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PHARMACOTHERAPY OF EPILEPSY IN CHILDREN

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Abstract

Pathomorphosis of epilepsy is a process of evolutionclinical (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 towards the development of protective and compensatory mechanisms of the body that help smooth out or reduce the manifestations of the disease; with a negative pathomorphosis, the opposite picture is observed.

Keywords: **To study drugs used for epilepsy in children.**

Introduction

Pathomorphosis of epilepsy is a process of evolution 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 towards the development of protective and compensatory mechanisms of the body that help smooth out or reduce the manifestations of the disease; with a negative pathomorphosis, the opposite picture is observed. Transformations in the clinical (clinical and neurophysiological) picture of the disease accompany the course of

most focal epilepsies in adults and are often the result of known causes [1,2]. Sometimes the changes that have arisen cannot be explained and the impression is created that they are spontaneous.

pathomorphosis.

Materials and Methods

The material for the analysis was the data of patients of the Neurosurgery Department of the Multidisciplinary Clinic of Samarkand State Medical University over the past 5 years and literature data.We analyzed data from case histories of children with epilepsy who were treated with Levetinol (levetiracetam). A total of 61 patients were examined (31 girls and 30 boys), aged from 2 to 17 years: 18 children from 2 to 6 years, 19 from 7 to 11 years, 24 from 12 to 17 years. Diagnosis of epilepsy was carried out based on the results of a clinical examination, video-EEG

monitoring, neuroimaging (computed, magnetic resonance imaging - MRI). Various forms of epilepsy were diagnosed: focal (idiopathic, cryptogenic and symptomatic) epilepsy, idiopathic generalized (childhood absence and juvenile absence, juvenile myoclonic, with isolated generalized seizures), Dravet syndrome, Lennox–Gastaut syndrome, Jeavons syndrome, atypical rolandic epilepsy, Duse syndrome. Most often in the observed group of patients, symptomatic (22.9%) and cryptogenic (19.6%) focal epilepsy, juvenile myoclonic epilepsy (13%). A third of patients - 21 (34.4%) had only one type of seizure, most often these were absence seizures, myoclonus or generalized tonic-clonic seizures. Changes on MRI of the brain were detected in 13 (21.3%) of the observed patients and were represented by the following pathological processes: cortical subatrophy - in 5, residual leukopathy - in 2, arachnoid cysts - in 4, cystic-gliotic changes - in 2.

Results

At the time of starting to take Levetinol, the duration of epilepsy ranged from 2 months to 10 years. The drug was prescribed in a therapeutic dose of 30 to 70 mg/kg per day. 23 (37.7%) children were on Levetinol monotherapy. In 6 cases, Levetinol was the first drug used to start treatment of epilepsy. The forms of epilepsy in which Levetinol was used as starting monotherapy were: idiopathic generalized with isolated generalized convulsive seizures, juvenile myoclonic, childhood absence, Jeavons syndrome, rolandic, idiopathic occipital (Panayotopoulos syndrome). In 17 out of 23 patients receiving monotherapy, replacement with Levetinol was made after treatment failure with the first/second prescribed antiepileptic drug (lack of effectiveness, side effects, deterioration in EEG) and, importantly, due to the negative attitude of parents towards the “old” antiepileptic drugs means. Transfer to monotherapy with Levetinol from other drugs was most often carried out in idiopathic forms (idiopathic focal, rolandic epilepsy, childhood absence, juvenile absence, juvenile myoclonic epilepsy). In 54% (n = 33) of cases, duotherapy was used, in 8.1% (n = 5) – 3 drugs were prescribed. Children with atypical rolandic epilepsy and cerebral palsy (CP) were on three drugs. Most often, Levetinol® (levetiracetam) in combination therapy was combined with the following antiepileptic drugs: valproic acid - in 19 children, carbamazepine - in 5, oxcarbazepine - in 2, topiramate – in 2, Frisium – in 2, lamotrigine – in 1, Sabril – in 1, stiripentol – in 1. Usually, the need for combined antiepileptic therapy arose when monotherapy was insufficiently effective and side effects of the first (second) drug occurred: changes in blood parameters, loss hair, abdominal pain, pharmacomonitoring data, weight gain when taking valproic acid; the appearance of salts in the urine, inhibition when taking metopiramate; allergic rash - during treatment with lamotrigine; dizziness during treatment with oxcarbazepine; changes in biochemical blood parameters (transaminases, alkaline phosphatase) during treatment with carbamazepine. A positive clinical effect was achieved in 53 children - most in the 3rd month of therapy (in some patients after dose adjustment), and in some cases already in the 1st-2nd month treatment, including: – reduction of attacks by 25% – in 2 children; – reduction by 50% – in 11; – reduction by 75% – in 3; – absence of attacks for 3–6 months – in 38 (62, 2%). The absence of a clinical effect (preservation of attacks) after 3–6 months of therapy with Levetinol was recorded in only 5 (8.1%), and in 2 children with extensive cystic-glial changes on MRI, an increase in attacks was observed. All these patients suffered from severe forms of epilepsy: symptomatic focal, atypical rolandic, Lennox-Gastaut syndrome, Dravet syndrome. Of the 6 patients,Four patients on initial monotherapy with Levetinol achieved clinical remission: with juvenile

