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ASPECTS OF HORMONAL REGULATION: THE EFFECT OF ESTROGENS ON THE DEVELOPMENT OF CARDIOVASCULAR DISEASES IN WOMEN

Tuychieva Sabokhat Kurakbaevna
Basic doctoral student of the Department of Internal diseases and cardiology № 2, Samarkand State Medical University
Tashkenbaeva Eleonora Negmatovna
Head of the Department of Internal diseases and cardiology № 2, Doctor of medical sciences, professor of Samarkand State Medical University
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ABSTRACT
Hormone regulation plays a key role in maintaining cardiovascular health in women. Estrogens, as the main sex hormones, have complex and multifaceted effects on the cardiovascular system, including regulating lipid metabolism, improving endothelial function, modulating inflammatory processes, and preventing oxidative stress. Their effect is especially important during reproductive age, but after menopause, estrogen levels are significantly reduced, which contributes to an increased risk of developing cardiovascular diseases (CVD). The article discusses the molecular mechanisms of action of estrogens, their protective role in the prevention of atherosclerosis, coronary heart disease and arterial hypertension. The article also analyzes current data on hormone replacement therapy, its benefits and risks in the prevention of CVD in postmenopausal women. The results obtained emphasize the need for further research to develop individualized approaches to the treatment and prevention of cardiovascular diseases in women, taking into account the hormonal status.

АСПЕКТЫ ГОРМОНАЛЬНОЙ РЕГУЛЯЦИИ: ВЛИЯНИЕ ЭСТРОГЕНОВ НА РАЗВИТИЕ СЕРДЕЧНО-СОСУДИСТЫХ ЗАБОЛЕВАНИЙ У ЖЕНЩИН

Туйчиева Сабохат Куракбаевна
Базовый докторант кафедры Внутренних болезней и кардиологии №2 Самаркандского государственного медицинского университета
Ташкенбаева Элеонора Негматовна
Заведующая кафедрой Внутренних болезней и кардиологии №2, доктор медицинских наук, профессор Самаркандского государственного медицинского университета
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ABSTRACT
Гормональная регуляция играет ключевую роль в поддержании сердечно-сосудистого здоровья у женщин. Эстрогены, как основные половые гормоны,

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Менопауза, эстроген, ИБС, гипертония, ССЗ.

оказывают сложное и многогранное воздействие на сердечно-сосудистую систему, включая регуляцию липидного обмена, улучшение эндотелиальной функции, модуляцию воспалительных процессов и предотвращение окислительного стресса. Их влияние особенно важно в репродуктивном возрасте, однако после наступления менопаузы уровень эстрогенов существенно снижается, что способствует повышению риска развития сердечно-сосудистых заболеваний (ССЗ). В статье рассматриваются молекулярные механизмы действия эстрогенов, их защитная роль в предотвращении атеросклероза, ишемической болезни сердца и артериальной гипертензии. Также анализируются современные данные о гормо-нозаместительной терапии, её преимущества и риски в профилактике ССЗ у женщин постменопаузального возраста. Полученные результаты подчеркивают необходимость дальнейших исследований для разработки индивидуализированных подходов к лечению и профилактике сердечно-сосудистых заболеваний у женщин с учётом гормонального статуса.

GORMONAL REGULYATSIYA ASPEKTLARI: AYOLLARDA YURAK-QON TOMIR KASALLIKLARINING RIVOJLANISHIDA ESTROGENLARNING TA’SIRI

Tuychiyeva Sabohat Quraqbayevna
Samarqand davlat tibbiyot universiteti 2-son Ichki kasalliklar va kardiologiya kafedrasi tayanch doktoranti
Tashkenbayeva Eleonora Negmatovna
Samarqand davlat tibbiyot universiteti 2-son Ichki kasalliklar va kardiologiya kafedrasi mudiri, tibbiyot fanlari doktori, professor
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ABSTRACT
Gormonlar ayollarda yurak-qon tomir kasalliklari rivojlanishida muhim rol o'ynaydi. Estrogenlar, asosiy jinsiy gormonalardan biri bo’lib, yurak-qon tomir tizimiga ta'sir ko'rsatadi, yani lipid almashinuvi, endoteliy funksiyasini yaxshilash, yallig'lanish jarayonlarini modulyatsiya qilish va oksidlanish stressining oldini olish kabilarni o’z ichiga oladi. Ularning ta'siri, ayniqsa, reproduktiv yoshda juda muhim, ammo menopauzadan so'ng estrogenlar darajasi sezilarli darajada pasayadi. Bu esa yurak-qon tomir kasalliklari (YQTK) rivojlanish xavfini oshiradi. Maqolada estrogenlarning molekulyar ta'sir mexanizmlari va ularning ateroskleroz, yurak ishemik kasalligi hamda

