

A New Approach to the Treatment of Pharmacoresistant Epilepsy Using Valparin XP

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Abstract Epilepsy is one of the most common forms of neurological pathology in childhood. According to the literature, the incidence of epilepsy in the population of children and adolescents under 15 years of age ranges from 0.3 to 1.7%. Modern approaches to treatment are focused on the use of monotherapy (Badalyan L.O. et al., 1980, Mukhin K.Yu., 2000, Petrukhin A.S., 2000, P. Temin. A., 1997, Shorvon S., 1996, Silanpaa M. et al., 1995).

Keywords Epilepsy, Valproic acid, Monotherapy, Psychocognitive, EEG, MRI

1. Introduction

Valproic acid preparations have been used in the treatment of epilepsy since the late 60s. Valproic acid and its salts are highly effective in all types of epileptic seizures: generalized and partial, which makes them the means of first choice in the treatment of most forms of epilepsy, including epileptic encephalopathies of childhood. In developed countries, it is the main antiepileptic drug and is used in 75-95% of cases. World research data indicate that valproic acid preparations are effective in 70-95% of cases in the form of monotherapy, which meets modern standards for the treatment of epilepsy. Important factors in the widespread use of valproic acid preparations are: positive psychocognitive effect, positive pharmacodynamic interactions with other antiepileptic drugs, stability of therapeutic concentration in blood plasma, good correlation of clinical and neurophysiological effects. The valuable quality of valproates is the ability to quickly increase the dose and low toxicity.

2. Materials and Methods

The purpose of this study was to analyze the antiepileptic treatment with Valparin XP in the form of monotherapy in patients with various forms of epilepsy. The study involved 87 patients aged 10 to 17 years.

3. The Results of the Study

Generalized epilepsy was observed in 39 (44.8%) patients. Of these, 9 (23.1%) had childhood absentee epilepsy, 7 (17.9%) had juvenile absentee epilepsy, and 23 (58.9%) had

epilepsy with generalized seizures. Focal epilepsy was diagnosed in 48 (55.2%). The structure of focal epilepsy was dominated by symptomatic cryptogenic forms in 46 (52.9%) patients. Of these, 19 (41.5%) had frontal epilepsy, 20 (43.7%) had temporal epilepsy, 2 (5.1%) had occipital epilepsy and 5 (9.7%) had parietal epilepsy. Benign childhood epilepsy with central temporal adhesions was diagnosed in 2 patients.

All patients received Valparin XP. The daily dose was 20 mg / kg - 60 mg / kg and was distributed in 2-3 doses. During the treatment, a pharmacokinetic study was conducted in dynamics.

The study confirmed the high clinical efficacy of Valparin XP in the treatment of all forms of epilepsy. The maximum effectiveness of Valparin XP (clinical remission) was noted in all forms of idiopathic generalized epilepsy — in 79.5% of patients: in childhood absentee epilepsy — in 92.3%, in epilepsy with isolated generalized seizures - in 85.2%, in juvenile absentee epilepsy — in 62.8%. A decrease in the frequency of seizures by more than 50% was achieved in 15.3% of patients. The lack of effect was observed in 5.1%, which required the appointment of additional therapy with carbamazepine and lamotrigine, as a result, drug remission was achieved in all cases.

As an illustration, we present a clinical observation.

Patient H., aged 14, was admitted to the Department of Pediatric Neurology with complaints of short bouts of unconsciousness and convulsions.

Anamnesis of the disease. The patient was 13 years old when, against the background of full health, attacks of tonic-clonic seizures appeared, accompanied by loss of consciousness, lasting up to 3 minutes. Seizures occurred 30 to 40 minutes after falling asleep, usually 3-4 times a year. There were 2 seizures. Neuroradiological and electroencephalographic examinations were not performed. Anticonvulsant therapy with phenobarbital 50 mg was

prescribed at night, against the background of which, after 1.5 years, the disease first caused seizures of turning off consciousness for 3-5 seconds, with a frequency of up to 9 per day. The dose of phenobarbital was increased to 100 mg per day. There was no effect from the treatment. Biographical history. From 2 physiological pregnancies, 2 urgent delayed deliveries at 42 weeks. Weight 4100, height 50 cm, screamed immediately. Early psychomotor development corresponded to age. The heredity of epilepsy is not burdened. The somatic status is without pathology. Weight 57 kg. There were no general cerebral, shell, or focal symptoms in the neurological status. The behavior is adequate. Intelligence is not changed.

