZANI TƏSDİQ EDİRƏM
Azərbaycan Tibb Universitetinin
ELMİ KATİBİ
Tibb elmləri doktoru, professor
Nazim Adil oğlu Pənəhov
08.05.24

GENERAL CHARACTERISTICS OF THE SCIENTIFIC RESEARCH WORK

Relevance and development rate of the topic. In recent years, there has been an increase in benign cervical diseases among women in both the reproductive and perimenopausal periods. Every year, 30 million women in the world are diagnosed with low grade dysplasia of the squamous squamous epithelium of the cervix, and more than 10 million women are diagnosed with intermediate and high grade dysplasia [1].

According to the information of the State Statistics Committee of the Republic of Azerbaijan, 6,614 women were registered with cervical diseases in 2010, and 10,758 in 2022 [2].

Dysplasia is a transition between the normal epithelium of the cervix and cancer in situ, it is considered a precancerous condition [1].

Every year, the approach to screening and early diagnosis of precancerous conditions is revised [3].

The main etiological factor of cervical cancer is human papilloma virus (HPV) [4]. Currently 100 species of have HPV been discovered, each with certain characteristics [5].

Ineffective and irregular screening programs in developed countries are underlined as another reason for the increased occurrence and

---

[1] Протасова, А.Э. Дисплазия шейки матки – этиопатогенез, диагностика, оптимальная тактика лечен. Учебное пособие / А.Э. Протасова, Т.И. Дзюбий, Г.А. Раскин [и др.]. - СПб.: 2014. - 22 с.

[2] Azərbaycan Respublikasının Dövlət Statistika Komitəsi. Rəsmi nəşr. Azərbaycanda səhiyyə, sosial müdafiə və mənzil şəraitİ. Statistik məcmuə. Bakı, - 2020. - 260 s.

[3] Zhang, S. / Cervical cancer: Epidemiology, risk factors and screening / S. Zhang, H. Xu, L. Zhang [et al.] // Chin J Cancer Res. - 2020. - Dec. - P. 720 - 728.

[4] İsayev, İ.H. Uşaqlıq boynu xərçənginin şüa terapiyasında boşluqdaxili və toxumadaxili braxiterapiya metodlarının tətbiqi ilə müştərək şüa müalicəsi / İ.H. İsayev, E.H. Quliyev, K.S. Əkbərov, N.S. Əliyeva // Azərbaycan onkologiya jurnalı, - 2016. N2,- s.82-84

[5] Субханкулова, А.Ф Эффективность радиоволнового метода лечения патологии шейки матки // Вестник Современной Клинической Медицины, - 2016, Том 9, вып 3.- с.35-38

mortality rate. Rigorous implementation of screening programs caused decreasing of prevalence and mortality rate of cervical cancer in developed countries [6].

Cytological screening is indicated as the main method for diagnosing of cervical cancer [7]. One of the main terms for increasing the efficiency of cytological screening is qualitative obtaining of the material. Therefore, numerous studies for improving of the screening examination of cervical diseases and the effectiveness of other alternative diagnostic methods are being studied[8]. According to several sources it is considered appropriate to use a liquid-based cytology method for solving of these problems[9]. Treatment of the benign cervical diseases ablation and excision can be used depending on cervical pathologies[10]. Using of broadband radio wave surgery and argon plasma coagulation - "FOTEK EA 141M" in ambulatory gynaecology allows to achieve good results in diseases of the cervix, uterus and vulva in women of different age groups. These methods minimally damage the tissue, preserves the anatomical integrity of organ, provides reliable haemostasis during surgical interventions[11].

---

[6] Sharma M., Using HPV prevalence to predict cervical cancer incidence / M. Sharma, L. Bruni, M. Diaz [et al.] // International J. Cancer, - 2013, v. 132, p. 1895-1900.

[7] Шабалова, И.П. Рак шейки матки в XXI веке: гинеколог, клинический цитолог, специалист по молекулярным исследованиям / И. П. Шабалова, А.В. Ледина, Л.Г. Созаева // Новости клинической цитологии России, - 2018, №22 (3-4). –с. 31-36

[7] Cəfərova, K.Ə. İnsan papilloma virusunun müxtəlif tipləri nəticəsində törəmələrin müasir diaqnostika metodları / K.Ə. Cəfərova, V.N.Cavadzadə // Azərbaycan onkologiya jurnalı, - 2020. N2, -s.43-45

[8] Nishio, H.Liquid-based cytology versus conventional cytology for detection of uterine cervical lesions: a prospective observational study /H. Nishio,T. Iwata,H.Nomura[et al.] // Jpn J Clin Oncol.,2018, Jun 1, 48(6), -p.522-528

[9] Əliyeva, N.R. Uşaqlıq boynu xərçənginin kimyaradioterapiyasından sonra əmələ gələn xroniki şüa proktitin konservativ müalicəsi// Azərbaycan onkologiya jurnalı, - 2019. N1, -s.38-43

[11] Бебнева, Т.Н. Современная концепция организации кабинета патологии шейки матки/Т. Н. Бебнева, С.И. Роговская // Медицинская наука и образование Урала, - 2012, №3. – с.114-118

The above-mentioned facts approve that studying of cervical pathologies, application of optimal diagnostic and effective treatment methods is one of actual problems of obstetrics and gynaecology. Successful treatment of benign cervical pathologies allows to obtain good forecasts for the successful course of many malignant cervical diseases in the future. All these facts prove that it is appropriate to conduct research in that direction.

A single algorithm for the diagnosis and treatment of benign cervical diseases with the Fotek device has not been developed, although these types of research works are conducted.

We want to determine the role of the liquid cytology method in the diagnosis of benign cervical diseases and the effectiveness of FOTEK hardware application in treatment of these diseases by conducting of systematic review of the studies conducted so far.

We think that, the results which we have achieved will be very important for diagnosing and selection of treatment tactics of cervical diseases.

Object and subject of the study. 150 women applied to the outpatient polyclinic department of the Scientific-Research Institute of Obstetrics and Gynaecology for consultation in 2017-2021 years are included to the study. They were divided into two groups: the main group - 130 women with benign cervical diseases and the control group included 20 women who had no complaints, who applied to the clinic for preventive gynecological examination, pregnancy planning and contraception.

The purpose of the study: Studying of the role of liquid-based cytology in diagnosing of benign cervical diseases and the efficiency of treatment with the "FOTEK EA 141M" device during cervical intraepithelial neoplasia.

The objectives of the study:

1. Comparison of prognostic values of liquid-based cytology and classical PAP smear results in women of reproductive, premenopausal and menopausal age with positive and negative HPV.

2. Determination of risk factors for the development of benign cervical diseases in women with positive and negative HPV, depending on age and reproductive functions.

3. Evaluation of recurrence after treatment of HPV positive women with benign cervical disease with "FOTEK EA 141M" device and diathermic electrocoagulation.

