

Features of the Course of Epilepsy in Women of Childbearing Age

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Abstract

This publication discusses the effectiveness of therapy in women with epilepsy. The data obtained in the course of studies on the hormonal background of patients with catamenial epilepsy are presented, which subsequently led to the development of a method of differentiated (personalized) therapy for epilepsy. The use of this therapy allowed to reduce the frequency and severity of epileptic seizures, and in 22% of cases to achieve a state of clinical remission (follow-up of 6 months), thereby affecting the quality of life of patients. In addition, the state of clinical remission allows women of fertile age to plan pregnancy and childbirth, i.e., the reproductive function of women improves.

1. Introduction.

The effect of epilepsy on a woman's body is a complex multi-level process that has an effect on the endocrine system, mineral metabolism, reproductive function, etc. The relationship between epilepsy and hormonal disorders has been illustrated for many years exclusively by one phenomenon, which, however, has a certain diagnostic value — an increase in the concentration of prolactin in the blood after generalized convulsive seizures. However, in the future, the interaction of epilepsy and the endocrine system began to be studied mainly in the context of reproductive function. The latter is of particular importance for women, whose ability to procreate largely determines the success of the life scenario and the quality of life [4]. It can occur in both women with generalized and focal epilepsy. Seizures in such patients are associated with their menstrual cycle. Diagnostic is a twofold and higher increase in the frequency of seizures in a certain phase compared to other phases. According to Herzog et al. (1997), women with catamenial epilepsy are divided into three subgroups: C1 (occurrence of seizures in the perimenstrual period, days from -3 to 3), C2 (ovulation, days from 10 to 13), and C3 (luteal phase, days from 10 to 13) [1].

The most studied potential mechanism explaining why seizures become more frequent in some women depending on the phase of the cycle is a cyclic change in the level of reproductive hormones. In humans and

animal models, it has been shown that estrogens have proconvulsive properties, while progesterone, in particular its active metabolite allopregnanolone, have an anticonvulsive effect (Reddy, Rogawski, 2009). The results of the conducted studies also suggest that these sex hormones have multiple pathways of influence, depending on factors such as the endocrine state, the concentration of sex hormones and metabolism (Scharfman, MacLusky, 2006). Probably, the periovulatory form of catamenial epilepsy (C2) occurs due to an increase in the concentration of estrogens in the middle of the cycle [3]. In women suffering from epilepsy, the frequency and intensity of seizures vary depending on the level of sex hormones during the menstrual cycle. Estrogens have a proconvulsive effect, progesterone has an anticonvulsive effect [2].

2. The Purpose of the Study.

To evaluate the effectiveness of treatment in women with epilepsy.

3. Materials and Methods of Research.

Among 120 women aged 18-55 who sought specialized help from an epileptologist, we identified 34 patients with disorders in the reproductive sphere and an increase in seizures associated with the menstrual cycle. The age of the onset of the disease in this group of patients varied from two to 45 years, the duration of active epilepsy - from three to 42 years.

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The examination included clinical and neurological examination, routine EEG and (or) EEG video monitoring, MRI of the brain, laboratory tests. Catamnesis for a period of one to five years (an average of three years) was monitored in 28 of 34 patients. All patients were prescribed current therapy with antiepileptic drugs (AEP) for the first time or underwent correction. The effectiveness of treatment was evaluated on the basis of attack diaries, independently filled out by patients. Remission was found in the complete absence of seizures during the entire period of catamnestic observation, improvement — with a decrease in the frequency of seizures by 50% or more, in other cases, therapy was regarded as ineffective. Disorders of reproductive functions were assessed on the basis of anamnesis, clinical examination, laboratory data, as well as diaries where patients noted the days of menstruation.

In order to clarify the clinical, biochemical, neurophysiological aspects of catamenial epilepsy, we examined 100 women with its various forms. The comparison group consisted of 20 women with symptomatic epilepsy that did not have a cyclical course. The control group consisted of 20 healthy women who did not suffer from epilepsy. All the examined patients underwent a clinical and neurological examination, which included the study of the cognitive sphere, neurophysiological studies (EEG), as well as laboratory studies of the level of female sex hormones during one cycle in the follicular and luteal phases.

There are a huge number of publications in the modern literature devoted to the problem of EEG in epilepsy, however, works devoted to the study of EEG in women with catamenial epilepsy are isolated, and therefore, we conducted a comparative analysis of EEG data from studies of women with catamenial epilepsy in various phases of the menstrual cycle. The study of the epileptic activity of the brain in the second phase of the menstrual cycle is dictated by the fact that this phase of the cycle is accompanied by primary progesterone (progestin) insufficiency, which in turn causes a decrease in the anticonvulsant effect of progesterone.

According to the results of the study, it turned out that EEG indicators in patients with catamenial epilepsy have differences from those in women with symptomatic epilepsy. Thus, the analysis showed differences in the types of EEG. So, if in patients with CE we more often found types I and II of EEG, then in patients with symptomatic epilepsy we more often found types II and V. This distribution varied depending on the phase of the menstrual cycle. The greatest changes in the second phase of the menstrual cycle were noted in the group of patients with CE. In particular, the representation of patients with type I EEG decreased from 35% to 3%, and the representation of type IV and V increased from 15 to 33 and from 1.6 to 30%, which indicates an increase in epileptic activity of the brain. This may explain the increase in generalized seizures in patients with CE in the second phase of the menstrual cycle.

