MODERN ASPECTS OF PREDICTION AND TREATMENT OF ENDOMETRIAL HYPERPLASIA IN THE PERI-MENOPAUSAL PERIOD.

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Summary. *Hyperplastic processes of the endometrium (HPE) are the most common pathology in gynecology, especially in women in perimenopausal age and are of significant value in the biomedical and socio-economic problem. According to many authors, almost 50-60% of women of late reproductive age and in the period of perimenopause suffer from HPE. The significant clinical significance of HPE lies in the fact that they are one of the main causes of uterine bleeding in women aged 35-55 years and their hospitalization. Another reason for the close attention to HPE is the possibility of their malignant transformation, since atypical hyperplasia progresses to invasive cancer with a frequency of up to 50% of cases. The above risk of developing malignancy of glandular hyperplasia and endometrial polyposis occurs in 4-5% and can reach up to 10% in peri-postmenopause. According to many authors, atypical hyperplasia progresses to invasive cancer with a frequency of up to 50% of cases. In this article, we decided to give opinions on this issue from all sides.*

Relevance. In peri- and postmenopausal women, pathological processes in the endometrium are most often asymptomatic, but the risk of malignant neoplasms is higher than the general population indicators, especially in the presence of bleeding and ongoing relapses of pathological processes in the endometrium.

Given that this age period is the peak of the incidence of endometrial cancer, effective early diagnosis and treatment of endometrial proliferative processes, which serve as a prerequisite for the onset of a malignant process, is one of the main preventive measures for this disease.

Hyperplasia due to dysfunction of cells is a precancerous condition; in some cases it is asymptomatic and its presence can be found out only after a diagnostic examination. however, most often outwardly endometrial hyperplasia is manifested by hormonal cycle disorders [4,19,24].

But in 30-40% of patients in the peri and postmenopausal period of life, GE can occur under conditions of a normal hormonal background for them due to the suppression of apoptosis processes, a violation of the receptor apparatus of the endometrium in relation to growth factors. An important achievement of recent years in modern gynecology is the determination of the heterogeneity of pathological processes in GE, including the growth of either normal polyclonal endometrium under the influence of hyperestrogenemia of various origins or focally altered abnormal monoclonal endometrium, which clearly defines two main paths in GE: hyperplasia or neoplasia.With the modern approach to the treatment of HE, it is first of all necessary to assess the presence or absence of cellular and then tissue atypia. Based on the above, the pathogenesis of HE should not be considered as a consistent increase in the severity of proliferative, cellular and structural changes, since the pathogenesis and clinical course of endometrial hyperplasia and neoplasia are heterogeneous.

Etiology and pathogenesis of endometrial hyperplasia.

Despite the fact that GP can be asymptomatic and not cause any discomfort to a woman, it poses a certain danger to her health, reproductive function and even life due to its complications, and therefore, with a long course without treatment, it can be a background for the development of endometrial cancer.

According to clinical statistics, in recent years there has been a progressive increase in the incidence of endometrial cancer. Every year, about 150,000 new patients with uterine cancer are diagnosed in the world and 42,000 women die from this pathology. The maximum incidence is

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observed at the age of 55-65 years and is 71.2 cases per 100,000 women. In 20-25% of cases, the disease is diagnosed in reproductive age, in 5% - in patients younger than 40 years.

The relationship between estrogen production and growth (proliferation) of the endometrium is obvious. Endometrial proliferation is a normal part of the natural menstrual cycle and occurs during the follicular or estrogen-dominant phase.

With prolonged estrogenic stimulation due to endogenous production of hormones or their exogenous administration, simple proliferation turns into endometrial hyperplasia. endometrial hyperplasia is "abnormal proliferation of both glandular and stromal elements of the mucosa with a violation of their histological architectonics."

According to the classification of the World Health Organization (2014.) endometrial hyperplasia is divided into two groups: hyperplasia without atypia and hyperplasia with atypia - endometrial intraepithelial neoplasia.

Some authors combine simple and complex hyperplasia without atypia into a single category - “hyperplasia”, and for atypical hyperplasia and adenocarcinoma they use the concept of “endometrial neoplasia”. Researchers at the Royal College of Obstetricians and Gynecologists indicate that the risk of developing endometrial cancer in HE without atypia is less than 5% over 25 years and that most cases of HE without atypia regress spontaneously over subsequent years. It should be noted that these data were obtained from the guidelines of the USA, China, Canada for the management of patients with endometrial hyperplastic processes. In routine practice in our Republic, gynecologists are guided by the "Standards for the diagnosis and treatment of gynecological diseases in medical institutions of the healthcare system of the Republic of Uzbekistan" 2018.

