Endometrial Hyperplastic Processes in Premenopause

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ABSTRACT

Hormonal therapy administered for endometrial hyperplastic processes is essentially a countercurrent therapy aimed at correcting the menstrual cycle, eliminating overt estrogenic influences and preventing the formation of endometrial hyperplasia. Doctors currently have a wide range of treatments for endometrial hyperplasia in their arsenal. These include progestins, combined oral contraceptives (OCs), antigonadotropic drugs, and gonadaliberin agonists. We examined the clinical and morphological efficacy of Midiana OC for the prevention of recurrent endometrial hyperplasticity in patients with concomitant cardiovascular disease in premenopause.

Keywords: premenopause, endometrial hyperplasia, hormone therapy.

Introduction

Endometrial hyperplasia (EH) is an extremely important, complex and multifaceted problem of practical gynecology. The tendency of GPE to a long, recurrent course, the absence of specific, pathognomonic symptoms, the complexity of differential diagnosis and the choice of treatment methods. In addition, this pathology is a proliferative process and, if left untreated for a long period of time, can be a background for the development of endometrial cancer. Over the past 20 years, there has been a steady increase in the incidence of cervical cancer, which ranks fourth among malignant neoplasms occurring in women (after breast, lung and colon cancer), and first among tumours of the female reproductive organs.

Objective

To determine the development of endometrial hyperplastic processes in premenopause

Materials of the Study:

We performed a clinical and laboratory examination and treatment of 60 patients aged 41 to 45 years with a history of recurrent endometrial hyperplasia. The mean age was 43.1±1.05 years. Oligomenorrhagia (in 63.9% of the patients) alternating with menometrorrhagia dominated in the menstrual history, 30 (27.8%) patients had menorrhagia, and 4.6% had oligomenorrhagia, whereas 3.7% of the women had no clinical manifestations of endometrial hyperplasia. In addition, 75% of the women were found to have premenstrual syndrome (PMS) with severe pain syndromes due to fluid retention during the second phase of menstruation. The pain syndromes included cephalgia (100%), mastalgia (70.6%) and fibromyalgia (52.8%). All patients had a history of repeated diagnostic uterine curettage. The mean number of previous diagnostic curettage procedures was 4.2±0.1. Histological examination of a history of 108 patients resulted in the diagnosis of PGE without atypia in 65 (60.2%) women and complex endometrial hyperplasia without atypia in 43 (39.8%) women. Taking into account the histological findings, all the women examined had previously been prescribed hormonal therapy. Progestagen therapy was given to 62 (57.4%)

patients, gonadoliberin agonists to 21.3%, IQT to 48 (44.4%) women for 6 months in standard doses. All the patients were diagnosed with cardiovascular pathology mainly represented by arterial hypertension manifested both as hypertensive disease I (66.7%) and as NCD in hypertensive type which was registered in 36 (33.3%) women. Diseases of the gastro-intestinal tract occurred in almost every second patient (44.4%) with endometrial hyperplasia. Of the diseases of the respiratory system, apart from frequent acute respiratory diseases, tonsillitis and pharyngitis, 22 (20.4%) women in the main group had chronic bronchitis. All the patients underwent transvaginal ultrasound scanning, hysteroscopy with a separate diagnostic scraping and subsequent histological examination of endometrial and cervical scrapings. The intrauterine intervention was indicated to assess the efficacy of hormone therapy. In 62 (57.4%) patients with POE were found to have no morphological signs of endometrial hyperplasia after 6 months of hormonal therapy, and 3 (2.8%) had preserved foci of hyperplastic endometrium. Only 29 (26.9%) patients with complicated endometrial hyperplasia after 6 months of hormonal therapy had no morphological signs of endometrial hyperplasia, while 14 (12.9%) had preserved foci of hyperplastic endometrium classified as PHE. All patients with recurrent hyperplasia after therapy were excluded from further studies due to the need for surgical treatment.

