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NEUROENDOCRINE MECHANISMS OF THE STRESS RESPONSE AND ITS MORPHOFUNCTIONAL EFFECTS ON ORGANISM SYSTEMS

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ABSTRACT: This research paper aims to scientifically and theoretically analyze the pathophysiological mechanisms of stressor agents on the human organism, specifically the morphofunctional transformations occurring in the neuroendocrine regulation, cardiovascular, and immune systems. The article elucidates the activation of the hypothalamic-pituitary-adrenal (HPA) axis during acute and chronic stress, as well as the destructive effects of catecholamine and glucocorticoid secretion on organ tissues within the framework of modern clinical and histological approaches. The research findings serve to understand the etiology of psychosomatic diseases, optimize the diagnostic process, and enhance the effectiveness of rehabilitative measures in preventive medicine.

Keywords: stress response, neuroendocrine system, hypothalamic-pituitary-adrenal axis, cortisol, psychosomatics, homeostasis, allostatic load, adaptation syndrome.

INTRODUCTION

Turning to the philosophical aspects of the history of medicine and ancient Eastern medicine, the integral connection between the human psyche and its somatic state has long been the focus of thinkers. In particular, Abu Ali ibn Sina (Avicenna) in his works scientifically substantiated the direct impact of mental suffering, anger, and emotional stress on body organs, primarily the cardiovascular and digestive systems. Today, these empirical conclusions find their full scientific confirmation through the achievements of modern neurophysiology and pathomorphology.

In modern science, the phenomenon of stress has been fundamentally studied within the framework of the "General Adaptation Syndrome" concept proposed by H. Selye. According to it, stress is not merely psycho-emotional discomfort, but a complex, multi-stage set of neuroendocrine and histomorphological reactions aimed at maintaining organism homeostasis and adapting to the negative factors of the external environment. However, against the background of modern urbanization, the excessive intensification of the digital information flow, and social pressures, the prevalence of continuous, chronic stress (distress) states among the population is reaching a dangerous level.

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From a physiological perspective, while short-term stress (eustress) mobilizes the organism's vital resources and improves the conductivity of the nervous system, a prolonged distress state triggers destructive changes at the cellular level, especially in the nervous and connective tissues. Degenerative processes observed in the histological structure of the nervous system, the weakening of synaptic connections, and morphological disorders in the vascular endothelium are the direct result of the influence of chronic stressor agents. Hormonal imbalance (especially long-term elevation of cortisol) disrupts tissue trophism, laying the groundwork for various severe psychosomatic diseases.

In clinical practice, the correct assessment of the psychosomatic state of patients has become an integral part of the medical diagnostic and treatment process. Therefore, in the modern medical education system, shaping the skills of a deep understanding of the role of stress in the etiology of diseases, relying on the principles of medical deontology and bioethics among future doctors, is of highly urgent importance. Applying the right psychological approach in "doctor-patient" relations is an important factor in increasing the adaptive capabilities of the organism, comparable to pharmacological agents.

Based on the above, the main objective of this study is to systematically and clinically assess the mechanisms of action of stressor agents on the hypothalamic-pituitary-adrenal (HPA) axis, and the impact of biochemical changes occurring during this process on the morphofunctional state of the cardiovascular, nervous, immune, and other systems.

MATERIALS AND METHODS

This research work is based on a complex approach, integrating experimental-morphological, biochemical, and retrospective clinical analysis methods. The research process was carried out in strict compliance with all international bioethical standards and principles of medical deontology.

1. **Formation of experimental and clinical groups:** During the study, changes in organism homeostasis under conditions of chronic stress and endogenous intoxication (including chronic toxic effects) were studied. As objects of analysis, groups subjected to chronic stressor factors and a control group (intact state) were taken, and comparative assessment work was carried out. During the observation, the activity of the hypothalamic-pituitary-adrenal axis and the functional indicators of parenchymal organs were taken under dynamic control.

2. **Histological and morphological examination methods:** In order to objectively assess the destructive impact of stressor factors at the tissue level, the morphology of the nervous system, vascular walls, and particularly, parenchymal organs (kidneys and liver) was studied in-depth. The obtained tissue samples were fixed in 10% neutral formalin and embedded in paraffin blocks using a standard method. The prepared 5-7 micron thick histological sections were stained using the generally accepted hematoxylin-eosin method to detect structural changes. Also, to differentially analyze the state of connective tissue elements (sclerosis processes) against the background of stress and to visualize the state of the microcirculatory bed, the Van Gieson special staining method was used. Histological preparations were studied using a modern light microscope, and morphometric measurements were carried out.

3. **Biochemical and enzyme-linked immunosorbent assays (ELISA):** To determine the reactivity of the neuroendocrine system, the concentration of stress hormones — cortisol, adrenocorticotropic hormone (ACTH), and catecholamines (adrenaline, noradrenaline) in the blood serum was measured using ELISA analyzers.

4. **Information technologies and statistical analysis:** In order to increase the significance of laboratory test results obtained through the application of computer technologies in medical education and practice, all acquired numerical data were processed using modern methods. The formation of the base of biometric and morphometric indicators, the calculation of the arithmetic

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mean (M), standard error (m), and variance analysis were performed directly in the **Microsoft Excel** software environment.

