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COMPLEX DIAGNOSIS AND TREATMENT OF HYPERPLASTIC PROCESSES AND ENDOMETRIAL CANCER

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ABSTRACT

The urgency of the problem of endometrial hyperplastic processes is due to the high risk of their malignancy, especially in women in peri- and postmenopause. The frequency of malignancy of endometrial hyperplastic processes varies within a fairly wide range (0.25-50%) and is determined by the morphological features of the disease, the duration of its recurrence, and the age of the patients. The aim of our work is to optimize the tactics of managing women with hyperplastic processes and endometrial cancer based on the development of an algorithm for diagnosing, treating and predicting the outcomes of therapy for this pathology using modern medical technologies. The complex use of clinical, laboratory, instrumental methods allows you to choose the best methods for diagnosing and treating endometrial hyperplastic processes.

KEYWORDS: *Endometrial Hyperplastic Processes, Endometrial Cancer, Diagnosis.*

INTRODUCTION

Over the past two decades in Russia, as in most countries of the world, there has been a clear trend towards an increase in the frequency of hormone-dependent tumors, and this primarily applies to hyperplastic processes and endometrial cancer (EC). Hyperplastic processes of the endometrium (HPE), precancerous conditions and endometrial cancer are most often found in a socially active group of women of reproductive and perimenopausal ages [4,6].

In most patients, pathological processes of the endometrium develop against the background of previous endocrine-metabolic disorders.These disorders, observed in patients with different frequency, form a clinical syndrome that has a single mechanism of age-related disorders of hypothalamic regulation, characteristic of normal aging and some tumor processes [10].

One of the main factors for the successful prevention of EH is the pathogenetically substantiated management of patients with hyperplastic and precancerous changes in the endometrium, the risk of developing cancerous transformation against their background reaches 23-57% [3]. This

problem is of particular importance in young women, when the question is not only about maintaining health, but also about restoring reproductive function. Among the factors contributing to the emergence of endometrial hyperplastic processes, the leading role is played by hyperestrogenia [5]

It is known that the risk of developing endometrial proliferative processes increases significantly against the background of obesity, diabetes mellitus, polycystic ovary syndrome, in which similar metabolic disorders are observed, such as insulin resistance and hyperinsulinemia, the role of which in stimulating cell proliferation has not been finally determined.

It has been established that, in addition to hormones, other biologically active compounds that perform autoparacrine regulation of cell growth, such as polypeptide growth factors and cytokines, which are closely associated with the immune system, can play a role in modulating the proliferative activity of the endometrium, in addition to hormones. An important role in the pathogenesis of EH and RE is played by genetic predisposition.[5,8,9]

Despite the fact that in recent years there has been an increased interest in the problem of RE, issues of morpho- and pathogenesis, there is a noticeable lag in the diagnosis, treatment and prevention of this disease. To date, a number of medical and organizational issues related to the examination of women in high-risk groups for the development of hyperplastic processes andendometrial cancer, the volume of diagnostic studies during preventive examinations and dispensary observation, the choice of effective screening methods for diagnosis and prevention.[11]

Untimely or inaccurate diagnosis of intrauterine pathology does not always lead to the correct choice of treatment method, long-term drug therapy, an unjustified number of invasive interventions and a large number of radical traumatic operations [2] With a significant number of studies devoted to certain aspects of RE, there are no works that reflect the assessment of the state of this problem at the regional level and open up ways to solve it from a medical and organizational standpoint.

Further improvement of the system of diagnostic and therapeutic measures for hyperplastic processes and endometrial cancer will help reduce morbidity and mortality in this pathology, improve long-term results.

MATERIALS AND METHODS

The paper presents the results of studies conducted on the basis of the Republican Clinical Oncological Dispensary, the Republican Perinatal Center,

The risk factors for the development of hyperplastic processes and endometrial cancer in 1500 patients were studied on the basis of a comprehensive examination. Age, patient complaints, obstetric and gynecological history, past extragenital diseases (diabetes mellitus, hypertension, obesity, diseases of the gastrointestinal tract), concomitant gynecological pathology (uterine fibroids, endometriosis, reproductive dysfunction, infertility) were studied using a specially designed map.

Clinical and laboratory research methods

The clinical examination was carried out according to the generally accepted scheme: the complaints of patients, the time of their appearance were clarified and evaluated, the anamnesis

was studied.At the same time, heredity, the course of pregnancy and childbirth in the mother, birth weight, living conditions at different age periods, the frequency and nature of infectious diseases, concomitant extragenital pathology, surgical interventions, injuries, and stressful situations were analyzed.

