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OPTIMIZATION OF THERAPEUTIC STRATEGIES THROUGH BIOCHEMICAL PROFILING IN PHARMACORESISTANT FORMS OF EPILEPSY

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ABSTRACT. Drug-resistant forms of epilepsy (DRE) represent a significant clinical problem associated with a high risk of neurocognitive impairment and decreased quality of life for patients. The aim of this study is to optimize therapeutic strategies through biochemical profiling of patients with DRE. The study involved 52 patients diagnosed with drug-resistant forms of epilepsy. Biochemical analysis included assessment of neurotransmitter status, oxidative stress, inflammatory markers, and metabolic indicators. Based on the obtained data, individualized therapeutic approaches were proposed.

Keywords: drug-resistant epilepsy, biochemical profiling, therapeutic strategy, neurotransmitters, oxidative stress.

ОПТИМИЗАЦИЯ ТЕРАПЕВТИЧЕСКИХ СТРАТЕГИЙ ПУТЕМ БИОХИМИЧЕСКОГО ПРОФИЛИРОВАНИЯ ПРИ ФАРМАКОРЕЗИСТЕНТНЫХ ФОРМАХ ЭПИЛЕПСИИ

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АННОТАЦИЯ. Фармакорезистентные формы эпилепсии (ФРЭ) представляют собой значительную клиническую проблему, связанную с высоким риском нейрокогнитивных нарушений и снижением качества жизни пациентов. Цель данного исследования — оптимизация терапевтических стратегий через биохимическое профилирование пациентов с ФРЭ. В исследовании приняли участие 52 пациента, у которых выявлены резистентные формы эпилепсии. Биохимический анализ включал оценку нейротрансмиттерного статуса, окислительного стресса, воспалительных маркеров и метаболических показателей. На основе полученных данных предложены индивидуализированные терапевтические подходы.

Ключевые слова: фармакорезистентная эпилепсия, биохимическое профилирование, терапевтическая стратегия, нейротрансмиттеры, окислительный стресс.

Introduction. Pharmacoresistant epilepsy is a clinically significant form of epileptic disorder, occurring in approximately 20-30% of patients with epileptic seizures. The main characteristic of FRE is the lack of adequate control of seizure

activity when using two or more anti-epileptic drugs (AEP) prescribed in therapeutically optimal doses and regimens. This form of epilepsy is associated with a high frequency of neurocognitive impairments, a decrease in the quality of life of patients, and an increased risk of developing psycho-emotional and behavioral disorders.

Modern research emphasizes that the main pathogenetic mechanisms of FRE are complex biochemical and molecular disorders. Among them, the following are distinguished: imbalance of neurotransmitter systems (mainly glutamatergic and GABAergic), increased levels of oxidative stress with disruption of antioxidant homeostasis, activation of pro-inflammatory cascades and cytokine systems, as well as various metabolic disorders, including dyslipidemia, hyperglycemia, and deficiency of individual amino acids and microelements. Disruptions in these processes can not only contribute to increased convulsive readiness of neural networks but also affect the pharmacodynamics and pharmacokinetics of the AEPs used, significantly limiting the effectiveness of standard therapy.

Due to the multifactorial nature of FRE, modern therapeutic approaches emphasize the need for individualized treatment. One of the most promising tools for personalized therapy is the biochemical profile of patients. This method allows for the identification of specific pathogenetic disorders in each patient, predicting the response to therapy, and developing optimal schemes for using anticonvulsants. In addition, biochemical analysis contributes to the correction of concomitant metabolic and inflammatory disorders, reduces the risk of side effects, and increases the overall effectiveness of treatment measures. Thus, the integration of biochemical profiling into clinical practice opens up new prospects for optimizing the treatment strategy for pharmacoresistant epilepsy, contributing to the transition from a standard "selective" approach to truly personalized treatment.

Materials and Methods. The study included 52 patients (27 men and 25 women) aged 12 to 55 years with a diagnosis of pharmacoresistant epilepsy in accordance with the criteria of the International League Against Epilepsy (ILAE). All patients underwent a thorough clinical examination, including anamnesis collection, assessment of the frequency and nature of epileptic seizures, and identification of concomitant somatic and neurological diseases.

