

The medical and organizational aspects of the management of patients with medical conditions associated with benign focal epileptiform discharges of childhood (BFEDC)

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**ABSTRACT**

**Relevance of the research**

Epilepsy, being one of the most common neurological diseases in the world, often entails the development of neurological, cognitive, emotional, psychological and social consequences. The latest systematic review and meta-analysis of international studies shows that the average incidence of epilepsy is 50-70 cases per 100.000 population per year. The mean prevalence of active epilepsy is 500-700 per 100.000 population (Beghi E., 2020). In 75% of cases, epilepsy manifests itself in childhood and adolescence up to the age of 15, which makes it the most important disease in pediatric neurology (Frolova B.M., 2020).

According to the WHO report "Epilepsy, a public health imperative", published in 2019 in collaboration with the International League against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE), this nosology is an important problem not only for neurology but also for public health and social medicine.

The strengthening of globalization processes and the ongoing integration of the Republic of Kazakhstan into the world health system make it imperative that the country introduces innovative methods of medical statistics that assess disease-burden indicators, expressed in the number of healthy years of life lost due to disease (YLD) or premature death (YLL). In this case, YLD is calculated using a disease-specific disability weight index (Dw) inversely proportional to the level of patients' quality of life.

In the second half of the 20th century, progress in child neurology was marked by the discovery of self-limited age-related epilepsies with a characteristic clinical semiology of seizures, the presence of benign focal epileptiform discharges of childhood (BFEDC), and a high probability of spontaneous remission of seizures before the end of puberty even in the absence of pharmacotherapy. Since that time, the previously unfavorable view of the diagnosis of "epilepsy" in children as a progressive disease has changed radically. In 2017, ILAE updated the classification of epilepsy for the first time since 1989 with the allocation of a group of self-limited childhood epilepsies. In addition, WHO launched a new International Classification of Diseases 11th Revision (ICD-11) in January 2022 in which the category of benign epilepsy of childhood was introduced into the nomenclature of diseases.

Nowadays, the possibility of comorbidity of BFEDC with structural brain changes has been proven and this should undoubtedly lead to adjustments being made to the generally accepted approaches to the diagnosis and treatment of children with cerebral palsy accompanied by convulsive seizures. Obviously, the disability weight

(Dw) of self-limited childhood epilepsy will be significantly lower than the Dw of symptomatic epilepsy. The official treatment protocols for childhood epilepsy in Kazakhstan do not take into account clinical cases of combined pathology. Thus, convulsive seizures with structural brain changes are diagnosed as "symptomatic epilepsy", followed by prolonged stigmatized anticonvulsant therapy.

This study is, therefore, very relevant to the need to modernize the existing management of epilepsy by improving methods for analyzing statistical data and integrating the treatment and diagnostic process of BFEDC-associated conditions into the primary health care system. This will in the future reduce the burden of disease and improve the quality of life in this category of patients.

**Purpose of the study:**

to develop and scientifically substantiate a set of measures for the management of children and adolescents with BFEDC-associated conditions based on an integrated assessment of the effectiveness of the treatment, taking into account the level of quality of life.

**Objectives of the study:**

1. Identify current global trends in the improvement of pediatric epileptological services.
2. To study the age-specific dynamics of the incidence and prevalence of epilepsy among the child population of Almaty.
3. To analyze the relationship between the quality of life of patients with Rolandic epilepsy and the use of various therapeutic approaches to anticonvulsant treatment.
4. Optimize a set of measures to organize medical and preventive care for patients with self-limited age-dependent epilepsy.
5. To develop an innovative model for management of children and adolescents with BFEDC-associated conditions at the level of primary health care organizations.

**Novelty of research findings:**

A comprehensive assessment of the age-specific dynamics of the incidence and prevalence of epilepsy among the child population of Almaty was carried out based on an analysis of retrospective statistical data and this has led to the definition of a critical period associated with the onset of idiopathic partial epilepsy.

The present work is the first prospective observational study of patients with self-limited focal childhood epilepsy with centrotemporal spikes (Rolandic epilepsy) carried out in Kazakhstan. For the first time, statistical proof has been established for the different approaches to treatments for self-limited focal childhood epilepsy which are most acceptable for the local population based on quality-of-life parameters.

The results obtained have made it possible to develop and scientifically substantiate an innovative model for the management of children and adolescents with BFEDC-associated conditions, including childhood focal epilepsy with structural changes in the brain and a pattern of BFEDC on the electroencephalogram (FESCB- BFEDC).

**Main Points for Defense Discussion:**

An analysis of the epidemiological indicators of the incidence and prevalence of epilepsy among the child population of Almaty demonstrates a clear dependence on

age, which correlates with the periods of manifestation and resolution of self-limited age-dependent epilepsies. An increase in the predicted levels of prevalence of idiopathic focal epilepsy necessitates the adoption of managerial decisions aimed at developing and implementing a model for the medical examination of children with conditions associated with BFEDC.

In childhood self-limited focal epilepsy with centrotemporal spikes with low frequency of seizures, indicators of emotional, social, physical functioning, as well as the overall level of health-related quality of life, are statistically significantly lower in children taking anticonvulsant therapy compared with patients observed without specific treatment.

The innovative model of integrated medical care for children with BFEDC-associated conditions corresponds to modern global trends in the organization of epileptological services and is a holistic, step-by-step monitoring system based on a patient-oriented approach and evaluation of treatment effectiveness, taking into account quality-of-life indicators.

### **Conclusions:**

1. Globally, the most significant area in relation to improving the pediatric epileptological service system is the identification and development of an organizational model of patient-oriented medical care for children with epilepsy at the level of primary health care, taking into account modern criteria for the effectiveness of treatment based on health-related quality of life parameters.