4. Assessment of efficiency of treatment of benign cervical diseases with FOTEK EA 141M" device and DEK

5. Optimization of treatment and prophylactics of benign cervical diseases.

Methods of the study:

According to the dissertation work studies cover several stages. On the first stage the articles of researchers in recent years were analysed for studying of application of epidemiology, etiology, pathogenesis, risk factors, diagnostics and modern treatment methods of cervical diseases. 26 domestic and 159 foreign sources were used for this purpose.

On the second stage clinical characteristics, laboratory and instrumental diagnostic aspects of cervical diseases in women of different ages were studied.

On the third stage we conducted comparative analysis of studied diagnostic criteria by groups. Comparative analysis of diathermic electrocoagulation and "FOTEK EA 141M" methods in treatment of benign cervical diseases in women have been analysed. On the fourth stage statistical processing of the results obtained separately for each group was carried out.

The main provisions to be defended:

1. The liquid-based cytology plays a prognostic role in morphological changes at the cellular and tissue level of the cervix and early diagnosis of cervical benign diseases.

2. Depending on age of woman, gynaecological anamnesis helps to form risk factors for development of benign cervical diseases.

3. Treatment of benign cervical diseases using the "FOTEK EA 141M" device allows to improve the indicators of recovery time and early recovery.

4. Character and selection of modes of "FOTEK EA 141M" device depending on type, depth and area of benign cervical diseases.

Scientific novelty of research work:

– The complex scientific examination of women with diagnosed

benign cervical diseases, have been conducted, using modern, informative diagnostic and treatment methods. The factors causing development of these diseases have been detected.

– The efficiency of application of "FOTEK EA 141M" device in treatment of benign cervical diseases was assessed. It was detected that the argon plasma ablation is a safe, effective, cost-effective, organ-sparing method and this method can be used in clinical practice for treatment of benign cervical diseases in women of different ages.

– The algorithms for selecting of tactics for treatment of benign cervical diseases based on early diagnostic criteria have been developed.

– Liquid cytology was compared with classic PAP smear and the association of abnormal cervical cytology with low, high oncogenic risk and negative HPV was evaluated.

– Comparative analysis of the clinical effectiveness of the treatment of cervical diseases in patients with positive and negative HPV have been conducted using the surgical methods such as diathermic coagulation, radio conization, argon plasma coagulation.

– It was determined that, argon plasma coagulation is an effective method for the treatment of benign diseases of the cervix in condition of type I and II transformation zone and it leads to complete elimination of complications caused by HPV infection.

– It was proven that, radio conization is both a diagnostic and therapeutic procedure, it allows to obtain material for histological examination with minimal coagulation under the conditions of type III transformation zone and helps in adequate interpretation of the result. Also, this method allows to treat the benign pathologies of the cervix, as well as the complete elimination of damage caused by HPV infection.

Theoretical and practical importance of the research work:

– Applying of the liquid-based cytology helped to efficiently conducting of the screening examination of benign cervical diseases.

– In case of in time diagnosing of benign cervical treatment with the FOTEK device, as a more effective method, has led to timely and uncomplicated elimination of these diseases.

– Results achieved as a result of the research work assisted obstetricians and gynaecologists in the early diagnosis of benign cervical diseases and the selection of treatment tactics.

Approbation of the dissertation work. Separate parts of the dissertation were discussed in the following scientific-practical meetings: III International Congress on Obstetrics and Gynaecology " New aspects in the diagnosis and treatment of obstetric conditions and gynaecological diseases " (March 4, 2020, Baku). Scientific-practical conference dedicated to the 60th anniversary of Topchubashov, Scientific Surgery Center named after academician M.A. Topchubashov (June, 2022, Baku), International Koru congress on pregnancy, birth and postpartum period (February 17-20, 2022, Turkey), 3rd Global virtual summit on Gynaecology Obstetrics and women's health (April 28-29, 2022 United Kingdom), İCWGCRM 2023, XVII International Conference On Women Gynecology, Childbirth and Reproductive Medicine (november 13-14,2023, Dubai, United Arab Emirates).

The first discussion of the case was conducted at the meeting of the Scientific Research Institute of Obstetrics and Gynaecology PC (protocol No. 12; 02.12.2022).

The scientific seminar of the work was held at the scientific seminar of the ED 2.06 dissertation council under Azerbaijan Medical University (protocol No. 08; 16.01.2024).

Application of the research work. The achieved results of the research work are used in the daily practice of the Scientific Research Institute of Obstetrics and Gynaecology PC. The scientific data obtained as a result of conducted clinical-laboratory-instrumental studies are also referred in the teaching process.

The organization where the dissertation work was performed. The dissertation work was performed in Scientific Research Institute of Obstetrics and Gynaecology PC.

The published scientific works: The main provisions and conclusions of the dissertation work are published as in 9 journals article (including 3 abroad) and 4 abstracts (including 3 abroad).

The volume and structure of the dissertation work. The dissertation work is printed on computer on 171 pages (total volume: 206.500 characters) and consists of sections "Content", "Introduction"

(volume: 11.000 characters), "Results of the study - 5 chapters", "Conclusion", "Results", "Practical recommendations" (volume: 30.800 characters) and "List of references".

The main content of the dissertation is divided into 5 chapters: Chapter I-"Literature review" (volume: 67.300 characters), Chapter II - "Materials and methods" (volume: 23.700 characters), Chapter III-"Achieved results of the study" (volume: 27.500 characters), Chapter IV -"Comparative analysis of the results of the groups included in the study" (volume: 14.800 characters), Chapter V- (volume: 31.400 characters).

185 literature sources were used in writing the dissertation, 26 of them are the works of scientists from Azerbaijan, 72 Russian and 87 of foreign scientists. The dissertation work is illustrated with 28 tables, 17 graphs and 11 pictures, 2 schemes.

MATERIALS AND METHODS OF THE STUDY

The clinical part of the research work was performed in the ambulatory polyclinic department of the Scientific Research Institute of Obstetrics and Gynaecology PC. The research work has prospective and retrospective character.

The clinical materials of 150 women who applied for consultation to the outpatient polyclinic department of the Scientific Research Institute of Obstetrics and Gynaecology PC during 2017-2021 were included for solving the tasks set in the research work. All patients were informed about conducted studies; they were included to the research based on their agreement. 130 women with benign cervical diseases in their anamnesis formed the main I group. The main group is divided into 3 subgroups (s/g): I s/g n=50 women of reproductive age; II s/g n=39 women in pre-menopause period; III s/g n=41 women in post-menopause period. The control group (NC) included 20 women who did not have any complaints, had a preventive gynecological examination, were planning a pregnancy and applied to the clinic for contraception. Women with atypical changes in the cylindrical epithelium of the cervical canal and cervical cancer were excluded from the study.

