Perinatal psychologists and psychotherapists can hardly solve their professional tasks without knowing the structure of a family planning the childbirth as well as family functioning and dynamics.

Perinatal psychologist should be able in a timely manner to recognize possible scenarios of disharmonic family relations and to prevent conflict or help constructively solving it.

Key words: woman, baby, perinatal period, family relationships.

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INFLUENCE OF POSTMENOPAUSE ON THE FORMATION OF CHRONIC HEART FAILURE IN WOMEN WITH ARTERIAL HYPERTENSION

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Chronic heart failure (CHF) is the leading cause of disability and mortality in the population, the prevalence of which is steadily increasing. CHF is three times more common in late postmenopausal women. The purpose of the work is the analysis of modern scientific ideas about the pathogenesis of CHF with arterial hypertension (AH) in postmenopausal conditions. The review presents the main ideas about the pathogenesis of CHF, the influence of hypoestrogeny on the molecular mechanisms of the development of hypertension, endothelial dysfunction, myocardial fibrosis, myocardial remodeling, and osteodysmetabolism. The leading role of the activation of systemic inflammation in the development of CHF, their importance in the postmenopausal period is indicated. The pro-inflammatory molecular cascades involved in the formation of CHF in postmenopausal women are presented. Common links were found in the pathogenesis of hypertension, CHF and processes accompanying postmenopause. Potential early markers of the development of CHF are presented, and possible directions of therapeutic influence are indicated. The review systematizes modern ideas about the pathogenetic mechanisms of the development of CHF in postmenopausal women against the background of hypertension, which determines the prospects for solving the problematic issues of diagnosis and treatment of CHF.

Key words: *chronic heart failure, arterial hypertension, postmenopause, pathogenetic mechanisms.*

Connection of the publication with planned research works. This work is a fragment of the science topic “Peculiarities of the course of cardiovascular pathology in patients of different age categories depending on the presence of components of the metabolic syndrome and comorbid conditions, ways of correcting the detected disorders and prevention”, state registration number 0119U1028.

Introduction. Chronic heart failure (CHF) is one of the most frequent causes of hospitalization, disability and mortality of the working population both in Ukraine and in the whole world. The prevalence of CHF is 1.5-2.0%, and among people older than 65 years, it reaches 6-10% [1, 2]. The annual mortality among patients with mild CHF is 10%, and in the case of a severe degree – 50-60% [3]. The five-year survival rate after the onset of clinical symptoms of CHF is 25% in men and 38% in women. The increase in the life expectancy of the population and, accordingly, its aging, is combined with a constant increase in the incidence of CHF, the prevalence of which reaches 37 million people in the [4]. Estimating the prevalence of CHF remains an epidemiological problem due to the dependence on the development of various methods of diagnosis and treatment [5, 6].

According to the New York Heart Association (NYHA), the prevalence of CHF of functional class II-IV in Ukraine is about 2 million people [7, 8]. The frequency of hospitalizations and mortality in CHF remains consistently high [9].

Recently, there has been a more significant growth rate of CHF in women; the ratio of the number of women to men at the age of 65 is approximately 3:1. However, the generalization of data from numerous clinical studies of CHF showed that women made up only 21 percent of the studied cohort [10].

Epidemiological studies have shown gender differences in the clinical picture, risk factors, and prognosis of CHF. In women, the phenotype of heart failure with

preserved ejection fraction (HFF) predominates, while mortality rates do not differ from those of individuals with systolic dysfunction [11].

In postmenopause, the frequency of arterial hypertension and coronary heart disease increases significantly, which creates conditions for the development of CHF [12]. More than 12.5 million patients with arterial hypertension (AH) are registered in Ukraine, which is 32.2% of the adult population of the country [13]. Hypertension is a leading risk factor for cardiac and cerebrovascular events, accounting for 88% of mortality from cardiovascular diseases [14]. Although it is determined that the prevalence of hypertension in men younger than 60 years is higher than in women, hypertension is a leading factor in the development of cardiovascular diseases and mortality in postmenopausal women [15, 16, 17].

