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HORMONAL DISORDERS IN WOMEN WHILE TAKING ANTIEPILEPTIC DRUGS.

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ANNOTATION: *The pathogenetic aspects of the hypothalamo-pituitary syndrome in patients with epilepsy is a very complex and multifaceted problem, which requires the study of the interaction of the nervous system and the endocrine system at different levels. This article provides information on the pathogenetic mechanisms of hypothalamo-pituitary syndrome associated with epilepsy, clinical manifestations, diagnostic and treatment methods. Epilepsy is a disease that contributes to the involvement of the patient's brain in the pathological process as a single functional system. In turn, a violation of the functional state of the patient's brain leads to an imbalance in the activity of nonspecific systems and manifests itself not only in electroencephalographic features, but also in characteristic disorders in the cognitive, mental and vegetative status of the patient.*

Key words: *T3, T4, TSH, TRH, pathological process, electroencephalographic features, pathogenetic mechanisms, epilepsy, patients, hypothalamic-pituitary syndrome, pituitary gland, hormones, treatment, nervous activity.*

INTRODUCTION

Hypothalamo-pituitary syndrome is a pathological condition caused mainly by the interaction of the hypothalamus and the pituitary gland. The hypothalamus is located at the upper level of the nervous system, and it carries out many physiological processes, including the production of hormones, temperature regulation, and control of sleep and wakefulness rhythms. The pituitary gland produces its own hormones

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under the influence of hormones produced by the hypothalamus. The development of hypothalamic-pituitary syndrome in patients with epilepsy is often associated with pathological changes in the hypothalamus. In this regard, the study of the functional status of the hypothalamic-pituitary system (HPS) in epilepsy will contribute to the expansion and in-depth study of pathogenetic mechanisms that will contribute to the optimization of modern diagnostic methods, which in turn will give a more complete picture of the clinical manifestation of this disease and optimize treatment methods.

The hypothalamus is an important link in the system of regulation of cerebral functions and regulates a number of processes outside the pituitary, on the one hand, and on the other hand, controls the state of the adeno-pituitary gland, constituting a single hypothalamic-pituitary system, hormones are modulators of epileptic activity, which is a prerequisite for optimizing the principles of treatment of this disease. Further study in this direction seems to be relevant and promising, since the low efficiency of antiepileptic drugs, according to many researchers, is 25%.

Most of the available research concerns the study of hormonal disorders, which were studied during or immediately after a seizure, when urgent mechanisms of regulation of hormonal homeostasis are implemented. Whereas between the seizure period and the formation of a chronic pathological process, which is provided by slowly acting mechanisms of adaptation, are practically not studied. The mechanism of chronic pathological adaptation is based on automatically proceeding metabolism, genetically predetermined with the participation of the regulatory role of the nervous and endocrine systems. Separate pathogenetic mechanisms of epilepsy, neurohormonal relationships and their influence on the characteristics of the course and prognosis of epilepsy have not been studied. Neurological manifestations of dysfunction of the hypothalamic-pituitary system in patients with epilepsy, as well as the role of the hypothalamic-pituitary system in the formation of clinical manifestations of this pathology, have not been sufficiently studied.

Purpose of the study: to study the peculiarity of clinical manifestations of imbalance and maladjustment of the hypothalamic-pituitary system in patients with epilepsy.

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Materials and methods of research: patients with epilepsy who were hospitalized in the Department of Neurology and Neurosurgery of the 1-Clinic Samarkand Medical institute for the period 2020-2021 were subject to examination, patients who were registered at the endocrinological dispensary in Samarkand, Tashkent. In accordance with the classification (international classification of epilepsy and epileptic seizures of the International League Against Epilepsy 2017), patients were examined with symptomatic epilepsy, cryptogenic epilepsy (idiopathic).

The total number of examined was 86, including 40 patients with epilepsy (group 1), 46 patients with epilepsy and signs of hypothalamic-pituitary syndrome (HHS; group 2).

To determine hormones in blood plasma, a radioimmunological method was used. All patients were tested for triiodothyronine (T3), thyroxine (T4), thyrotropin (THG), adrenocorticotropic hormone (ACGH), and cortisol levels (using standard commercial kits).

Assessment of the functioning of the autonomic nervous system is carried out according to the method of determining the autonomic index (VI) of Kerdo. In accordance with the state of the autonomic nervous (VNS) system, 5 tones are distinguished: pronounced parasympathicotonia - the predominance of parasympathetic tone, indicator values> (-31); parasympathicotonia - an intermediate state between the norm and parasympathetic tone, values from (-16 to -30); norm - balance of sympathetic and parasympathetic influences, values from (-15 to +15); sympathicotonia - an intermediate state between the norm and sympathetic tone - from +16 to +30; pronounced sympathicotonia - predominance of sympathetic tone, indicator values> (+31).

All patients underwent dynamic EEG studies. Basically, the structure of the brain was studied using magnetic resonance computed tomography (MRI).

Statistical processing was carried out using the Microsoft Excel program package (version 14.0). During the statistical processing, the methods of parametric and nonparametric statistics were used.

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Research results. During the examination of patients, attention is drawn to the specificity of the external data of patients of group 2, in particular, overweight in 16 patients ($\chi 2 = 10.656$; $p = 0.453$), while in group 1 it is 2 times less. Striae are clearly visible in the area of the abdominal wall. Young women, 18-28 years old (9), complained about headache and periodic dizziness (taking into account the main problem of epileptic seizures).

The duration of the disease in the groups was identical (10.5 ± 2.3 years and 10.9 ± 1.9 years, respectively, in groups), despite these indicators, epileptic seizures in group 2 were severe, seizures were more prolonged and frequent.