The reliability level of the difference in intergroup indicators was calculated using Student's t-test, and a value of $p < 0.05$ was considered statistically significant. Furthermore, to demonstrate the integral relationship between hormonal changes and morphological disorders in tissues, correlation graphs and histograms were created using the Excel program.

RESULTS

As a result of the comprehensive clinical-laboratory and experimental-morphological studies conducted, a number of important biochemical and structural changes regarding the impact of stressor factors on organism systems were recorded. The obtained data showed that depending on the duration and intensity of stress, destructive processes in tissues deepen.

1. **Dynamics of neuroendocrine and biochemical indicators:** In the initial (alarm) stage of the study, due to the sharp activation of the hypothalamic-pituitary-adrenal (HPA) axis, the amount of cortisol and catecholamines in the blood serum was found to increase by an average of 2.5-3 times compared to the control group. The analysis of the data obtained from laboratory tests, conducted in the Microsoft Excel program, showed that in the state of chronic stress (at the end of the resistance stage and during the exhaustion period), the hormonal imbalance took on a stable character, and the concentration of ACTH and cortisol in the blood demonstrated high stability ($p < 0.01$). It was statistically proven that this state of hypercortisolemia intensifies protein catabolism in tissues, reducing the overall adaptive resources of the organism.

2. **Histological state of the nervous system and connective tissues:** Under the influence of chronic stress, pronounced degenerative processes were observed in the histological structure of the central nervous system. Examinations conducted with a light microscope showed the vacuolization and breakdown of the myelin sheath of nerve fibers, as well as the thinning of interneuronal connections that provide synaptic transmission. Under the long-term influence of stressor agents, structural disorders occurred in the connective tissues (specifically, collagen and elastin fibers) in the vascular walls and organ stroma. On histological sections, interstitial edema and the formation of initial sclerotic foci were noted as a result of microcirculatory disruption.

3. **Impact on the morphology of parenchymal organs (On the example of kidney tissues):** The most severe complications of stress and endogenous intoxication were observed in parenchymal organs. In particular, when evaluating the morphological state of the kidneys of offspring born to mothers affected by chronic toxic hepatitis, ischemia in the renal glomeruli apparatus and desquamation of the capillary endothelium were identified against the background of stressor factors. The development of protein and fatty dystrophy in the epithelial cells of the tubules, and the occurrence of necrobiosis in some foci, were visually confirmed using histological analyzes. As a result of the combination of toxic effects and distress, spasms of the microcirculatory bed and tissue hypoxia sharply intensified in the renal parenchyma.

4. **The importance of information technologies in laboratory analyzes:** The significance of laboratory test results obtained through the application of computer technologies in medical education and scientific research was once again confirmed in this study. The database of all morphometric and biochemical indicators was formed in a computerized system. The differences ($M \pm m$) obtained when comparing the destructive changes in the observation group (changes in the diameter of renal tubules, an increase in the connective tissue index) with the control group were found to be absolutely reliable ($p < 0.05$). Graphic visualizations clearly demonstrated the existence of a direct correlation between the duration of stress and the severity of histological disorders.

DISCUSSION

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The empirical data and morphological analysis results obtained show that the effect of stressor factors is not of a local nature but is a systemic pathogenetic mechanism that disrupts the homeostasis of the entire organism. The changes in the histological structure of the central nervous system and the degeneration processes in the connective tissue elements recorded in our study are in line with the conclusions of a number of foreign and local scientists. In particular, against the background of hypercortisolemia, damage to the myelin sheath of nerve fibers and spasms in the microcirculatory bed sharply reduce the trophic supply of tissues, creating a basis for irreversible morphofunctional disorders.

The particularly acute manifestation of this pathological process can also be clearly seen against a number of intoxication backgrounds, for example, in assessing the morphological state of the kidneys of offspring born to mothers affected by chronic toxic hepatitis. The combined (synergistic) effect of endogenous intoxication and stress accelerates ischemia of parenchymal organs, specifically renal glomeruli, and causes protein-fatty dystrophy in tubular epithelial cells. This, in turn, scientifically proves how powerfully psycho-emotional and somatic stresses affect the architecture of organs under pathological conditions.

While analyzing these processes, turning to the philosophical aspects of the history of medicine and Ancient Eastern philosophy is highly relevant. Eastern thinkers interpreted the inner world of a person (psyche) and the physical body in integral unity, as a whole microcosm. Today, the obtained histological and biochemical evidence confirms the absolute scientific validity of these ancient philosophical approaches. From this point of view, in clinical practice, it is important not only to be limited to the treatment of somatic symptoms but to actively apply the principles of bioethics and medical deontology. Ethical-psychological interaction in doctor-patient relations serves as a powerful therapeutic tool in reducing the patient's mental stress and alleviating the allostatic load.

At the same time, in modern medical education, mastering these complex pathophysiological and morphological processes by students requires innovative approaches. The widespread introduction of information technologies in higher education institutions, including medicine, the statistical processing of the obtained laboratory test results in application programs such as "EXCEL," and the visualization of their pedagogical-statistical assessment elevate the analytical thinking of future specialists. An advanced digital educational environment allows medical students to more deeply understand the integral connection between histological changes at the cellular level and general clinical symptoms.

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