Numerous pathogenetic mechanisms are associated with estrogen deficiency during menopause, leading to the formation of hypertension and its consequences. This is a violation of endothelium-dependent vasodilatation, and activation of the renin-angiotensin-aldosterone system (RAAS), sympathoadrenal system (SAS), increased sensitivity to sodium chloride, increased vascular resistance, dyslipidemia, insulin resistance, which together belong to the postmenopausal metabolic syndrome [18, 19].

Disturbances in the hormonal status manifested by the climacteric syndrome create conditions for masking the clinical manifestations of the initial stages of CHF. In postmenopause, CHF runs for a long time in a hidden, asymptomatic form, is poorly diagnosed and, in the absence of treatment, progresses rapidly.

Therefore, it is relevant to study the characteristics of CHF against the background of hypertension in postmenopausal women with the aim of timely diagnosis and treatment of CHF in the initial stages.

The purpose of the work is an analytical study with the determination of the leading pathogenetic mechanisms of the formation of chronic heart failure against the background of arterial hypertension in postmenopausal women.

Main part. The fact of neurohumoral activation has definitely been proven in the pathogenesis of CHF, but this theory is not exhaustive. It has been proven that hemodynamic overload and myocardial ischemia activate immune defense, which, in turn, can cause systolic and diastolic dysfunction of the myocardium [20, 21]. The leading mechanism of the development of CHF is also a violation of the metabolism of the extracellular matrix, which causes myocardial fibrosis with subsequent remodeling of the myocardium, especially in CHF with preserved left ventricular ejection fraction [22, 23].

Recently, a new concept of the development and progression of CHF has become relevant, which consists in the influence of immune activation and systemic inflammation [24, 25]. Proinflammatory cytokines (CK) regulate the level of apoptosis of cardiomyocytes, which determines the type of myocardial remodeling and, accordingly, the progression of CHF [26, 27, 28].

Today, a whole spectrum of proinflammatory CKs is known, which have a damaging effect on the endothelium of vessels, cellular and matrix structures of the myocardium, which mediates vasoconstriction, apoptosis, fibrosis and remodeling of the myocardium. Fractalkin/CX3CL1, neopterin and a number of others are among the recently established markers of CHF development and progression Proinflammatory CCs cause endothelial dysfunction and oxidative stress, which are one of the main factors in the formation and progression of AH and CHF [29].

To date, the cardiovascular protective properties of estrogens have been proven, estrogen receptors have been found on the surface of cardiomyocytes and vascular smooth muscle cells [30]. A decrease in the level of estrogens in postmenopausal women is an independent factor that leads to the activation of the RAAS and SAC, and an increase in the level of angiotensin II (AT-II) production. Along with the well-known pressor effects, AT-II stimulates the production of pro-inflammatory CK, aldosterone, vasoactive molecules, endothelin-1. Aldosterone stimulates the synthesis of collagen by fibroblasts, mediates inflammatory reactions in the vascular wall, causes increased excretion of calcium from the body, especially in conditions of vitamin D deficiency, which provokes secondary hyperparathyroidism [31, 32]. Parathyroid hormone activity also increases with age. AT-II and parathyroid hormone activate the proliferation of osteoclasts and their metabolic activity. Pro-inflammatory CKs stimulate osteoclastogenesis and inhibit the functional capacity of osteoblasts, in turn, increased osteoclast activity mediates osteoporosis, increased stiffness of myocardial arteries, causing deepening of morpho-functional disorders both in hypertension and CHF with negative consequences for the body as a whole [33]. Thus, the mechanisms of hypertension, CHF and the processes accompanying menopause are similar and potentiate each other.

It is known that B-type natriuretic peptide (BNP) and N-terminal BNP peptide (NT-proBNP) are the "gold standard" for CHF diagnosis. In 1998, McDonagh and colleagues published the results of a large-scale study, establishing that a BNP level ≥17.9 pg/ml with a sensitivity of 77% and a specificity of 87% can be used as a marker of left ventricular (LV) dysfunction [34].

However, these markers cannot reflect the ways of development and progression of CHF, since elevated levels are determined only in clinically expressed CHF, and also, high variability of the values of these markers is noted depending on gender, age, body weight, hormonal imbalance, kidney diseases, previous infection [35].