arterial gipertoniyani oldini olishdagi roli ko'rib chiqiladi. Shuningdek, menopauza davridagi ayollarda YQTK profilaktikasi uchun gormonal o'rin bosuvchi terapiya, uning afzalliklari va xavflari haqida tahlil qilinadi. Olingan natijalar, gormonal holatni hisobga olgan holda ayollarda yurak-qon tomir kasalliklarini davolash va profilaktikasi uchun individual yondashuvlarni ishlab chiqish zarurligini ta'kidlaydi.

Introduction. Cardiovascular disease (CVD) is the leading cause of death worldwide. As the population ages and the prevalence of obesity and diabetes rises, the cost of treating CVD will skyrocket globally .The incidence of CVD varies by gender, with premenopausal women having a lower risk of hypertension, atherosclerosis, heart failure, and myocardial ischemia compared to age-matched men. However, this advantage gradually diminishes after menopause, increasing the risk of CVD in postmenopausal women compared to men of the same age. This trend is largely attributed to the role of female hormones in this process [13, 9].

These features emphasize the need to study the role of estrogens in the pathogenesis of CVD, especially in the context of hormonal changes at different periods of a woman's life.

Studying the influence of estrogens on the pathogenesis of cardiovascular diseases (CVD) is of key importance in the context of increasing the effectiveness of prevention and treatment of these pathologies in women. Estrogens have a variety of effects on the cardiovascular system, including regulation of vascular tone, improvement of endothelial function, reduction of atherogenic lipoprotein levels and modulation of inflammatory processes. These properties play an important role in protecting women from the development of atherosclerosis and other CVDs during reproductive age [33].

Declining postmenopausal estrogen levels are associated with a sharp increase in the risk of cardiovascular disease, including myocardial infarction, stroke and chronic heart failure. This is due to deterioration of endothelial function, increases in cholesterol and blood pressure, and an increase in overall vascular stiffness [5,30]. However, the mechanisms underlying these processes are not fully understood, which creates gaps in the understanding of pathogenesis. Moreover, taking into account the gender characteristics of the pathogenesis of CVD is of great importance for the creation of gender-specific recommendations and treatment standards [2]. Thus, studying the role of estrogens in the pathogenesis of CVD in women helps to improve the diagnosis, prevention and treatment of cardiovascular diseases, which makes this topic extremely relevant in modern medical science [33].

The study of the influence of hormones on the cardiovascular system began in the late 19th and early 20th centuries, when researchers began to notice differences in the course of CVD in men and women. One of the first steps was the understanding that women before menopause are less likely to suffer from cardiovascular disease, which is associated with the protective effect of estrogen.

Modern medicine uses various approaches to assess hormonal status and its effect on cardiovascular diseases. Modern research makes it possible to more accurately identify and

evaluate hormonal changes that influence the development of CVD in women. Modern methods can accurately measure the levels of hormones such as estrogens, progesterone and testosterone in the blood, which is important for assessing the health of the hormonal system [16]. In addition, hormonal tests are widely used to help assess the level of activity of the pituitary gland and ovaries, as well as identify possible hormonal imbalances.Research suggests that changes in estrogen levels may serve as a risk marker for CVD. For example, low postmenopausal estrogen levels are associated with an increased risk of atherosclerosis, hypertension, and other vascular diseases. Important markers also include the HDL/LDL ratio, triglyceride levels and C-reactive protein, which reflects inflammation in the body [29].

In recent decades, scientific debate has developed regarding the benefits and risks of HRT in the context of cardiovascular disease. Modern research shows that HRT can have both positive and negative effects on the cardiovascular system, depending on the time of initiation of therapy, the dose of hormones and the individual characteristics of the patient. For example, starting therapy at a young age may have a protective effect, whereas starting therapy late may increase the risk of CVD [12].

