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Combination therapy of uterine cervical ectopy in young nulliparous women

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Abstract

Actuality of the study of cervical pathology is caused by a significant degree of abnormality detection in young nullipara and the probability of further malignancy, especially if it is associated with papillomavirus infection. According to the literature data uterine cervical ectopy occurs in 38.8 % of the female population and in 54.2 % of gynecological patients; 49.2 % of women with ectopy are under 25 years of age. Increasing frequency of cervical pathology background in nulliparous women, correlates to the growth of diseases of the genital system, sexually transmitted infections, including human papillomavirus of high oncogenous risk. These abnormal conditions attract practitioners' and scientists' attention, as they can be the basis of malignancy. The research is based on examination of 52 nulliparous women from 18 to 25 years of age (average age was 22.3 ± 0.42 years) with diagnosed cervical ectopy on the background of hormonal dysfunction. Depending on the chosen treatment, women were divided into 2 groups. Group I included 25 women. They were made argon plasma coagulation on the 5th-7th day of menstrual cycle, depending on the duration of their menstrual discharge. The treatment in this group of patients was characterized by the administration of hormonal contraceptive drug "Jazz plus" from the first day of the menstrual cycle on which APC was scheduled, with further drug administration for the period of 6 months. Group II counted 27 women, who were made the argon plasma coagulation only. The use of minipill hormone oral contraceptive combined with argon plasma coagulation of the cervix in young women provides an opportunity to accelerate regeneration processes of multilayer squamous epithelium and normalize the menstrual function and level of sex hormones.

Keywords: cervical ectopy; nulliparous women, argon plasma coagulation.

1. Introduction

Preservation of reproductive health of the female population is an integral part of the demographic policy. That is why oncological morbidity of women is one of the problems that need solving at the State level. Over the past two decades there have been significant changes in the structure of cancer pathology. Incidence rate among women of reproductive age is noted. Cervical cancer ranks second in the structure of cancer pathology of the female reproductive organs in Ukraine. The share of reproductive age women among all ill with cervical cancer is 48.5 %. In a world the increasing number of dysplasia in young women up to 30 years, a growing number of elementary forms of cancer at the age of 33-34 years, and mortality in the age range 25-49 years are observed [1].

Actuality of the study of cervical pathology is caused by a significant degree of abnormality detection in young nullipara and the probability of further malignancy, especially if it is associated with papillomavirus infection. According to the literature data endocervicosis (ectopy) occurs in 38.8 % of the female population and in 54.2 % of gynecological patients; 49.2 % of women with ectopy are under 25 years of age [2]. Increasing frequency of cervical pathology background (including endocervicosis) in nulliparous women, correlates to the growth of diseases of the genital system, sexually transmitted infections, including human papillomavirus (HPV) of high oncogenous risk [3]. These abnormal conditions attract practitioners' and scientists' attention, as they can be the basis of malignancy [4].

Investigation of the etiology and pathogenesis of cervical diseases background illustrates the important role of sexually transmitted infections in the development of this pathology (STD) [5]. Epidemiological data have clearly shown that genital papillomavirus infection is a real risk factor for precancerous changes and cervical cancer. In the process of studying the interrelation between HPV and cervical pathology the following data were detected: oncogenous HPV carriers were in 76 % of cases, 48 % of patients with ectopy without cell abnormalities had HPV, and human papillomavirus was present in 100 % of patients with epidermoid carcinoma and cervical neoplasia [6].

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According to many scientists the risk factors of HPV infection are early sex life, frequent change of sexual partners and a large number of sexual partners (more than 3 sexual partners), the presence of STIs, dysimmunity. Currently more than 200 types of HPV are known and more than 40 of them can contaminate the genital tract and which are divided into groups of high and low oncogenic risk [7].

By ectopic zone the place of microflora persistence which has all conditions for maintaining chronic inflammation is meant. Immature epithelium in the transformation zone of girls in the age under 18 years in the first years after beginning of sexual life is considered to be especially susceptible to infections [8].

While cervix inflammation is getting chronic pathological cycle supporting the existence of ectopic nidi occurs, and the processes of epithelium regeneration are decreased. Due to research results a certain role in support of ectopy is played by connection between immunomorphologic phenomena and epithelium proliferation in exocervix [9].

According to another scientists, the inflammation is not an etiologic factor of hormone-dependent ectopys [10]. It can play only a secondary role. Lymphohistiocytic and lymphoplasmacytic infiltration in underlying stroma is, as a rule, of diffuse nature. Predominance of plasma cells on lymphocytes is often observed, and among the latter small lymphocytes more commonly seen. Similar infiltrates consisting of immunocompetent cells have nothing in common with inflammation and are most likely to be the result of metabolic processes activation.

