THE ROLE OF THE EPIPHYSIS HORMONE IN THE DEVELOPMENT OF EPILEPTIC SEIZURES IN YOUNG MEN

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Summary. This article discusses the role of monoaminergic systems, namely the role of the pineal gland hormone in the pathogenesis of epilepsy. The functions of melatonin in this pathology in young men are also considered.

Keywords: epilepsy, epiphysis, metabolism, melatonin, young men

Introduction
The term epilepsy (epilepsis, epilepsy) first appears in the writings of Hippocrates, as a definition of a special brain disease manifested by epileptic seizures [1]. Epilepsy is an independent nosological unit that differs significantly in etiology and pathogenesis from acute cerebral pathology and focal diseases of the brain that have epileptic seizures in their clinical picture [2].

According to the definition of the Task Force of the International League Against Epilepsy (ILAE) epilepsy is a disease of the brain defined by any of the following conditions:
1. At least two unprovoked (or reflex) seizures occurring >24 h apart
2. One unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years
3. Diagnosis of an epilepsy syndrome [3].

According to the World Health Organization (WHO), today in the world more than 65 million people suffer from epilepsy, which is about 1% of the world's population [4]. The study of the mechanisms of formation and regulation of epileptic activity and the development of new ways to correct it is one of the most important problems of modern epileptology [5].

There is no doubt about the pathogenetic role of disturbances in neurotransmitter systems in the pathogenesis of epilepsy. Monoaminergic systems deserve special attention in the context of the problem of formation of epileptic activity. The prerequisite for this is that monoaminergic neural systems form
pathways to the neocortical divisions, limbic system, cerebellum, hypothalamus; have an activating or inhibitory effect on the structures of the intermediate, anterior and neocortical parts of the brain; have not only neurotransmitter, but also neuromodulatory properties; involved in the regulation of brain homeostasis; are defined in the structures having low convulsive thresholds; in the process of metabolism in the brain form a large number of products characterized by neurotropic activity.

One of these products is melatonin. Its synthesis occurs in the epiphysis, the source is tryptophan, which is converted through a number of intermediate compounds into serotonin, and later into melatonin (Fig. 1). Changes in the functional state of the epiphysis, and primarily the production of its hormone melatonin, play a significant role in the pathogenesis of epilepsy.

Fig. 1. The pathway of melatonin synthesis in the epiphysis

Melatonin (N-acetyl-5-methoxytryptamine) is a multifunctional hormone that is a neuroprotective agent and an antioxidant, plays a key role in the coordination and synchronization of the nervous system. It has a high permeability through the blood-brain barrier, therefore fluctuations in its concentration in the peripheral blood have a significant effect on the functional state of the brain neurons. Melatonin has a subtle specific inhibitory effect, speeds up the falling asleep process.

The purpose of this research is to study the level of melatonin in young men with epilepsy, depending on the severity of the disease, the type and frequency of seizures.

Materials and Methods

The clinical material was analyzed on the basis of the survey of 256 young men with epilepsy aged 18-44 years. According to the WHO classification, all the subjects belonged to the group of young people. The average age of the patients was 31.8±2.12. On the basis of the multifactorial analysis of the clinical data, three groups of patients were singled out: the 1st group – patients with an unfavorable, progressive disease course; the 2nd group – patients with a favorable course of the disease; the 3rd group – patients with the onset of epilepsy. The severe adverse course of the disease was confirmed by the presence of pronounced EEG changes. The control
group (52 practically healthy young men) had no actual acute or chronic pathology, CNS diseases.

The studies were carried out on the basis of clinical symptoms and instrumental data analysis. The detection of melatonin in the blood serum was carried out by applying a modified Cole and Crank fluorometric method with orthophthalic aldehyde. Taken into account the circadian rhythms of melatonin production, the studies were conducted from 7:00 to 8:00 am, during the period of maximum secretion. The EEG and EEG-video monitoring were used as screening techniques.

The Student's t-test and Pearson’s agreement test ($\chi^2$) were used for statistical processing.

**Results**

In all young men, a significant decrease in morning melatonin secretion was found on average by 25.6% in comparison with the control group indicators (Table 1).

<table>
<thead>
<tr>
<th>Indices</th>
<th>patient population</th>
<th>Patients total</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1-st group</td>
<td>2-nd group</td>
<td>3-rd group</td>
</tr>
<tr>
<td>Mean value</td>
<td>0,491± 0,019</td>
<td>0,581± 0,017</td>
<td>0,753± 0,021</td>
</tr>
<tr>
<td>Dispersion</td>
<td>0,019</td>
<td>0,006</td>
<td>0,005</td>
</tr>
<tr>
<td>$N_{deviation}$</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

$N_{deviation}$ – a sign of deviation from the norm ($P<0,001$);
[author's development]

Analysis of the clinical characteristics of epilepsy and their relationship with changes in melatonin levels in the interictal period revealed a number of characteristic features: a fairly close functional relationship between seizures, frequency of seizures, the presence of "epileptiform" electroencephalographic changes and dynamics of melatonin levels in patients 1 and 2nd groups. Correlation ratios for the 3rd group were not calculated, having no significant decrease in melatonin in these patients (Table 2).

<table>
<thead>
<tr>
<th>Groups of patients</th>
<th>Clinical factors</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Type of seizures</td>
</tr>
<tr>
<td>1-st group</td>
<td>All</td>
</tr>
<tr>
<td></td>
<td>Night</td>
</tr>
<tr>
<td>2-nd group</td>
<td>All</td>
</tr>
<tr>
<td></td>
<td>Night</td>
</tr>
</tbody>
</table>

* - correlations in the 1st group are probably higher than in the 2nd group ($P<0,05$);
[author's development]
A low level of melatonin was characteristic of patients with primary and secondary generalized convulsive attacks, as well as with prolonged complex partial attacks: an average of \( 0.478 \pm 0.017 \) μM / L in the 1-st group and \( 0.566 \pm 0.012 \) μM / L in the 2-nd one. In the third group, in the presence of generalized tonic-clonic seizures, a sufficiently low content of this hormone was also detected, on average \( 0.702 \pm 0.014 \) μM / L.

In patients with epileptic seizures associated with the sleep cycle, the melatonin level was significantly lower than on a par in the groups (Table 3).

**Table 3**

<table>
<thead>
<tr>
<th>Indices</th>
<th>Patient population</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1-st group</td>
<td>2-nd group</td>
</tr>
<tr>
<td>Mean value</td>
<td>0.473± 0.024</td>
<td>0.579± 0.017</td>
</tr>
<tr>
<td>Dispersion</td>
<td>0,016</td>
<td>0.003</td>
</tr>
<tr>
<td>N_deviation</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

*N_deviation* – a sign of deviation from the norm \((P<0.001)\)

In 28 patients with generalized convulsive epileptic seizures associated with sleep, an EEG with sleep deprivation was made. The deterioration of the EEG pattern in 89.3% of cases was accompanied by the appearance of new epileptiform phenomena: spikes, "spike-slow wave" complexes, high-amplitude sharp waves (Fig. 2). In 57.1% of patients, a significant focal “slowing down” of the EEG was registered.

**Conclusion**

Thus, melatonin deficiency can be one of the reasons for increasing the activity of excitatory systems. The correlation between epileptiform changes in the EEG and
certain decrease in melatonin level has also been detected. The higher the melatonin level in young men, the lower is the convulsive readiness of the organism and the more favorable course of epilepsy.

Conflict of interest. The authors declare the absence of a conflict of interest in the preparation of this article.

References: