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# ANTIEPILEPTIC PHARMACOTHERAPY IS A LEADING FACTOR IN THE INDUCED PATHOMORPHOSIS OF EPILEPSY

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**ABSTRACT**

*Only 47 (52%) patients with MG, 21 (57%) with M and 26 (48%) with F were prescribed therapy at the onset of the disease, and it was rationally selected only in 41 (45%) cases – in 19 (51%) with M and 22 (41%) with F (p> 0.05). Of the 82 (100%) patients receiving therapy at the time of examination, 37 (45%) were taking basic, 20 (24%) modern, 24 (29%) a combination of basic and modern AEDs and in about 2% of cases a combination with the use of 1st generation drugs. Monotherapy was carried out in 45 (55%), polytherapy – in 37 (45%) of them. Of the 19 (100%) patients taking CBZ as starting monotherapy, 10 (52%) took the drug in a non-prolonged form, twice a day.*

## INTRODUCTION

Pathomorphosis of epilepsy is the process of evolution of the clinical (neurophysiological, epidemiological) picture of the disease under the influence of various factors or their combination related to the internal and external environments of the body. Pathomorphosis can be natural and induced, positively and negatively directed. Positive pathomorphosis is characterized by a tendency to develop protective and compensatory mechanisms of the body that contribute to smoothing or reducing the manifestations of the disease, while negative pathomorphosis is characterized by the opposite picture. Transformations of the clinical (clinical-neurophysiological) picture of the disease accompany the course of most focal epilepsies in adults and are often a consequence of known causes [1,2].

## MATERIALS AND METHODS

The study of the process reflecting the variability of the clinical (clinical-neurophysiological) picture of epilepsy over time is an urgent task, since understanding the patterns of pathomorphosis allows for timely identification, and often foreseeing a variant of change in the course of the disease and giving it the “right” direction, for example, by influencing from the outside with the help of antiepileptic drugs (AEDs) [3,4]. In epilepsy, two extreme, diametrically opposed states characterizing positive and negative pathomorphosis are: 100% control over seizures, while maintaining a high quality of life and pharmacoresistant course of the disease, with a low quality of life. The leading factor capable of inducing both of the above-mentioned variants of development of events is antiepileptic pharmacotherapy (AET). Today, AET is the most effective method of treating epilepsy, the use of which allows, on average, in 75% of patients, to successfully control seizures. For these cases, the new classification of

epileptic seizures and epilepsies (MPEL, 2017) includes the term “pharmacoreactive”, that is, sensitive to AED therapy [5]. On the other hand, AEDs can become a source of formation of undesirable tendencies in the clinical and neurophysiological picture of the disease. The range of issues determining the influence of AET on the pathomorphosis of the disease is associated with the timeliness and rationality of the initial and subsequent treatment, the pharmacokinetic effects of AEDs, drug interactions, issues of replacing one AED with another, the use of generic analogues, drug monitoring of AEDs, compliance, undesirable paradoxical reactions and side effects, features of use in men and women in different age groups [1].

The study included 91 (100%) patients with CFE and SFE in the general group (OG). The patients sought specialized care. Among them were 37 (41%) men (M) and 54 (59%) women (F). At the time of the study, 82 (90%) patients were taking AEDs, 33 (89%) M and 49 (91%) F. The age of patients in the OG ranged from 18 to 78 years, with an average of 37.5 years. The onset of epilepsy was noted at the age of 4 to 71 years. The duration of the disease ranged from 1 to 52 years, with an average of 16.1 years. A follow-up period of 1 to 2.5 years was monitored in all patients. Patients underwent clinical, neurological, laboratory and instrumental examination methods, which included anamnesis, clinical and neurological examination, neuropsychological testing using the MMSE, FAB, HADS scales, assessment of the severity of attacks using the NHS3 scale, quality of life using the QOLIE-31 scale, and assessment of laboratory parameters of internal organ function.

**RESULTS AND DISCUSSION**

Only 47 (52%) MG, 21 (57%) M and 26 (48%) F patients were prescribed therapy at the onset of the disease ($p>0.05$), while it was rationally selected only in 41 (45%) cases, in 19 (51%) M and 22 (41%) F ($p>0.05$). At the time of the initial examination, 82 (90%) MG, 33 (89%) M and 49 (91%) F patients were taking AEDs. Of these, 43