Endometrial hyperplasia is an abnormally increased proliferation of endometrial glands that are irregular in shape and size. This pathology differs from typical anovulatory manifestations primarily in the degree and volume of histological changes in the endometrium. Risk factors for the development of this pathology include early menarche, late menopause, no history of childbirth, metabolic syndromes, obesity, ovarian-menstrual cycle disorders, endocrine infertility, polycystic ovary syndrome, estrogen-secreting ovarian tumors, hormone replacement therapy in postmenopause [5,11].Simple hyperplasia does not often progress to carcinoma, but is still considered a definite risk factor as a precancerous condition. With this type of hyperplasia, excessive proliferation of glandular elements and endometrial stroma is noted. this form of hyperplasia should be differentiated from the normal variant of the structure of the endometrium in the perimenopausal period with cystic involution, which is not a pathological condition.

Compound endometrial hyperplasia is an abnormal proliferation of glandular elements without concomitant proliferation of stromal elements. Many authors believe that adenomatous hyperplasia is a true intraepithelial neoplastic process, and it can be detected microscopically as very small foci against a background of normal proliferative endometrium.

Atypical hyperplasia is characterized by cellular atypia and impaired maturation and is a particularly serious precancerous condition, characterized by a 20-30% risk of malignant transformation.

Endometrial polyps are focal hyperplasia of the endometrium, often arise from a hyperplastic basal layer of the endometrium and consist of stroma and glands, the lumen of which can be expanded, the so-called glandular and glandular cystic polyps. Fibrous polyps are connective tissue formations, often collagenized, without or with a very small number of glands.

In the pathogenesis of hyperplastic processes of the endometrium, metabolic and endocrine disorders have a significant place. However, hyperplastic processes of the endometrium can also develop with undisturbed hormonal ratios. The development of science in molecular biology, medical genetics, clinical immunology contributed to the identification of a complex system of factors involved in clinical regulation.Along with female steroid hormones, a number of biologically active

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compounds are involved in the regulation of the proliferative activity of endometrial cells: growth factors, cytokines, arachidonic acid metabolites, as well as the system of cellular and humoral immunity. Scientists around the world have proven that in tissue homeostasis and the pathogenesis of proliferative diseases, an important role belongs to the imbalance between the processes of cell proliferation and programmed cell death. The resistance of endometrial cells to apoptosis leads to the accumulation of altered and excessively proliferating cells, which is a characteristic feature of neoplastic changes in the endometrium. As stated above, the pathological transformation of the endometrium is a complex biological process that affects all parts of the neurohumoral system of a woman's body.

The presence of an active estrogen receptor apparatus of the uterus can cause endometrial hyperplasia under conditions of relatively low estrogen levels, and this process may be associated with local dysregulation of cell proliferation and local changes in tissue metabolism.

In addition to systemic changes, an adequate response of the endometrium to hormonal effects is of great importance in the formation of HPE. The role of disturbances in hormonal-receptor interactions in the development of HE, which are modulated by specific cytoplasmic and nuclear receptors, is widely discussed in the literature. These disorders in HPE may be associated with a deficiency of progesterone receptors in the cellular elements of the mucous membrane of the uterine body (Kuznetsova I.V. 2009., Sukhikh G.T., Shurshalina A.V. 2010). There is an opinion that PGEs can be genetically determined.

According to a number of authors, the occurrence of HPE is promoted by hereditary burden, damaging effects during fetal life, diseases during puberty and associated disorders of menstrual, subsequently reproductive function and previous gynecological diseases, surgical interventions on the genitals according to Dobrokhotova Yu.E. and Saprikina L.V. (2021), GE women had menstrual irregularities in 46.92% of cases, aggravated heredity in 34.62% of cases, and reproductive dysfunction (20%).

From the modern point of view, endometrial hyperplasia is considered as a polyetiological pathological process; many different reasons can contribute to the progression of this pathology. Based on numerous studies, it has been proven that one of the necessary conditions for the development of endometrial hyperplastic processes is absolute or relative hyperestrogenemia (Kuznetsov I.V. 2009., Kiselev I.V. 2011., Sheshukova N.A. 2011)

In addition to estrogenic stimulation, which is the main etiological factor in the development of the disease, factors such as immunosuppression and infection may also be involved in the pathogenesis of HE. According to many authors, a retrospective analysis revealed a twofold increase in the number of cases of HE in the group of kidney transplant recipients with abnormal uterine bleeding compared with control patients without a transplant [6,14].At the same time, information about the features of systemic immunity in tumors of the female genital organs is scarce and ambiguous, the issue of impaired immune system in patients with GE remains debatable and requires clarification, since the tactics of managing and treating patients largely depend on how affected the patient's immune system is. . To optimize the existing methods of treatment and prevention of HE, a deeper study of the immunological aspect of the development of this pathological process is necessary.

