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Hormonal characteristics and indicators of life quality in women of fertilal age with idiopathic epilepsy

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Abstract

The clinical material of the study was 82 patients with idiopathic epilepsy. A study of the hormonal profile in women with IE through the phases of the menstrual cycle revealed that the dominant patients with idiopathic epilepsy were:hypoestrogenemia, hyperandrohinemia, hyperprolactinemia, hypoprogesteroemia. Tropic hormones LH, FSH were characterized by low concentrations in both phases of the cycle in all groups, which indicates the presence of secondary hypogonadism. Patients with IE were dominated by moderate depression on the background of increased self-esteem as a whole, as well as the dominance of individuals in the socially maladaptive risk of group 1. The MMSE and LISAT-11 tests revealed a decrease in cognitive functions at the level of mild dementia and the presence of increased self-esteem of quality of life. Finally, the Hamilton scale determined the presence of mild depression.

Keywords: idiopathic epilepsy, women, fertile age, hormones

INTRODUCTION

Despite the fact that the effect of epilepsy on hormonal status and reproductive functions in women has been studied extensively, however, this problem continues to attract the attention of doctors of various specialties [1]. To some extent, this is due to the fact that in the majority of works devoted to female epilepsy, disorders in the endocrine and mental spheres are considered in isolation, while almost no comprehensive interdisciplinary studies have been performed in this direction [2, 3]

The effect of epilepsy on the lives of women is very different compared to men, since it affects the areas of sexuality, reproduction, the menstrual cycle and contraception, in addition to the teratogenicity of antiepileptic drugs [4, 5].

A study of the medical literature and a comprehensive review of published summaries and reports of international meetings on epileptology over the past five years have shown that sensitization of women with epilepsy begins in adolescence with education and preparation for sexual life and available contraceptive methods to avoid unwanted pregnancies and serious consequences that they can cause.

Approximately 1/3 of women with epilepsy experience disease variations associated with the menstrual cycle, possibly due to the neurotoxic effects of estrogens (not balanced by progesterone hormones) [6].

Despite the urgency of the problem, there are few works on this topic in the literature. There are no multicenter, placebo-controlled studies on the effects of AED on the reproductive organs of women. There are few publications (dissertations, articles).

All of the above served as the reason for the present study.

The purpose of the study was to assess the hormonal characteristics of women of childbearing age with epilepsy of various origins on the 7th, 14th and 21st days of the menstrual cycle.

MATERIAL AND METHODS

The clinical material of the study was 82 sick women with idiopathic epilepsy of childbearing age who applied to 1 Republican Clinical Hospital on an inpatient and outpatient basis, to 3 clinics of the Tashkent Medical Academy, as well as 20 healthy women of childbearing

age not suffering from epilepsy. At the time of statistical processing, the age of women ranged from 16 to 45 years. The debut age of epileptic seizures ranged from 1 month to 45 years. The duration of epilepsy in women of childbearing age ranged from 1 month of life to 35 years.

In accordance with the goal and objectives, for an in-depth study of this study, we divided the clinical cases into 3 groups (according to the Classification of Epilepsy of the International Antiepileptic League ILAE: review and update of 2017). The diagnosis of epilepsy was based on a combination of clinical, electroencephalographic data, as well as various methods of neuroimaging.

The choice of examination methods was based on 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 epilepsies and epileptic syndromes were used (ILAE 1981, 1989), as well as the requirements for a list of diagnostic measures in patients with epilepsy.

Table 1 shows the distribution of patients by age.

Table 1: Distribution of sick women by age (according to WHO)

Age, years	Idiopathic epilepsy n=82
16 – 29	13 (15,8%)
30-44	60 (73,1%)
45-59	16 (19,5%)
60-74	-
Total:n=82	82(46,9%)

In addition to the study of general somatic and neurological statuses, general clinical, biochemical (total bilirubin, total protein, Alt, AcT, alkaline phosphatase, amylase, urea, creatinine, blood sugar); immunological (ciliaryneurotrophic factor) and hormonal (estradiol, progesterone, LH, FSH, St. testosterone, prolactin); blood tests. Instrumental methods of research included: echo-electroencephaloscopy, electroencephalography, MRI and CT of the brain with contrasting with gadolinium (according to indications), vascular program (according to indications) (MagnetonEspree 1.5 Tc (Siemens, USA).

In addition, scales were used to perform co-metric studies: social adaptation and maladaptation according to Novikova, EuroQol tests - 5D, MMSE, LISAT-11, Beck depression scale.

The data obtained were processed using computer programs Microsoft Excel and STATISTICA_6 (136-140). The significance of differences in quantitative indicators (n> 12) was determined by the Wilcoxon method for unrelated ranges, to determine the reliability of small samples (n <12), the non-parametric randomization criterion for the Fisher components for independent samples was used, for the qualitative values, the exact Fisher-Irwin criterion was used.

