BRITISH MEDICAL JOURNAL

British Medical Journal Volume-1, No 2
10.5281/zenodo.5155134
British Medical Journal
Volume 1, No 2., 2021
Internet address: http://ejournals.id/index.php/bmj
E-mail: info@ejournals.id
Published by British Medical Journal
Issued Bimonthly
3 knoll drive. London. N14 5LU United Kingdom
+44 7542 987055
Chief Editor
Dr. Fiona Egea

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Assessment of the severity of postmenopausal complications and clinical and laboratory parameters in the dynamics of treatment of women with a history of PCOS.

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Abstract. The study of clinical and laboratory parameters during the treatment of menopausal disorders in postmenopausal women with a history of PCOS was conducted. To study the features of postmenopausal disorders, such markers as the age of menopause, the severity of menopausal disorders, body weight, body mass index (BMI), the ratio of waist circumference to hip circumference, blood lipid spectrum were used. It was revealed that MGT in the composition with drospirenone, prescribed to women with menopausal complications with PCOS in the anamnesis, relieves menopausal disorders, has a favorable effect on the lipid profile, preventing the development of fatal complications of menopause.

Keywords: menopause, polycystic ovary syndrome, menopausal disorders, body mass index (BMI), lipidogram, cardiovascular diseases (CVD), menopausal hormone therapy (MHT).

Introduction.

Currently, the medical community is facing an acute problem of maintaining the activity and efficiency of postmenopausal women. The relevance of this topic is due to the increase in the life expectancy of women and the change in their social status. The results of scientific research in recent years indicate that menopausal hormone therapy (MHT) is the main method of treating menopausal disorders. Taking into account the features and genesis of the pathological course of menopause, the use of MHT is pathogenetically justified and its effectiveness is scientifically proven [5, 6]. Menopausal hormone therapy (MHT) is used for the prevention and treatment of cardiovascular diseases, osteoporosis, correction of neuropsychiatric and urogenital disorders. MHT is not an unacceptable intervention in the natural course of menopause, since this type of treatment both prophylactically and therapeutically affects vegetative and metabolic deviations from the

10.5281/zenodo.5155134
physiological course of the "transition" period and leads to a significant improvement in women's well-being and an increase in the quality of life. Studies show that cardiovascular diseases (CVD) occupy a leading position in the structure of causes of death in postmenopausal women. An important risk factor for the progression of cardiovascular diseases is arterial hypertension, the frequency of which increases significantly in women with the onset of menopause. The most significant increase in the frequency of hypertension was observed in women with initial endocrinopathies, in particular in patients with a history of hyperandrogenism. In the development of hypertension, along with insulin resistance and hyperinsulinemia, tromobophilic factors, neurogenic factors, disorders in the renin-angiotensin-aldosterone system are important. Currently, MHT is recognized as a safe and effective method for both the correction of menopausal disorders and the prevention of the development of late metabolic disorders of the postmenopausal period. When conducting MGT, we should adhere to the principles that provide for an individual approach to the choice of the drugs. An individual selection of medicines is necessary, taking into account the characteristics of each patient, including age, the stage of the menopausal period, concomitant somatic and gynecological diseases. If a consensus has been reached regarding the expediency of prescribing estrogens to women in the menopausal period, then the opinions of researchers differ on the progestogenic component. Many well-known progestogens, providing protection of the endometrium, have an adverse effect on the metabolic profile. This issue is particularly relevant in patients with an initial imbalance of steroid hormones. It is known that in the menopausal period, an imbalance of hormones is observed due to a decrease in the secretion of estrogens with a stable synthesis of androgens. The choice of a drug for MHT in patients with initial hyperandrogenism containing the progestogen drospirenone, which has an antiandrogenic effect, is more appropriate [3].

The aim of the present study was to study the effect of MGT with drospirenone on the function of the vascular endothelium and the peripheral circulatory system, the metabolic profile and the degree of insulin resistance in patients with a history of PCOS.

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Research materials and methods.

The criteria for including women in the study were: postmenopause, the presence of menopausal disorders, an indication of a history of polycystic ovary syndrome, the woman's consent to the examination. We studied the clinical manifestations of menopausal disorders in a group of women with a history of PCOS in the dynamics of treatment. The average age of the patients was 52.5±1.06 years. Before the start of therapy, the examination included a consultation with a gynecologist with an assessment of individual and family history. Ultrasound examination of the pelvic organs, mammography, smear assessment for oncocytology, determination of blood sugar, blood lipid spectrum, hemostasiogram indicators and hormonal profile – follicle-stimulating hormone, estradiol, thyroid hormones, prolactin, total testosterone, globulin-binding sex hormone, electrocardiogram were performed. According to the results of the examination, 9 patients (43%) were diagnosed with arterial hypertension, 11 (52%) – small uterine fibroids, indications of endometriosis and endometrial hyperplastic processes in the anamnesis. Type 2 diabetes mellitus was detected in 1 patient, insulin resistance was detected in 7 (33.3%), obesity of 1-2 degrees was registered in 14 cases (67%), congenital hyperbilirubinemia (Gilbert's syndrome) was confirmed in one patient. Varicose disease were detected in 12 out of 21 patients. Dyslipidemia was registered in 15 women (71.4%). Hirsutism occurred in 4 patients with a normal level of free testosterone. Thus, the examined patients can be considered as a high-risk group for the development of cardiomeiabolic complications of postmenopause.

All patients received a continuous combination of 17p-estradiol 1 mg/drospirenone 2 mg, 1 tablet daily.

Research results and discussion.

The results of the total demographic, anthropometric, anamnestic and clinical data of the examination in the dynamics of treatment reflect the effectiveness of the use of combined MGT in a monophasic mode, with the content of estradiol 1 mg/drospirenone 2 mg for 24 weeks and are presented in Table 1.