Despite many scientific studies on this pathology, the molecular and biological mechanisms of their development and its influence on the increase in the risk of malignancy of the process, the issues of prediction, early diagnosis and treatment of its subclinical forms are still not fully understood and scientifically substantiated.

Determination of risk factors and preclinical diagnosis of endometrial hyperplasia.

The most basic direction of scientific research remains the assessment of risk factors for the development of endometrial hyperplasia and its malignant transformation. According to Klinyshkova

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T.V., Tuchaninov D.V. and Frolova N.B. (2020), risk stratification in population categories is the main optimal step in planning an individualized management strategy for women with endometrial hyperplasia. Despite a significant number of research works devoted to this problem, a unified scale for assessing the risk of developing GE has not yet been developed and is often very controversial.

The main risk factors for the formation of endometrial hyperplasia in the perimenopausal period of women's life are currently considered by many authors to be such pathological processes as diabetes mellitus, obesity, gynecological history factors, and the use of hormonal drugs for various indications. The main factor in the gynecological history, affecting the development of GE and its transition to neoplasia and malignant transformation, many authors consider the absence of a childbirth in the anamnesis. RaglanO. et al (2019) showed a decrease in the incidence of endometrial cancer among patients who gave birth, compared with nulliparous. The above data can be explained by the hormonal changes that occur during pregnancy and are characterized by an increase in progesterone secretion.

Many researchers note that such diseases as endometrial hyperplasia develops mainly in women with one form or another of endocrine-metabolic disorders (EON): hyperinsulinemia (HI), insulin resistance (IR), impaired glucose tolerance (IGT), diabetes mellitus (DM) and overweight.

E.S. Akhmetova et al. (2006) in the study of risk factors for endometrial diseases noted that among the somatic pathology, EON was the most common: obesity, nodular goiter, type 2 diabetes mellitus, respectively, and hypertension.

In 2009 L.N. Bogatyreva, in her work on risk factors for the development of endometrial hyperplastic processes, indicated that in patients with a recurrent form of endometrial hyperplasia, the body mass index (BMI) was 30.4 + -0.62 kg / m2, and 27.8% of them were overweight , 43.1% - suffered from obesity of varying severity.

In 2011, E.V. Korneva et al. in their work showed that among women of perimenopausal age, 71.8% of women showed increased glucose tolerance and insulin resistance, and 66% of patients were overweight. From the above data, it is clear that endocrine and metabolic disorders are one of the main background conditions for the development of proliferative diseases of the endometrium and a manifestation of hormonal imbalance.

According to Kacalska-JanssenO. Et.al (2013) insulin resistance in perimenopausal women was significantly more common and they proved the correlation of insulin levels in the blood after a load test with glucose and with the presence of endometrial pathology. A number of authors have proven that the presence of concomitant diabetes mellitus in patients significantly increases the risk of developing endometrial cancer, without being accompanied by an increase in mortality (Baburin D.I. 2017, Kolesova T.E. 2017. Giovannucci E., Harian D.M., Archer M.C., et al. 2015).Thus, according to the systematic review of Tsilidis K.K. (2015), the incidence of endometrial cancer in patients with diabetes is 1.7 times higher than in women without carbohydrate metabolism disorders. Hyperinsulinemia, which is the main trigger for the development of type 2 diabetes mellitus, this situation is realized through a direct myogenic effect, or through a possible increase in the bioavailability of estrogen, which binds sex hormones. Obesity, insulin resistance, diabetes mellitus were often combined with hypertension in perimenopausal women, and late menopause in this category of patients occurred in 40-50% of cases.

Currently, breast cancer occupies the main place all over the world, and tamoxifen is widely and long-term used in the complex therapy of its hormone-sensitive forms. This drug is a selective ER modulator, the therapeutic effect of which is achieved by antagonistic action against the tumor ER, while the effect of the drug on ERb leads to negative effects in the form of an increase in the incidence of endometrial pathology, including hyperplasia, atypia and malignancy (Katzellenbogen B.S., Katzellenbogen J.A. 2000). It can be assumed that rational metabolic correction of hormonal and EON in patients with endometrial hyperplasia in combination with metabolic syndrome and a

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high risk of malignancy will help reduce the risk of endometrial cancer. To achieve this goal, it is necessary to develop both methods for predicting and early diagnosis of HE against the background of the metabolic syndrome, and options for the rehabilitation of these patients.