In the light of the new concept of the progression of CHF, which is based on the idea of immune activation and systemic inflammation, the biomarker ST2 (Growth Stimulation expressed gene 2), also known as IL1RL1, a member of the interleukin-1 receptor family (IL-1), which plays a central role in the regulation of the pro-inflammatory response. ST2 has been identified in two forms: membrane-bound (ST2L) and soluble, circulating in the bloodstream (sST2). The membrane-bound form of ST2 is expressed on cardiomyocytes [35, 36, 37].

The functional ligand of ST2, interleukin 33 (IL-33), secreted by fibroblasts, provides a cardioprotective effect in response to myocardial stretch. In contrast, the soluble isoform (sST2) blocks the effects of IL-33, causing the activation of cardiac remodeling and fibrosis [38, 39].

The ST2/IL-33 signaling system is likely to be key in regulating the inflammatory response in the myocardium. At the same time, it was established that the de-

gree of increase in sST2 in the blood does not depend on the etiology of CHF, gender, heart rate, body mass index (BMI), hemoglobin level, the presence of atrial fibrillation, etc., unlike BNP/NT-proBNP [40]. The advantage of ST2 also lies in the ability to determine the presence of CHF in the clinically asymptomatic phase, unlike natriuretic peptides [41, 42].

Over the past 5 years, a number of large-scale studies have been conducted: LURIC, PROTECT, the results of which demonstrated the leading role of the ST2/IL-33 system in the pathogenesis of CHF [43, 44].

Due to its special properties and potential role in the diagnosis and prediction of asymptomatic remodeling, fibrosis and CHF, as well as mortality, ST2 claims to be a risk predictor of CHF and adverse cardiovascular events.

Estrogen deficiency in postmenopausal women also causes an imbalance in the functioning of the RANKL/RANK/OTG signaling system, which is responsible for the formation of osteoporosis and implements its mechanisms due to the activation of systemic inflammation. RANK is a receptor-activator of nuclear factor kappa B (NF-kB), which is presented on activated osteoblasts, RANKL is a ligand, a glycoprotein synthesized by osteoblasts and activated T-lymphocytes, belongs to the tumor necrosis factor (TNF-α) superfamily [45, 46]. NF-kB plays a key role in the activation of the pro-inflammatory cascade [47].

The RANKL/RANK signaling pathway, mediated by TRAF6 and NF-kB signaling, triggers osteoclast maturation and differentiation and, accordingly, bone resorption is activated. OTG (osteoprotegerin) – produced by osteoblasts, vascular endothelium, stroma, B-lymphocytes, competitively binds with RANK, affecting osteogenesis, by inhibiting the maturation of osteoblasts [48].

Estrogens, binding to the intracellular receptors of osteoblasts, increase their functional and proliferative activity, leading to the activation of the formation of osteoprotegerin, which in turn indirectly stimulates the RANK/OTG cascade, suppressing the activity and maturation of osteoclasts [49].

Osteoprotegerin, according to foreign researchers of the last five years, is recognized as an important marker for the development of CHF in postmenopausal women [50].

The above demonstrates the complex multifactorial mechanisms involved in the formation of CHF, the determining pathogenetic role of the activation of chronic systemic inflammation in hypertension and CHF, the importance of a differentiated gender approach and early diagnosis, prevention and treatment of CHF.

To date, there are insufficient data on the early detection and prevention of CHF in postmenopausal women with hypertension. Also, there are no developed ways to prevent CHF in conditions of hormonal and metabolic shifts mediated by menopause. Numerous studies on the use of hormone replacement therapy (HRT) in postmenopause did not give a clear conclusion about its importance in the prevention of cardiovascular complications and safety [51, 52, 53, 54].

Recently, agents based on polyphenols of plant origin have been actively researched, which have shown reliable effectiveness in relation to many links of pathogenetic processes in cardiovascular diseases and other pathological conditions, possessing a wide spectrum of activity (antioxidant, anti-inflammatory and immunomodulatory effect) [55, 56, 57, 58, 59]. One of the leading mechanisms of action of polyphenols is the anti-inflammatory effect due to the blockade of signaling, by activating systemic inflammation, in particular, with the participation of NF-kB [60, 61].

