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Research Article

EPILEPSY IN WOMEN OF FERTILE AGE

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ABSTRACT

Epilepsy in women is caused by the hypothalamic-pituitary-ovarian system, and women with epilepsy have a higher incidence of disorders such as menstrual irregularities, polycystic ovary syndrome, and infertility. The incidence of sexual dysfunction in the group of women with epilepsy ranges from 14 to 50%.

It was found that epileptic seizures and long-term use of antiepileptic drugs (AEDs) lead to reproductive disorders of the female body, affecting the endocrine, hormonal, and sexual spheres of the female body.

KEYWORDS

Epilepsy, antiepileptic drugs, reproductive function, women.

INTRODUCTION

It should be emphasized that the connection between epileptic seizures and the days of menstruation was found in 14,5% of women. The above menstrual irregularities (MMC) can be interpreted as increased excitability of the hypothalamic-pituitary system caused by the underlying disease, which led to secondary disorders of the reproductive system. According to our research data, the testosterone level against the background of monotherapy was 1,6-2,2 nmol / l, and in the polytherapy group 2,1-2,7 nmol / l (p> 0,05), an increase in testosterone levels was found in 21,7% and amounted to 3,75 ± 0,05 nmol / l. Thus, the study of the hormonal profile in women with different forms of epilepsy by menstrual cycle MC phases made it possible to establish that hyperestrogenemia, hyperandro genemia, hyperprolactinemia, hypoprogesteronemia were dominant in all groups of patients. The tropic hormones LH and FSH were characterized by low concentrations in both phases of the cycle in all groups, which indicates the presence of

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secondary hypogonadism. All these disorders require hormone replacement therapy and correction under the control of an endocrinologist, neurologist, and EEG.

Being a woman with epilepsy is not the same as being a man with epilepsy. Epilepsy affects sexual development, the menstrual cycle, aspects of contraception, fertility, and a woman's reproduction. The diagnosis of epilepsy and the use of antiepileptic drugs (AEDs) confront women of childbearing age with many challenges; both the disease and its treatment can alter the menstrual cycle and fertility [1].

A number of studies have shown that the peculiarity of epilepsy in women is due to the hypothalamic-pituitary-ovarian system with daily and monthly cycles, accompanied by diverse changes inherent only in the body of a woman: pregnancy, childbirth, lactation [2]. These and other studies show that women with epilepsy have a higher incidence of disorders such as menstrual irregularities, polycystic ovary syndrome, and infertility. The frequency of sexual dysfunctions in the group of women with epilepsy ranges from 14 to 50% [5].

It was found that epileptic seizures and long-term use of antiepileptic drugs (AEP) lead to impaired reproductive function of the female body, affecting the endocrine, hormonal, and sexual spheres of the female body [3]. However, what is paramount in influencing the reproductive function of a woman with epilepsy remains debatable, since it is believed that the undesirable effects of AEDs on a woman's fertility are genetically determined [3,6] or whether epileptic seizures still affect the reproductive function of a woman, the question remains open. [4].

A number of authors have found that changes in estrogen secretion in women with epilepsy lead to depressive disorders. At the same time, the seizures themselves can lead both to changes in the levels of certain hormones and to mental disorders in women with epilepsy, but this issue also remains insufficiently studied [8]. Epilepsy and pregnancy, management of pregnancy and childbirth remains a big problem for women with epilepsy. According to Russian researchers, over the past decades there has been a fourfold increase in the number of births among women with epilepsy [2,3]. In the world, 0.3% of newborns are born annually from women suffering from epilepsy [9,10].

The impact of epilepsy on women's lives is very different compared to men, as it affects the areas of sexuality, reproduction, the menstrual cycle, and contraception, in addition to the teratogenicity of AEDs.

Purpose of the study: to study the role of hormonal changes in the course of epilepsy in women of reproductive age, against the background of taking antiepileptic drugs, and on this basis to develop treatment tactics.

MATERIALS AND METHODS OF RESEARCH

15 patients with epilepsy of childbearing age who applied to the 4th City Clinical Hospital named after I.I. At the time of statistical processing, the age of women ranged from 16 to 44 years (average age 30 years). The age of onset of epileptic seizures ranged from 1 to 44 years.