As can be seen from the data presented, patients with epilepsy in most cases have sympathicotonia, moreover, in patients with HGS burden, sympathicotonia was observed in 52.1% of cases, while in patients of group 1 - in 36.8% of cases; parasympathetic was observed in 29.8% of patients with epilepsy in combination with HGS, while in patients with epilepsy - in 34.7%. The balance of sympathetic and parasympathetic influences was 2.6 times more often observed in patients of group 1.

Expressed autonomic symptoms, autonomic lability, unstable arterial hypertension, more often against the background of headaches. The most reliable was the absence of the menstrual cycle (aminaria), which confirms the hypothalamic-pituitary syndrome in these patients.

The clinical study contributed to the establishment of the functional state of HGS in patients with epilepsy, which showed a pronounced polymorphism of pathological syndromes and symptoms caused by epilepsy, which regulates vegetative-trophic and endocrinological functions. The severity of symptoms depended on the presence of a pathological imbalance in the function of the HGS, i.e. in patients of group 2.

Dysfunctions of the HGS are most often manifested by the presence of neurotrophic syndrome ($\chi 2 = 2.877$; $p = 0.233$), sleep and wakefulness disorders ($\chi 2 = 2.523$; $p = 0.219$) and the development of emotional and psychological disorders ($\chi 2 = 6.044$; $p = 0.333$). A comparative analysis of the data obtained allows us to

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conclude that there is a more pronounced pathology in patients with epilepsy and HGS.

Neurological examination revealed diffuse symptoms in most patients, however, in patients with epilepsy not aggravated by HGS, disorders were observed mainly at the cortical-subcortical level, and in patients with HGS with this disease, the stem level of the vestibular system was involved in the pathological process.

Changes in bioelectric activity in epilepsy, observed by us in the interictal period, are similar to those described in the literature, however, computer processing of the electroencephalogram revealed differences between the data of studies in patients of the 1st and 2nd groups. The day of patients with epilepsy aggravated by HGS was characterized by a shift in the average effective frequency of the spectrum towards pathological slow wave activity, as well as the presence of signs of dysfunction of the mid-depth structures of the brain and a change in correlative relationships between the main EEG rhythms.

In the study of the hormonal status in patients with epilepsy, data were obtained indicating the presence of significant changes in the hormonal function of the hypothalamic-pituitary system, which is manifested by an imbalance of the hypothalamic-pituitary-adrenal and hypothalamic-pituitary-thyroid axis. When examining the content of ACTH in patients with epilepsy during the interictal period, no significant changes in its concentration were found. An increase in the level of ACTH according to the literature, during seizures and its normal content in the inter-paroxysmal period, suggests that ACTH is a factor in the adaptation of the body to stress.

A significant increase in the level of cortisol varied depending on the duration of the disease and was maximal in patients who were ill over 5 years (mean values 7.4 ± 0.09 years).

Since glucocorticoids increase the synthesis of serotonin, reduce the level of GABA in the brain, increase the permeability of neuronal membranes for Na + and Ca +, and decrease protein synthesis in the brain, an increase in cortisol levels can cause a decrease in the seizure threshold and a characteristic sign of an epileptic

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seizure. An increase in cortisol levels with normal ACTH values is a manifestation of dysregulation in the hypothalamus-pituitary-adrenal system. A decrease in the content of T3 in the blood plasma of patients with epilepsy and a significant variability in the level of T4 and TSH in all examined patients were found. Moreover, the severity of changes in thyroid status correlates with the severity of epilepsy, clinical signs of hypothalamic pathology, as well as the duration of the disease, the frequency and type of seizures.

Under stress (of any nature), a synergistic increase in the activity of the suprarenal and thyroid complexes at the hypothalamic, pituitary and peripheral levels occurs only in the initial phase. But in the future, activation of the adrenal complex inhibits the function of the thyroid gland at the hypothalamic-pituitary and peripheral levels. These mechanisms explain the presence of subclinical hypothyroidism in the examined patients during the interparoxysmal period.

Thus, the hypothyroid state disrupts bioelectrical processes in organs with a high level of metabolism, including the brain, where the activity of glycolytic and oxidative enzymes decreases. In addition to energy metabolism, the exchange of mucopolysaccharides in the vascular wall is disrupted, the tone of the cerebral vessels decreases.

It is known that repeated epileptic seizures of various origins are accompanied by persistent disorders of energy metabolism, in particular, a decrease in the rate and coefficient of phosphorylation. Along with this, anticonvulsants lead to a decrease in the respiratory activity of the brain tissues, dissociation of respiration by sforphorylation, and this aggravates the disturbances in the bioenergetics of patients with epilepsy caused by the epileptic process.

T3 deficiency leads not only to a distortion of the hormonal status of the body, but also due to the variety of the influence of thyroid hormones to the development of a pathological energy and metabolic state, which aggravates the course of the disease and creates a pathological basis for its progression.

Thus, functional restructuring of the state of the brain in patients with epilepsy significantly alters the activity of the hypothalamic-pituitary system. This is

confirmed by the identified autonomic disorders, changes in the bioelectrical activity of the brain, disorders in the hypothalamus-pituitary-thyroid gland and hypothalamus-pituitary-adrenal glands, and disruption of the integrated connections between these systems.

Conclusions:

1. The clinical and neurological picture of maladjustment of the hypothalamic-pituitary system is characterized by disorders of the autonomic nervous system with a predominance of sympathetic orientation.

2. The hypothalamic-pituitary system, affects the functional restructuring of the brain in patients with epilepsy and is manifested by polymorphic symptoms on the one hand, dysfunction of the HGS enhances arousal through biologically active substances, on the other hand, reduces the level of arousal through the synthesis of some neurotransmitters and disorders of the autonomic nervous system.

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