Particular attention was paid to the analysis of the formation of the menstrual function, the nature of the menstrual cycle disorder, its dynamics in the course of the disease. The possible causes of the onset and duration of the disease were clarified. An analysis was made of the generative function, previous hormonal therapy and its effectiveness. Gynecological diseases were recorded, in addition to the pathology of the endometrium, as well as previously performed gynecological operations.

A general examination of the patients was carried out, during which the nature of the physique, the condition of the skin (the presence of hirsutism, striae, acne, hyperpigmentation), the measurement of the height and weight of the patients, followed by the calculation of the body mass index (BMI) or the Brey index according to the formula: BMI = body weight (kg) / height (m). Values from 18 to 25 kg/m were regarded as an indicator of normal body weight, from 25 to 30 kg/m - as overweight, more than 30 kg/m - as obesity.

The general clinical examination also included examination and palpation of the mammary glands, a gynecological examination, which assessed the nature of the development of the external genital organs, the condition of the cervix and the condition of the appendages, the presence or absence of adhesions in the small pelvis.To identify the frequency, structure, dynamics of morbidity and mortality from endometrial cancer, a retrospective study of the results of examination and treatment of patients for 2012-2022 was carried out. based on the analysis of medical documents of the oncological dispensary (form No. 025-u) The risk factors for the development of hyperplastic processes and endometrial cancer in 1861 patients were studied on the basis of a comprehensive examination. Age, complaints of patients, obstetric and gynecological history, past extragenital diseases (diabetes mellitus, hypertension, obesity, diseases of the gastrointestinal tract), concomitant gynecological pathology were studied using a specially designed map (uterine fibroids, endometriosis, reproductive disorders, infertility).

RESULTS AND DISCUSSIONS

105 patients with endometrial cancer were examined and treated. The age of the patients ranged from 24 to 55 years, with an average of 42.3 ± 3.1 years; 61 patients were in the reproductive period and 44 were in the perimenopausal period (Table 1).

TABLE 1 DISTRIBUTION OF PATIENTS WITH PATHOLOGICAL PROCESSES OF THE ENDOMETRIUM DEPENDING ON AGE

Age, years	До 30		31-35		36-40		41-45		46-50		51-55		Total	
Number	abs.	%	abs.	%	abs.	%	abs.	%	abs.	%	abs.	%	abs.	%
	4	3,8	17	16,2	19	18,1	21	20,0	26	24,8	18	17,1	105	100

Early onset of menarche (before 1 year) was noted in 5 (4.8%) patients, later than 17 years - in 3 (2.9%), mean age - 14.2 ± 0.66 years; the duration of menstruation ranged from 3 to 8 days, on

average - 4.9 ± 0.18 days; the duration of the menstrual cycle - from 21 to 32 days, on average - 27.8 ± 0.56 days. Anovulatory cycles in history occurred in 11 (10.5%) patients. There were no births in history in 10 (9.5%) women, abortions - in 11 (10.5%).

Of the concomitant extragenital diseases, obesity occurred in 32 (30.5%) patients, diseases of the gastrointestinal tract - in 22 (21.0%), hypertension - in 10 (9.5%), diabetes mellitus - in 8 (7 .6%). Of the gynecological diseases in history, uterine fibroids were in 28 (26.7%) patients, endometriosis - in 19 (18.1%), inflammatory diseases (metroendometritis, salpingoophoritis) - in 15 (14.3%), menstrual disorders - in 11 (10.5%), infertility - in 8 (7.6%), polycystic ovaries - in 5 (4.8%).

All patients underwent diagnostic hysteroscopy with separate diagnostic curettage of the uterine mucosa. Indications for hysteroscopy were various menstrual irregularities, bloody discharge from the genital tract, and ultrasound examination data.

More often, clinical manifestations were associated with concomitant gynecological diseases (uterine fibroids, polycystic ovaries, adenomyosis).

Hysteroscopic pictures in endometrial cancer may be similar to the normal uterine mucosa in one of the phases of the menstrual cycle. In these cases, to make a diagnosis, it is necessary to compare the nature of the hysteroscopic picture with the clinical picture of the disease and the day of the menstrual cycle.

In the anamnesis, 52 (49.5%) of the examined had from 2 to 4 separate diagnostic curettage of the uterine mucosa due to various menstrual irregularities, endometrial hyperplastic processes were detected.

