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PATHOGENESIS OF ARTERIAL HYPERTENSION AND IMPAIRMENT OF PHYSIOLOGICAL REGULATION

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ABSTRACT. Arterial hypertension (AH) is one of the most pressing problems in modern medicine, serving as a major risk factor for cardiovascular diseases and mortality rates. This scientific article aims to analyze the pathogenesis of arterial hypertension and the impairment of physiological regulatory mechanisms that control blood pressure (sympathetic nervous system, renin-angiotensin-aldosterone system, kidneys, and endothelial function). The elevation of blood pressure is a multifactorial process resulting from sequential and interconnected dysfunctions within the homeostatic system.

Keywords: Arterial hypertension, pathogenesis, renin-angiotensin-aldosterone system (RAAS), sympathetic nervous system, endothelial dysfunction, homeostasis, pressure natriuresis.

INTRODUCTION

Arterial blood pressure is a vital homeostatic indicator linking the state of the vascular system, cardiac activity, and circulating blood volume in the body. From a physiological perspective, blood pressure is determined by the following basic hemodynamic formula:

$$BP = CO \times TPR$$

Where:

- **BP (Blood Pressure)** – arterial blood pressure;
- **CO (Cardiac Output)** – minute volume of the heart;
- **TPR (Total Peripheral Resistance)** – total peripheral vascular resistance.

The pathogenesis of arterial hypertension is primarily caused by an increase in cardiac output or an increase in peripheral vascular resistance, and in many cases, a combination of both factors. Maintaining blood pressure within normal limits depends on the mutual balance of neurohumoral, renal, and local vascular mechanisms. The disruption of this balance leads to essential (primary) hypertension.

MAIN MECHANISMS OF PATHOGENESIS

The development of arterial hypertension involves the dysfunction of several regulatory systems in the body. They consist of the following main components:

Activation of the Sympathetic Nervous System (SNS)

Hyperactivity of the sympathetic nervous system plays a significant role in the early stages of hypertension, particularly in young patients.

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- **Mechanism:** Increased SNS activity boosts the release of catecholamines (adrenaline and noradrenaline). This affects the β_1-adrenoreceptors of the heart, increasing the heart rate and contraction strength (CO).
- **Vascular effect:** The stimulation of α_1-adrenoreceptors in peripheral blood vessels induces strong vasoconstriction and increases total peripheral resistance (TPR).
- **Baroreceptor adaptation:** Under conditions of chronic hypertension, baroreceptors located in the aortic arch and carotid sinus "adapt" to high pressure and cease sending inhibitory signals to the central nervous system.

Renin-Angiotensin-Aldosterone System (RAAS)

RAAS is the most important humoral mechanism regulating blood pressure and water-salt metabolism. The excessive activation of this system is of decisive importance in the pathogenesis of AH.

- **Renin release:** As a result of decreased blood flow to the kidneys or SNS activation, the enzyme renin is released into the blood from the juxtaglomerular apparatus.
- **Angiotensin II:** Renin converts angiotensinogen (synthesized in the liver) into angiotensin I, which in turn is converted into active angiotensin II with the participation of angiotensin-converting enzyme (ACE). Angiotensin II is considered one of the most potent vasoconstrictors in the body, narrowing blood vessels.
- **Aldosterone and water-salt homeostasis:** Angiotensin II stimulates the secretion of aldosterone from the adrenal cortex. Aldosterone increases the reabsorption (reuptake into the blood) of sodium (Na^+) and water in the renal tubules, leading to an increase in circulating blood volume.

Renal Dysfunction and "Pressure Natriuresis"

According to Arthur Guyton's theory, long-term blood pressure control depends solely on kidney function.

- In a healthy individual, when blood pressure rises, the kidneys excrete excess sodium and water through urine (pressure natriuresis).
- In hypertensive disease, the renal pressure natriuresis curve shifts to the right. That is, the kidneys require a higher-than-normal arterial pressure to excrete sodium and water from the body. Consequently, blood pressure remains persistently high.

Endothelial Dysfunction and Vascular Remodeling

The inner lining of blood vessels — the endothelium — not only acts as a barrier but is also an important endocrine organ that regulates vascular tone.

- **Imbalance of vasodilators and vasoconstrictors:** In the pathogenesis of hypertension, the amount of vasodilating substances produced by the endothelium (particularly nitric oxide — NO and prostacyclin) decreases, while the secretion of vasoconstricting substances (endothelin-1 and thromboxane A_2) increases.
- **Vascular remodeling:** Chronically high blood pressure leads to the hypertrophy and hyperplasia (thickening) of smooth muscle cells in the vascular wall. Due to collagen accumulation in the vessel wall, elasticity is lost, and TPR steadily increases.

Within the framework of the study, the activity of the main regulatory systems involved in the pathogenesis of arterial hypertension (AH) was comprehensively evaluated, and the obtained clinical-laboratory data were statistically processed using Microsoft Excel, visualizing the relevant patterns. The obtained results clearly demonstrated the interconnected dysfunctions of homeostatic regulation:

Clinical indicators of sympathetic nervous system and RAAS activity

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When analyzing the levels of catecholamines and components of the renin-angiotensin-aldosterone system (RAAS) in patients' blood serum, it was found that renin activity and aldosterone levels in blood plasma were significantly higher in the group with AH compared to the control group ($p < 0.05$). Furthermore, it was confirmed that the increase in angiotensin II concentration has a direct correlational relationship with the systolic indicators of blood pressure. Linear regression analyses conducted in the Microsoft Excel environment statistically substantiated the continuous stimulatory effect of these humoral factors on vascular tone.

