

Optimization of Approaches to the Treatment of Endometrial Pathology in Women in the Perimenopausal Period with Extragenital Pathology

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Abstract. Prompt diagnosis of menopausal pathologies is one of the principal factors that affects the women life expectancy at the working age at the peak of social activity. The intensions of formation at risk groups are to improve the quality of women`s life in early menopause and to do the prevention of distant complications. Perimenopausal syndrome is accompanied by significant abnormalities in women`s body system in many different forms that depend on specific clinical symptomatic. The major aim of the work is to find clinically justified way of treatment of endometrial pathology in women in the age of 46 to 60 years with extragenital pathology. The main group of patients consisted of two groups that were then divided according to the treatment and prevention approach, and were compared to the control group of healthy women. The notable improvements in the fibrinolysis system were noticed in a Group 1 month after the beginning of the treatment. The Group 1 got magnesium supplements and prophylaxis against TEC. Eventually the cytological findings of the aspirates from the uterine cavity, indicated the absence of atypical or pre-tumorous processes after intrauterine craniocervical surgery. The results of the following research allow to develop pathogenetically substantiated algorithm of treating patients with HPE and adenomyosis in the perimenopausal period (46–60 years old), and also to provide secondary prevention of somatic pathologies. Expected improvements included during next two years after received treatment are: absence of complaints during bimanual examination, decreased uterine size (ultrasound diagnostic), uterine endometrial thickness of 3-4 mm, pathomorphological examination of uterine cavity aspirates.

Keywords: Endometrial hyperplasia, Endometrium, Endometrial neoplasia, Perimenopausal period, Extragenital Pathology, Endometrial pathology, Fibrinolysis system, Female patients

1 Introduction

Statistical data and scientific literature show a steady increase in the high incidence of hyperplastic endometrial processes (HPE) and endometrial cancer [1, 2, 3, 4, 5]. Perimenopausal women are the most susceptible to endometrial cancer, and approximately half of their cancers are the result of low incidence of HPE [5, 6, 7].

The perimenopausal period is associated with a biologic transformation of the female organism, reduction and subsequent elimination of the ovarian function. As a result, the central autonomic nervous system, which has been functioning in a cyclic mode for the last ten years, is overworked, vegetative and psycho-emotional disorders manifest themselves, the general health status is deteriorating and the risk of intrauterine pathology is growing [8]. This is the very period of a woman's life when neurovegetative, psycho-motional and metabolism-endocrine disorders appear together [10, 11, 12].

The relevance of the problem is also due to the fact that 65% to 80% of perimenopausal women have various extragenital pathologies that are contraindications for the use of specific hormonal therapy and surgical treatment [13, 14].

The use of hormones for the treatment of pre-tumours of the endometrium and myometrium has a low level of contraindications. Hormonal therapy is not reasonable for severe forms of pre-tumor mandibular pathology, and often its use is associated with severe complications, including thromboembolic complications [16, 17, 19]. Also, hormonal replacement therapy prescription at early perimenopause and at intact coronary arteries is believed to decelerate formation of atherosclerotic lesions and to result in decreased mortality from cardiovascular diseases [20].

Radical methods (surgical interventions such as suprapubic amputations and uterine extirpation) are traumatic and often lead to organ removal, surgical castration (incidence of ovariectomy after 45 years of age reaches 90.0%), the following psychosomatic problems associated with the loss of menstrual and reproductive function in women. Moreover, surgical and psychological trauma, adverse effects of anesthesia, and reduced manual activity in the post-operative period, in women over 45 years of age, genital and somatic pathologies are risk factors that lead to a high risk of thromboembolic complications (TEC) in this category of patients [21, 22].

The statements above are the reason for the unfortunate state of the issue of immediate, effective, relapse-free and safe treatment of sporadic uterine and endometrial pathology in women in the early reproductive years. Lack of follow-up care, extensive discective treatment without subsequent prescription of adequate treatment or absence of treatment in general lead to recurrence of the disease, its progression to severe forms of hyperplasia (adenomatosis) and endometrial cancer.

The aim of the study is to increase efficacy and reduce the incidence of complications after treatment of endo- and menometrium pathologies in perimenopausal patients with extragenital pathology and menometrium in perimenopausal patients with extragenital pathology through optimization of approaches and organ preservation therapy based on the results of a comprehensive examination for such pathology.