The results of the above studies allow us to draw the following conclusions: risk factors for the development of hyperplastic processes and endometrial cancer are hyperestrogenemia, obesity, hypertension, impaired carbohydrate metabolism, diabetes mellitus, late menopause, no history of pregnancy and childbirth.

Early markers and prognostic criteria for preclinical diagnosis of endometrial hyperplasia.

In most countries of the world, there is an increase in the incidence of endometrial cancer.According to the statistics of our Republic of Uzbekistan, over the past 5 years, this pathology has increased by 23.6%. It is known that the development of endometrioid adenocarcinoma is associated with endometrial hyperplasia, especially its recurrent forms, however, data on its prevalence are extremely scarce, since there is no official registration of this insidious pathology, although the assessment of the incidence of HE plays an important role not only in the aspect of management tactics associated with uterine bleeding women in the perimenopausal period, but also to prevent the development of endometrial cancer. Proliferative processes in the endometrium are considered as a precancerous condition with varying degrees of probability of malignancy [1,20].

The frequency of malignancy for HE without atypia if is up to 1-3%, while for women with atypical hyperplasia and endothelial intraepithelial neoplasia, it is more than 30% (SobczukK 2017., Selen S. Et.al. 2020). Such a close relationship and a steady increase in the incidence of HE and endometrial cancer dictates to specialists and scientists the need to search for effective markers for preclinical diagnosis and prediction of this formidable pathology in patients of late reproductive age.

Screening methods for diagnosing HE are transvaginal ultrasound, with an ambiguous echographic picture, it is possible to perform HSG, less often aspirate from the uterine cavity. Hysteroscopy and separate diagnostic curettage of the uterine mucosa can be reliable diagnostic methods.Hysteroscopy allows for direct visual examination of the endometrium and directed biopsy of suspicious areas, it also makes it possible to diagnose polyps, submucous forms of fibroids and various structural anomalies of the uterine cavity. The final diagnosis is verified on the basis of a histological examination of the endometrium.

The clinical picture of GE is characterized by the so-called anovulatory uterine bleeding, which usually occurs after a delay in menstruation and they can be prolonged with moderate blood loss or profuse, profuse. With GE, sometimes appear "unscheduled" spotting, especially while taking menopausal hormone therapy (MHT). The 2019 Canadian Guidelines for the Management of Patients with GE stated that it was intermenstrual bleeding and manifest bleeding in postmenopausal age that may be associated with an increased risk of endometrial hyperplasia and it is often combined with mastopathy. With large endometrial polyps, cramping pains in the lower abdomen can be observed, but sometimes polyps can remain asymptomatic, especially in postmenopausal women.

Ultrasound examination (ultrasound) of the pelvic organs (without bleeding) is of great informative value for the prediction and early diagnosis of endometrial hyperplasia, especially its pathological forms, and is the main prognostic marker. Transvaginal ultrasound scanning is a highly informative, non-invasive, safe method for diagnosing endometrial hyperplastic processes. This method is performed in order to determine the pathology of the endometrium on the 5th-7th day of the menstrual cycle in women of perimenopausal age; normally, the M-echo should not exceed 5-7 mm. With an M-echo value of less than 7 mm, the probability of the presence of HE is extremely low. On ultrasound, the hyperplastic endometrium has a diffusely heterogeneous echo structure. What can be manifested by the presence of echo-positive and echo-negative inclusions, the absence of a line of closure of the mucous membrane of the uterine cavity and its uneven contour, as well as an indistinct border "endometrium-myometrium".

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The active form of glandular hyperplasia of the endometrium is ultrasonographically manifested by an increase in the weekly increase in the thickness of the mucous membrane up to 5-12 mm in one week, with a maximum height of up to 16-30 mm before the onset of menstrual bleeding. At the same time, at all stages of the cycle, the uterine mucosa can retain a three-layer structure, which is normally inherent in the late stage of the first phase of the cycle with a predominance of echo-negative areas of overdeveloped functional epithelium.With an inactive form of glandular hyperplasia of the endometrium, a homogeneous tissue of medium or high density is determined in the uterine cavity, repeating the outlines of the cavity. In general, the hysteroscopic picture resembles the phase of early proliferation.

With glandular-cystic hyperplasia, filling defects are detected, while changes in the shape and size of the uterine cavity may not occur, and in cases of an endometrial polyp, marginal defects in the filling of the uterine cavity with a wavy contour are determined and have a visual resemblance to the secretion phase.