The greatest changes were noted in the second phase of the menstrual cycle in the group of patients with CE. In particular, the representation of patients with type I EEG decreased from 35% to 3%, and the representation of type IV and V increased from 15 to 33% and from 1.6 to 30%, which indicates an increase in epileptic activity of the brain. This may explain the increase in generalized seizures in patients with CE in the second phase of the menstrual cycle. To clarify the quantitative characteristics of the EEG in patients with Kins, the paroxysmal activity index and the index of the main brain rhythm - alpha rhythm in various phases of the menstrual cycle were further studied. We performed a quantitative analysis of these neurophysiological indicators in three different functional states: rest, mental load and hyperventilation for 1.5-2 minutes.

The analysis of the brain paroxysmal index in patients of groups I and II revealed characteristic differences in both indicators among patients of both groups, and in different phases of the menstrual cycle. The data of the analysis of the index of paroxysmal activity of the brain in patients of groups I and II are presented in Table 1.

Table 1. Indicators of the paroxysmal index in the examined patients

Brain condition	Groups of patients	Cycle phase
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		luteal	follicular
In peace	Group I (n=70)	6,8±0,4	8,2±0,7
	Group II (n=70)	8,9±0,5*	9,1±0,6
Intellectual load	Group I (n=70)	6,2±0,4	7,5±0,3
	Group II (n=70)	7,9±0,4*	8,2±0,6
Hyperventilation	Group I (n=70)	7,8±0,4	12,3±0,8
	Group II (n=70)	12,8±0,7*	14,7±0,9*

* - significant differences with group I patients (p0, 05)

As can be seen from the presented table, the paroxysmal index tends to fluctuate, depending both on the functional state of the brain and the phase of the menstrual cycle. The index of paroxysmality in patients of group II was initially significantly higher (p0. 05) than in patients of group I. As the analysis of the paroxysmal index showed, it was different in different brain conditions and depended on the phase of the menstrual cycle. The greatest fluctuations were noted by us during hyperventilation in group I of patients. At values of 7.8±0.4 in the luteal phase, in the follicular phase, it increased to 12.3±0.8. Slightly smaller fluctuations were observed in group II, at values of 12.8±0.7 in the luteal phase, in the follicular phase it reached the figure of 14.7±0.9. In comparison with group I, the dynamics of this indicator was slightly lower. This confirms the importance of hyperestrogenemia in the development of epileptic brain activity. It is important to note that in all brain conditions, the dynamics of the paroxysmal index of the brain in patients of the first group I in the follicular phase was higher than in patients of the second group.

It should be noted that the results obtained indicate the presence of signs of congenital channelopathy in women with catamenial epilepsy, which requires in most cases a revision of treatment tactics, and in particular the replacement of AEP with a modern one with better pharmacokinetic indicators. Our choice fell on the AEP of the topiramate group. This is dictated by a number of facts. First, modern AES, which are topiramates, not only ensure the safety of long-term use, have greater bioavailability than carbamazepine, are better excreted from the body, which allows you to properly control the dose of the drug in the blood, do not affect the polysomal enzyme system of the liver,

thereby do not affect the metabolism of female sex hormones, which, as is known, affects the course of catamenial epilepsy. We have prescribed the drug Topepsil at a dosage of 200 mg/day. As our research has shown, the observation and management of women suffering from catamenial epilepsy is a process that requires a multidisciplinary approach, since its pathogenesis is based on hormonal balance disorders. Proper and timely conduct of certain types of studies (examination of a neurologist-epileptologist, examination of a gynecologist, endocrinologist, regular neurophysiological studies, biochemical analyzes, leads to a decrease in the frequency and duration of epileptic seizures.

4. The Results of the Study.

The onset of seizures before menarche was noted in 25% of patients, most often epilepsy debuted at the age of 13-20 years — in 37.5% of patients. In the third and fourth decades of life, seizures began in 25% and 10.9% of individuals, respectively. Only one patient (1.6%) had the onset of seizures after 40 years.

The duration of active epilepsy was less than five years in 10.9% of patients, sixty years — in 26.6%, 11-15 years - in 21.9%, 16-20 years — in 20.3%, 21 years or more-in 20.3%.

In most patients, seizures persisted for a long time, which was the reason for the appointment of AEP in 83.6% of cases, while in 41.2% they were used in insufficient doses and (or) irrational combinations.

5. Conclusions.

1. The interaction of epilepsy and the reproductive system in women of childbearing age with epilepsy in our study was detected in 14.3% of cases (34 patients out of 120). The main patterns of the above-mentioned interaction are CE and menstrual cycle disorders.

2. After correction of treatment, normalization of the menstrual cycle was observed in 48% of patients. Remission among patients of this group was noted in 57.1% of cases, improvement — in 14.3%, lack of effect - in 28.6%.

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