Current research and clinical practice use a variety of instrumental methods to assess vascular risk, including ultrasound assessment of intima-media thickness (IMT), cardiac performance tests (ECG, echocardiography), and coronary angiography to detect atherosclerosis. Estrogens are steroid hormones, the synthesis of which occurs primarily in the ovaries of women of reproductive age.

Main forms of estrogens:

Estradiol (E2) is the most active form, dominant during the reproductive period.

Estrone (E1) is a less active form that predominates in postmenopause.

Estriol (E3) - actively produced during pregnancy. Sources of synthesis in different periods of life

Reproductive age: The main organ of synthesis is the ovaries (follicles). The production of estrogen is regulated by the hypothalamic-pituitary axis through the secretion of gonadotropins (FSH and LH).

Pregnancy period: A significant portion of estrogens is synthesized by the placenta.

Postmenopause: The main source is adipose tissue, where estrone is formed from androstenedione with the help of aromatase.

In addition to the ovaries, a small amount of estrogens is synthesized in other tissues: adipose tissue, adrenal glands, and brain.These sources play a particularly important role after menopause.

The main effects of estrogens on the cardiovascular system. Estrogens play an important role in maintaining normal vascular endothelial function, which is critical for regulating vascular tone and preventing the development of cardiovascular diseases (CVD). Estrogens activate endothelial NO synthase (eNOS), which increases NO production. NO causes relaxation of vascular smooth muscle cells, improving blood flow and lowering blood pressure. Estrogens suppress the expression of adhesion molecules such as ICAM-1 and VCAM-1, preventing the attachment of monocytes to the endothelium. Reduced proliferation of vascular smooth muscle cells, which prevents the development of atherosclerotic plaques [16].

Estrogens have a significant effect on the blood lipid profile, reducing the risk of developing atherosclerosis: HDL helps remove cholesterol from the vascular wall and transport it to the liver for further utilization. Estrogens reduce LDL synthesis, preventing the accumulation of atherogenic cholesterol in the vascular wall. Increased metabolism of triglycerides reduces their concentration in blood plasma [13].

Estrogens have strong antioxidant properties that protect the cardiovascular system from damage caused by oxidative stress. Estrogens reduce the formation of ROS, which contribute to endothelial cell damage and LDL oxidation, an important step in the development of atherosclerosis. Estrogens increase the activity of superoxide dismutase, catalase and glutathione peroxidase, which neutralize free radicals [29].

Mechanisms of estrogen influence on the development of cardiovascular diseases (CVD). Before menopause, estrogens play a key role in protecting women from developing cardiovascular disease. Estrogens have positive effects on various aspects of the cardiovascular system, including vascular function, lipid metabolism and inflammatory processes [18]. These hormones provide a number of protective effects that reduce the risk of developing atherosclerosis, hypertension and other CVDs. Estrogens increase the activity of endothelial NO synthase, which leads to increased production of nitric oxide. This molecule helps relax blood vessels, reducing their resistance and maintaining normal blood flow. This prevents the development of hypertension and promotes better blood supply to organs and tissues. Estrogens help maintain endothelial cell health by preventing cell damage and inflammation [13,31]. This reduces the risk of developing atherosclerosis, since damaged endothelium promotes the formation of atherosclerotic plaques.Estrogens stimulate the synthesis of HDL, which act as cholesterol “scavengers,” clearing blood vessels of atherogenic cholesterol (LDL) and ensuring its removal to the liver for further processing. It helps prevent cholesterol from building up in artery walls [28]. Estrogens reduce the synthesis of LDL, which reduces the risk of the formation of atherosclerotic plaques and blockage of blood vessels. It also helps reduce total cholesterol in the blood, which is important for the prevention of CVD.

Estrogens have an antiphlogistic effect, which is manifested by a decrease in the levels of inflammatory cytokines such as interleukin-6 (IL-6) and C-reactive protein (CRP). Inflammation is an important factor in the development of atherosclerosis and other vascular diseases, and suppressing it helps prevent vascular damage [3,15]. Estrogens reduce the expression of molecules that promote the attachment of monocytes and other inflammatory cells to the walls of blood vessels, which prevents the development of atherosclerotic plaques and vascular damage. Estrogens have pronounced antioxidant properties, reducing the level of free radicals and preventing the oxidation of LDL. This reduces the risk of damage to the vascular walls, which plays a key role in the development of atherosclerosis. Estrogens stimulate the activity of enzymes such as superoxide dismutase and catalase, which neutralize free radicals, protecting blood vessels and cardiac tissue from oxidative damage. Estrogens help improve tissue sensitivity to insulin, which reduces the risk of developing type 2 diabetes, which is an important risk factor for CVD [17].