2 Materials and Methods

The clinical, laboratory and instrumentalexamination was performed in 130 female patients with somatic pathology in the perimenopausal period (46–60 years old), who were divided into representative groups. The main group consisted of 100 patients with HPE and adenomiasis. The control group consisted of 30 healthy women without endometrial or myometrial pathology. The main group of patients was divided into two groups according to the treatment and prevention approach. Group I included 50 women who underwent hysteroscopy and intrauterine craniocutaneous surgery, magnesium supplements and prophylaxis against TEC. Patients of the II group (50 patients) underwent hysteroscopy and prophylactic treatment according to the Ukraine's Ministry of Health Protocol (No. 676 of December 31, 2004).Hysteroscopic interventions were performed according to the generally accepted method using a "KARL STORZ" 26050E hysteroresectoscope, Germany, "HOPKINS" optics.

Cryosurgical interventions were performed with the help of "Cryo-Pulse" equipment, where liquid nitrogen was used as a cooling agent. To prevent inflammatory complications in the postoperative period, broad-spectrum antibacterial medications and rectally thrombolytics were administered. Patients with moderate or high risk of TEC were additionally treated with specific low-molecular-weight heparin (LMWH) and non-specified (elastic compression) prophylaxis, as well as treatment with vascular medications for 2-3 months.

The results were optimized through statistical processing of the data using the Microsoft Excel analysis package and the computer programs included in the Microsoft Office Professional 2000 package, Russian Akademik OPEN No Level license.

3 Results

The age of the patients examined and treated by us ranged from 46 to 60 years and averaged 54.2-6.7 years in the Main and 53.1-5.9 in the control group ($p > 0.05$). Depending on the ultrasound and pathomorphological examination, all the patients were divided into the following groups: simple nonatypical EH in 42 patients (42.0%), complex nonatypical EH (23.0%), polyp (lamellar and lamellar-fibrotic) endometrium in 35.0%. All cases of EH were associated with stage I and II adenomiasis. The structure of extragenital pathology was dominated by: varicose veins of the lower extremities in 61 patients (61.0%), arterial hypertension stage 2-3 in 46 cases (46.0%); coronary heart disease, angina pectoris in 8 cases (8.0%); obesity in 43 cases (43.0%), liver, gastrointestinal and pancreatic ducts in 52 cases (52.0%). In 78.0% of patients somatic pathology was represented by two or more diagnoses. The reproductive history of HPE patients in association with adenomatosis is characterized by early menarche (up to 14 years old in 85.3% of patients), a high number of pregnancies (four and more in 80.0%), most of which ended in miscarriages (three and more in 68.0%). The study of hemostasis system indices in perimenopausal female patients with HPE and adenomiasis and extragenital pathology showed an abnormality in the platelet-endothelial line system, which manifests itself in a significant decrease in platelet count to $159.5 \pm 12.7 \times 10^9/l$ and an increase of their aggregation capacity to $42.3 \pm 4.4\%$, as compared with the same indices in healthy women (respectively $226.5 \pm 11.3 \times 10^9/l$; $29.5 \pm 2.8\%$).

A significant increase of plasma lysis was detected in the fibrinolysis system ($p < 0.05$) from 154.3 ± 9.1 sec in the control group to 213.9 ± 11.2 sec in the patients, decrease of AO-III (from $71.3 \pm 2.2\%$ to $57.3 \pm 3.3\%$) and an increase in soluble fibrin (+) in 3 times that is 3.9 ± 0.4 ($p < 0.05$).

Such parameters indicate maximal tension of the hemostasis system in patients with HPE and adenomiasis. The unstable equilibrium of the hemostasis system in this case is related to the phase I (hypercoagulation) of SICS syndrome. It is also confirmed by the fact that we found a positive reaction in the ethanol test in 97.3% of patients with sporadic uterine and endometrial pathology, which is significantly different from the indices of healthy women by 30.7%.