RESULTS

The analysis of gynecological morbidity did not reveal a specific gynecological pathology. Among the patients, symptoms dominated by hirsutism (29.8%), dysmenorrhea (16.2%), follicle persistence (9.7%), infertility (9%).

We have conducted research on the basal values of blood serum hormones in three phases of the menstrual cycle of women: follicular phase, ovulation and luteal phase with the use of AEDs.

Table 2 shows the average values of hormones in patients with IE by the days of the menstrual cycle.

Table 2: Average values of hormones in the group with idiopathic 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	15,3±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
Freetestosterone, ng/mg	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	22,4±1,5	35,6±2,2	25,5±1,2

Table 2 cont'd

Контроль,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 control group <0.05

As can be seen from table 2, for patients with IE, on the 7th, 14th and 21st day of the cycle, a significant decrease in basal levels of the average values of LH, FSH and ovarian hormones (estradiol, progesterone) was observed against the background of hyperprolactinemia and hyperandrogenism.

At the next stage of the work, we set out to study the effect of estradiol, progesterone, LH, FSH levels in the follicular and luteal phases of the menstrual cycle in patients with affective disorders on psychopathological indicators on the scales of self-assessment and quality of life.

Table 3 shows the correlation of the average values of hormones with indicators of psychometric scales in patients with idiopathic epilepsy in the folliculin/luteal phase.

Table 3: Correlation of mean hormone values with psycho-metric scales in patients with idiopathic epilepsy in the follicular / luteal phase (n=25)

Hormones	**Level 1 socialdisadaptation**	**EuroQol - 5D: QoL assessment at an average level**	**LISAT-11: IncreasedQoL**	**Test MMSE MildDementia**	**Hamilton Scale: MildDepression**
Estradiol	- 0,30/-0,25	-0,30/-0,28	-0,20/-0,24	**-0,56**/-0,51****	**- 0,59*/-0,90***
Progesterone	0,24/0,32	0,33/0,33	0,11/0,36	**0,74**/-0,28**	0,33 / **-0,63***
LH	-0,29/0,29	-0,41/-0,18	-0,12/-0,16	**-0,55*/-0,59***	**-0,54*/-0,97***
FSH	-0,29/0,18	-0,24/-0,20	-0,38/-0,24	**-0,51*/-0,56***	**-0,52*/-0,59***
Free Testosterone	-0,32/-0,29	-0,40/-0,32	-0,36/-0,12	**-0,52*/-0,56***	**-0,64**/ 0,74***
Prolactin	**-0,54/-0,54**	-0,28/-0,28	-0,36/-0,36	-0,30 /-0,30	-0,07/ -0,07

Note: statistically significant correlations are shown in bold; * - p <0.05, ** - p <0.01, *** - p <0.001, **** - p <0.0001.

From table 3 it is seen that previously in patients with idiopathic epilepsy, the dominance of individuals with socially maladaptive risk of group 1 was revealed. Tests MMSE and LISAT-11 revealed a decrease in cognitive functions at the level of mild dementia and the presence of an increase in self-esteem of quality of life. And finally, the Hamilton scale determined the presence of mild depression. In patients with IE, moderate depression dominated against a background of increased self-esteem in general [6-9].

The correlative characteristics of indicators of scales and hormones in the follicular and luteal phases in patients with IE revealed the following changes.

In patients with mild depression who dominated IE, progesterone levels in the follicular phase of the menstrual cycle positively correlated with mild dementia (r= 0.74, p<0.01) on the MMSE scale. The progesterone level in the luteal phase of the menstrual cycle positively correlated with depression indicators on the Hamilton scale (r= 0.63, p <0.05).

The values of estradiol in the follicular phase had a negative correlation with all scales, while it was significantly with the data of the Hamilton scale (r= –0.59, p <0.05) and the MMSE scale (r= –0.56, p<0.05). Values of estradiol in the luteal phase had a negative correlation with all scales, while it was reliable with the data of the Hamilton scale (r= –0.90, p <0.05) and the MMSE scale (r= –0.51, p <0.05) . So, in patients with mild depression and low levels of estradiol, higher rates were observed on all scales of self-esteem in both phases of the cycle, which is confirmed in studies by Zheleznova E.V., 2012.

Further, a study of the correlation of LH values in the follicular phase in patients with IE showed that the LH level in the follicular phase of the menstrual cycle also negatively correlated in patients with moderate depression (IE group) with MMSE and Hamilton score (r = –0.55, p < 0.05 and r = –0.54, p <0.05, respectively). Further, a study of the correlation of LH values in the luteal phase in patients with IE showed that the LH level in the luteal phase of the menstrual cycle also negatively

correlated in patients with moderate depression (IE group) with MMSE data and with Hamilton indicators (r = –0.59 , p <0.05 and r = –0.97, p <0.05, respectively).

