THE EFFECT OF THE POLYCYSTIC OVARY SYNDROME ON THE COMPLICATED COURSE OF THE MENOPAUSAL PERIOD

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Abstract. *Polycystic ovary syndrome (PCOS) is considered to be the most common endocrine disorder in women. The etiology of PCOS is multifactorial and still not fully understood. Insulin resistance and subsequent hyperinsulinemia are major features of PCOS. Additionally, increased androgen levels facilitate the release of free fatty acids from visceral fat tissue, what exacerbates insulin resistance. Insulin resistance in PCOS is also associated with abdominal obesity and other components of metabolic syndrome. All these abnormalities place females with PCOS at an increased risk of cardiovascular disorders later in life. Current data indicate that in women with PCOS there is a significant cancer risk, at least for endometrium. This finding should facilitate proper screening strategies, lifestyle changes and insulin resistance's treatment as a primary intervention what may decrease the risk in PCOS population.*

Keywords: *polycystic ovary syndrome, insulin resistance, menopausal period abdominal obesity, weight gain, hyperandrogenism, metabolic syndrome, cardiovascular disorders, atherogenic lipid profile, endometrial cancer risk.*

ВЛИЯНИЕ СИНДРОМА ПОЛИКИСТОЗНЫХ ЯИЧНИКОВ НА ОСЛОЖНЕННОЕ ТЕЧЕНИЕ КЛИМАКТЕРИЧЕСКОГО ПЕРИОДА

Аннотация. *Синдром поликистозных яичников (СПКЯ) считается наиболее распространенным эндокринным заболеванием у женщин. Этиология СПКЯ многофакторна и до конца не изучена. Инсулинорезистентность и последующая гиперинсулинемия являются основными признаками СПКЯ. Кроме того, повышенный уровень андрогенов способствует высвобождению свободных жирных кислот из висцеральной жировой ткани, что усугубляет резистентность к инсулину. Инсулинорезистентность при СПКЯ также связана с абдоминальным ожирением и другими компонентами метаболического синдрома. Все эти аномалии подвергают женщин с СПКЯ повышенному риску сердечно-сосудистых заболеваний в более позднем возрасте. Текущие данные свидетельствуют о том, что у женщин с СПКЯ существует значительный риск рака, по крайней мере, эндометрия. Это открытие должно способствовать правильному скринингу, изменению образа жизни и лечению резистентности к инсулину в качестве основного вмешательства, что может снизить риск СПКЯ в популяции.*

Ключевые слова: *синдром поликистозных яичников, инсулинорезистентность, менопаузальное абдоминальное ожирение, прибавка массы тела, гиперандрогения, метаболический синдром, сердечно-сосудистые нарушения, атерогенный липидный профиль, риск рака эндометрия.*

Polycystic ovary syndrome (PCOS) is considered the most common endocrine disorder in women and, depending on diagnostic criteria, makes up approximately 10% of women in perimenopause [1]. The clinical manifestation of PCOS is heterogeneous, varies widely between patients, but the diagnosis of the classical phenotype is mainly based on a triad of symptoms that

include hyperandrogenism (both clinical and biochemical), oligovulation or anovulation and the presence of polycystic ovaries during an ultrasound scan. The etiology of PCOS is multifactorial and has not yet been fully understood [5]. Numerous studies on its pathogenesis indicate a predisposition to PCOS in the presence of familial and genetic factors [2-3]. Research data suggests that there may be potential programming at the molecular level of adipose tissue dysfunction, insulin resistance, inflammation, oxidative stress, and endothelial dysfunction during fetal development [4]. However, the main pathophysiological mechanism for the development of PCOS has not yet been established. Insulin resistance and subsequent hyperinsulinemia are the main features of PCOS and are found in 80% of women with this pathology and almost all women with PCOS are obese [8]. It has been proven that insulin as such, through the signaling of IGF-1 or through classical insulin receptor signaling, can enhance the secretion of androgens and cause the development of polycystic ovaries. In addition, hyperinsulinemia inhibits the hepatic production of sex hormone-binding globulin (SHBG), and in this case, the level of free testosterone in serum increases. In addition, an increased level of androgens contributes to the release of free fatty acids from the tissue of visceral fat, which aggravates insulin resistance. Insulin resistance in PCOS is also associated with abdominal obesity and other components of the metabolic syndrome. All these disorders in women with PCOS lead to an increased risk of cardiovascular diseases in the age of menopause [6,7].

The purpose of the study was to study the peculiarities of the course of menopause in women who suffered from polycystic ovary syndrome at a fertile age and entered menopause in a state of insulin resistance.

Materials and methods

We examined 124 women with a complicated course of postmenopause. The main group consisted of 80 patients with complicated menopause and a history of PCOS. The comparison group with her was formed by 44 women without a history of PCOS. We studied the frequency and nature of clinical manifestations of menopausal disorders in women with a history of PCOS compared with the control. Anamnestic analysis was also carried out, the age of menopause, height-weight indicators, the nature of the distribution of adipose tissue, glycemic indicators were studied.

To study the lipid profile, blood lipid spectrum parameters were determined: cholesterol (HC), triglycerides (TG), high, low low density lipoproteins and very low density lipoproteins (HDL, LDL, VLDL) – produced on the Cypress Diagnostics analyzer (Belgium) using special standard techniques and electrophoresis systems followed by computer processing in the laboratory of functional diagnostics.

Statistical analysis of the data obtained was carried out using standard software packages Statistica for Windows 6.0, Microsoft Exel. The arithmetic mean (M), arithmetic mean error (m), frequency (M±m) were analyzed. The probability of error was assessed according to the Student's criterion.