A full laboratory-clinical examination according to the accepted

scheme in the ambulatory polyclinic department of the Scientific-Research Institute of Obstetrics and Gynaecology was carried out for all patients. This examination scheme consists of: detailly collection of anamneses; conducting an objective review (weight-height index, type of body structure, nature of hair); conducting a gynaecological examination; ultrasound examination of small pelvic organs (via a vaginal probe); bacterioscopy of uterine discharge; bacteriological examination; HPV (DNA); PAP test - liquid-based cytology and classical pap smear; histological examination; ZPR in herpes; simple and extended colposcopy. Also, 6 months after treatment, HPV-DNA genotyping, liquid-based PAP smear, and simple and extended colposcopy were repeated to the patients.

Liquid-based cytology was performed with the "CellScan 100A" device, overcomes the shortcomings of traditional cytology. This device reduces the field of view of the microscope by creating a monolayer slide that directly propagates cervical cells and provides accurate reading with 100% efficiency without cytopathic changes. This device allows the removal of mucus, inflammatory elements and blood cells from the sample by spinning the cytological specimen in a centrifuge. The studied cells retain their properties, as they are stored in a special solution.

The "FOTEK EA 141M" device currently is the most suitable among the surgical treatment methods of cervical pathologies, at the same time is capable in producing of excisional and ablative effects.

It is important to perform the surgical intervention on the 5th-9th day of menstruation, for the prevention of relapses of cervical diseases and endometriosis. Full recovery after the procedure happens in 2 months and 3-6 months later it is possible to plan pregnancy.

We used this device in different operating modes. So that, Cervical polyps and condylomas were excised with a 0.3 mm diameter pet electrode in the "SMES" mode at 50-70Wt power. The coagulation depth was 1mm, reliable hemostasis was ensured. An argon plasma torch in the "SPRAY" mode affected the tissue with a power of 50-60 Wt. in a time interval of 3-5 seconds to a depth of no more than 3 mm for coagulation of endometrioid heterotopias. Cervical ectopy and ectropion are ablated at a depth of 1-2 mm under the influence of an argon torch

with a power of 60-70 Wt. in a time interval of 2-4 seconds using the “SPRAY” mode. It coagulates the tissue during leucoplakia in "SPRAY" mode up to a depth of 2.5-3 mm at a power of 50-70 Wt. in 4-7 seconds time interval. The electrode is kept in a distance 0.5 cm from the cervix in case of argon plasma ablation. If pulsatile bleeding is not observed during the procedure, the argon coagulation from the periphery to the center, holding the electrode at a distance of 5 mm from the wound area with the "FULGUR" mode was implemented. In case of intensive bleeding, it was stopped by using 70-80 W power with ball electrode in "SOFT" mode.

The method of diathermic coagulation (DTC) has a high electric current and causes the tissues to heat up due to high temperature. In case of using DTC, it is necessary to control the frequency and duration of the electric current. Because, during coagulation, it generates endogenous heat up to 60-100 degrees in the tissue, what can cause irreversible consequences in tissue. While using the method, a passive electrode is placed under the patient's buttocks and the pathological area is coagulated with power 70-100Wt during 7-12.

Research work was determined as analytical-by design; clinical-by the method; selective-by volume; scientific- by type; retrospective and prospective – by the material; transverse and longitudinal –by the duration; clinical -by location.

Statistical analysis was conducted in MS EXCEL 2019 and IBM Statistics SPSS-26 programs using variance (U-Mann-Whitney, KU-Kruskal-Wallis, W-Wilcoxon), discriminant (Chi-square Pearson), correlation (ρ-Spearman), dispersion (ANOVA test), ROC-analysis and proven medical methods.

THE RESULTS OF PERSONAL RESEARCH AND THEIR DISCUSSION

The clinical features of benign cervical diseases in women of different ages. The highest frequency of benign cervical diseases is seen among women in the reproductive age group. The reason for this high frequency is explained with the active sex life of women in the reproductive age group.

Most women included to the research group live in the Republic of Azerbaijan, preferably in the city of Baku. No significant difference was found during the study of their social and economic status. Patients have a status of housewives or working women and their working conditions were not related to professional damages. Anamnesis about extragenital diseases of women in the research group was collected, these diseases were detected mostly in women in the postmenopause age group. Anaemia was observed in 15% of women, arterial hypertension in 13% of women, diseases of the thyroid gland in 9% of women, diseases of the genitourinary system and digestive organs (gastritis) in 10% of women, and diabetes in 7% of women.

Among the inflammatory diseases, non-specific vaginitis was found in 2(4%) women in the reproductive group, 4(10.3%) in the premenopausal period, 4(9.8%) in the postmenopausal period, and 1(5%) in the control group (CG). Ectopy and endocervicitis were detected in 29(58%) women of subgroup I, in 14(35.9%) women in subgroup II, in 17(41.5%) women in subgroup III. In CG only endocervicitis was seen in 6(30%) women. As it is seen, ectopy in the I group was registered 2 times more common compared to group II, and 1.5 times more compared to group III. At the same time, in the second group, condyloma was found 1.5 times more than in group III (12.8%), and in the third group, leucoplakia was found 1.5 times more (14.6%). Atrophic vaginitis did not occur in any woman of I, II and control groups, also leucoplakia did not occur in any woman of the control group. Among hormone depended diseases cervical polyps were noted in 4 women in the reproductive group, in 3 women in the premenopausal group, and in 2 women in the postmenopausal group, and the uterine endometriosis was noted in 3 women in the reproductive group and in 5 women in the premenopausal group.

The following nosological forms of benign diseases were found during comprehensive clinical and laboratory examination of 150 women included in the study.

Only 1 woman among CG patients had polyp. Cervical ectropion was seen in 3(6%) women in reproductive group, in 3(7.7%) women in premenopausal group, in 1(2.4%) woman in postmenopause group, and in 1 woman in CG ($p_U < 0.001$), ($p_н = 0.521$). It is known that an

indicator of reproductive health was an indicator of menstrual function. Comparative analysis of this function showed almost equal menarche age (12.1 ± 0.2, 12.4 ± 0.2 and 11.9 ± 0.3 years, respectively) among patients of I, II and III subgroups (table 3.1.2). in CG this indicator was 12.6 ± 0.3 years. Thus, 74% of the women in the reproductive group had normal menstruation, 18% had oligomenorrhea, 4% polymenorrhagia, and 4% algomenorrhea. 53.8% of women in the premenopausal group had normal menstruation, 30.8% had oligomenorrhea, 5.1% polymenorrhea, and 10.3% algomenorrhea. 95.1% of women belonging to the menopause group had normal menstruation in their anamnesis, 4.9% suffered from oligomenorrhea. 70% of women in CG had normal menstruation, 15% oligomenorrhea, 15% algomenorrhea were found ($p_u<0.001$) ($p_H< 0.001$).