In medical literature the term "congenital erosion," i.e. cervical ectopy in nulliparous women is often found. This question has been a subject of debate for a long time. Many authors believe that all cervical ectopies in nulliparous women are congenital, and exist in girls in their pubertal period, and are detected for the first time with the beginning of sexual life [8].

Acquired ectopy of columnar epithelium is regarded as a polyetiologic disease, caused by the interaction of a number of factors. Acquired cervical ectopies are caused by endogenous and exogenous factors including mechanisms maintaining pathological differentiation of cervix reserve cells into columnar epithelium. Exogenous factors include: infectious – viral (early sex life, a large number of sexual partners, inflammations of genital organs in the history), traumatic (cervical trauma during delivery and abortion, the use of barrier methods of contraception). The endogenous factors include: hormonal hemostasis disorders (menarche in the age under 12 years, disorders of menstrual and reproductive functions), immune changes (presence of chronic extra genital and gynecological diseases, occupational hazards). Hereditary predisposition, the influence of combined oral contraceptives and smoking on the development of cervix ectopia are discussed [11].

Optimal methods of background diseases treatment in young nulliparous women, are such that combine an effective influence on the pathological process not causing traumatic cervical injury and negative influence on the reproductive health of a woman and the future course of delivery. Among the modern methods of treatment of cervical pathology with the use of nidus destruction are the following: chemical, cryogenic and laser destruction, diathermocoagulation, radio wave therapy and argon plasma coagulation. The spectrum of the use of these methods for young nulliparous women is limited to those that do not leave cicatricial deformity on the cervix. Among the latter chemodestruction, laser vaporization, and argon plasma coagulation should be given attention to.

The duration of medical rehabilitation of patients, the processes of epithelium regeneration and associated with it possibility of infecting, pathological proliferation and epithelium and connective tissue metaplasia are important in the choice of destruction method [8].

The aim of the work was to study the method of complex treatment of endocervicosis in nulliparous women, with abnormalities of menstrual cycle, using the local nidus destruction by method of argon plasma coagulation combined with administration of hormonal contraceptive medications in postoperative period, in the context of the study of cervical epithelium regeneration processes, colposcopic assessment in dynamics, complications after the treatment.

2. Materials and Methods

The research is based on examination of 52 nulliparous women from 18 to 25 years of age (average age was 22.3 ± 0.42 years) with diagnosed benign cervical pathology on the background of hormonal dysfunction.

The women were selected for the study after the following procedures: the initial examination, questionnaire survey, simple and extended photo-colposcopy, cytologic screening of smear from exocervix and endocervix, screening for sexually transmitted infections, determine HPV and its type, taking cervical biopsy for histological examination.

Hormonal dysfunction was diagnosed on the basis of menstrual cycle disorders complaints, ultrasound investigation and hormonal screening. In assessing menstrual functions the attention was paid on the age of menarche, character of the menstrual cycle, the duration and the character of menstrual and intermenstrual discharge, the presence of algodismenorrhea and premenstrual syndrome. Hormone research for identification of hormones in blood serum (estradiol, progesterone, testosterone, luteinizing and follicle-stimulating hormone, prolactin) was made on the 7th-9th, 19th-21th days of menstrual cycle by the radioimmunoassay technique using standard test kits.

Depending on the chosen treatment, women were divided into 2 groups. Group I included 25 women. They were made argon plasma coagulation (APC) on the 5th-7th day of menstrual cycle, depending on the duration of their menstrual discharge. The treatment in this group of patients was characterized by the administration of hormonal contraceptive drug "Jazz plus" from the first day of the menstrual cycle on which APC was scheduled, with further drug administration for the period of 6 months. Group II counted 27 women, who were made the argon plasma coagulation only.

Destruction of the cervix pathologically altered areas was made by argon plasma coagulation of tissue using the apparatus "FOTEK-EA-142" («FOTEK-EA 142») in "Spray" mode, 36 W power, argon consumption – 7 liters per minute. Coagulation was made by argon plasma torch circularly from the periphery to the center within the healthy tissue until appearance of light yellow cervical tissue. APC is a method of monopolar high-frequency surgery, in the course of which the energy of high-frequency current is applied to the tissue by the electrode in non-contact way with the use the ionized argon gas (plasma), and the argon plasma torch is made between the electrode and the tissue. Under the influence of the torch on the tissue the local heating and coagulation not more than 3 mm deep occurs [9, 12].