myoclonic epilepsy and idiopathic generalized epilepsy with generalized convulsive seizures. In 9 of 17 patients on monotherapy with Levetinol (after a change in monotherapy), clinical remission was achieved; the rest, after 3–6 months, were additionally prescribed a second antiepileptic drug (valproic acid, oxcarbazepine, lamotrigine). In 2 cases, the drug was discontinued after 3 months.

administration due to ineffectiveness (increased attacks), in 5 patients - after 6 months of administration and increasing the dose until a therapeutic effect was achieved. The majority (78.7%) of patients tolerated Levetinol therapy well, and it was not accompanied by adverse events. Side effects while taking the drug occurred in 13 (21.3%) patients and were represented by: sleep disturbance (intermittency) in 6, increased tics in 1, residence, aggressiveness - in 5, allergic rash - in 1. It is important to note that in no case were the side effects so significant that discontinuation of the drug was required. Attention was drawn to the fact that children with these side effects even before starting Levetinol had problems with sleep, neurotic reactions. During a dynamic assessment of the EEG while taking Levetinol (carried out in 39 patients), only in 4 cases (after 6 months of treatment) a disappearance was noted and a significant decrease in index epileptiform activity (mainly diffuse peak-polypeak-wave activity). With initially recorded focal epileptiform activity, especially against the background of regional slowing, the presence of benign epileptiform discharges of childhood, the effect of the drug on the EEG pattern was weak (absent after 3–6 months). Important factors determining the choice of an antiepileptic drug, in addition to the type of seizures, form of epilepsy, age, are comorbid disorders. In table Table 2 lists concomitant diseases that were noted in 47 of the 61 patients with epilepsy examined, which required a particularly careful approach to the selection of an antiepileptic drug. In particular, concomitant neurological disorders were observed in 25 patients. They were represented by cerebral palsy (in 5 patients), malformations of the brain (in 1 – Arnold-Chiari anomaly, in 1 – hypoplasia of the corpus callosum). Delayed neuropsychic development was observed in 12 children, general underdevelopment of speech – in 4, attention deficit hyperactivity disorder – in 1, tics – in 1. During the dynamic observation, attention was drawn to the absence