Factors such as the number of abortions, trauma to the cervix during childbirth, early sexual intercourse, and methods of contraception play an important role in the development of cervical diseases.

Number of non-smoking patients in both groups was equal. But smoking women prevail among those with papilloma virus. The results of collected questionnaires showed that, 24% of women in the reproductive group, 15.4% of premenopausal women, 24.4% of women in the postmenopausal group, and 20% of women in the CG smoked. So, can be concluded that, smoking is not the only risk factor for papilloma virus development, also is a cofactor for the progression of cervical intraepithelial neoplasia. Naturally, it affects the development and carcinogenicity of dysplasia. It is known that, smoking is a factor that contributes to the initiation and development of HPV because of decreasing number of Langerhans cells ($p_U= 0.876$), ($p_H=0.578$).

COMPARATIVE ANALYSIS OF CLINICAL-DIAGNOSTIC ASPECTS OF BENIGN CERVICAL DISEASES IN WOMEN

The analysis of implemented surgical operations showed that, cervical polypectomy - 7.3%, anterior and posterior colporrhaphy - 7.3%, subtotal amputation of the uterus - 7.3%, ovarian cystectomy - 4.9%, tubectomy - 2.4% were seen among women included to the third group

2 times more than women belonging to other groups.

Women in the second group were performed hysteroscopy - 2.6% and ovariectomy -2.6% and women in the reproductive age group underwent cervical excision - 2% and tubal sterilization - 2% (pн=0.016). According to the questionnaires collected from the examined women, it was found out that, infection with HPV is more common among women whose partners do not use contraception and condoms. That is why these women are more sensitive to sexually transmitted diseases. Clinical laboratory smear analysis and monitoring of ZPR (chlamydia, ureoplasma, mycoplasma) in the examined women showed that, the sexually transmitted diseases and bacterial infections such as papilloma virus, mostly are associated with other urogenital infections.

Mixed urogenital infections were detected in 78% of women in reproductive age group, 74,4% women in premenopausal group, 75,6% women in postmenopausal group and 55% of patients in CG (p_U=0.047, ($p_н$=0.984). Sexually transmitted diseases in the main group were detected more than the control group.

Among them: candidiasis was found in 12% of women in subgroup I; in 15.4% of women in subgroup II; in 9.8% of women in subgroup III, in 5% of patients in CG, bacterial vaginosis was found in 6% of women in subgroup I; 2.6% in subgroup II; 14.6% in subgroup III; in 5% of patients in CG; trichomoniasis was detected in 2% of patients in subgroup I; 2.6% in subgroup II; 4.9% in subgroup III; gonorrhoea was detected in 2% of patients in subgroup; I 7.7%– subgroup II ; 2.4% - subgroup III; ureoplasma, mycoplasma and chlamydia is seen in 8% of patients in subgroup I; 4.9% in subgroup III; 5% in CG; non-specific vaginitis in subgroup I was 48%; in subgroup II - 46.2%; in subgroup III - 39% of patients; 40% - CG; herpes was found in 14% of patients I subgroup; in 10.3% of patients in subgroup II (pU=0.178), (pн=0.053).

Women underwent ultrasound examination within the frames of retrospective and prospective study, while studying the results of the examination it became clear that, 44(88%) of women of reproductive age had normal indicators, 2(4%) had ovarian cyst, 4(8%) - uterine adenomyosis, indicators of women 30(78.9%) in premenopausal age

were normal, 6(15.8%) had uterine fibroids, 2(5.3%) - uterine adenomyosis, indicators of 29(87.9%) women in postmenopausal age were normal, 3(9.1%) had uterine fibroids, 1(3%) - endometrial polyp (p_U= 0.170), ($p_н$= 0.347).

Currently HPV is widespread virus and according epidemiological examinations its types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, 82) are on high-risk group, 12 types (6, 11, 40, 42, 43, 44, 54, 61, 70, 72, 81 & 89) are on low-risk group.

We had detected the incidence rate of "low" and "high" oncogenic risk of human papilloma virus in women with benign cervical diseases. The results of performed analysis showed that in 36 (72%) of women in reproductive age group, 15 (38.5%) of women in premenopausal age group, 5 (12.2%) of women in postmenopausal age group. HPV type with high oncogenic risk was positive in 6 (30%) of women in CG.

HPV type with low oncogenic risk was positive in 11 (22%) of women in the reproductive age group, 10 (25.6%) of women in the premenopausal age group, and 7 (17.1%) of women in the postmenopausal age group. In the control group, this type was positive in 2 (10%) women (p_U=0.229), ($p_н$< 0.001).

While assessing the cytological parameters it should be noted that, PAP smears were taken from all examined women by liquid-based cytology method.

In 7(14%) women of reproductive age, 10(25.6%) premenopausal women, and 17(41.5%) postmenopausal women NMİL were detected. But in 23 (46%) women of reproductive age AS-CUS; in 16(32%) women - LSİL, in 4(8%) women HSİL were detected. In premenopausal age group AS-CUS was detected in 13(33.3%) women, LSİL – in 3(33.3%) women, HSİL – in 2(5.1%) women; AGUS – in 1(2,6%) woman. In postmenopausal age group AS-CUS was seen in 11(26.8%) women; LSİL - in 7(17.1%) women; HSİL - in 2(4.9%) women, AGUS – in 4 (9.8%) women ($p_н$=0.013). Also, cytogram was normal in 20(100%) of women in CG (p_U< 0.001).

While comparing the results of traditional PAP smear among groups, 7(23.3%) women in the reproductive group had NMİL, 12(40%) women had AS-CUS, 6(20%) women had LSIL, 2(6.7%)

women had blood elements, 1(3.3%) woman had inflammation elements identified as insufficient in 2 (6.7%) women. In 7(30,4%) women of premenopausal age indicators were normal, AS-CUS in 6(26.1%) women, LSIL in 7(30.4%) women, inflammatory elements in 2(8.7%) women, in 1(4.3%) woman identified as inadequate. In 5(22,7%) women of postmenopausal age indicators were NMİL, AS-CUS in 6(27.3%) women; LSIL in 2 (9.1%) women, HSIL in 3 (13.6%) women, AGUS in 2 (9.1%) women, blood elements in 3 (13.6%) women, inflammation in 1 (4.5%) woman elements were determined (pH = 0.556). Totally, 2(100%) women in CG gave an analysis and the result was normal (p_U= 0.001).

Totally, in terms of quality, in 5 cases in subgroup I, in 3 women in subgroup II, in 4 women in subgroup III the results of traditional cytological analysis were unsatisfactory and no cytological diagnosis was made. Causes of unsatisfactory smear were, lack of endocervical cells for analysis in the micropreparation because the smear is mixed with inflammatory elements and blood cells.

