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## THE EFFECTIVENESS OF THE USE OF MODERN ANTIEPILEPTIC DRUGS DURING PREGNANCY IN WOMEN

**Zoirov Sunnat Ro'zimurodovich, Edgorov Zhasurbek Juraevich**

*Student of Bukhara State Medical Institute, Bukhara, Uzbekistan*

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### Abstract

In this article, patients are divided into two groups. Comparative data on the effectiveness of lamotrigine and Convulex used in the treatment of epilepsy during pregnancy in women are presented. The research group consisted of 88 pregnant women aged 20 to 40 years who were diagnosed with epilepsy. The first group included 42 patients who were prescribed lamotrigine. In the second group there were 46 pregnant women who were diagnosed with epilepsy, who were prescribed seizures. We observed prenatal and 30-day-old patients in the postpartum period. It is proved that the optimal condition for the treatment of epilepsy during pregnancy is monotony with a minimum dose of anticonvulsants.

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**Relevance.** Epilepsy is one of the most common neuropsychiatric diseases, ranking third among organic brain diseases. Epilepsy is registered with a frequency of 1% in the population, and 25-40% of patients are women of childbearing age. In 10-13% of women, epilepsy debuts during pregnancy, 5% have more frequent seizures during and after childbirth [2, 3, 5]. According to P.N.Vlasov, about 0.3–0.4% of newborns are born from mothers with epilepsy. Physiological pregnancy in 20-25% of cases leads to an increase in seizures during pregnancy and in 30-35% – to an increase in seizures in the first trimester. During pregnancy, the risk of such a life-threatening condition as epileptic status is high, the frequency of which reaches 3%. During puberty and under the age of 30, the prevalence of epilepsy is significantly higher in women. Epilepsy in women is characterized by a number of additional problems related to reproductive function: menstrual cycle, sexual development, fertility, contraception, as well as pregnancy, childbirth, lactation and menopause [8, 10, 11]. Due to epilepsy and exposure to antiepileptic drugs (PEP), fertility in women decreases, and they also cause various endocrine disorders [12].

There are different opinions about the course of epilepsy in pregnant women and the effect of pregnancy on the epilepsy clinic, methods of pregnancy management, methods of delivery. Some authors note an improvement in the course of the underlying disease during pregnancy [1, 4], while others express the opposite opinion, believing that pregnancy adversely affects the course of the epileptic process, causing its exacerbation or manifestation [9]. The range of issues that the attending physician has to solve during pregnancy in patients with epilepsy is extremely wide: what will be the mutual influence of epilepsy and pregnancy, the peculiarities of childbirth, the prognosis of the birth of

a healthy child, the likelihood of developing epilepsy [6, 7]. The data of a number of authors are relatively different; the issue of the combination of epilepsy and pregnancy is covered in the literature somewhat one-sided. Despite the frequent combination of epilepsy and pregnancy, discussion of this problem and issues related to pregnancy management arise constantly. But there is not enough work devoted to these issues, which necessitates further research.

**The purpose of the study.** Comparative analysis and evaluation of the safety of antiepileptic drugs during pregnancy.

**Research objectives.** To study the clinical and dynamic features of epilepsy in pregnant women. To develop recommendations on the choice of optimal antiepileptic therapy for this category of women.

**Material and methods of research.** The study involved 88 women aged 20-40 years suffering from epilepsy. Pregnant women were observed in the maternity complex of the Bukhara region, they underwent clinical diagnostics, collected anamnesis of the disease (length of service, frequency of seizures, type of therapy, treatment plan) and other medical data concerning the course of pregnancy, childbirth, as well as the development of the child. The patients underwent electroencephalography and ultrasound examination (ultrasound) to assess the condition of the mother and fetus during pregnancy.