Therefore, the search for ways to prevent and correct CHF in patients with hypertension in the postmenopausal period is extremely relevant and timely, and the addition of polypotent polyphenols to standard CHF therapy may prove to be a promising direction for both treatment and prevention of these pathological conditions.

Conclusions. The analysis of the data available in the scientific literature made it possible to systematize modern ideas about the pathogenetic mechanisms of the development of chronic heart failure in women in the postmenopausal period on the basis of arterial hypertension and to identify certain problematic issues that are controversial in the discussion by various authors and do not have a final solution until now.

Prospects for further research. On the basis of the presented analytical study, it is planned to conduct prospective cohort studies aimed at studying the characteristics of CHF in women with arterial hypertension in the postmenopausal period. Cytokine levels, particularly ST2 and osteoprotegerin (OTG), in early postmenopausal women need to be studied to determine the CHF phenotype. It is expedient to study the relationships between clinical, immunological, and biochemical indicators in the postmenopausal period, which can reveal predictors of cardiovascular risk in women. The given data are the basis for the search for pathogenetically justified therapeutic and preventive measures for CHF in postmenopausal women.

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ВПЛИВ ПОСТМЕНОПАУЗИ НА ФОРМУВАННЯ ХРОНІЧНОЇ СЕРЦЕВОЇ НЕДОСТАТНОСТІ В ЖІНОК З АРТЕРІАЛЬНОЮ ГІПЕРТЕНЗІЄЮ

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Резюме. *Вступ.* Хронічна серцева недостатність (ХСН) є однією з провідних причин інвалідізації та смертності населення, з високою розповсюдженістю у світі і невпинними темпами зростання захворюваності. Останнім часом спостерігається усе більша поширеність ХСН у жінок, у похилому віці, у порівнянні з чоловіками, її розповсюдженість стає втроє більша. У постменопаузі суттєво зростає частота артеріальної гіпертензії (АГ), ішемічної хвороби серця, що створює умови для розвитку ХСН. Тому актуальним є вивчення особливостей ХСН на тлі АГ у жінок постменопаузального віку з метою своєчасної діагностики й лікування на початкових стадіях.

Метою роботи – аналітичне дослідження з визначенням провідних патогенетичних механізмів формування ХСН на тлі АГ в жінок у постменопаузі.

Основна частина. В огляді представлені основні уявлення про патогенетичні механізми розвитку та прогресування ХСН. Зазначена роль нейро-гуморальної активації, гемодинамічного перенавантаження в умовах АГ, порушення метаболізму позаклітинного матриксу з формуванням жорсткості міокарду. Основну увагу приділено новій концепції розвитку ХСН, що полягає у впливі імунної активації та системного запалення. Зазначено роль прозапальних цитокінів у розвитку ендотеліальної дисфункції, ремоделюванні міокарду та прогресуванні ХСН. Незалежним фактором патогенетичних змін у розвитку ХСН є гіпоестрогенія у постменопаузі. Наведені механізми активації пресорних систем в умовах дефіциту естрогенів та опосередковані ефекти, у тому числі молекулярні механізми дисметаболізму сполучної тканини, кардіогемодинамічні наслідки та їхній взаємозв'язок. Знайдені спільні ланки у патогенезі АГ, ХСН та процесів, що супроводжують постменопаузу. Детально викладені прозапальні сигнальні каскади, що задіяні та активуються у механізмах формування ХСН в жінок у періоді постменопаузи, зокрема, за участю інтерлейкіна ST2, остеопротегерину. Обгрунтовано значення гіпоестрогенії у активації прозапальних механізмів з розвитком остеодисметаболізму, міокардіального фіброзу та ремоделювання та їхній взаємозв'язок крізь призму системного запалення. Представлені потенційні ранні маркери розвитку ХСН, зазначені можливі напрямки терапевтичного впливу.

Висновки. В огляді систематизовано сучасні уявлення про патогенетичні механізми розвитку ХСН в жінок у постменопаузі на тлі АГ що визначає перспективи вирішення проблемних питань діагностики та лікування ХСН.