When comparing both methods of PAP smears taken from women we had found ASCUS in liquid-based PAP smear of 8 women and LSIL in 2 patients with normal result in conventional PAP smear.

In 22 women with normal PAP smear results we found ASCUS as a result of liquid-based PAP smear, LSİL in women.

Also, the traditional PAP smear detected LSİL in 15 women. But according the results of liquid-based PAP smear the results of 1 woman was normal, 1 had ASCUS, 11 results confirmed traditional PAP, i.e. LSİL was detected. In 1 patient - HSIL and in 1 patient - AGUS was prescribed. In 1 of 3 patients, with HSIL detected in classic smear, HSIL was also detected and AGUS was detected in 2 patients as a result liquid-based PAP. In two women with AGUS diagnosed by PAP analysis the results of both PAP smear methods were similar.

As we stressed, while analysing the traditional PAP smear examination the uterus excretion and in some cases blood, inflammation prevent correct results. So, liquid-based PAP smear did not reveal dysplasia in 1 patient with blood-covered visual field, in 2 women - AS-CUS, in 2 women - LSIL were registered. In 3 women with inflammatory cells in the field of vision dysplasia was not detected as a result

of liquid-based cytology, LSIL was detected in 1 woman. As a result of the classic cytology the analysis was considered insufficient because there were no endocervical cells in the smear of 3 women. On the contrary, liquid-based cytology also determined LSIL in 1 of these patients, ASCUS in 1, and a normal response in 1 ($p<0.001$).

Comparison of values of sensitivity, specificity, and prognostic between conventional PAP smear and liquid-based cytology was conducted (table).

Table. Comparison of results of liquid-based cytology and traditional PAP test by histology

Traditional PAP smear	Pathology		
	Yes	No	Hysto-logy
	48	17	65
+	39	5	44
-	9	12	21
Se	81,3	±	5.6
Sp	70,6	±	11.1
Ppv	88,6	±	4.8
nPV	57.1	±	10.8
LR+	2.76	Satisfactory	
LR-	0.27	Satisfactory	
GDV	78.5	±	5.1

Li-quid	Pathology		
	Yes	No	Hysto-Logy
	87	63	150
+	81	15	96
-	6	48	54
Se	93.1	±	2.7
Sp	76.2	±	5.4
pPV	84.4	±	3.7
nPV	88.9	±	4.3
LR+	3.91	Satisfactory	
LR-	0.09	Excellent	
GDV	86.0	±	2.8

So that, sensitivity of liquid-based cytology detected under the study was 93.1%, which is higher than sensitivity of traditional PAP test. But in traditional PAP test this indicator was 81.3%. As for specificity, this indicator was 76.2% in liquid-based cytology, which is higher than traditional PAP test for 70.6%. The positive prognostic value (PPV) was calculated as 84.4as a result of liquid-based cytology and was 88.6% in traditional PAP test results. The negative prognostic value (nPV) was 88.9% in liquid-based cytology result and 57.1% in traditional PAP test result. Indicators of general diagnostic value at liquid-based cytology was 86% and 78.5% at traditional PAP test. As the quantity of false, negative and non-satisfactory detected by liquid-based cytology was little, the probability of getting a correct result in women with cervical diseases is higher. As the liquid-based cytology

has more sensitivity and specificity, is more preferable than traditional PAP test in detection of cervical neoplasia. All patients underwent a colposcopic examination after receiving material for cytological testing within the frames of the screening program. For detecting the occurrence of pathological changes in cervix, the patients underwent simple or extended colposcopy.

In 1(2%) woman of reproductive age, in 4(10.3%) premenopausal women and in 7(17.1%) postmenopausal women, who underwent colposcopy examination, the colposcopic image was normal. In the control group the normal colposcopic image was in 8(40%) women(p_U<0,001).

In 17(34%) women of reproductive age the colposcopic image was abnormal, 4(8%) had leucoplakia, 2(4%) - endometriosis, 3(6%) - ectropion, 15(30%) - ectopy, 3(6%) - condyloma, 1(2%) - cervical polyp, 3(6%) cervical stenosis (p_H = 0.047). In 3(7.7%) women of premenopausal age the colposcopic image was abnormal, 7(17.9%) leucoplakia, 4(10.3%) endometriosis, 3(7.7%) ectropion, 9(23.1%) ectopy, 5(12.8%) condyloma, 3(7.7%) %) cervical polyp were identified. In 17(36.6%) women of postmenopausal age the colposcopic image was abnormal, 5(12.2%) leucoplakia, 1(2.4%) ectropion, 5(12.2%) ectopy, 4(9.8%) condyloma, 1(2.4%) cervical polyp, 1(2 .4%) cervical stenosis was determined. Among women of CG 6(30%) abnormal colposcopic images, 1(5%) endometriosis, 1(5%) condyloma, 1(5%) ectopy, 2(10%) cervical stenosis were detected (P_U< 0.001).

Biopsies were taken using the FOTEK device, from aceto-white areas in case of abnormal colposcopic image. Materials for histological examination were taken from totally from n=122 women.

Analysis was taken from n=48 women in reproductive age group, results of 6(12%) histological examination were normal, 37(74%) - CIN 1; 7(14%) - CIN 2 were found out. Analysis was taken from n=35 women in premenopausal age group, results of 11(31.4%) histological examination were normal; 19(54.3%) - CIN 1; 5(14.3%) - CIN 2 were found out. Analysis was taken from n=37 women in postmenopausal age group and results of 16(43.2%) histological examination were normal, 16(43.2%) - CIN 1; 2(5.4%) CIN 2 - 1(2.7%) CIN 3 - 2(5.4%) condyloma were found out (pU = 0.368), (p_H = 0.001).

IMPROVEMENT OF TREATMENT OF BENIGN CERVICAL DISEASES IN WOMEN OF DIFFERENT AGES

42 women with benign cervical diseases were applied conservative treatment and 88 women were treated by surgical method. 38 women among them underwent diathermic electrocoagulation, 50 women underwent argon plasma ablation and excision with the "FOTEK EA 141M" device. It should be noted that, patients for the surgical operations were selected taking into consideration their biopsy results and complaints.

The efficiency of treatment implemented with both methods was assessed according to complaints, clinical gynaecological examination and colposcopic examination, as well as epithelization on the surface of the wound, complication or relapse on the 30th, 45th, 60th day.

Women with different complaints were treated with the method of diathermic electrocoagulation: intracervical neoplasia I, II and high oncogenic type of HPV positive, contact bleeding etc.

Some patients after DEC had complaints such as pain in the lower abdomen, bloody discharge and, a white film on the wound surface was developed in all women immediately after the procedure, a curve was formed on the 7^{th} day in 22(57.9%) women ($p_W < 0.001$), and only in 37(97.4%) patients on the14th day ($p_W < 0.001$). A scab is a hard, thick crust that forms from blood clots and dead cells after a burn for covering the surface of a wound. The watery excretion and bloody staining came from the genital tract of the patients during 30-45 days.