(53%) patients, 13 (41%) M and 30 (61%) F, had a history of three or more therapy attempts ($p>0.05$). At the same time, attacks were not controlled for various reasons, including iatrogenic, in 76 (93%) patients. Of the 82 (100%) patients receiving AEDs, 37 (45%) were taking basic, 20 (24%) were taking modern, 24 (29%) were taking a combination of basic and modern AEDs, and in about 2% of cases, a combination with the use of 1st generation drugs. Of the 19 (100%) patients taking CBZ as starting monotherapy, 10 (52%) were taking the drug in a non-extended form, at a low dose, twice a day, in the morning and in the evening, at the time of the initial examination. Monitoring of the AED PC at the time of the initial examination was performed in 6 (7%) patients; after the initial examination, monitoring was recommended to 28 (34%) patients, including 19 (68%) due to the inefficiency of AEDs used in a standard dose, 6 (21%) due to the development of intoxication symptoms, 3 (11%) to control the bioequivalence of a generic analogue. In two cases, severe hand tremor was detected when using VPA at a dose of 600 mg / day, and PC analysis revealed indicators 1.2-1.5 times higher than the upper limit of normal values. Violation of the titration rate was noted in the anamnesis of 3 (4%) patients taking AEDs. In a timely manner, at the onset of the disease, the diagnosis was established only in 47 (52%) patients of the MG, 21 (57%) M and 26 (48%) F. Routine EEG examination in the anamnesis was carried out in 79 (87%) patients of the MG, 32 (87%) M and 47 (87%) F. Epileptiform changes were detected in 34 (43%) of them, 12 (37%) M and 22 (47%) F ($p> 0.05$).

Video-EEG monitoring was performed in 20 (22%) MG, 8 (22%) M and 12 (22%) F patients. Epileptiform changes were detected in 11 (55%) of them, 7 (88%) M and 4 (33%) F ($p<0.05$). MRI examination was performed in 69 (76%) MG, 29 (78%) M and 40 (74%) F patients. Structural epileptogenic changes were detected in 37 (54%) of them, 21 (72%) M and 16 (40%) F ($p<0.05$). At the time of examination, out of 82 (100%) patients receiving AEDs, monotherapy was performed in 45 (55%), polytherapy – in 37 (45%) of them. The most frequent factor inducing attacks was stress, in 54% of cases in the MG, 49% in men and 57% in women. The second most frequent factor was discontinuation/missing an AED dose in men in 25% and menstruation in women of reproductive age in 46% of cases. More than 1 year but less than 5 years of remission were noted in the anamnesis of 25 (27%) patients in the MG, 12 (32%) in men and 13 (24%) in women ($p>0.05$). The subsequent relapse of attacks in 13 (52%) cases was associated with discontinuation, in 3 (12%) with dose reduction and in 4 (16%) with replacement (including with a generic analogue) of AED. An attempt to discontinue therapy after 5-year remission, with subsequent return to taking AEDs, was revealed in the anamnesis of 2 patients (2%). An attempt to replace AEDs was made in 61 (74%) patients from among those taking AEDs, 20 (61%) men and 41 (84%) women. The reason for making such a decision in 22 (36%) cases, along with the ineffectiveness of therapy, was the development of persistent severe AEs. A one-stage replacement of CBZ with OKZ, due to AEs, was made in two patients. A history of using generic analogs was revealed in 43 (52%) patients receiving therapy. At the same time, 28 (65%) of them noted low efficacy and poor tolerability of analogs, in comparison with original drugs. In 48 (53%) patients of the MG, cognitive impairment of varying degrees was detected. Severe cognitive deficit was observed in 5 (14%) men and 11 (20%) women ($p>0.05$). Anxiety-depressive disorders were detected in 42 (46%) patients of the MG, 16 (43%) men and 26 (48%) women ($p>0.05$). Only 21 (26%) patients taking AEDs, 7 (21%) men and 14 (29%) women ($p>0.05$), were absolutely compliant from the onset of the disease.

At the time of the initial examination, full awareness of the rules for using AEDs was revealed in 23 (28%) patients receiving therapy, 9 (27%) men and 14 (29%) women. Remission was noted only in 6 (7%) patients receiving therapy during the initial examination. In the rest, seizures were not controlled, including due to iatrogenic reasons. In 37% of cases, patients took the drugs in low doses, in 12%, a drug that was not the first line was prescribed at the onset, in 9%, non-prolonged forms were used, in 9%, an irrational replacement was made, in 4%, AEDs were prescribed without taking into account the form of epilepsy and the type of seizures, in 5%, a drug with the potential for aggravation was prescribed. The phenomenon of aggravation was noted in the anamnesis of 6 patients (7%), 2 (6%) men and 4 (8%) women ($p> 0.05$), and was associated with the use of LTZ in 2 (33%), CBZ in 2 (33%), TPM in 1 (17%) and NNS in 1 (17%) case. In 2 (33%) of them, the phenomenon of VBS was detected during the EEG study. In 43 (52%) patients from among those receiving therapy, 15 (45%) men and 28 (57%) women, some adverse reactions were detected ($p> 0.05$).

**CONCLUSION**

Antiepileptic pharmacotherapy plays a leading role in the emergence of evolutionary changes in the picture (clinical, neurophysiological) of epilepsy. Timeliness and rationality of therapeutic measures, taking into account the pharmacokinetic features of AEDs, as well as adherence to the basic provisions of rational pharmacotherapy of epilepsy, are the key to the

induction of favorable scenarios for the pathomorphosis of the disease. At the same time, AET itself may carry the potential for decompensation of the course of epilepsy and associated disorders, which is especially important in the treatment of elderly and elderly patients. An important component of the success of AET is the full awareness of patients about the methods of pharmacotherapy and the risks associated with it, which significantly increases compliance rates and, in this regard, improves the prognosis.

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