Research results

According to the results of the study, a more unfavorable course of the menopausal period was noted in the main group of women. At the same time, the average age of menopause in the group of women with a history of PCOS was 50.6 ± 0.6 years, which is significantly later than the indicators obtained in the control. In the women of the main group, the height and weight index, the distribution of adipose tissue, and glycemic indicators differed from those

obtained in the control. Thus, the body mass index (BMI) in the main group of menopausal women with a history of PCOS was significantly higher than in the control group – 29.7±0.3 kg/m2 and 26.9±0.4 kg/m2, respectively (p<0.001). It should be particularly noted that there is a significant difference between the main and control groups in the nature of fat distribution, which reflects the OT/OB index, which, in turn, is one of the clinical criteria for metabolic syndrome. Thus, in the main group, the OT/O index was 1.11±0.0, which is significantly higher than the same indicator in the control group – 1.01±0.0 (p<0.001). Attention is drawn to the long-term and stable hypertensive condition in women of the main group, on average, for 9.0 ± 3.57 years, in women of the control group, the duration of hypertension was 2.5 ± 2.89 years. The indicators of glycosylated hemoglobin in the main group amounted to 7.89 ± 0.1%, against kontol – 5.4± 0.1% (p<0.001). As for the concentration of glucose measured on an empty stomach, in the group of women with PCOS, the indicator was 5.6± 0.1 mol/l, whereas in the control, the same indicator was significantly lower and amounted to 4.6± 0.07 mol/l. The same trend can be traced in the indicators of C-reactive protein. The content of this indicator in women of the main group was 4.8±0.1 mg/l versus 3.6±0.06 mg/l (p<0.001).

In the group of postmenopausal women with a history of PCOS, a high level of newly diagnosed hypertension was noted in 135 (77.6%) women, CHD in 58 (33.3%) women, these parameters in the control group were recorded in 21 (26.3%) and 16 (20.0%) cases, respectively. It should be noted that in 117 (67.2%) women of the main group, a violation of glucose tolerance (HTG) and type 2 diabetes was detected for the first time – in 23 (13.2%) women. Also in the main group, significantly high rates of immunoreactive insulin and the insulin resistance index (HOMA-IR) were noted. Thus, the insulin index in the main group was significantly higher – 11.9 ± 0.1 pmol/l compared with the control – 10.3±0.1 pmol/l (p<0.001). The index of insulin resistance (HOMA-IR) also demonstrated significant differences between the groups. In women with complicated menopause and PCOS in the anamnesis, HOMA-IR was 1.6±0.0, which is significantly higher than HOMA-IR in the control group – 1.4±0.0 (p<0.001). In the group of women with concomitant endocrinopathy, glucose values measured on an empty stomach and after 2 hours were 5.6±0.0 mmol/l and 7.1±0.1 mmol/l. Whereas in the control group, these indicators were, respectively, 4.6= 0.1 mol/l and 6.9= 0.1 mol/L. Glycosylated hemoglobin in the main group was significantly higher than the control indicator – 7.9 ± 0.1% versus 5.4±0.1% (p<0.001). There was an increase in the level of the so-called atherogenic fraction of low-density lipoproteins (LDL) in menopausal women with a history of PCOS, which was 4.7±0.1 mmol/l, while in the control group the LDL level was 3.9±0.1 mmol/L, this difference was significant (p<0.001). In the women of the main group, a significant increase in the indices of atherogenic fractions of very low density lipoproteins (VLDL) was also revealed – 0.7±0.0 mmol/l, compared with the control – 0.6±0.0 mmol/l (p<0.001). As mentioned above, a similar pattern can be traced in the indicators of triglycerides. In the main group of women with a history of PCOS, hypertriglyceridemia was recorded – 3.9±0.1 mmol/l. Whereas in the control group, the triglyceride level was significantly lower and amounted to 1.2 = 0.01 mol/l (p<0.001). The level of the anti–atherogenic fraction of high-grade cholesterol - lipoproteins (HDL-Cholesterol) was lower in the main group of women with a history of PCOS and amounted to 0.6±0.0 mmol/l, in the control group the HDL index was significantly higher than 1.1±0.0 mmol/l (p<0.001).

It is known that the prognostic sign of the risk of atherosclerosis is not so much the absolute values of the concentration of atherogenic and antiatherogenic fractions of blood

lipoproteins, as their ratio, i.e. the coefficient of atherogenicity (atherogenicity index) – IA (LDL / HDL). IA was significantly higher in women of the main group and amounted to 3.9±0.1 mmol/l relative to the control group – 3.7±0.1 mmol/l ($p<0.001$).

Conclusions

Thus, the course of menopause in women with a history of PCOS is accompanied by an increased risk of hyperlipidemia. Analysis of the effect of insulin-resistant state on dyslipidemia showed the following patterns. Women had significantly high levels of total cholesterol and triglycerides, increased the content of atherogenic fractions of cholesterol – low-density lipoproteins and very low-density lipoproteins. At the same time, the level of the anti-atherogenic fraction of high-density lipoproteins in the main group of women with a history of PCOS is significantly lower than the control indicators. It is well known that the prognostic sign of the risk of atherosclerosis and cardiovascular complications is not so much the absolute values of the concentration of lipid fractions, as the ratio of atherogenic and anti-atherogenic fractions to each other. This is an indicator of the atherogenicity index – IA, the level of which was also significantly higher in women with a history of PCOS and showed significant differences compared to the control group. The negative tendency to increase atherogenic lipid fractions increases with age, which is typical for both patients with PCOS and healthy women.

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