Genetic and epigenetic factors play an important role in how estrogens influence the development of CVD. At the molecular level, hormonal changes can influence the expression of

genes that regulate lipid metabolism, inflammation, and vascular function [28]. For example, genetic changes in estrogen receptors may be associated with an increased risk of atherosclerosis in postmenopausal women. Epigenetic mechanisms, such as DNA methylation and histone modifications, can regulate the expression of genes associated with inflammation, oxidative stress, and lipid metabolism [8]. For example, decreased estrogen levels in postmenopause may alter the epigenetic activity of genes responsible for inflammation and lipid metabolism, which increases the risk of atherosclerosis and hypertension [14].

Hormonal changes during periods of a woman's life and their impact on cardiovascular diseases (CVD). During the reproductive age of women, the level of estrogen, progesterone and other hormones varies depending on the phase of the menstrual cycle. These hormones have a significant effect on the cardiovascular system, providing protection against CVD. During the reproductive period, thanks to the action of estrogen, women have lower cholesterol levels and a normalized lipid profile (increased HDL levels and decreased LDL), which reduces the risk of atherosclerosis and other vascular diseases. Estrogens also help maintain normal vascular endothelial function by increasing nitric oxide production and reducing vascular resistance [1].

Progesterone affects the relaxation of vascular smooth muscle and also regulates water and electrolyte balance, which can affect blood pressure. However, its effect on the cardiovascular system is less pronounced than that of estrogens [23].

Menopause is characterized by a sharp decrease in the levels of estrogen and other sex hormones, which leads to many changes in a woman's body, including an increased risk of developing CVD. After menopause, a decrease in estrogen levels leads to a deterioration in lipid metabolism (increased LDL and decreased HDL), increased triglyceride levels and a general increase in cholesterol levels, which accelerates the development of atherosclerosis. There is also deterioration of endothelial function and a decrease in vascular elasticity, which contributes to increased blood pressure and an increased risk of hypertension [1,23]. A decrease in estrogen levels after menopause leads to increased blood viscosity and increased blood clot formation, which increases the risk of blood clots and vascular events such as myocardial infarction and stroke [25].

Hormone replacement therapy (HRT) is a treatment based on replacing estrogen and/or progesterone levels in postmenopausal women. However, HRT has both benefits and risks to health, including the cardiovascular system. HRT helps increase HDL levels and reduce LDL and triglyceride levels, which helps reduce the risk of atherosclerosis. HRT may improve endothelial function by increasing nitric oxide production, which improves vascular tone and lowers blood pressure [7]. Although not directly associated with CVD, HRT helps prevent loss of bone mineral density, which is important for postmenopausal women [22].

Risks of HRT: One of the main risks of HRT is the increased likelihood of blood clots, which increases the risk of heart attacks and strokes. The use of a combination of estrogen and progesterone in HRT may be associated with an increased risk of breast cancer. Although HRT may have a protective effect on the cardiovascular system when starting therapy in early postmenopause, there is a risk of increased cardiovascular disease if HRT is started later [13].

Modern approaches to the use of HRT are based on an individual approach and a thorough assessment of the risks and benefits for each patient. Research shows that starting

hormone replacement therapy in the first 10 years after menopause can have a positive effect on the cardiovascular system, reducing the risk of developing atherosclerosis and hypertension. An important component of modern recommendations is a personalized approach to prescribing HRT. Assessing risk factors, such as age, family history of CVD, and the presence of diseases associated with blood clots, is an important step in deciding whether to use HRT [6]. In case of contraindications to traditional HRT, modern approaches suggest the use of alternative methods, such as the use of estrogens or phytohormones alone, as well as neurohormonal drugs, which may have less impact on the cardiovascular system [22].

Impact of comorbidities. Women with diabetes mellitus (especially type 2 diabetes) have a significantly increased risk of cardiovascular disease. High levels of glucose in the blood contribute to damage to the vascular wall, increased inflammation and oxidative stress, which increases the development of atherosclerosis**.** In this context, decreased estrogen levels after menopause may enhance these effects, increasing vascular susceptibility to injury and impairing endothelial function. [13]. Even despite the potential protective effects of estrogens, in women with diabetes their effects on the cardiovascular system may be attenuated by the presence of insulin resistance and chronic inflammation. [11,32].