The medication "Jazz-plus" is chosen for hormonal correction of menstrual cycle due to its unique dosing regimen – 24 + 4 and the presence of levomefolate calcium 0.451 mg in its

composition. The dosing regimen helps to reduce the hormone fluctuations associated with the menstrual cycle which are observed when the standard 27/7 dosing regimen for hormonal oral contraceptives is used. Levomefolate calcium is a salt of natural folic acid. The folate deficiency correlates with increased risk of neural tube defects in newborns. Prevention of folate deficiency is recommended before the onset of pregnancy in order to achieve a proper folate status in early stages of pregnancy. That is why “Jazz-plus” is actual for use in young nulliparous women who are planning a pregnancy, which are under the investigation.

Patients diagnosed for pathogenic organisms or human papilloma viruses, were administrated anti-inflammatory and immune-modulating therapy taking into account the discharged microflora before starting the specific treatment of endocervicosis.

The studied groups were matched and statistically homogeneous. The results of treatment in both groups were evaluated on the 30th and 60th days after the start of treatment.

3. Results and Discussion

As a result of the study of patients' menstrual function it was found that 29 patients (55.77 %) had their menarhe under 12 years of age. Three patients (5.76 %) began to menstruate after 15 years of age. As regards abnormalities of the menstrual cycle, the hyperpolymenorrhea was detected in 18 women (34.61 %) that constituted 9 patients in each group; algodysmenorrhea was diagnosed in 33 (63.46 %) cases, 16 of which were in group I and 15 in group II. Irregular menstrual cycle was observed in 23 women (44.23 %), 12 of which were in group I and 11 in group II.

In patients with algodysmenorrhea the pain sensation in the lower abdomen and the lumbar area during menstruation, nausea, weakness, and irritability disappeared in 8 of 9 patients (88.89 %) in group I and 5 of 9 women in group II (55.56 %). Normalization of menstrual cycle for 6 months was observed only in patients and group I in the course of treatment with hormonal medication.

Colposcopic examination revealed round scarlet cervical ectopy with smooth even fine-grit surface, and a clear margin of two epithelium types. In most cases, ectopy extended to zone II on the periphery – 31 women (59.62 %) and to zone III in 17 patients (32.69 %), in 4 cases ectopy was limited to zone I (7.69 %). The external os was round or fissured. In 5 cases (9.62 %) plicae semilunares covered with sharply defined big caruncles were found on anterior and posterior lips of cervix uteri. In five patients (9,62%) ectopy combined with acetowhite epithelium and iodine negative zone. Incomplete benign transformation zone in the form of pale-pink “flames”, extending onto the columnar epithelium from the periphery of ectopy to the cervical canal was found in 11 cases (21.15 %).

On the 30th day following the treatment the colposcopic examination showed the following results: in 22 women (78.51 %) of group I and 16 patients (64.0%) of group II the zones II and III were covered with multilayer squamous epithelium, in some parts adaptive vascular hypertrophy was found. Under the influence of acetic acid vessels were contracted moderately. Schiller test with newly formed epithelium was negative that showed its immaturity. In the first zone the epithelium transformation was not yet complete in all cases.

After 60 days the colposcopic findings were as follows: in 25 cases (92.59 %) of group I in 21 women (84.0 %) of group II ectocervix was covered with multilayer squamous epithelium,

it was pale pink with a little increased subepithelial lymphocapillary network. In some cases the formation open glands was found in zone I.

Assessment of sexual hormones secretion showed that hypoestrogenism was found on the 7th day of the menstrual cycle in 6 patients (24%) of group I and in 7 women (25.93 %) of group II. Hypoprogesteronemia was observed on the 21th day in 8 patients (32 %) of group I and 6 (22.22 %) of group II.

In the study of sex hormones secretion after 6 months of treatment in women of group I the normalization of hormone concentration was found out. Pathological hormones secretion indices in patients of group II hardly differed from the original values.

It should be noted that 2 patients in group I got pregnant after treatment.

4. Conclusions

Benign cervical pathology in young nulliparous women concomitant with dishormonal states is the most commonly comorbid with algodysmenorrhea, combined with irregular menstrual cycle and hyperpolymenorrhea. Cervical ectopy affected by hormonal disorders is characterized by colposcopic peculiarities. Hyperestrogenism affected by progesterone deficiency stimulates epithelium proliferation pathological processes in the zone of ectopia altering differentiation of cells.

The use of minipill hormone oral contraceptive combined with argon plasma coagulation of the cervix in young women provides an opportunity to accelerate regeneration processes of multilayer squamous epithelium and normalize the menstrual function and level of sex hormones.

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