In addition, for women of perimenopausal age, a discrepancy between the echogenicity of the endometrium and the phase of the menstrual cycle is characteristic. It is best to conduct a study immediately after menstruation, when a thin M-echo corresponds to the complete rejection of the functional layer of the endometrium, and an increase in the anterior-posterior size of the M-echo throughout or locally should be regarded as a pathology. It should be noted that in most cases it is not possible to distinguish glandular hyperplasia of the endometrium from atypical one with ultrasound.

The use of Doppler ultrasound techniques is important for assessing the state of the endometrium; in patients with HE, the blood flow in the spiral arteries is recorded, and in patients without endometrial pathology in the M-echo projection, the blood flow in these arteries is not visualized. It should be noted visualization of blood flow in the spiral arteries, which can be attributed to early markers predicting the development of proliferative processes and the formation of pathological endometrial hyperplasia.

In patients in the perimenopausal period, pathological processes in the endometrium may be asymptomatic. However, the risk of malignant neoplasms may be higher than the general population indicators, especially in the presence of bleeding and recurrence of pathological processes in the endometrium. It should be noted that the diagnosis can be established on the basis of ultrasound screening. Considering that normally, at the end of the perimenopausal period and postmenopause, intraendometrial blood flow is not visualized during Doppler examination, it can be assumed that vascularization of the endometrial cavity in postmenopause is a diagnostic criterion for endometrial hyperplasia with atypia. It should be noted that there is often a discrepancy between the conclusion of an ultrasound scan and the results of a histological examination, as a rule, difficulties arise in the differential diagnosis of the pathology of the endometrium and submycotic myoma nodes of small sizes - up to 1 cm in diameter. as about the presence or absence of HE [6,10,16].The recognition of GE is of particular importance for the choice of treatment and prevention of endometrial cancer, and the diagnosis of GE requires histological examination of endometrial tissue. Endometrial biopsy should be performed in accordance with accepted algorithms, with special attention to women 40 years of age and older or with a body mass index of 30 kg/m2 or more [13,16,23].

To control treatment, as well as in the order of screening examination of women, there is a need to use cytological methods for studying the contents of the uterus, obtained by aspiration, but this method does not give a clear idea of the nature of endometrial hyperplasia, and therefore, it can mainly be used for the selection of patients for further detailed morphological study.

The endometrium is a functionally active layer of the uterus, which is extremely sensitive to hormonal imbalances in the body. Microscopically, during the development of hyperplastic processes in the endometrium, the architectonics of the functioning layer of the endometrium is disturbed,

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undifferentiated basal, functional layers are determined on sections of the endometrium, and the most characteristic feature of this process is an increase in the stromal and glandular components.

When glandular-cystic hyperplasia is detected, the glands may be tubular, cystic, or branching.As the time of action of estrogens, which is not compensated by the effects of progesterone, increases, cystic glands appear, tubal metaplasia develops, blood clots form in small vessels, and in adjacent areas, the stroma is destroyed and reactive changes in the epithelial cover develop. When examining the average value, the frequency of occurrence and the degree of proximity of the glands change from one field of view to another, this can be regarded as an important marker for predicting pathological endometrial hyperplasia and its neoplasia.

After a comprehensive study and the establishment of a clinical and morphological diagnosis, it will be necessary to address the issues of therapy, evaluation of the effectiveness of treatment and the choice of the optimal gynecological tactics for managing women of perimenopausal age.

Tactics of management and treatment of women in the perimenopausal period with proliferative processes.

Treatment in women of different ages with identified proliferative processes of the endometrium consists of stopping bleeding, restoring menstrual function in the late reproductive period or achieving atrophy and subatrophy of the endometrium at an older age, as well as preventing the recurrence of pathological proliferative processes of the endometrium.

Hyperplastic processes of the endometrium tend to have a long course and recurrence, they are also characterized by the absence of specific pathological symptoms and the complexity of differential diagnosis [8,15].

The incidence of GE varies depending on its form and the age of the woman from 10 to 30%, most often GE is recorded at the age of 45-55 years, and according to some authors, in 50% of patients in the late reproductive period. The high frequency of recurrence of HE requires the need to improve the tactics of managing patients and revising the principles of hormone therapy [7,12,14,18].

It should be noted that in 30-40% of cases, HE can also occur under normal hormonal levels due to the suppression of apoptosis processes. In the diagnosis of GE, any form of menstrual irregularity is of great importance - from amenorrhea to abnormal uterine bleeding (AMB).

An analysis of the literature data indicates that various approaches to the treatment of HE are currently used - removal of the pathologically altered endometrium, hormonal therapy and surgical treatment.It should be noted that the treatment tactics for GE is selected after the morphological verification of the diagnosis depends on the age of the patient, the presence of somatic and gynecological pathology [8,11,14].