In patients with IE, the level of FSH in the follicular phase of the menstrual cycle negatively correlated with MMSE and the Hamilton scale (r = –0.51, p <0.05 and r = –0.52, p <0.05, respectively). In patients with IE, the level of FSH in the luteal phase of the menstrual cycle negatively correlated with MMSE and the Hamilton scale (r = –0.56, p <0.05 and r = –0.59, p <0.05, respectively).

Further, in patients with IE, the testosterone level in the follicular phase of the menstrual cycle negatively correlated with MMSE and the Hamilton scale (r= –0.52, p<0.05 and r= –0.64, p<0.01, respectively). Further, in patients with IE, the testosterone level in the luteal phase negatively correlated with MMSE and the Hamilton scale (r= –0.56, p<0.05 and r= –0.74, p<0.01, respectively).

Finally, in patients with IE, prolactin level in the follicular phase of the menstrual cycle negatively correlated with indicators of social maladaptation of level 1 (r= –0.54, p<0.05). Prolactin level in the luteal phase of the menstrual cycle negatively correlated with indicators of social maladaptation of level 1 (r= –0.54, p<0.05).

Thus, in patients with IE, it was found that the average values of all indicators on all psychometric scales were higher in women with lower levels of estradiol in the blood. In other words, the lower the level of estradiol, the more pronounced the anxiety-depressive symptoms.

Patients with depression and low estradiol showed higher rates on all self-assessment scales. The levels of progesterone, LH, FSH in both phases of the cycle correlated (progesterone - positively, the rest - negatively) with indicators of depression and MMSE test.

The discussion of the results. So, our study showed an ambiguous effect of the level of various hormones on the concomitant psychopathological symptoms in women with epilepsy. Moreover, the obtained results confirm the data that with a decrease in estrogen levels, depressive states more often develop [5,7].

It has long been proven that the effect of estrogen on brain structures, in particular on the hippocampus, is similar to the action of antidepressants that selectively inhibit serotonin reuptake. However, these mechanisms of action of steroid hormones are not fully understood. However, it is known that estrogens lead to an increase in serotonin concentration in those areas of the brain that are responsible for mood. In the hypocampus, there are receptors for estrogens and androgens [2]. As far back as 2003, Scharfman H.E. et al. Found that estrogens contribute to the synthesis in the hippocampus of a neurotrophic factor - BDNF (brain-derived neurotrophic factor) which, along with serotonin, is able to regulate the development and plasticity of the nerve pathways involved in the formation of mood disorders. Therefore, a decrease in estrogen levels leads to an increased risk of developing depression. [3]. All together worsens significantly other indicators of quality of life, which we have identified.

In other words, female sex hormones, acting on the hippocampus, have a definite effect on both epilepsy and the development of depressive symptoms, and the high comorbidity of these disorders apparently explains the existence of a single pathogenetic mechanism of their development [19].

This is also confirmed by the results obtained in this work, which showed that in patients with depression with two or more types of seizures compared with patients who clinically have epilepsy with one type of seizures, a higher level of estrogen in the follicular phase of the menstrual cycle is noted. In addition, it was found that with a lower level of estradiol, more pronounced depressive symptoms were observed.

In our study, the level of progesterone correlated with all individuals with IE was significantly lower than normal and correlated only with MMSE, LISAT-11 tests. So, according to some authors, there is an assumption about the depressive effect of progesterone in women [16].

Studying the role of FSH and LH,it should be emphasized that pathological discharge activity in the brain disrupts the production of LH and FSH, which in turn, changes the concentration of estradiol and progesterone. To date, there is no direct evidence of the influence of tropic hormones on affective status. [17, 18]. In our study, the tropic hormones LH, FSH were characterized by low concentrations in both phases of the cycle in all groups, which indicates the presence of secondary hypogonadism.

In the present study, prolactin concentration was negatively correlated with the level of social maladaptation in patients with PT epilepsy (r = –0.59, p <0.05).

Thus, a study of the hormonal profile in women with different forms of epilepsy in the MC phases revealed that the dominant in patients with IE were: hypoestrogenemia, hyperandrogenemia, hyperprolactinemia, hypoprogeste-rogenemia

CONCLUSION

1. A study of the hormonal profile in women with different forms of epilepsy in the MC phases revealed that the dominant in patients with IE were: hypoestrogenemia, hyperandrogenemia, hyperprolactinemia, hypoproge-sterogenemia
2. Tropic hormones LH, FSH were characterized by low concentrations in both phases of the cycle in all groups, which indicates the presence of secondary hypogonadism.
3. In patients with IE, moderate depression dominated against the background of increased self-esteem in general, as well as the dominance of individuals with

socially maladaptive risk of group 1. MMSE and LISAT-11 tests revealed a decrease in cognitive functions at the level of mild dementia and an increase in self-esteem of quality of life. And finally, the Hamilton scale determined the presence of mild depression.

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