Obesity is another important factor that modifies the effects of estrogen on the cardiovascular system. Excess body weight increases insulin levels and inflammation, and also disrupts lipid balance, which increases the risk of developing atherosclerosis and hypertension. [29,32]. In obese women after menopause, decreased estrogen levels may worsen lipid imbalance and promote the accumulation of visceral fat, which increases the likelihood of developing cardiovascular disease. At the same time, obesity can reduce the effectiveness of hormone replacement therapy (HRT), which necessitates an integrated approach in the treatment of such patients.

Women with hypertension, especially postmenopausal women, are at higher risk of stroke, heart attack, and heart failure. Declining estrogen levels after menopause contribute to decreased vascular elasticity and increased vascular resistance, which can worsen hypertension. In such cases, the effect of estrogen on blood pressure may be less pronounced, and treatment should include not only hormonal drugs, but also antihypertensive drugs [18].

Lifestyle and behavioral factors. Diet plays an important role in modulating the effects of estrogen on the cardiovascular system. Diets high in saturated fat, trans fat, and carbohydrates may reduce the effectiveness of estrogens in maintaining normal lipid profiles and vascular function. In contrast, diets high in omega-3 fatty acids, fiber, antioxidants, and micronutrients such as magnesium and calcium improve lipid metabolism and reduce inflammation, which enhances the protective effects of estrogens. In women with poor diets, cholesterol, triglycerides, and insulin levels may be elevated, reducing the beneficial effects of estrogen on vascular health [27].

Regular physical activity has a positive effect on lipid profile, blood pressure and vascular function. In women who lead an active lifestyle, the effect of estrogen on the cardiovascular system may be more pronounced. Exercise helps lower LDL levels and increase HDL levels, thereby improving protection against atherosclerosis [4]. In sedentary women, decreased estrogen levels after menopause may be associated with a more rapid development of cardiovascular disease. [11].

Chronic stress can significantly reduce the protective effects of estrogen on the cardiovascular system. Stress promotes activation of the sympathetic nervous system, increased cortisol levels and inflammation, which can impair endothelial function and contribute to increased blood pressure. In women with chronic stress, the effects of estrogen on vascular health may be weakened, increasing the risk of hypertension, atherosclerosis, and other cardiovascular diseases. Therefore, managing stress and psycho-emotional state is an important element in the prevention of cardiovascular diseases in women. The effect of estrogen on the cardiovascular system can vary significantly depending on the presence of concomitant diseases and the woman's lifestyle [18,26]. Diabetes mellitus, obesity, hypertension and other chronic diseases can weaken the protective effects of estrogens, increasing the risk of developing cardiovascular diseases. At the same time, a healthy lifestyle that includes good nutrition, regular physical activity and stress management can significantly enhance the protection provided by estrogen. Consideration of these factors is important for the development of personalized strategies for the prevention and treatment of CVD in women, especially in the context of hormonal changes in postmenopause [34].

Conclusion. Effect of estrogens on the cardiovascular system: Estrogens play a key role in maintaining cardiovascular health in women, especially during the reproductive period. They help improve the lipid profile, maintain normal endothelial function, reduce oxidative stress and inflammation, and maintain vascular tone. These effects reduce the risk of developing atherosclerosis, hypertension and other cardiovascular diseases. With the onset of menopause and a decrease in estrogen levels in women, the risk of developing cardiovascular diseases increases. This is associated with a deterioration in lipid metabolism, increased blood pressure, impaired vascular elasticity and an increased risk of thrombosis. All these changes can lead to accelerated development of atherosclerosis and other vascular diseases. Comorbid medical conditions, such as diabetes and obesity, as well as lifestyle choices, including diet, physical activity, and stress, can significantly influence the degree of protection that estrogens provide to the cardiovascular system. Inadequate diet, sedentary lifestyle and chronic stress can reduce the effect of estrogen, increasing the risk of developing CVD.

Early intervention, including hormonal correction, can prevent or slow the development of CVD, improving the quality of life of postmenopausal women. Hormone replacement therapy, when used correctly and individualized, can be an effective tool for preventing CVD, but it must be carefully selected based on the risks and benefits for each woman.

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