Hormone therapy remains one of the most widely used treatments for HE without atypia. According to scientific studies and various publications, proliferative activity in the endometrium depends on the dose and time of use of estradiol. The concept that free estrogen is associated with an increased risk of endometrial proliferative processes has long been known, however, the combined use of estrogen and progesterone in menopausal hormone therapy (MHT) in women for the conservative treatment of this pathology has become the standard.

The endometrium can be easily protected from the proliferative action of estrogens by following simple rules:

* it is necessary to use specific progestogens as well as estrogens and their doses in a continuous, not cyclic mode;

* it should be noted that normethyltestosterone derivatives are more effective for endometrial protection than pregnane and microdosed progesterone;

* microdosed progesterone and dydrogesterone should be used as the first line of combined MHT;

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* it is important to explain to women about the need to comply with the dosage of progestogens and their duration of use.

The effectiveness of hormonal therapy for HE without atypia, according to a number of researchers, is high and reaches up to 42% [5,9].

Several groups of hormonal drugs are used to treat GE.Progestogens and their ability to cause regression of the endometrium has been proven by many researchers, since progestogens, by increasing the activity of apoptosis, led to a pronounced reduction in the glandular apparatus of the endometrium [4, 17, 19, 21].

A highly selective progestogen that specifically binds to progesterone receptors is dydrogesterone, which has few side effects. For the treatment of HE, dydrogesterone is prescribed 10 mg 2 times a day continuously for 6-12 months under the control of ultrasound monitoring of the M-echo of the thickness of the endometrium. Duphaston has no estrogenic, androgenic or corticoid activity and has an antiestrogenic effect only in some target tissues, including the endometrium. This hormonal preparation does not change the parameters of the coagulation system, blood lipids, glucose, insulin and does not have a significant effect on water and electrolyte metabolism. Unlike other progestogens, it very effectively activates progesterone receptors, and therefore it can be used in cases of impaired endometrial tissue receptivity.

Progestins can be used in any form of GE, the choice of progestin and the mode of its administration must be modified by morphological data. As a monotherapy for GE, many authors recommend the use of GnRH agonists based on the fact that they can have an antiproliferative effect on endometrial cells by binding to high-affinity specific receptors for gonadotropin-releasing hormones [3,5,20,22].

Combined oral contraceptives (COCs) - may be the drug of choice for simple endometrial hyperplasia diagnosed in women of active reproductive age. It is optimal to carry out 6-12 cycles of taking drugs according to the usual standard scheme. Given the polyetiology of endometrial hyperplasia, since infectious and traumatic factors can play an important role in the development of this pathology, it is necessary to carry out complex therapy aimed at eliminating the causative agent of the inflammatory process and reducing the activity of the viral infection. To this end, traditionally, at the first stage of therapy, antibacterial and antiviral drugs are used in combination with immunostimulants, and the second stage of treatment of chronic endometritis should be aimed at restoring the morphofunctional potential of tissues, eliminating metabolic disorders, hemodynamics and activity of the uterine receptor apparatus [2,4,23] .A relapse of the endometrial hyperplastic process may indicate hormonally active processes in the ovaries, which requires clarification of their condition, including visual diagnostic methods (ultrasound, laparoscopy, ovarian biopsy). The absence of morphological changes in the ovaries makes it possible to continue the initiated hormonal therapy with higher doses of drugs or to use a progestogen containing IUDs.

In recent years, in many countries in clinical practice for the treatment of GE by intrauterine exposure to levanorgestrel (LNG), based on the fact that this method provides a sufficiently high concentration of LNG in the endometrium (100-500 times higher than with oral) and reaches a high the effectiveness of the progestogenic effect on the uterus. Mirena is a hormonal intrauterine system that provides contraceptive protection for 5 years and has a number of therapeutic advantages. The mechanism of its action is multifactorial: a decrease in the vascularization of the endometrium; decrease in the level of prostaglandins and inhibition of fibrinolytic activity of the blood.

According to L.V. Tkachenko and N.I. Sviridov 2019 it was found that in 95.4% of patients with pathological endometrial hyperplasia, after 6 months of using the LNG-IUD in the control study, morphological signs of HE were absent, regardless of its form.

In order to reduce the risk of complications of hormone therapy prescribed at any age for endometrial hyperplastic processes, hepatoprotectors, anticoagulants, and antiaggregants are

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recommended in parallel [1,9,18]. The main criteria for the effectiveness of conservative treatment can be the relief of clinical symptoms of the disease, the absence of relapses, and the normalization of menstrual function. It should be noted that none of the currently existing options for conservative treatment is the main etiopathogenetic one, its progress is not excluded during therapy, which may require surgical corrections.