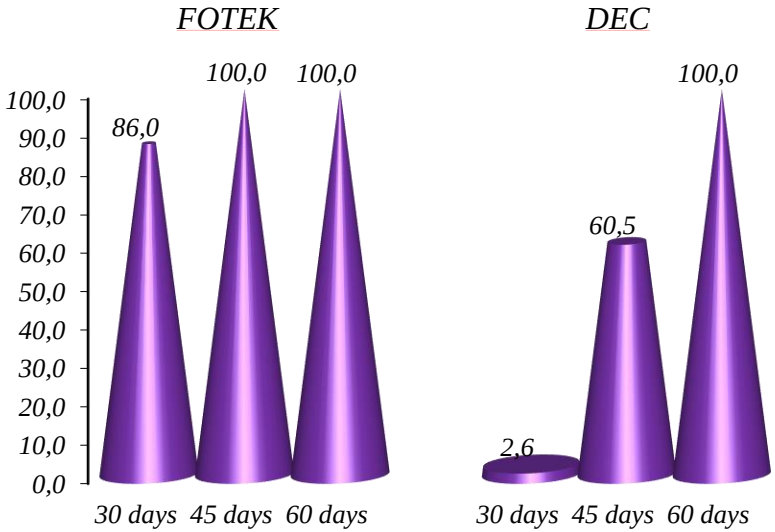
Women underwent a gynaecological examination on the 30^{th}, 45^{th} and 60^{th} day for controlling the degree of epithelization and healing of the wound after DEC. So, on the 30^{th} day after DEC epithelization of the wound surface was observed in 1(2.6%) patient and in 23(60.5%) women on the 45^{th} day. On the 60^{th} day after the treatment complete epithelialization of the wound surface was observed in all 38(100%) women ($p_W = 0.317$), ($p_W < 0.001$), ($p_W < 0.001$).

Both early and late complication were detected after using DEC. Bleeding due to early complications was observed in 6 patients in 15.8% of cases while applying the procedure. Late complications

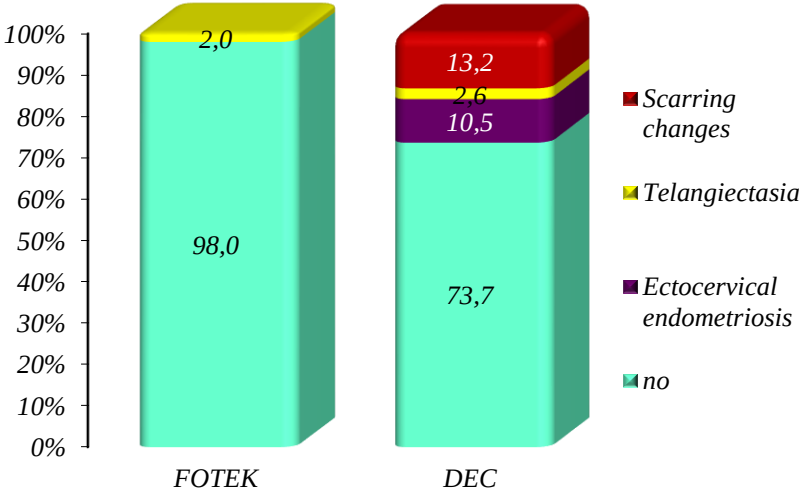
were registered in 10(26.3%) cases. Among them ectocervical endometriosis was found in 4 (10.5%) patients, telangiectasia in 1 (2.6%) patient, and scar changes in 5 (13.2%) women. HPV DNA and PAP smear were taken for detecting relapses after the treatment and 9(23.7%) women had relapses.

"FOTEK EA 141M" method, argon plasma coagulation was performed in women with contact bleeding, IPV high oncogene type positive and intraepithelial neoplasia (CIN1) as a biopsy result. But, excision was performed in only 12 women, including cervical intraepithelial neoplasia (CIN2).

While using "FOTEK" no one of patients had complications. The watery excretion came from the genital tract of the most of patients during 4-6 days, and bloody staining was observed during 5-7 days. It should be noted that, we had observed shortening of duration of hydrorhea by approximately 2 times compared to the traditional method of treatment. A fibrin layer was observed on the wound surface on the 7^{th} and 14^{th} days after the treatment with "FOTEK". Fibrin is a thin film formed as a result of the drying of a blood clot. The fibrin layer was observed in 6(50%) patients after excision(p_W= 0,014), in 19(50%) patients after argon plasma ablation(p_W< 0,001), on 14^{th} day in 37(97.4%) patients after APC (p_W< 0,001), in 12(100%)women after excision (p_W= 0,001).The effectiveness of the treatment was assessed by epithelialization of the wound surface. A gynaecological examination and a colposcopic examination were performed, and the healing rate of the wound surface was evaluated on 30^{th}, 45^{th} and 60^{th} days after the treatment. Epithelialization of the wound was observed in 34(89.5%) patients on 30^{th} day after APC (p_W< 0,001) and in 9(75%) patients while excision (p_W= 0,003). Complete epithelization of the wound surface was noted in 38 (100%) women (p_W < 0.001) and in 12 women on 45^{th} day after APC, which is 100% of cases after excision (p_W = 0.001). After 6 months, as late complication, telangiectasia was observed in only 1 (2%) woman, who was examined by colposcopy (graph 1). Thus, the reproductive group was the group with the most relapses and late complications, while bleeding from early complications occurred most often in premenopausal age group (graph 2).



Graph. 1. Epithelialization of the wound surface depending on applied treatment methods.