**Discussion of the results of the study.** The study analyzed information about pregnant patients with epilepsy who took monotherapy and were diagnosed with developmental abnormalities. Monotherapy was understood as cases of taking only one (PEP) antiepileptic drug from the first trimester or in subsequent trimesters. Epileptic seizures pose a significant risk to the health and even the life of the mother, having a great impact on her quality. Therefore, most women who have got rid of seizures, when planning pregnancy, are reluctant to think about the cancellation of therapy and the likelihood of their recurrence.

The survey of women revealed the reasons for refusing PEP therapy during pregnancy is the fear of harming the unborn child. When collecting anamnestic data, it was found that 20 (22.7%) women had epileptic seizures more frequently during pregnancy. The postpartum period for women suffering from epilepsy is vulnerable due to changes in the pharmacokinetics of PEP, a violation of the quality and duration of night sleep, breastfeeding problems and postpartum depression, which can lead to an increase in epileptic seizures.

78 (88.6%) women who took PEP in the first trimester gave birth to completely healthy children. 82 (93.2%) women who took PEP in the second trimester gave birth to completely healthy children. Malformations were registered in 6 (6.8%) newborns and fetuses on the background of convulex and in 7 (8%) - on the background of lamotrigine.

**Table 1. Severity of symptoms of epilepsy in the treatment of PEP**

Symptoms	Lamotrigine (n=42)		Convulex (n=46)	
	Абс.	%	Абс.	%
Ataxia	12	28,6	17	37,0
Dizziness	14	33,3	15	32,6
Dermatitis	16	38,1	16	34,8
Diplopia	11	26,2	18	39,1
Cardiacarrhythmias	15	35,7	10	21,7
Drowsiness	14	33,3	11	23,9
Encephalopathy	10	23,8	13	28,3

Headaches, dizziness, diplopia, cardiac arrhythmias, drowsiness, cognitive impairment, increased frequency of seizures and encephalopathy were most often recorded in patients.

In the study, an increase in seizures was registered in 31 (35.2%) patients, which can be explained by

non-compliance with the regime, sleep deprivation, psychoemotional overstrain and violation of compliance with therapy in 25 (28.4%) of them.

In the case of positive clinical and electroencephalographic dynamics against the background of treatment and the absence of adverse reactions, the dose of convulex was reduced by 25%. On the part of the psycho-emotional sphere, emotional disorders and depression, irritability, aggression and disobedience were registered in patients.

**Table 2. Severity of symptoms of epilepsy in pregnant women**

Symptoms	(n=88)	
	Абс.	%
Emotional disorders	28	31,8
Depression	26	29,5
Irritability	38	43,2
Aggression	22	25,0
Disobedience	24	27,3
Anxiety	39	44,3

Early reports on the effect of lamotrigine on infants during breastfeeding showed that most full-term infants have little problems with breastfeeding, but careful monitoring of toxicity is recommended, especially in hypotrophic or premature infants (Lander C.M., 2008). In more recent studies, lamotrigine has also been classified as a safe PEP for women during breastfeeding with rare and usually moderate side effects among newborns exposed to high concentrations of the drug and its metabolites in milk (Dalili H. et al., 2015). The literature provides data according to which convulex served as the only drug in monotherapy with a low risk of seizures during pregnancy. According to scientists, resistance to PEP is observed in 20-30%.

To simplify the analysis, pregnancy outcomes against the background of taking PEP were classified into two groups, the group without malformations and the group with malformations. All fetal disorders were attributed to malformations.

**Table 3. Distribution of malformations depending on the type of PEP taken during pregnancy**

Name Of the PEP	Number of women (n)	Number of malformations (abs)	Malformations (%)
Lamotrigine	42	1	7,1*
Convulex	46	5	19,5

Note: \* - significantly compared with patients who took convulex  $P < 0.001$ .

The frequency of registered malformations against the background of taking lamotrigine and convulex was 12 (13.6%) out of 88 newborns, and there were no stillbirths. It is important to remember that malformations can manifest themselves in the long-term period after birth, but these data are very difficult to collect and analyze. The study showed that, in general, 96% of children born to mothers who took lamotrigine during pregnancy did not have malformations. In comparison with lamotrigine and convulex, lamotrigine turned out to be statistically safer in terms of the development of paroxysms. (see Table 3).