Ключові слова: хронічна серцева недостатність артеріальна гіпертензія, постменопауза, патогенетичні механізми.

INFLUENCE OF POSTMENOPAUSE ON THE FORMATION OF CHRONIC HEART FAILURE IN WOMEN WITH ARTERIAL HYPERTENSION

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Abstract. *Introduction.* Chronic heart failure (CHF) is one of the leading causes of disability and mortality in the population, with a high prevalence in the world and an unrelenting rate of increase in morbidity. Recently, there has been an increasing prevalence of CHF in women, in old age, compared to men, its prevalence becomes three times greater. In postmenopause, the frequency of arterial hypertension (AH), coronary heart disease, which creates conditions for the development of CHF, increases significantly. Therefore, it is relevant to study the characteristics of CHF on the background of hypertension in postmenopausal women with the aim of timely diagnosis and treatment in the initial stages.

The purpose of the work is an analytical study with the determination of the leading pathogenetic mechanisms of the formation of CHF against the background of hypertension in postmenopausal women.

Main part. The review presents the main ideas about pathogenetic mechanisms of CHF development and progression. The role of neuro-humoral activation, hemodynamic overload in conditions of hypertension, violation of the metabolism of the extracellular matrix with the formation of myocardial stiffness is indicated. The main attention is paid to the new concept of the development of CHF, which consists in the influence of immune activation

and systemic inflammation. The role of pro-inflammatory cytokines in the development of endothelial dysfunction, remodeling of the myocardium and the progression of CHF is noted. An independent factor of pathogenetic changes in the development of CHF is hypoestrogeny in postmenopause. Mechanisms of activation of pressor systems in conditions of estrogen deficiency and mediated effects are presented, including molecular mechanisms of connective tissue dysmetabolism, cardiohemodynamic consequences and their interrelationship. Common links were found in the pathogenesis of hypertension, CHF and processes accompanying postmenopause. The pro-inflammatory signaling cascades involved and activated in the mechanisms of CHF formation in postmenopausal women, in particular, with the participation of interleukin ST2, osteoprotegerin, are described in detail. The importance of hypoestrogenia in the activation of pro-inflammatory mechanisms with the development of osteodysmetabolism, myocardial fibrosis and remodeling and their relationship through the prism of systemic inflammation is substantiated. Potential early markers of the development of CHF are presented, and possible directions of therapeutic influence are indicated.

Conclusions. The review systematizes modern ideas about the pathogenetic mechanisms of the development of CHF in postmenopausal women against the background of hypertension, which determines the prospects for solving the problematic issues of diagnosis and treatment of CHF.

Key words: chronic heart failure, arterial hypertension, postmenopause, pathogenetic mechanisms.

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PROGRESS AND PROBLEMS OF VACCINATION AGAINST CORONAVIRUS INFECTION COVID-19

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This article is devoted to the main achievements and problems associated with vaccination against the COVID-19 coronavirus infection. This problem remains relevant as the coronavirus infection is a highly contagious disease that spreads widely worldwide. Vaccination is currently the most effective way to prevent the occurrence of a coronavirus infection or its severe consequences. The difficulty is that vaccination against COVID-19 is effective only when the antigenic structure of the circulating virus matches the antigens contained in the vaccine (or, in the case of RNA and DNA vaccines, the viral antigens programmed into the genetic code). However, the coronavirus is constantly changing its genetic structure, resulting in new strains that differ from circulating variants and have pandemic potential, against which existing vaccines may be ineffective. This study aimed to determine the main approaches to creating a vaccine's advantages and disadvantages of vaccination through bibliographic analysis. A literature search was conducted among published peer-reviewed articles, books, textbooks, and monographs. The obtained data were systematized and processed. Attention was paid to the main approaches to creating vaccines against COVID-19; the problems of immunological imprinting and antibody-dependent enhancement of infection were assessed. It was established that strategies based on the use of DNA and RNA vaccines to solve the problem of their low immunogenicity in humans are a real alternative for the future development of medicine in the prevention of infectious diseases.

Key words: *vaccination, coronavirus infection, COVID-19, vaccine, immunological imprinting, antibody-dependent enhancement of infection.*