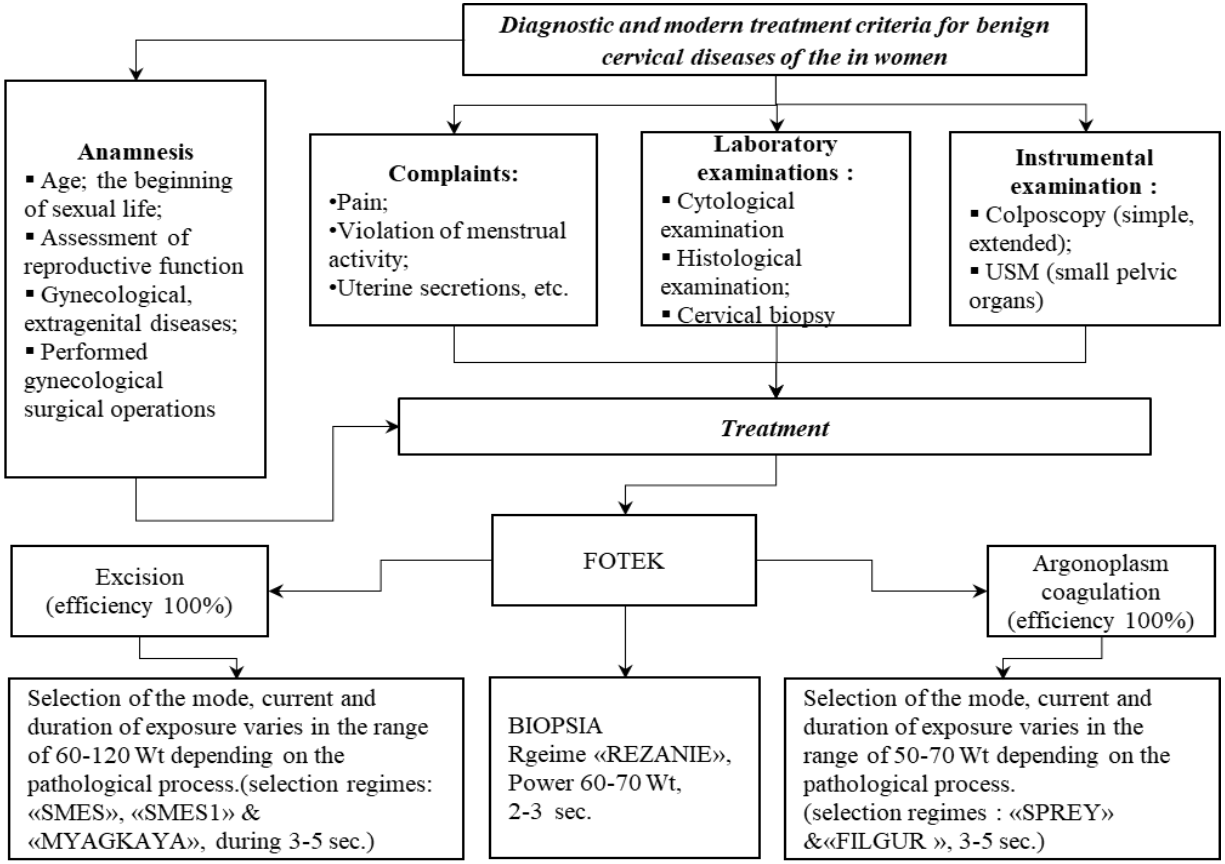
Graph. 2. The comparative chart of complications depending on used treatment methods

Patients were invited for examination in order to assess the effectiveness of the treatment. Gynaecological examination of women was implemented by simple and extended colposcopy, liquid-based pap smear and HPVDNA genotype analysis was repeated. HPV with low oncogenic risk was positive in 1 (3,6%) patient, HPV with high oncogenic risk was positive in 8 (14,5%) patients with recurrent disease (p=0.012).

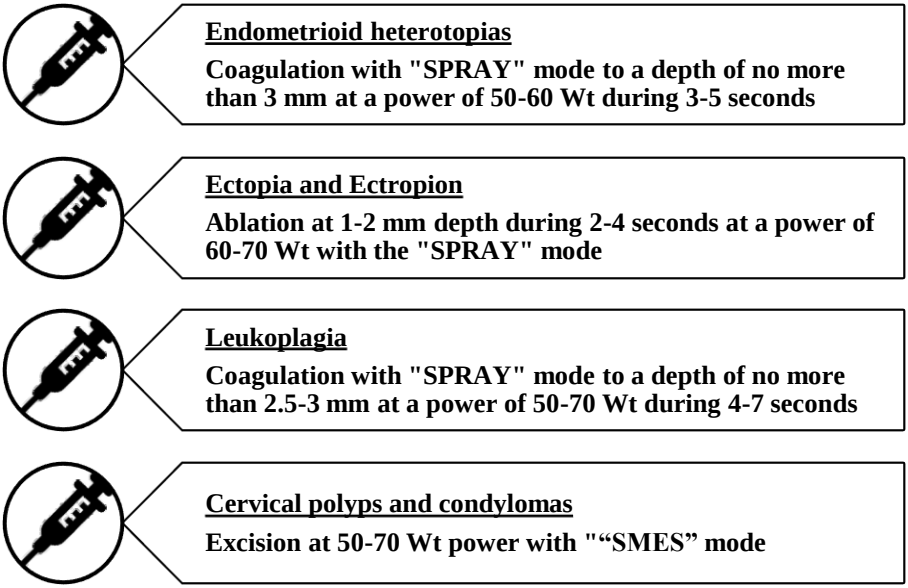
However, in 1(3.6%) woman HPV with low oncogenic risk was positive, HPV with high oncogenic risk was positive in 3(5,5%) women with late complication – cervical scar changes, in 2(3.6%) women with telangiectasia, in 3(5.5%) women with ectocervical endometriosis (p=0.107). It can be concluded that, the type of HPV with high oncogenic risk plays a role in the formation of relapses and complications, as well as delaying wound healing. Monitoring of HPV status and PAP smear in women with benign diseases of the cervix after treatment is a prognostic marker of treatment. Using argon plasma coagulation for treatment of patients with benign diseases of the cervix allows to eliminate the complications caused by HPV and achieve recovery by removing the pathologically changed epithelial layer without damaging the deep tissues. In particular, the soft effect of argon-plasma coagulation on the cervix prevents the formation of a rough scar and deformation, what makes to using of the method even in women who have not given birth possible. "FOTEK EA 141M" device was highly effective and well tolerated and provides epithelialization of ectocervix and endocervix.

We have developed an algorithm for diagnosing and treatment of women of different age groups with benign diseases of the cervix according to the achieved results (scheme 1, 2).

Using of presented set of diagnostic methods and the proposed algorithm will help to select optimal and different tactics for treatment depending on cervical pathologies found in women.



Scheme1. Algorithm of diagnostic and modern treatment criteria for benign cervical diseases of the in women



Scheme 2. Algorithm of modern treatment criteria with "FOTEK EA 141M" device for treatment of benign diseases of the cervix in women.

FINDING

1. Sensitivity of liquid-based cytology was 93.1% and traditional PAP test – 81.3%. Specificity of liquid-based cytology was detected as 76.2% and traditional PAP test –70,6%. General diagnostic value in liquid-based cytology was calculated as 86%, and 78.5% in traditional PAP test [5,8].

2. According to the collected anamnesis,46% of women in reproductive age group, 79.5% of women in premenopausal age group, 78% of women in menopausal age group had abortion. In 32% of women in reproductive age group, 12.8% of women in premenopausal age group, 14.6% of women in menopausal age group one of postpartum complications – laceration of the soft birth canal, especially the cervix was found. 70% of women in reproductive age group, 69.2% of women in premenopausal age group, 95.1% of women in menopausal age didn't use any contraceptive method [6,10].

3. HPV status or pap smear of women with benign diseases of the cervix were monitored in 6 months after treatment and none of patients had relapses after treatment with "FOTEK EA 141M" device. But relapses were found in 23.7% of patients treated with DEC [7].