Histological examination of the uterine mucosa in all patients was diagnosed with endometrial cancer; they were prescribed hormone therapy with various drugs (stage I of treatment). After 6 months, against the background of hormone therapy, a control hysteroscopy was performed with separate diagnostic curettage of the uterine mucosa. The list of used hormonal drugs and their effectiveness are presented in Table. 2.

Estrogen-gestagens (monophasic COCs) were used for 6 months in a cyclic mode. They have a permanent (non-cyclic) effect on the level of gonadotropins, slightly reducing it, preventing the proliferation of the endometrium (Logest, Novinet, Marvelon).

Treatment was also carried out with gestagens, derivatives of progesterone and 19-norsteroids. Pure gestagendufaston was prescribed at a dose of 10-20 mg per day from the 5th to the 26th day of the menstrual cycle for 6 months (after diagnostic curettage of the uterine walls).

Danazol - a synthetic derivative of 17 a-ethinylestradiol - causes a state of hypogonadism and atrophic changes in the endometrium. The drug was administered at 400 mg per day for 6 months continuously.

17-hydroxyprogesterone capronate (17 GPC) t has an antitumor effect, inhibits DNA synthesis in tumor cells.It was used at 250 mg intramuscularly 2 times a week in the second phase of the menstrual cycle for 3-6 months.

Medroxyprogesterone acetate (MPA) - an antitumor drug - is a progestogen, does not have estrogenic activity. Suppresses the secretion of pituitary gonadotropins, which prevents the

maturation of follicles, causing anovulation in women of childbearing age. It was prescribed 100 mg 2 times a week for 3-6 months continuously.

At stage II of hormonal treatment, women of reproductive age were prescribed clomiphene, whose action is based on the blockade of estradiol receptors, in order to restore the ovulatory cycle. After its cancellation by the feedback mechanism, GnRH secretion increases, which normalizes the release of LH and FSH and, accordingly, the growth and maturation of follicles. The drug was used from the 5th to the 9th day of the menstrual cycle, 50 mg per day for 2-3 months. This method of treatment was used in 14 patients.

TABLE 2 THE EFFECTIVENESS OF VARIOUS HORMONAL DRUGS IN THE TREATMENT OF ENDOMETRIAL GLANDULAR HYPERPLASIA

Hormonal drug	Duration duration of treatment (months)	Age up to 45 years (n = 61)		Age from 46 to 55 years (n = 44)	
		Effect	No effect	Effect	No effect
Estrogen (COCP) (Logest, Novinet, Marvelon)	6	15	4	—	—
Antiestrogens (danazol)	6	5	3	6	2
Gestagens (duphaston)	6	14	6	4	4
Progestogen (17 - OPC)	3 - 6	4	2	8	4
Progestogen (medroxyprogesterone acetate)	3 - 6	5	3	12	4
Total		43	18	30	14

As can be seen from Table. 2, the effectiveness of hormonal treatment in patients of reproductive age was noted in 43 (70.5%) patients, no effect - in 18 (29.5%), in patients in perimenopause - in 30 (68.2%) and 14 (31.8%) %) respectively. Treatment failure was noted in the form of relapses of endometrial hyperplasia (according to ultrasound data) and repeated uterine bleeding. Recurrences of uterine bleeding were more often observed in patients with uterine myoma, adenomyosis. Thus, the effectiveness of hormone therapy was noted in the reproductive age in 70.5% of patients, in the premenopausal age - in 68.2%. In the next 6 months after hysteroscopy and hormone therapy, 6 patients underwent hysterectomy. Indications for surgery were uterine bleeding, not amenable to hormonal treatment against the background of uterine fibroids or adenomyosis.

Long-term results were followed up in 92 patients with endometrial glandular hyperplasia over a period of 1 to 3 years. In 32 (34.8%) patients, a recurrence of FGE was detected, they underwent transcervical electrosurgical resection of the endometrium, of which 18 women were of

reproductive age and 14 were of the perimenopausal period.

Previously conducted hormonal therapy in this group of patients was as follows: 4 women of childbearing age were prescribed estrogen-gestagens, danazol - 3, Duphaston - 6, 17 OPC - 2, medroxyprogesterone acetate - 3; women in perimenopause: danazol - 2, Duphaston - 4, 17 OPC - 4, medroxyprogesterone acetate - 4.

Of the gynecological diseases in this group, 14 (43.8%) patients had uterine myoma, 10 (31.3%) had adenomyosis (according to hysteroscopy and ultrasound).Thus, in most patients who underwent surgical treatment, there was an increase in the size of the uterus up to 6-7 weeks (75.1%). It was revealed that previously 11 (34.4%) patients had complicated childbirth and abortion (manual separation and separation of the placenta, bleeding with curettage of the walls of the uterus, metroendometritis).