2. The dynamics of the incidence of epilepsy among children and adolescents in Almaty in 2015-2021 is characterized by a stable increase in indicators from age one (107.4;  $m=23.8$ ,  $\sigma=58.2$ ,  $Cv=54.2$ ) to 9 (209.0;  $m=44.4$ ,  $\sigma=108.8$ ,  $Cv=52.1$ ), followed by a decrease to 129.1 ( $m=22.4$ ,  $\sigma=54.9$ ,  $Cv=42.5$ ) cases per 100,000 child population by age 15-17. The prevalence of epilepsy follows a similar trend, with an increase in indicators from the age of one (477.1;  $m=31.8$ ,  $\sigma=77.8$ ,  $Cv=16.3$ ) to 15 (662.0;  $m=22.8$ ,  $\sigma=55.9$ ,  $Cv=8.5$ ), and a decrease to 454.9 ( $m=44.2$ ;  $\sigma=108.3$ ;  $Cv=23.8$ ) by the end of puberty (age 15-17).

3. An analysis of the results of a comprehensive study using the methods of extrapolation of existing trends based on regression models showed a forecast for the near future in relation to the main indicators of the pediatric epileptological service: the incidence of epilepsy among children in Almaty aged 0-17 years tends to increase from 320 per 100,000 children in 2021 to 502-648 by 2023-2024. The level of predictive values for the prevalence of idiopathic focal epilepsy is positive linear with an increase of 103 per 1,000 children with epilepsy aged 0-17 in 2021 to 117-120 in 2023-2024. The trend steadily increases in 6-9 years old and 9-12 years old from 104 and 110 cases per 100,000 child population in 2021 to 133 and 129 by 2024, while for those aged 12-15 and 15-17 the forecast values tend to decrease.

4. The demographic characteristics of childhood self-limited focal epilepsy with centrotemporal spikes in a prospective observational study in Almaty showed similar global trends in terms of the age of onset of clinical manifestation and the sex ratio of patients: in 65.1% of cases, Rolandic epilepsy manifests itself at the age of 5 to 8 (range 3–12), with boys accounting for up to 62.8%. All observed children under the

age of 15 achieved remission of seizures lasting for at least two years, regardless of the use of AEDs.

5. The average indicators of emotional (90.1, Me=88.95, IQR=4.75), social (88.0, Me=87.5, IQR=5.4) and physical (85.8, Me=86.1, IQR = 9.7) functioning in patients with a history of fewer than four seizures and who were taking anticonvulsant therapy were statistically significantly reduced compared with the observed subgroup without AED- (98.6; 98.4; 98.7) at  $p<0.01$ . At the same time, similar indicators in the AED-subgroup did not reveal statistically significant differences in comparison with conditionally "healthy" children (100.0).

6. The final calculations of the overall quality of life index in the AED+ subgroup (89.2, Me=87.43, IQR=4.76) turned out to be statistically significantly lower ( $p<0.01$ ) than the AED- subgroup (98.0, Me=100, IQR=3.3). There was no significant difference between the general indicators of the quality of life of patients in the AED subgroup and "conditionally healthy" children.

7. Based on scientific and organizational approaches, an innovative integrated model of dynamic monitoring of children and adolescents with BFEDC-associated conditions in primary health care has been developed, based on three stages: (1) preventive screening examinations at certain ages; (2) clarification of the diagnosis according to the developed algorithm of diagnostic process, followed by the distribution of children into health groups; (3) selection of therapeutic approaches based on quality of life indicators and scheduled follow-up examinations.

#### **The practical significance of the study:**

1. The results of the comparative assessment of quality of life indicators among patients with self-limited focal epilepsy with various therapeutic approaches may be used to optimize the organization of medical care for this category of patients.

2. In order to reduce the epilepsy burden, the proposed model of integrated patient-oriented management plan for children with BFEDC-associated conditions is recommended for use by local health organizations responsible for statistical processing and the clinical and epidemiological analysis of childhood epilepsy in Kazakhstan.

3. The results of the study were integrated into the clinical practice of pediatric neurologists at three locations in Almaty: the "Sunkar" medical center, Polyclinic #55 and the Center for Social Adaptation and Vocational Rehabilitation of Children and Adolescents with Mental and Physical Disabilities.

#### **Approbation of the thesis**

The main results of the research set out in this dissertation have been presented at the following conferences:

- 5th International Congress "Health for all: Integration of all services for the health of the nation on the basis of modernization of practical medicine and public health" (Almaty, Kazakhstan, June 21-22, 2017);

- 14th World Congress on Controversies in Neurology (CONy), (London, UK, March 26-29, 2020);

- 5th World Congress on Public Health and Health Care Management (Miami, USA, July 20-21, 2020).

#### **Publications on the topic of the dissertation:**

Doctoral dissertation materials were published in seven scientific papers, including three publications in the proceedings of international scientific and practical conferences, two articles in journals recommended by the Committee for Control of Education and Science in the Ministry of Education and Science for the Republic of Kazakhstan, and two publications in Web of Science Core Collection and Scopus journals.

Two copyrights have been developed and certificates have been obtained for state registration of rights in connection with the scientific works entitled “Benign focal epileptiform discharges of childhood” (No. 20825, October 12, 2021) and "Outpatient management of patients with benign focal epileptiform discharges of childhood " (No. 20824, October 12, 2021).

#### **Volume and structure of the thesis**

The dissertation consists of an introduction, five sections, a discussion, conclusions, practical recommendations and a list of references. The thesis is 160 pages in length and contains 31 tables, 34 figures, 5 appendices and 161 references.