Based on careful clinical, EEG, neuroimaging research methods, we first diagnosed epilepsy in 3 women (20%) cases, and in 12 women (80%) the diagnosis was previously established. All patients were divided according to etiological factors into the following: idiopathic form of epilepsy (hereditary form),

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symptomatic form and cryptogenic or epilepsy of unknown etiology. Among all forms, the symptomatic form prevailed - 7 (50%), then the idiopathic form - 4 (25%) and the cryptogenic form - 4 (25%) cases.

The choice of examination methods was based on the modern and most informative and promising methods for a comprehensive study of neurological disorders and the functional state of the brain. Classifications of types of seizures and epilepsy and epileptic syndromes (ILAE 1981, 1989) were used, as well as taking into account the requirements for a list of diagnostic measures in patients with epilepsy. All patients underwent a thorough collection of complaints and anamnesis during the clinical and neurological examination. Particular attention was paid to the cause that led to the development of epileptiform seizures, to the initial manifestations of epileptic seizures, their frequency, the duration of epileptic manifestations, the clinical picture, the course of the post-seizure state, the presence of status epilepticus in the anamnesis, drug therapy, family history burden (data were obtained from the patients themselves as well as from relatives). Conducted electroencephalography (EEG), laboratory research methods, hormonal profile (estradiol, progesterone, LH, FSH, testosterone, prolactin).

RESULTS OF THE STUDY

The study of the clinical and laboratory characteristics of patients showed that symptomatic (50%), idiopathic (25%) and cryptogenic (25%) epilepsy ($p<0.05$) prevailed in women of childbearing age in terms of etiology.

Juvenile myoclonic epilepsy (JME) was statistically significant among idiopathic forms of epilepsy. Less common were idiopathic occipital epilepsy (2.4%), and autosomal dominant frontal lobe epilepsy (4.9%). The benign course of the pharmacoinduced form of epilepsy prevailed statistically significantly - in 82.9% of cases, the benign course - in 14.6% of cases. The status course of idiopathic epilepsy was registered in 2.4% of cases.According to the etiology of symptomatic epilepsy, epilepsy against the background of trauma (25.2%), mesial temporal sclerosis (18.7%), and congenital anomalies of the central nervous system (CNS) (19.4%) prevailed statistically significantly. Clinical remission in symptomatic epilepsy was observed in 22.2% of cases, which is more common than in the idiopathic form (13.4%), and in 8.9% of cases there was clinical and electrophysiological remission. The duration of remission in symptomatic epilepsy is from 1 to 18 years. The debut of symptomatic epilepsy in childhood was noted at 1 year of age against the background of congenital hereditary diseases of the central nervous system. The debut of symptomatic epilepsy in adulthood was noted at the age of 17±2.7 years on the background of a brain injury and neuroinfection. Among the reasons for the late diagnosis of symptomatic epilepsy was the complexity of diagnosis and the untimely appeal of patients to neurologists.

Among all the studied forms of epilepsy, a low proportion accounted for cryptogenic epilepsy - 25%. The status course of cryptogenic epilepsy was noted in 7.0% of cases. An analysis of the study of patients with epilepsy of childbearing age showed that there were no statistically significant differences in the age of patients at the time of observation, the time from the onset of the disease to the provision of qualified neurological care ($p<0.05$).

In patients with symptomatic epilepsy, 3 peaks of the disease were noted: the first peak was at the age of 1 to 15 years and amounted to 17%; the second - from 16 to 28 years old and amounted to 25.2%; the third - after 32 years and amounted to 13.3%. In patients with

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idiopathic epilepsy, the peak of the disease occurred at the age of 12-17 years, cryptogenic epilepsy - 15-20 years. In terms of frequency, generalized tonic-clonic seizures (GTCS) over the past year in patients with idiopathic and cryptogenic forms did not show statistically significant differences - 14.1% and 13.4%, respectively; with a symptomatic form - 5.9% of cases. Remission of epilepsy was more often achieved in patients with the cryptogenic form and amounted to 32.4% of cases; in idiopathic and symptomatic forms - 13.4% and 22.2%, respectively ($p<0.05$).

In general, the study of complaints and anamnesis of patients showed that the type of epileptic seizures was dominated by primary generalized epilepsy - (39.2%) cases, second place - secondary generalized epilepsy - (32.3%) cases, and the third - focal epilepsy - (28.5%) cases.

Analysis of the development of the rhythm of menstruation in patients with epilepsy showed that in the vast majority of cases (69%), the age of menarche was 12.5±0.3 years. However, every fourth patient had an early menarche. In patients, the menstrual cycle while taking antiepileptic drugs was normoponic in 75% of cases. Postponic nature of menstruation according to the type of oligomenorrhea was detected in 25%, extremely rarely (2.3%) secondary amenorrhea was observed.

