# THE ROLE OF HOMOCYSTEIN IN THE PATHOGENESIS OF POLYCYSTIC OVARIAN SYNDROME IN WOMEN

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**Annotation:** Currently, scientists pay great attention to the study of the role of endothelial dysfunction as one of the causes of the development of polycystic ovary syndrome (PCOS). It is known that in addition to the barrier function, the vascular endothelium takes an active part in the regulation of the processes of vascular vasoconstruction and vasodilation, the synthesis and activity of vascular proliferation factors, fibrinolysis factors and platelet aggregation, and inflammatory reactions. According to many scientists, high concentrations of homocysteine, which has a pronounced toxic effect on cells, especially on the inner surface of blood vessels, lead to the development of endothelial dysfunction. Based on this, the problem of hyperhomocysteinemia is a subject of interest for researchers.

**Key words:** endothelial dysfunction, homocysteine, hyperhomocysteinemia, polycystic ovary syndrome, methionine.

# РОЛЬ ГОМОЦИСТИНА В ПАТОГЕНЕЗЕ СИНДРОМА ПОЛИКИСТОЗА ЯИЧНИКОВ У ЖЕНЩИН

**Аннотация:** в настоящее время учёные большое внимание уделяют изучению роли эндотелиальной дисфункции в качестве одной из причин развития синдрома поликистозных яичников (СПКЯ). Известно, что кроме барьерной функции, эндотелий сосудов принимает активное участие в регулиции процессов сосудистой вазоконструкции и вазодилатации, синтеза и активности факторов пролиферации сосудов, факторов фибринолиза и агрегаци тромбоцитов, воспалительных реакций. К развитию эндотелиальной дисфункции, по мнению многих учёных, приводят высокие концентрации гомоцистеина, который оказывает выраженное токсическое действие на клетки, особенно на внутреннюю поверхность сосудов. На основании этого, проблема гипергомоцистеинемии является предметом интереса исследователей.

**Ключевые слова:** эндотелиальная дисфункция, гомоцистеин, гипергомоцистеинемия, синдром поликистозных яичников, метионин.

## INTRODUCTION

Among the many laboratory markers of endothelial dysfunction in polycystic ovary syndrome, homocysteine occupies one of the leading places [3, 4].

## MATERIALS AND METHODS

Homocysteine (HC) is a sulfur-containing amino acid that is a homologue of the amino acid cysteine. Homocysteine is a product of the conversion of methionine. As a chemical

derivative, it was described in 1932 by chemists Butz and Vigneaud as a product obtained by the reaction of high concentration acid methionine.

Homocysteine does not enter the body with food, therefore, under physiological conditions, the only source of homocysteine in the body is the conversion of methionine. In excess, homocysteine accumulated in the body can be converted back into methionine. The cofactors of the enzymes of the metabolic pathways of methionine in the body are vitamins: folic acid, riboflavin (vitamin B1), pyridoxine (vitamin B6), cyanocobalamin (vitamin B12) [1, 5, 11].

Factors that cause an increase in the level of homocysteine are: genetic - gene mutations that encode the synthesis of an enzyme involved in the formation of homocysteine; non-genetic - autoimmune processes, the use of large amounts of caffeine, kidney disease, smoking, insufficient intake of vitamins B1, B6, B12, folic acid. Homocysteine levels can also rise in the elderly.

Homocysteine has a toxic effect on the cell. To prevent the cell from damaging its action, special mechanisms are triggered to remove it from the cell into the blood. Therefore, if it increases in the body, it begins to accumulate in the blood, and the main site of its damaging effect is the inner surface of the vessels. Under the influence of an increased content of homocysteine, there is an increase in the expression of pro-inflammatory cytokines, a change in the bioavailability of nitric oxide, induction of oxidative stress, activation of apoptosis and defective methylation. Insufficient supply of deoxyribonucleic acid (DNA) methyl groups, protein and lipid methylation impairs the proliferation and differentiation of granulosa cells, thereby inhibiting oocyte and follicular maturation, as well as steroidogenesis in the ovaries [17, 21, 22].

Homocysteine is a metabolite that has both thrombovascular and atherosclerotic effects. With an increase in the concentration of homocysteine in the blood, it has a damaging effect on the inner wall of the arteries. In these damaged areas, cholesterol begins to be deposited, gradually forming atherosclerotic plaques. As a result, atherosclerosis develops, and the likelihood of blood clots increases. Microthrombus formation and microcirculation disorders lead to impaired placentation, which can cause infertility as a result of implantation defects of the embryo.

According to some sources, the rate of blood HC levels ranges from 10-11 μmol / l. In other sources, the level of HC in blood plasma should be in the range of 5-15 μmol/l. At the same time, it should be noted that the concentration of HC in the blood during life tends to increase, which is associated with a reduced excretory function of the kidneys [5, 6, 12].

In young women with PCOS, a high frequency of hyperhomocyteinemia (HHC) is a risk factor for increased levels of ET-1 (endothelin-1) and the formation of endothelial dysfunction, which can lead to impaired blood supply to the pelvic organs, impaired folliculogenesis in the ovaries, anovulation and contribute to the development of long-term somatic complications of this pathology [2]. When studying the marker of endothelial dysfunction ET-1, some authors found that an increase in the concentration of ET-1 occurred in 64 (80%) patients with PCOS, and its content in blood serum (2.4±0.4 fmol/ml) exceeded ($p<0.05$) average indicators of healthy women (0.83±0.2 fmol/ml) [2].

**RESULTS AND DISCUSSION**

According to some studies, the study of the content of HC in the blood serum showed that its levels in women of the control group averaged 8.1 ± 0.2 μmol / l and coincide with a number of some authors who believe that the normal concentration in the blood of HC in women of reproductive age should not exceed 8-10 μmol/l [11]. In patients with PCOS, the level of HC averaged 10.3±0.4 μmol/l and significantly ($p<0.05$) exceeded that of healthy women 8.1±0.2

µmol/l. In 33 (50.8%) patients with PCOS, the blood levels of HC exceeded 10 µmol/l and averaged (12.2±0.3 µmol/l). Consequently, half of the women with PCOS had HHC [2, 14, 19].

However, there are conflicting data on the concentration of HC in patients with PCOS: while some researchers speak of an increase in the concentration of HC compared with healthy women [7, 13], others deny the presence of hyperhomocysteinemia (HHC) in this group of patients [9, 15, 18].

Data on elevated serum levels of HC in women with PCOS, leading to impaired follicle development and egg maturation, continue to be discussed [8, 10, 16, 20].

**CONCLUSIONS**

Thus, an increase in the concentration of homocysteine in women with PCOS is a reason for further in-depth study of its secretion in order to improve treatment methods.

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