**Table 4. The number of seizures in each trimester when using PEP during pregnancy as monotherapy**

Medication	Firsttrimester	Secondtrimester	Thirdtrimester	Третий триместр
Lamotrigine	1	2	3	6
Convulex	1	1	1	3

The incidence of malformation on the background of lamotrigine in some cases is comparable to that of healthy mothers. The experience of using new AES during pregnancy has not been fully studied, therefore, large epidemiological studies are required to assess the safety of these drugs. When choosing PEP for any patient, as a rule, factors such as the effectiveness of the drug, its tolerability, safety and ease of use are taken into account. Despite the fact that the quality of life of patients with epilepsy is determined by the control of seizures, there is no doubt about the priority of achieving complete control over them.

**Table 5. Psychopathological disorders before and after birth with the use of PEP as monotherapy**

Symptoms	Treatments days	Group of patients											
		Group 1 Lamotrigine (n=42)						2 Convulex group (n=46)					
		1 point		2 point		3 point		1 point		2 point		3 point	
		ābc	%	ābc	%	ābc	%	ābc	%	ābc	%	ābc	%
Asthenia	Beforebirth	12	28,6	14	33,3	5	11,9	13	28,2	15	32,6	6	13,0
	Afterbirth	8	19,1	6	14,3	7	16,7	8	17,4	7	15,2	5	10,9
Dysphoria	Beforebirth	20	47,6	14	33,3	4	9,5	19	41,3	15	32,6	6	13,0
	Afterbirth	12	28,6	7	16,7	2	4,8	10	21,7	5	10,9	2	4,3
Anxiety	Beforebirth	14	33,3	12	28,6	8	19,1	18	39,1	14	30,4	7	15,2
	Afterbirth	10	23,8	7	16,7	3	7,1	9	19,6	6	13,0	4	8,7
Sleep disorders	Beforebirth	15	35,7	10	23,8	5	11,9	17	36,9	12	26,1	7	15,2
	Afterbirth	11	26,2	7	16,7	1	2,4	8	17,4	7	15,2	1	2,2
Mood decline	Beforebirth	14	33,3	9	21,4	3	7,1	15	32,6	10	21,7	5	10,9
	Afterbirth	8	19,1	5	11,9	1	2,4	8	17,4	9	19,6	3	6,5
General discomfort	Beforebirth	12	28,6	10	23,8	7	16,7	13	28,3	11	23,9	8	17,4
	Afterbirth	9	21,4	6	14,3	2	4,8	7	15,2	5	10,9	3	6,5

Note: 1 point - mild degree of symptom severity, 2 points - moderate degree of symptom severity, 3 points - severe degree of symptom severity.

In 18 out of 88 cases, pregnant women were delivered by planned cesarean section on the recommendation of a neurologist and a psychiatrist due to the presence of pronounced changes on the EEG. The refusal to breastfeed a newborn is completely unjustified, since during pregnancy, the penetration of PEP into the baby's blood is usually higher than with mother's milk. Breastfeeding should be carried out in a supine position in order to avoid injury in the event of a seizure. The organization of sleep and wakefulness, avoiding shortening the duration of night sleep are important steps to prevent epileptic seizures. The patient's relatives can take care of the child at night, including feeding him. All the maternity women had uncomplicated course of the postpartum period, were discharged home in satisfactory condition, breastfeeding was carried out in 90.9% of cases.

**Conclusions.** Women of reproductive age should not give up antiepileptic drugs, excluding severe forms of the disease. One should always strive for monotherapy with the use of a minimum dose. Reducing the number of seizures during pregnancy can be achieved with convulex or lamotrigine. Having studied the treatment of pregnant patients with epilepsy, it shows that malformations in newborns were higher in patients receiving convulex and valproate than in patients receiving lamotrigine. Summarizing the above, it can be argued that one of the safest drugs for the treatment of epilepsy in women is lamotrigine.

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