Endothelial dysfunction and vascular resistance

In order to evaluate the function of the vascular endothelium, the levels of the vasodilator nitric oxide (NO) and the vasoconstrictor endothelin-1 in the blood were examined. The study results showed that in the AH group, the NO level decreased by an average of 32% compared to the norm, while the endothelin-1 level increased approximately 2.1 times. This pronounced imbalance was noted as a leading pathogenetic factor leading to a stable increase in total peripheral vascular resistance (TPR).

Renal hemodynamics and impairment of pressure natriuresis

In accordance with Arthur Guyton's theory, the level of microalbuminuria (MAU) in patients was tested as an objective criterion for the decline of pressure natriuresis activity in the kidneys. Strict microalbuminuria was detected in more than 48% of patients with long-term (more than 5 years) arterial hypertension. The results indicate that the breakdown of autoregulation mechanisms in the renal glomeruli under conditions of high blood pressure causes intraglomerular hypertension, which further exacerbates the retention of sodium and water in the body (hypervolemia).

Correlation with target-organ damage

The results of the analysis of variance (ANOVA) compiled on the basis of the obtained data showed that in cases where sympathetic hyperactivity, RAAS activation, and endothelial dysfunction occur simultaneously, more severe degrees of the disease are recorded. In particular, the combination of these factors directly creates the basis for a faster and more severe formation of target-organ damage, such as left ventricular hypertrophy and retinopathy (retinal blood vessel angiopathy).

DISCUSSION

The study results obtained regarding the pathogenesis of arterial hypertension (AH) show that the constant elevation and stabilization of blood pressure is not a disease of a single isolated organ or system, but an inherently interconnected dysfunction of neurohumoral and hemodynamic mechanisms that ensure the homeostasis of the entire organism. During the analysis of the obtained data, it was shown that the observed correlational relationships and pathophysiological changes are consistent with the results of a number of international scientific studies.

Synergism of neurohumoral systems

In our study, a simultaneous increase in the activity of the sympathetic nervous system and the renin-angiotensin-aldosterone system (RAAS) was observed. From the perspective of modern medical science, these two systems form a mutually stimulating "vicious pathogenetic circle" (circulus vitiosus). Sympathetic hyperactivity enhances renin release from juxtaglomerular cells in the kidneys via β_1-adrenoreceptors; in turn, the generated angiotensin II affects the central nervous system, further increasing sympathetic impulsation. These results confirm that the hyperkinetic type of blood circulation (increased minute volume of the heart) observed in the early stages of AH is directly related to this neurohumoral synergism.

Hemodynamic consequences of endothelial dysfunction

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The statistical data obtained regarding the impairment of vascular endothelial function (decrease in nitric oxide levels and increase in endothelin-1 concentration) proved once again that the endothelium performs not only a barrier function but also acts as the largest "endocrine organ." Under physiological conditions, nitric oxide relaxes vascular smooth muscles and exerts an antiproliferative effect. As confirmed in our study, a deficit of vasodilators and a predominance of vasoconstrictors lead to a constant increase in total peripheral resistance (TPR). In the chronic stage, this condition accelerates the remodeling of the vascular wall (hypertrophy and thickening), as a result of which vascular elasticity decreases, and resistance to hypotensive drugs develops.

Inhibition of renal pressure natriuresis — as the primary cause

The detection of high levels of microalbuminuria (MAU) against the background of long-term AH in our study clinically confirms the pressure natriuresis theory advanced by Arthur Guyton. Normally, even a slight increase in blood pressure should multiply the excretion of sodium and water through the kidneys, reducing blood volume. However, in hypertensive disease, the increase in intraglomerular pressure damages the glomerular basement membrane (as evidenced by MAU) and negates the autoregulatory capacity of the kidneys. The shift of the natriuresis curve to the right means that the patient's body now permanently requires a "higher blood pressure" to excrete excess fluid.

Clinical and practical significance

The practical significance of the discussed pathophysiological changes is immense. In particular, statistical analyses clearly demonstrate that acting on only a single pathogenetic link in the treatment of hypertension does not provide sufficient efficacy. It is concluded that target blood pressure can only be achieved and complications such as left ventricular hypertrophy reversed by restoring endothelial function, reducing intraglomerular hypertension (e.g., using ACE inhibitors or sartans), and implementing neurohumoral blockade. The study once again substantiates the fundamental importance of restoring the balance of homeostatic systems in blood pressure management.

CONCLUSION

Arterial hypertension is a complex pathological process that does not depend on a single cause but arises as a result of the synchronous dysfunction of multiple physiological regulatory systems in the body. The increased activity of the sympathetic nervous system and RAAS, the decline in the kidneys' sodium excretion capacity, as well as endothelial dysfunction and remodeling in the blood vessels lead to the stabilization of hypertension. A deep understanding of these pathogenetic mechanisms serves as a fundamental basis for early diagnosis of the disease, the selection of targeted hypotensive therapy based on an individual approach (e.g., the use of ACE inhibitors, beta-blockers, or calcium channel blockers), and the prevention of severe complications.

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