Results of the Study

To prevent endometrial hyperplasia, all patients with a positive effect of hormonal therapy (endometrial atrophy) were prescribed the combined low-dose monophasic oral contraceptive Midiana (Gedeon Richter) in a prolonged regimen. Midiana was developed in the search for positive non-contraceptive effects and ways to improve the tolerability of oral contraceptives. It contains 30 μg of ethinylestradiol and 3 mg of drospirenone. Drospirenone in Midiana OC is a derivative of 17α-spironolactone whose pharmacological properties represent a unique combination of progestagenic, anti-mineralocorticoid, and anti-androgenic effects without estrogenic and glucocorticoid activity. Drospirenone has a pharmacological profile similar to that of endogenous progesterone. In normal menstruation, estrogen-induced fluid retention is compensated by the anti-mineralocorticoid action of progesterone. When taking OCs, this balance disappears, which may result in weight gain due to fluid retention in the body. The anti-mineralocorticoid effect of Midiana OCs can restore the lost balance between fluid retention and excretion and achieve stabilisation of body weight and blood pressure (BP). The patients were followed up for 1 year. According to the study protocol, clinical and laboratory parameters were monitored at baseline and during Midian administration: body weight and BP dynamics were assessed. Endometrial mucosa morphological control was carried out after 6 months of Midian administration by endometrial biopsy. The endometrial thickness was monitored after 3, 6 and 12 months. It is noteworthy that acyclic haemorrhage was detected in the first 2 menstrual periods in 3 patients. Due to this fact, 2 patients refused further use of the drug. Against the background of taking Midiana OCs after 6 months, oligomenorrhoea was detected in 58 (63.7%) patients. At the end of one year oligomenorrhea was diagnosed in 73 (80.2%) patients. During the use of Midiana OC, body weight decreased and further stabilised. On the average in the 3rd month of use 45.1% of patients body weight decreased by 0.5 kg or more, in 6 months of use a decrease in body weight (which remained during the year) of 1-2 kg was found in 35 (35.2%) patients. Thus, the antimineralocorticoid activity of drospirenone helps to stabilise body weight and prevent its increase in patients with GBE. An additional result of drospirenone's anti-mineralocorticoid effect is BP stability. The dynamic control of BP against Midian OC has revealed a tendency for its decrease in 74 (81.3%), while against other OCs [2] there is a tendency for its increase. It should be noted that there was no significant difference in BP change compared to baseline parameters. Although the positive anti-mineralocorticoid effect of Midian OCs is undisputed, they should not be considered as an alternative to spironolactone or other agents used to increase diuresis and stabilise BP.

In addition, the study has conclusively proved that Midiana OCs have a positive effect on PMS symptoms, which reduce the quality of life of patients with HpE. As a result of the therapy, 68 (74.7%) women with PMS experienced a therapeutic effect. At the start of Midian® OC the mean endometrial thickness was 4.2±0.2 mm and did not change significantly over 6 months (after 3 months - 4.0±0.1 mm, and after 6 months - 3.8±0.2 mm). A more detailed analysis showed that 45.1% of women had an endometrial thickness of less than 5 mm in the first 6 months, 50.5% of cases ranged from 5 to 10 mm, and only 4.4% of patients had an endometrial thickness greater than 10 mm at 6 months. In 12 months of Midian OC use, a clear trend was seen in the reduction of median M-echo, its mean value decreased significantly with respect to the initial one to 3.1±0.2 mm. To assess the efficacy of the therapy, endometrial tissue samples obtained by endometrial biopsy were examined histologically after 6 months of Midian's OC use. Morphological signs of endometrial hyperplasia were found to be absent in 87 (95%) patients after 6 months of using the drug, whereas 4 (4.4%) women had foci of hyperplastic endometrium.

Conclusions

Thus, the results obtained in the present study suggest that the use of Midiana OC as a highly effective agent for the prevention of recurrent GEE in women with concomitant cardiovascular pathology in premenopause is scientifically justified.

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