All patients of childbearing age had menstrual irregularities in the form of prolonged and heavy bleeding, and in perimenopausal patients, the main complaint was spotting.

Operations were performed under intravenous anesthesia. For irrigation of the uterine cavity, a 5% glucose solution or a polyglucin solution was used. Operations were performed under close monitoring of the amount of fluid used. Transcervical resection (ablation) of the endometrium was performed according to the method of combined electrosurgical resection of the endometrium. The operation began with ablation of the uterine angles and fundus of the uterus with a ball electrode 2 mm in diameter in the "coagulation" mode with a current power of 50-60 W, then the endometrium was resected with a 4 mm loop electrode in the "cut" mode with a current power of 100-110 W, starting from the back the walls of the uterus, then the side walls and lastly the anterior wall. The endometrium was cut along with the adjacent myometrium in the form of shavings to the area of the internal os in the direction from top to bottom. The operation was completed by coagulation of bleeding areas in the "coagulate" mode, changing the loop electrode to a 4 mm ball electrode with a current power of 50-60 W. The duration of the operation was from 15 to 40 minutes. Intraoperative complications were not observed. In the postoperative period, no treatment was prescribed. 3 patients had subfebrile temperature during the first two days.

In all operated patients, bloody discharge from the uterus lasted from 10 to 30 days, averaging 23.3 ± 1.8 days. In 4 patients, a month after the operation, small spotting was noted for 1-2 days. After the operation, the patients were followed up dynamically: after 3, 6, 12, 24, and 36 months. Long-term results after surgery were monitored in all patients. The nature of the uterine discharge was assessed, and a gynecological examination and ultrasound scanning were performed.

The long-term results of resection (ablation) of the endometrium in patients of the reproductive and perimenopausal periods were analyzed separately. The results obtained are presented in the table. 3. The efficiency of resection (ablation) of the endometrium was higher in the group of patients of reproductive age (94.4%) with endometrial glandular hyperplasia. %).

Amenorrhea occurred in 23 (71.9%) patients, hypomenorrhea - in 6 (18.8%) operated patients. The operation was ineffective in 3 (9.4%) patients. Recurrent uterine bleeding occurred in 1 patient of reproductive age, in 2 - in the period of perimenopause. They underwent a hysterectomy. Hysterectomy was performed in 2 patients aged 42 and 50 years with recurrent

glandular hyperplasia of the endometrium against the background of adenomyosis, one at the age of 54 years with recurrent glandular hyperplasia of the endometrium and uterine fibromyoma. A recurrence of PGE and uterine bleeding occurred in them during the first year after endometrial resection, the size of the uterus corresponded to 6-7 weeks of pregnancy.

TABLE 3 LONG-TERM RESULTS OF TREATMENT OF PATIENTS OF REPRODUCTIVE AND PERIMENOPAUSAL AGE AFTER RESECTION (ABLATION) OF THE ENDOMETRIUM

Period of life	Long-term results		
	Amenorrhea (n = 23)	Hypomenorrhea (n = 6)	No effect (n = 4)
Reproductive (up to 45 years) (n= 18)	12	5	1
Perimenopause (46-55 years) (n = 14)	11	1	2

From the anamnesis, it was revealed that in the group of patients with FGE, early and late menarches were observed in 7.7% of patients, anovulatory menstrual cycles - in 10.2%, infertility - in 7.6%. The ineffectiveness of hormone therapy was noted in 18 (29.5%) patients of reproductive age and in 14 (31.8%) patients of the perimenopausal period, more often in combination with uterine myoma, adenomyosis. The results of endometrial ablation showed the effectiveness of the operation in 90.6% of patients.

In the absence of the therapeutic effect of hormone therapy, recurrence of uterine bleeding and glandular hyperplasia of the endometrium, the small size of the uterus, a hysteroscopic operation, resection (ablation) of the endometrium, is quite effective.

CONCLUSION

The complex use of clinical, laboratory, instrumental methods (transabdominal and transvaginal ultrasound, Doppler, hysteroscopy) allows you to choose the best methods for diagnosing and treating endometrial hyperplastic processes, including endoscopic ones, which significantly reduces the risk of recurrence of this pathology. The development of an endometrial tumor increases the formation of reactive oxygen species in the homogenate of its tissue, and at the same time, antioxidant activity decreases.

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