4. Epithelization of the wound surface occurred in 2.6% of cases30 days after diathermic electrocoagulation, epithelization was in 86% of women treated by using "FOTEK EA 141M". Full epithelization was in 100% of women 45 days after using "FOTEK EA 141 M" device, in 60.5% of women treated with DEC on 45^{th} day after treatment and in all patients on 60^{th} day [1].

5. The algorithm designed for diagnosis and treatment of women with benign diseases of the cervix consists of collection of detailed anamnesis, laboratory examinations such as bacteriological and bacterioscopic examination of the smear, cytological examination, determination of HPV genotype, histological examination, colposcopy (simple and extended), USM of the pelvis [9].

PRACTICAL RECOMMENDATIONS

1. Given that liquid cytology has a higher detection rate of squamous epithelial lesions than conventional PAP smear, the liquid cytology is an effective method for diagnosing of benign diseases of the cervix, also is recommended to be used in a mass screening program for cervical cancer.

2. For treatment of women with benign diseases of the cervix coagulation of endometrioid heterotopias with the "FOTEK EA 141M" device in regime “SPREY” during 3-5 seconds at a power of 50-60 Wt. to a depth of no more than 3 mm for coagulation of endometrioid heterotopias is recommended.

3. Ablation of ectopia and ectropion with the "FOTEK EA 141M" device in regime “SPREY” during 2-4 seconds at a power of 60-70Wt. to 1-2 mm depth is recommended. In case of leucoplakia coagulation in regime “SPREY” during 4-7 seconds at a power of 50-70 Wt. to 2.5-3 mm depth is recommended.

4. Excision of cervical polyps and condylomas with "FOTEK EA 141M" device in regime “SMES” at a power 50-70 Wt. can be used.

5. Treatment with the "FOTEK EA 141M" device is safe, effective, organ-preserving method is recommended for the treatment of women with benign cervical diseases at any age.

List of published scientific works on the subject of the dissertation

1. Qurbanova, C.F., Məcidova, N.B., Əhmədova, L.Y. Uşaqlıq boynunun xoşxassəli xəstəliklərinin müalicəsində diatermoelektrokoaqulyasiya üsulunun qiymətləndirilməsi. // Azərbaycan onkolojı jurnalı,- 2022, N 1, - səh. 70-72
2. Məcidova, N.B. Qurbanova F.A., Kərimova A.C. Uşaqlıq boynunun xoşxassəli xəstəliklərinin diaqnostika və müalicəsinin təkmilləşdirilməsi. // Jurnal Müasir ginekologiya və perinatologiyanın aktual məsələləri, -2019, cild 6, N 04,- səh. 25-32
3. Məcidova, N.B. Uşaqlıq boynunun xoşxassəli xəstəliklərinin müalicəsinin təkmilləşdirilməsi. // Azərbaycan təbabətinin müasir nailiyyətləri, 2020, N1, - səh.78-84
4. Məcidova, N.B. Uşaqlıq boynunun xoşxassəli xəstəlikləri olan qadınların kliniki xarakteristikası. // Sağlamlıq jurnalı, - 2021, N 3,- səh. 53-58
5. Məcidova, N.B. Qadınlarda onkoginekoloji xəstəliklərin diaqnostikasında maye əsaslı PAP yaxma və adi PAP – klassik sitoloji üsulların müqayisəli təhlili. // Jurnal Müasir ginekologiya və perinatologiyanın aktual məsələləri, - 2022, cild 9, N 01,- səh. 37-42
6. Məcidova, N.B. Xoşxassəli uşaqlıq boynunun xəstəliklərinin risk faktorlarının yaş qrupları üzrə təhlili.//Tibb Jurnalı, - 2022, N 2,- səh. 67-63
7. Majidova N.B. Modern methods of treatment of benign diseases of the cervixin women. // Bisnik problem biologii i medicine / Bulletin of problems in biology and medicine.-2022, vol.2, t.1(154), p. 204-207
8. Majidova N.B., Gurbanova C.F., Gurbanova F.A. Impotance of Cytological Screeninq in the Diaqnosis of Cervical Diseases. // Ukraininan Journal of Medicine, Biology and Sport. -2022, vol. 7, N 3(37), p.159-164
9. Majidova N.B.A modern view on the etiology and pathogenesis of cervix diseases. // 5 uluslararası koru gebelik doğum lohusalık kongresi, - Türkiyə, 2022, -p. 482-483

10. Majidova N.B. The role of reproductive function in the development of non-malignant diseases of the cervix. // "World Gynecology 2022: 3rd Global Virtual Summit on Gynecology, Obstetrics & Women's, 2022,vol. №2 - p.47

11. Qurbanova, C.F., Məcidova, N.B. İnsan papillomavirusu ilə əlaqəlı olan uşaqlıq boynu neoplaziya risklərinin qiymətləndirilməsi. // Summary of the scientific conference dedicated to the 60th anniversary of the Surgery Center named after M.A. Topchubashov - Baku, 2022, №2 - page 73

12. Курбанова, Д. Ф., Меджидова, Н. Б. Сравнительный анализ различных методов лечения заболеваний шейки матки в репродуктивном возрасте. // Репродуктивное здоровье Восточная Европа, - 2023, том 13, №6 –с. 614-622

13. Majidova N.B., Gurbanova C.F., Ali-zade., Hasanova A., Mikailzade P. Characteristics of Clinical and Diagnostic Aspects of benign Diseases of Cervix in Women // World Academy of Science, Engineering and Technology International Journal of Health and medical Engineering Vol 17, №11,2023

List of abbreviations

AGUS – atypical granular cells
APC – argon plasma coagulation
ASC-H – internal injury of differentiated squamous cell epithelial (Squamous cell carcinoma)
ASCUS – atypical squamous cells of unknown significance
CC – cervical cancer
CG – control group
CIN – cervical intraepithelial neoplasia
DEC – diathermic electrocoagulation
HSIL – highly differentiated squamous intraepithelial lesion
HPV – human papillomavirus
LSIL – low differentiated squamous intraepithelial lesion
NiLM – normal, no intraepithelial damage
WHO – World Health Organization
PCR – polymerase chain reaction

The defence will be held on “10” “June” 2024, at 16:00 at the meeting of the Dissertation council ED 2.06 of Attestation Commission under the President of the Republic of Azerbaijan operating at Azerbaijan Medical University

Address: AZ 1022, A. Gasimzade street 14, Baku.

The dissertation is available in the library of the Azerbaijan Medical University.

Electronic versions of the dissertation and its abstract are available on the official website of the Azerbaijan Medical University (http://www.amu.edu.az).

Abstract was sent to the required address on “___” “_____” 2024

Signed for print: 01.05.2024
Paper format: 60 x 84 1/16
The volume: 35.500 characters
Number of copies: 20