It should be emphasized that the relationship of epileptic seizures with the days of menstruation was found in 14.5% of women. The above menstrual disorders (NMC) can be interpreted as increased excitability of the hypothalamic-pituitary system caused by the underlying disease, which led to secondary disorders of the reproductive system.

The most frequently reported complaints were: irregular menstruation in (27.7%), dysmenorrhea in (16.2%). In addition, there were drawing pains in the lower abdomen in (7.5%), heavy menstruation in (3.1%), premenstrual spotting and dyspareunia in (1.6%) girls and women.

According to our research data, the level of testosterone during monotherapy was 1.6 - 2.2 nmol / l, and in the polytherapy group 2.1 - 2.7 nmol / l ($p> 0.05$), which fully coincides with the point of view of J .Isojarvi, 1990. We found an increase in testosterone levels in 21.7% and amounted to 3.75±0.05 nmol/l.

As we found earlier, patients with IE were characterized by mild depression according to the Hamilton Depression Scale, patients with PT, PI, VA, OH had severe depression, and patients with CE had moderate depression.

The patients had the following manifestations of the gynecological status, such symptoms as hirsutism (29.8%), dysmenorrhea (16.2%), follicle persistence (9.7%), infertility (9%) dominated.

We have studied the dependence of the type of epileptic seizures on the hormonal background in two phases of the menstrual cycle. It was found that in patients with depression in the presence of two or more types of seizures, compared with patients in whom epilepsy is clinically manifested by one type of seizures, there was a higher level of estrogen in the follicular phase of the menstrual cycle.

We conducted studies of the basal values of blood serum hormones in three phases of the menstrual cycle of women: the follicular phase, ovulation and luteal phase while taking AED.

The processes that take place during the menstrual cycle can be described as phases corresponding to changes in the ovaries (follicular, ovulatory and luteal) and in the endometrium (menstrual, proliferative and

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secretory phases). Table 1 shows the mean hormone levels in the IE group by day of the menstrual cycle.

As can be seen from Table 1, for patients from the group, on the 7th, 14th and 21st day of the cycle, a significant decrease in the basal levels of the average values of LH, FSH and progesterone against the background of hyperestrogenemia, hyperprolactinemia and hyperandrogenmia was characteristic.

Table 1.

Average values of hormones in the group with epilepsy on days 7, 14 and 21 of the cycle.

Hormones	7th day	14th day	21st day
LH, ME/L	5,7±0,6	14,3±2,5	4,9±0,4
Control, ME/L	12,3±0,4	51,7±2,1	10,2±0,6
p	<0,05	<0,05	<0,05
FSH, ME/L	3,6±0,3	9,8±2,3	3,4±0,4
Control, ME/L	6,6±0,4	17,2 ± 2,3	4,1±0,2
p	<0,05	<0,05	>0,05
Prolactin, ng/ml	15,6±0,3	16,3±0,5	15,6±0,6
Control, ng/ml	5,7 ±0,3	5,4±0,5	5,5 ±0,2
p	< 0,05	<0,05	<0,05
Free Testosterone, ng/ml	2,2±0,01	2,5±0,03	1,7±0,02
Control, ng/ml	0,2±0,01	0,2±0,01	0,2±0,01
p	<0,05	<0,05	<0,05
Estradiol, pg/ml	322,4±1,5	335,6±2,2	325,5±1,2
Control, pg/ml	345,3±9,2	285,3±8,2	247,5±6,2
p	> 0,05	<0,05	<0,05
Progesterone, nmol/l	0,1±0,03	0,3±0,02	6,1±0,4
Control, nmol/l	1,5±0,03	9,8±1,3	49,5±3,2
p	<0,05	<0,05	<0,05

Note: p - significance of differences with the control group < 0.05

Thus, the study of the hormonal profile in women with different forms of epilepsy by MC phases made it possible to establish that the following were dominant in all groups of patients: hyperestrogenemia, hyperandrogenemia, hyperprolactinemia, hypoprogesteronemia. Tropic hormones LH, FSH were

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characterized by low concentrations in both phases of the cycle in all groups, which indicates the presence of secondary hypogonadism.

Against the background of the treatment of epilepsy with antiepileptic drugs, a teratogenic effect occurs that affects reproductive function, and all these disorders require hormone replacement therapy and correction under the supervision of an endocrinologist, neurologist, and EEG.

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