Indications for two-stage surgical treatment of endometrial hyperplasia are low efficiency of hormonal conservative therapy, recurrent endometrial hyperplasia and its transition to neoplasia. Endometrial ablasia can be used as the first stage of surgical correction, which includes electrical destruction of the endometrium using electrodes with a wide base, resection of the mucosa using an electric loop. The recurrence of endometrial hyperplastic processes, as well as the combination of this pathology with uterine myoma or adenomyosis in patients in pre- and perimenopause, requires the expansion of indications for radical operations - hysterectomy.The main method of treating patients with an endometrial polyp is targeted polypectomy, and after removal of endometrial polyps, it is necessary to perform hormonal therapy, the type and duration of which depend on the age of the patients, the morphological structure of the polyp, comorbidity, and the hormonal therapy regimen in perimenopausal age corresponds to those for endometrial hyperplasia without atypia.

In the presence of GE in pre- and menopause, it is reasonable to perform a hysterectomy. The choice of access depends on the presence of somatic and concomitant gynecological pathology, as well as the skills of surgeons.

Prevention of endometrial neoplasia is the elimination of the listed risk factors and, in fact, is aimed at eliminating hyperestrogenism: weight loss, compensation for diabetes mellitus, restoration of reproductive function, normalization of menstrual function, elimination of the causes of anovulation, timely surgical treatment for feminized tumors, etc. However, the most effective measures of secondary prevention are aimed at timely preclinical diagnosis and treatment of background and precancerous endometrial proliferative processes: adequate examination and treatment, screening of women once a year using transvaginal echography, the formation of risk groups with regular targeted medical examination.It should be noted that to date, markers of preclinical diagnosis of the development of endometrial hyperplasia have not been identified, which could be objective predictors of the dynamics of progress or regression of this pathological process and the likelihood of malignant degeneration. Based on clinically significant risk factors, the selection of individual tactics for management, treatment and medical examination is a promising approach to improve the effectiveness of endometrial hyperplasia therapy and improve the lifestyle of perimenopausal women.

Conclusion. Thus, in the context of deteriorating indicators of women's gynecological health, the most promising are the issues of early diagnosis, prevention and correction of conditions leading to the development of the threat of pathological endometrial hyperplasia in women in the critical perimenopausal period of life. The reduction of oncological problems in the late reproductive age of women in our Republic of Uzbekistan depends on how early this pathology is predicted and subclinically diagnosed.

Literature.

1. Kogan E.A., CHernuha G.E., Dumanovskaya M.R., Asaturova A.V. CHastota vyyavleniya i struktura giperplazii endometriya v razlichnye vozrastnye periody // Akusherstvo i ginekologiya. - 2015. № 3. S. 40-44.
2. Ismailova Z.I. Rannyaya diagnostika i profilaktika giperplasticheskih processov endometriya : nauchnoe izdanie / Z. I. Ismailova // Novosti dermatovenerologii i reproduktivnogo zdorov'ya. - Tashkent, 2013. - N3- - C. 127-128

ISSN 2277-3630 (online), Published by International journal of Social Sciences & Interdisciplinary Research., under Volume: 11 Issue: 09 in September-2022
https://www.gejournal.net/index.php/IJSSIR