negative impact of Levetinol® (levetiracetam) on the state of higher mental functions both in the entire group of patients examined and in patients with comorbid neurological disorders. Somatic complications occurred in 6 cases and were represented by diseases of the gastrointestinal tract (in 4 children), kidney disease (in 1), dermatitis (in 1), chronic viral infection (in 1). 13 patients suffered from endocrine diseases, including 5 with menstrual irregularities, 4 with hyperinsulinism, 3 with exogenous constitutional obesity, and 1 with diabetes mellitus. It should be emphasized that in none of the patients with somatic burden and endocrine disorders, the prescribed treatment with Levetinol was not accompanied by an increase in these disorders. Levetiracetam has a favorable safety profile – low incidence of adverse effects, no negative impact on cognitive function. At the same time, the drug has anticonvulsant synergism with many antiepileptic drugs, without showing synergy in neurotoxic effects. There are no clinically significant pharmacokinetic interactions with either antiepileptic or other drugs. Therefore, it can be considered the optimal drug for the combined treatment of epilepsy. The listed characteristics lead to improved adherence to treatment on the part of patients and parents, which is of great importance in outpatient practice. This is also facilitated by the simplicity and convenience of its use - a simple dose titration scheme, taken 2 times a day, regardless of meals. In addition, the prescription of the drug does not require determination of its concentration in the blood serum and laboratory monitoring (blood tests, urine tests, determination of liver enzyme activity). It is well

known that the burden of epilepsy increases in the presence of concomitant diseases [8]. Long-term treatment with levetiracetam carried out

in an outpatient setting, is well tolerated and is not accompanied by clinically significant drug interactions. This is of particular importance for patients with epilepsy receiving polytherapy, as well as those with concomitant diseases, for which drugs of other groups are prescribed in addition to antiepileptic drugs. Drug interactions can worsen both the effectiveness and tolerability of antiepileptic therapy. Levetiracetam, a new generation antiepileptic drug with a linear pharmacokinetic profile, has a clear advantage over other drugs for the treatment of children and adolescents with epilepsy and concomitant pathologies. Children with epilepsy have mental retardation and regression in mental development are observed only in a limited number of forms of the disease. Most patients with epilepsy have intact intelligence and can study in a comprehensive school program. However, at least 50% of them have behavioral and emotional disorders and learning difficulties [4]. Cognitive difficulties are based on damage to brain structures, localization of the epileptic focus, nature, severity and frequency of attacks, the presence of subclinical epileptiform activity on the EEG, previous status epilepticus, insufficient effectiveness or side effects of an antiepileptic drug. As long-term follow-up studies have shown, the consequences of epilepsy with onset in childhood often persist until adulthood and are determined by early onset concomitant cognitive, behavioral and emotional disorders [4]. Taking this into account, the process of treating epilepsy in children should include special measures aimed at the timely and most complete overcoming of cognitive, behavioral and emotional disorders. The presence of delayed neuropsychic development determines the doctor's tactics when caring for the child

with epilepsy. If this delay arose as a result of the ongoing epileptic process, then the main efforts should be aimed at stopping the attacks and suppressing epileptiform activity on the EEG. If the child had normal intelligence before the onset of seizures, then priority is given to a drug that is effective for the type of seizures present and has minimal effect on cognitive functions. The advantage of levetiracetam in such cases is due to the fact that it not only does not have a negative effect on the state of higher mental functions, but also has a positive effect on them with long-term use. As studies have shown, therapy with levetiracetam improves memory, attention, reaction time, organization and control of mental and motor processes [9]. When choosing a drug for both initial treatment of epilepsy and polytherapy, in addition to the type of epileptic seizures and the form of epilepsy in children and adolescents, it is important to take into account the characteristics of somatic status. In our group of patients, the choice of Levetinol in patients with carbohydrate metabolism disorders (diabetes mellitus, congenital hyperinsulinism) was determined by the advantages of the drug's pharmacokinetics and the absence of a negative effect on metabolic processes. No less important is the absence of interaction between Levetinolas and other drugs, which was important when choosing it for use in patients with concomitant chronic somatic diseases.

Conclusion

Levetinol (levetiracetam) has demonstrated high therapeutic efficacy, particularly in achieving remission, in children with both generalized and focal forms of epilepsy. The greatest clinical effect was observed in idiopathic forms. Levetinol has shown a high level of safety and good

tolerability, which allows its use in polytherapy of epilepsy, including in children with concomitant neurological, somatic and endocrine diseases.
diseases that require a particularly careful approach to the choice of antiepileptic drug. Levetiracetam is a modern quality standard for the treatment of epilepsy, which has an advantage over other antiepileptic drugs for use in outpatient neuropediatric practice.

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