The results of a comprehensive examination of perimenopausal patients with combined endo- and menometrial pathology on the basis of extragenital pathology showed that thrombophilic risk factors in this category of patients should include endo- and menometrial pathology, preoperative surgery (hysteroscopy, intrauterine craniocerebrocopy), age over 45 years, use of hormonal medications, cardiovascular diseases (hypertension, varicose veins) and other severe extragenital pathologies. Thrombogenic potential in patients with combined pathology of endo- and myometrium is increased by the presence of haemodynamic disorders in the affected organ, magnesium deficit in the body of the patient and the presence of psychogenic disorders. The presence of these factors combined with changes in the hemostatic system (platelet-junction, plasma hemostasis and fibrinolysis system) indicated the presence of a medium to high risk of TEC occurrence and required thromboprophylaxis. It consisted of additional prescription of specific low molecular weight heparin (LMWH) and non-specified (elastic compression, magnesium) prophylaxis, as well as of vascular medications for 2-3 months.

4 Discussions

The conducted analysis of the results of clinical, laboratory, instrumental, immunohistochemical, psychological examinations, and determination of the hemostasis system status before and after 1, 3 and 6 months after hysteroscopy and endocrine surgical treatment of endometrial pathology in association with adenomyosis have shown that the method of treatment used to prevent thromboembolic and inflammatory complications in such patients is highly effective.

The results of the examination of the hemostasis system in 1 month after treatment showed a positive effect of the suggested method of treatment on this system. Thus, first of all, in contrast to the patients with HPE and adenomyosis ($159.5 \pm 12.7 \times 10^9$), the platelet count was normalized ($189.7 \pm 9.1 \times 10^9$), and did not differ from that of healthy women ($226.5 \pm 11.3 \times 10^9$). The normalization of platelet aggregation capacity was evidenced by the index of their aggregation. The post-treatment values ($29.7 \pm 4.1\%$) authentically decreased ($p < 0.05$) and were close to those of the healthy women ($29.5 \pm 2.8\%$) ($p > 0.05$).

Significant positive changes in the fibrinolysis system in 1 month after the use of our treatment (Group I) indicated its benefits. Plasma lysis values (161.8 ± 5.8) and AO-III (65.9 ± 2.1) hardly differed from those of healthy women (154.3 ± 9.1 and 69.3 ± 2.2 accordingly). After the general therapy (Group II) the fibrinolysis values were significantly ($p < 0.05$) higher (plasma lysis (sec) - 227.9 ± 7.2 ; AO-III (%) - 59.2 ± 3.1), in comparison with the same indicators in the CG (154.3 ± 9.1 and 69.3 ± 2.2) and in the group of patients after perioperative treatment and prophylactic measures for prophylaxis of TEC and flammable diseases.

The normalization of the fibrinolysis system is also evidenced by the positive reactions of the ethanol test, the number of which decreased in contrast to the pre-treatment figures, namely from 97.3% to 63.6%. In our opinion, it indicates the absence of a negative effect of the applied therapy method on the hemostasis system and the high efficiency of hysteroscopy in the complex with endocrine and menometric treatment of endometrial pathology in patients with extragenital pathology of the perimenopausal period.

An ultrasound examination obtained 3 months after treatment showed the absence of signs of uterine hyperplasia and decreased antero-posterior uterine dimensions.

The cytological findings of the aspirates from the uterine cavity, which we received 3 months after intrauterine craniocervical surgery, indicated the absence of atypical or pre-tumorous processes.

Based on the results of a comprehensive examination before and after the use of the therapy and prevention of complications of treatment of combined pathology endo- and myometry in patients with extragenital pathology and based on the results of dispensary observation of our patients for 1 to 6 years, we have established criteria for the efficacy of therapy. After 3 months and during the next 2 years of dispensary observation, we will expect: absence of complaints, absence of complaints during bimanual examination, decreased uterine size (ultrasound diagnostic), uterine endometrial thickness of 3-4 mm, pathomorphological examination of uterine cavity aspirates.

Thus, the clinical, laboratory and cytomorphological examination and ultrasound findings demonstrate the efficacy of the suggested approach to the diagnosis and prophylaxis of TEC, the efficacy of the suggested minimally invasive treatment (hysteroscopy and intrauterine craniocutaneous surgery) and prophylaxis of TEC and inflammatory endometrial and menometrial pathology in perimenopausal women with extragenital pathology the rate of the treatment was 82.0%, the rate of prophylaxis of TEC and occlusive complications was 100%. The generally accepted approaches resulted in treatment efficacy of 36.0 %, prevention of TEC of 96.0 %, and prevention of flammable complications of 78.0 %.

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