Laboratory and instrumental studies.

Oculist's examination: the fundus is without pathology.

EEG: discharges from grouped peaks and sharp waves are detected in the background. During photostimulation, hypersynchronous generalized discharges of peak-slow wave complexes with a frequency of 3-3.5 Hz are recorded. MRI: without pathology.

Diagnosis: Juvenile absentee epilepsy.

In the hospital, phenobarbital was completely abolished and Valparin XP was prescribed in a daily dose of 20 mg / kg of weight. The attacks of absences stopped within a week.

The medical history demonstrates a typical case of juvenile absentee epilepsy and characteristic miscalculations in the diagnosis and treatment tactics of patients with epilepsy. Features of this observation: the debut of UAE in the pubertal period with generalized convulsive seizures and with the combination of simple absences 1.5 years after the onset of the disease. The administration of Valparin XP led to clinical remission.

Clinical remission with monotherapy with Valparin XP symptomatic cryptogenic focal epilepsy was achieved in 50% of patients. A decrease in the frequency of seizures by more than 50% - in 40.7%, no effect—in 4%.

When analyzing the effectiveness of Valparin XP, depending on the nature of seizures, the greatest effectiveness was noted in isolated secondary generalized seizures (59.2%) and simple and complex focal seizures (56.3%). In the presence of polymorphic seizures, the effectiveness of therapy is significantly lower—36.8%. In all cases of resistance to monotherapy with Valparin XP, polytherapy using carbamazepine, topiramate, and lamotrigine was prescribed.

Patient P., 13 years old, was admitted complaining of seizures accompanied by an aura in the form of headache and loss of consciousness, pallor, grasping movements in his hands. The duration of the attack is up to 2 minutes, the frequency is 1-2 times a week. Attacks of generalized tonic-clonic seizures lasting up to 5 minutes, frequency up to 1-2 times a week.

Biographical history. A child from 1 pregnancy, 1 urgent spontaneous birth, which proceeded without pathology. Birth weight 3100, length 49 cm. Early psychomotor development corresponded to age.

Anamnesis of the disease. The first symptoms of the disease appeared at the age of 7 years and were manifested

by loss of consciousness, gaze arrest, cessation of motor activity, automatism in the form of grasping movements in the hands, lasting up to 2 minutes. In the future, the attacks were repeated up to 4-5 times a week. The child was observed by a neurologist with a diagnosis of "episyndrome". He was repeatedly subjected to electroencephalographic examination. Combination therapy with phenobarbital (50 mg / day) and suxilep (500 mg / day) was prescribed. Against the background of treatment, there was a decrease in the frequency of paroxysms up to 2 times a week. The nature of anticonvulsant therapy has not changed for 5 years. During the last 3 months, the course of seizures has changed: the above-described seizures began to end with generalized tonic-clonic seizures, and their duration increased. Somatic status without pathology. Weight 43 kg. There were no general cerebral, shell, or focal symptoms in the neurological status. Intelligence is not changed.

Laboratory and functional studies.

Clinical and biochemical blood and urine tests—without pathology.

The fundus is without pathology.

ECG is rhythmically sinus, the vertical direction of the electrical axis of the heart.

EEG—multiple acute waves, peak-slow wave complexes with a frequency of 3 Hz, the predominance of abnormal activity in the parietal-central parts of the right hemisphere of the brain.

CT scan of the brain — no pathology was detected.

Diagnosis: Cryptogenic temporal lobe epilepsy.

In the department, phenobarbital and suxilep were canceled, Valparin XP monotherapy was prescribed at a daily dose of 40 mg / kg. After 2 weeks, the secondary generalized seizures stopped and a month after the start of treatment, therapeutic remission was achieved.

This observation demonstrates the transformation of complex partial seizures into secondary generalized ones against the background of unjustified combination therapy. The transfer to Valparin XP monotherapy at an average daily dose (40 mg/kg) led to drug remission.

Clinical recovery was observed in all patients (2) with benign epilepsy with central temporal adhesions.

We also studied the dynamics of EEG during monotherapy with Valparin XP: first of all, generalized epileptiform activity regressed in all forms of epilepsy. A complete reduction of generalized epileptiform activity in generalized epilepsy was observed in 61.7% of cases, and a decrease in severity in 38.3%. In focal epilepsy, generalized and focal epileptic activity was leveled less frequently. Complete or partial reduction of epileptic activity was noted in 53.7% of patients. EEG dynamics were not observed in 46.3% of children.