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Table 1. Indicators of the severity of menopausal syndrome according to the MMI index in the dynamics of treatment.

The severity of postmenopausal complications according to the MMI index	Initial data (n =174)	MHT (24 weeks)	OR	Lower bound	Upper bound
	n=174	n=174			
Mild severity	26 (14,9±2,6 %)	77 (44,3±3,7 %)	0,22	0,13	0,37
Moderate severity	85 (48,9±3,8 %)	57 (32,8 ±3,6 %)	1,96	1,27	3,03
Heavy severity	63 (36,2±3,7 %)	31 (17,8±2,9 %)	2,62	1,59	4,0

In the dynamics of treatment (after 24 weeks), there was a decrease in the severity of the postmenopausal complications. Thus, only 26 women out of 174 examined from the main group of patients with complicated menopause and PCOS of mild symptoms, which was 14.9±2.6 %. After treatment, 77 women, which is 44.3±3.7% ($p<0.001$), had mild menopausal disorders. The number of women with moderate and severe symptoms of complicated menopause also significantly decreased: 57 (32.8 ±3.6 %) and 31(17.8±2.9 %) compared to the data before the start of treatment: 85 (48.9±3.8 %) and 63 (36.2±3.7 %) before the start of treatment, respectively ($p<0.001$). There was a significant decrease in the modified menopausal index (MMI) in the dynamics of treatment. In women with a history of PCOS, the initial MMI scores were 56.3±0.7, while taking MHT for 6 months, the MMI scores in patients of this group significantly decreased to 37.2±0.4 ($p<0.001$).

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We evaluated the data of clinical and laboratory studies in patients during the treatment.

Table 2.

Studied parameters	Initial data (n =174)	MHT (24 weeks) (n =174)
BMI, kg/m2	29,7±0,4	27,5±0,7**
Waist/hip circumference	1,1±0,0	1,0±0,02**
Waist circumference	96,6 ± 1,5	91,2±2,2*
Cholesterol, mmol/L	6,5 ± 0,1	5,8±0,1*
Triglycerides, mmol/L	3,9±0,1	3,1±0,21*
HC-HDL (mmol/L)	0,6±0,0	1,1±0,05*
HC-LDL (mmol/L)	4,7±0,1	4,1±0,1**
v-LDL (very low density lipoproteins)	0,7±0,0	0,6±0,04*
Atherogenicity index (AI)	8,3 ± 0,2	3,9 ± 0,1**

Note: ** p<0,01, - * p< 0.05 compared to the original value.

When studying the dynamics of the body mass index (BMI) during treatment, a significant decrease in BMI was noted from 29.7±0.4 to 27.5±0.7 (p<0.01).

However, it is worth noting that the distribution of adipose tissue is a more pathognomonic indicator of insulin resistance. In contrast to BMI, the dynamic change in the index waist/hip circumference (W/HC) was significant. A significant decrease in the W/HC index occurred against the background of MHT for 24 weeks. If before the start of taking MHT drugs, the W/HC index was calculated as 1.1±0.0, then after treatment it was 1.0±0.02, which was significantly lower than the initial indicator (p<0.01).

After 24 weeks, there was a significant decrease in the level of cholesterol while taking MHT. Thus, the initial indicators of total cholesterol were 6.5 ± 0.1 mmol/l, in the dynamics of observation against the background of taking the drug, a

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significant decrease was noted – 5.8±0.1 mmol/l. In the group of women taking MHT, there was a significant decrease in the level of triglycerides (TG) – from 3.9±0.1 mmol/l to 3.1±0.21 mmol/l.

Significant decreases in low-density lipoprotein fractions were noted in the dynamics of treatment for 24 weeks. Thus, LDL values during treatment significantly decreased from 4.7±0.1 (mmol/l) to 4.1±0.1 (mmol/l. There was also a significant decrease in the level of very low density lipoproteins (v-LDL). The initial v-LDL values were 0.7±0.0 mmol/l, in the dynamics of observation against the background of taking the MHT drug, a significant decrease in the level of very low density lipoproteins was noted – 0.6±0.04 mmol/l.

In contrast to the LDL and HDL fractions, there was a favorable increase in the non-atheromatous HDL fraction during treatment. The HDL level shows a significant increase from 0.6±0.0 mmol/l to 1.1±0.05 mmol/l. The above-mentioned changes in the parameters of lipid fractions during treatment created prerequisites for a favorable decrease in the atherogenicity index, which decreased in the dynamics of observation from 8.3 ± 0.2 to 3.9 ± 0.1, which is significantly lower than the baseline values. The above-mentioned changes in the parameters of lipid fractions during treatment created prerequisites for a favorable decrease in the atherogenicity index, which decreased in the dynamics of observation from 8.3 ± 0.2 to 3.9 ± 0.1, which is significantly lower than the initial indicators.

Thus, MHT in the composition with drospirenone, prescribed to women with menopausal complications with PCOS, stops menopausal disorders, has a favorable effect on the lipid profile, prevents the development of fatal complications of postmenopause. It should be emphasized that the progestogen drospirenone is metabolically neutral, does not affect glucose tolerance and insulin resistance.

Thus, both the literature data and the results of our own research indicate the effectiveness and safety of taking the combination of estradiol/drospirenone in postmenopausal patients. In addition, there was a decrease in urogenital complaints against the background of taking the drug. Patients note an increase in the quality of life and satisfaction with the results of treatment [7].

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In conclusion, it should be noted that the combination of estradiol/drospirenone is effective and safe for use in patients with hyperandrogenism and insulin resistance, with a high risk of cardiometabolic risk.

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