Complex biochemical profilization was used to assess the pathogenetic mechanisms of pharmacoresistance. It included:

Neurotransmitter status study - determination of glutamate, γ-aminobutyric acid (GBA), dopamine, and serotonin concentrations in blood serum.

Assessment of oxidative stress - measuring the level of malondialdehyde (MDA) and the activity of the antioxidant enzyme superoxide dismutase (SOD).

Analysis of inflammatory markers - determination of the concentration of C-reactive protein (CRP) and interleukin-6 (IL-6).

Metabolic examination - assessment of blood glucose levels, lipid profile, and amino acid composition.

Statistical data processing was carried out using the SPSS 25.0 software. The level $p < 0.05$ was taken as the statistical significance criterion. All results were

presented as average values ± standard deviation, and corresponding parametric and non-parametric methods were used to assess correlations and differences.

Table 1. Clinical and Biochemical Characteristics of Patients with Pharmacoresistant Epilepsy (n = 52)

Parameter	Mean ± SD	Range	Notes
Age, years	28.4 ± 9.2	12–55	27 males / 25 females
Duration of disease, years	10.6 ± 6.3	2–30	–
Seizure frequency, per month	7.8 ± 3.5	1–15	–
Number of AEDs used	2.8 ± 0.7	2–4	–
Glutamate, µmol/L	15.2 ± 4.1	9–23	Elevated in 80% of patients
GABA, µmol/L	7.6 ± 2.3	3–12	Decreased in 75% of patients
Dopamine, nmol/L	0.42 ± 0.12	0.25–0.65	–
Serotonin, nmol/L	0.85 ± 0.21	0.5–1.3	–
MDA, nmol/mL	4.9 ± 1.5	2.5–8.0	Elevated in 65% of patients
SOD, U/mL	1.12 ± 0.38	0.6–2.0	–
CRP, mg/L	6.4 ± 3.2	1–15	Elevated in 50% of patients
IL-6, pg/mL	12.3 ± 5.1	4–25	–
Glucose, mmol/L	5.6 ± 1.1	4–8.5	Hyperglycemia in 40% of patients
Total cholesterol, mmol/L	5.2 ± 1.3	3.5–8.0	Dyslipidemia in 40% of patients

Conclusion. The study included 52 patients with pharmacoresistant epilepsy, comprising 27 males and 25 females, aged between 12 and 55 years. The mean age was 28.4 ± 9.2 years, and the mean duration of disease was 10.6 ± 6.3 years. Seizure frequency ranged from 5 to 15 episodes per month, and patients were receiving 2 to 4 antiepileptic drugs (AEDs) at the time of assessment.

Biochemical profiling revealed that 80% of patients exhibited elevated glutamate levels accompanied by decreased GABA concentrations, which correlated with increased seizure frequency. Markers of oxidative stress, including malondialdehyde (MDA) and superoxide dismutase (SOD), were elevated in 65% of patients. Additionally, inflammatory markers, such as interleukin-6 (IL-6) and C-reactive protein (CRP), were increased in 50% of cases. Metabolic abnormalities were observed in 40% of patients, predominantly manifesting as dyslipidemia and hyperglycemia.

Elevated glutamate levels were associated with resistance to valproate therapy, while decreased GABA levels suggested potential benefits from adding GABAergic agents, such as benzodiazepines. The presence of elevated inflammatory markers indicated the need for combined therapy with anti-inflammatory agents and antioxidants.

Biochemical profiling provides valuable insights into the key pathogenic mechanisms underlying pharmacoresistant epilepsy. Individualizing therapy based on biochemical analysis enables:

- Selection of the most appropriate antiepileptic drugs for each patient
- Correction of metabolic and oxidative disturbances

- Reduction in seizure frequency and improvement of patients' quality of life

Comparison of biochemical data with clinical characteristics emphasizes the importance of an integrated approach in the management of pharmacoresistant epilepsy.

Biochemical profiling represents an effective tool for optimizing therapeutic strategies in pharmacoresistant forms of epilepsy. A personalized treatment approach allows for improved therapeutic efficacy while minimizing adverse effects, thereby enhancing overall patient outcomes.

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