Side effects on the background of monotherapy with Valparin XP were observed in 29 (33.9%) children, early—in 17 (58.6%), long—term—in 12 (41.4%). In most cases, they were dose-dependent and transitory in nature.

The structure of early adverse effects was dominated by disorders of the gastrointestinal tract and the central nervous

system (in 11 and 5 patients, respectively). Adverse reactions from the gastrointestinal tract manifested nausea, abdominal discomfort, decreased appetite, vomiting, diarrhea.

Changes from the central nervous system manifested by weakness, drowsiness, static tremor of the hands, decreased concentration of attention were observed with a rapid increase in the dose of the drug and regressed with a decrease in the dose.

As an illustration, we present a clinical observation.

Patient R., 6 years old, complained of seizures of "fading" with the eyeballs turned up, lasting 10-20 seconds, with a frequency of up to 50-60 times a day.

Biographical history. A child from 2 pregnancies that occurred with toxicosis of the 1st half of pregnancy, 2 urgent spontaneous births. Weight 3700, height 47cm. She screamed right away. Early psychomotor development corresponded to age. Heredity is not burdened.

Anamnesis of the disease. She has been ill since the age of 5.5, when, against the background of complete well-being, there were attacks of turning off consciousness for 20-30 seconds, with a frequency of up to 20-30 per day. Somatic status without pathology. The weight is 32 kg.

There were no general cerebral, shell, or focal symptoms in the neurological status. Intelligence is preserved. During examination, up to 7 bouts of unconsciousness lasting up to 30 seconds with the eyeballs turned up were observed.

Laboratory and instrumental research methods.

Oculist's examination: fundus without pathology.

EEG: there is no normal rhythm in the background. Discharges of spike-slow wave complexes with a frequency of 3-3.5 Hz of high amplitude are constantly observed.

Diagnosis: Childhood absentee epilepsy.

Treatment. I have not received antiepileptic treatment before. The clinic prescribed monotherapy Valparin XP in a daily dose of 600 mg (20 mg / kg). It is recommended to gradually increase the dose by 150 mg per week. However, the child's parents carried out a dose increase for 3 days. A week after taking the full daily dose, the child experienced repeated vomiting and refusal to eat. At the same time, the biochemical parameters of the blood remained within the normal range. The above complaints regressed after reducing the dose of Valparin XP to 450 mg/day. The seizures were completely stopped. No further side effects of the drug were noted. Currently, he is in drug remission.

The presented medical history demonstrates a typical case of childhood absentee epilepsy. The rapid increase in the dose of Valparin XP led to the development of early side effects of Valparin XP in the form of gastrointestinal disorders, which regressed after reducing the dose of the drug.

Among the long-term side effects, isolated increases in liver enzymes in the blood were most common (7 patients). The increase in the level of transaminases exceeded the standards

by 1.5-2.5 times, was transient and was not accompanied by clinical and somatic manifestations. Transient thrombocytopenia was observed in 3 children, while transient clinical manifestations (petechiae, nosebleeds) were observed in 2 patients. Laboratory parameters returned to normal after reducing the dose of Valparin XP. Neuroendocrine disorders developed in 2 patients and were manifested by a slight increase in body weight.

One of the indicators of quality of life is the social adaptation of epilepsy patients, in particular, the possibility of learning. The patients were successfully enrolled in secondary school or received education at higher educational institutions. 7 patients were home-schooled, which is associated with the severe course of the disease, the persistence of epileptic seizures, and an underestimated assessment of the child's abilities by teachers and parents. The study showed the high efficacy of Valparin XP in all forms of epilepsy, and primarily in idiopathic generalized epilepsy. The prevalence of side effects was 23.7%, which generally showed good tolerability of Valparin XP. The side effects of Valparin XP were dose-dependent in 93.1% of cases and had a transitory character.

4. Conclusions

It is important to note that this observation confirms the literature data on the high efficacy and good tolerability of relatively low doses of Valparin XP — in this study, the doses of the drug were moderate. In accordance with the recommendations of the World Antiepileptic League, the goal of epilepsy treatment is to achieve remission with a minimum number of adverse events. The conducted research in clinical practice has confirmed the high efficacy and very good tolerability of Valparin XP in monotherapy for childhood forms of epilepsy.

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