3. Orazov M.R., Pokul' L.V., CHugunova N.A., Lebedeva M.G. Giperplasticheskie processy zhenskih reproduktivnyh organov: rasshirenie vozmozhnostej diagnostiki i al'ternativnoj terapii. // Medicinskij alfavit, - 2018. T. 2. № 13 (350). S. 45-51.
4. Sinchihin S.P., Kostenko E.V., Stepanyan L.V. Sravnitel'naya effektivnost' gormonal'nyh preparatov dlya podgotovki endometriya k ablacii u pacientok premenopauzal'nogo perioda. // Arhiv akusherstva i ginekologii im. V.F. Snegireva. - 2019. T. 6. № 3. S. 151-156.
5. Strizhakov A.N., Davydov A.I. ZHelezistaya giperplaziya endometriya: principy diagnostiki i gormonal'noj terapii. // Voprosy ginekologii, akusherstva i perinatologii. - 2008. T. 7. № 4. S. 20-2
6. Ashurova N. G., Rahmatullaeva M. M., Navruzova N. O. Rol' kol'poskopii v rannej diagnostike zabolevanij shejki matki //Al'manah molodoj nauki. – 2018. – №. 4. – S. 21-23.
7. Clarke MF, Dick JE, Dirks PB, Eaves CJ, Jamieson CH, Jones DL, Visvader J, Weissman IL, Wahl GM. Cancer stem cells–perspectives on current status and future directions: AACR Workshop on cancer stem cells. Cancer Res. 2006; 66(19):9339-44.
8. Clement NS, Oliver TR, Shiwani H et al. Metformin for endometrial hyperplasia: a Cochrane protocol. BMJ Open. 2016; 6 (8): e013385.
9. Cottreau CM, Ness RB, Modugno F, Allen GO, Goodman MT. Endometriosis and its treatment with danazol or lupron in relation to ovarian cancer. Clin Cancer Res. 2003; 9:5142-4.
10. Dellinger TH, Planutis K, Tewari KS, Holcombe RF. Role of canonical Wnt signaling in endometrial carcinogenesis. Expert Rev Anticancer Ther. 2012. 12(1):51–62.
11. Dolapcioglu K, Boz A, Baloglu A. The efficacy of intrauterine versus oral progestin for the treatment of endometrial hyperplasia. A prospective randomized comparative study. Clin Exp Obstet Gynecol. 2013; 40:122–6.
12. Dong P, Kaneuchi M, Watari H, Hamada J, Sudo S, Ju J, Sakuragi N. MicroRNA-194 inhibits epithelial to mesenchymal transition of endometrial cancer cells by targeting oncogene BMI-1. Mol Cancer. 2011. 10:99.
13. Donnenberg VS, Landreneau RJ, Donnenberg AD. Tumorigenic stem and progenitor cells: implications for the therapeutic index of anti-cancer agents. J Control Release. 2007. 122(3):385–391.
14. Du H, Taylor HS. The Role of Hox Genes in Female Reproductive Tract Development, Adult Function, and Fertility. Cold Spring Harb Perspect Med. 2015; 6(1):a023002.
15. Dueholm M, Hjorth IM. Structured imaging technique in the gynecologic office for the diagnosis of abnormal uterine bleeding. Best Pract Res Clin Obstet Gynaecol. 2017; 40:23-43.
16. Negmatullaeva M.N., Hamdamova, M.T, Hotamova M.T. (2022). Konservativnaya miomektomiya u zhenshchin reproduktivnogo vozrasta. ZHurnal vestnik vracha, 1(1), 62–64. https://doi.org/10.38095/2181-466X-2020931-61-63
17. Negmatullaeva, M.N., Dustova, N. K. (2012). Mochevaya kislota-marker razvitiya preeklampsii. Problemy biologii i mediciny, 1, 26.
18. Tuksanova D.I., Avakov V.E., Nazhmutdinova D.K., Negmatullaeva M.N., Ahmedov F.K. Osobennosti pochechnogo i pechenochnogo krovotoka u beremennyh s preeklampsiej. Rossijskij vestnik akushera-ginekologa. 2013;13(5):41-43.
19. Tuksanova, D. I., SHaripova, M. A. (2018). Osobennosti izmenenij pokazatelej sistemnogo i organnogo krovotoka u zhenshchin pri tyazhyoloj preeklampsiej. Mezhdunarodnyj Kazahsko-Tureckij Universitet “Sovremennaya medicina tradicii i innovacii”.–Kazakstan, 151-155.

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https://www.gejournal.net/index.php/IJSSIR

20. Tuksanova, D. I. (2019). Osobennosti sostoyanie parametrov gomeostaza i kardiogemodinamiki u zhenshchin s fiziologicheskim techeniem beremennosti. Novyj den' v medicine-Tibbiyotda yangi kun-2019, 1(25), 159-163.
21. Tuksanova, D. I. (2019). Features of the state of parameters of homeostasis and cardiodynamics in women with the physiological course of pregnancy. Tibbietda yangi kun.-Tashkent, (1),
22. .Nurkhanova N.O. Assessment of the risk of endometrial hyperplasia in the perimenopausal period. / International Journal of Advanced Research in Engineering and Applied Sciences, 2022. Vol. 11. No. 6. P. 8-15. https://garph.co.uk/IJAREAS/June2022/2.pdf
23. Zaripova D.Ya., Tuksanova D.I., Negmatullaeva M.N. Osobennosti techeniya perimenopauzal'nogo perekhoda zhenshchin s ozhireniem. Novosti dermatovenerologii i reproduktivnogo zdorov'ya. № 1-2.2020 Str.39-42.
24. Zaripova D.Ya., Negmatullaeva M.N., Tuksanova D.I., Ashurova N.G. Vliyanie magnij deficitnogo sostoyaniya i disbalansa steroidnyh gormonov zhiznedeyatel'nosti organizma zhenshchiny. Tibbiyotda yangi kun 2019; 3 (27) Str- 14-18.

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