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## KETOGENIC DIET IN THE TREATMENT AND REHABILITATION OF CHILDREN WITH EPILEPSY

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### Abstract

**Introduction.** Pharmacoresistant epilepsy and epileptic syndromes in children remain a pressing clinical problem. The ketogenic diet (KD), a high-fat and low-carbohydrate metabolic intervention, is considered an effective method to reduce seizure frequency and improve neurocognitive status.

**Aim.** The aim of this study was to evaluate the efficacy and tolerability of KD in children with pharmacoresistant epilepsy in a rehabilitation setting.

**Materials and Methods.** A prospective observational study was conducted at the National Center for Child Rehabilitation (Astana, Kazakhstan) from January 2022 to March 2025. The study included 30 patients aged 1 to 18 years (median age – 8 years) with confirmed pharmacoresistant epilepsy or epileptic syndromes. KD was applied in the classic ratio of 2:1, 3:1, and 4:1 alongside antiepileptic therapy. Effectiveness was assessed by reduction in seizure frequency at 4, 6, 12, and 12–18 months of therapy. Additionally, EEG dynamics, cognitive status, and adverse effects were evaluated. Statistical analysis was performed in SPSS 25.

**Results.** After 4 months of therapy, a clinically significant response ( $\geq 50\%$  reduction in seizure frequency or remission) was observed in 22 patients (73.3%). At 6 months, positive dynamics persisted in 13 patients (56.5%), at 12 months – in 7 of 15 (46.7%), and at 12–18 months – in 7 of 17 (41.2%). The presence of pronounced cognitive impairment was associated with lower KD effectiveness ( $p=0.04$ ). Completion of the full course of the diet was significantly more frequent among patients with a positive effect ( $p=0.006$ ). Adverse effects were more common in the non-responder group ( $p=0.03$ ); no severe complications were recorded.

**Conclusion.** The ketogenic diet is an effective and safe method of treating pharmacoresistant epilepsy in children, including patients with severe neurodevelopmental disorders. High adherence and multidisciplinary support contribute to clinical improvement. Controlled studies with larger samples are needed to confirm long-term efficacy.

**Keywords:** ketogenic diet, epilepsy, resistance, children, rehabilitation, diet therapy.

**Introduction.** Epilepsy is one of the most common chronic neurological disorders in children, with a global prevalence of the active form ranging from 6.8 to 18.6 per 1000 of the pediatric population [1]. In children with focal cortical dysplasia, therapy resistance reaches 74% [2]. Pharmacoresistant epilepsy is closely associated with a high risk of severe cognitive impairments, delays in speech and motor development, behavioral disorders, and social maladaptation [3]. The risks of injury, social isolation, and sudden unexpected death in epilepsy (SUDEP) also increase, especially in cases of frequent generalized seizures [4].

Low pharmacotherapy efficacy is the key problem in the treatment of pediatric epilepsy. The term «pharmacoresistance», according to the consensus of the International League Against Epilepsy (ILAE), is defined as a failure to achieve seizure control when using two adequately chosen antiseizure medications (ASMs), and is observed in approximately 20–30% of children with epilepsy [5].

There is a high prevalence of resistance even among patients who have undergone surgical treatment or vagus nerve stimulation. In children with focal cortical dysplasia, the rate of drug-resistant epilepsy (DRE) reaches 74% [6].

Prolonged lack of response to ASMs leads to the progression of cognitive deficits, delays in speech development, and deterioration of quality of life – all effects well described in studies on childhood epilepsy [7]. The risk of sudden unexpected death in epilepsy (SUDEP) also increases, particularly with frequent uncontrolled generalized seizures [4].

In addition to lack of efficacy, long-term ASM use is associated with risks of cognitive side effects, adverse reactions, and financial burden. In adults, cognitive adverse effects are reported with drugs such as phenytoin and valproate, requiring caution in pediatric practice [8].

At the same time, alternative treatments such as surgery and vagus nerve stimulation are less accessible for children or have limited effectiveness in complex epilepsy forms. Surgical interventions are not always feasible in generalized epilepsies and systemic encephalopathies, highlighting the need for additional non-pharmacological approaches.

The ketogenic diet (KD), characterized by high fat and low carbohydrate content, has been used in drug-resistant epilepsy since the early 20th century. Numerous randomized controlled trials have shown that 35–56% of children receiving a classical or modified KD achieved  $\geq 50\%$  seizure reduction (RR = 5.1, 95% CI 3.18–8.21;  $p < 0.001$ ) compared to the control group without diet [9].

Meta-analyses and reviews confirm that approximately 16% of children achieve complete remission, 32% experience  $>90\%$  seizure reduction, and about 56% achieve  $\geq 50\%$  reduction [10].

Among patients with severe epileptic syndromes, such as West syndrome and Lennox–Gastaut syndrome, KD demonstrates improvement in 75–90% of cases, including full seizure control [11].

The mechanism of KD is complex and multifactorial. It is hypothesized that ketone bodies (acetoacetate,  $\beta$ -hydroxybutyrate), produced in the liver during ketosis, provide stable energy supply to neurons, increase resistance to energy-dependent stress, and modulate GABAergic and glutamatergic neurotransmission [12]. Experimental models have shown that KD increases mitochondrial density and functionality and stabilizes ion channel activity [13]. In addition to its antiepileptic effect, the diet may improve cognitive functions, behavioral responses, and quality of life in children due to its influence on neuronal plasticity and metabolic regulation [14].

KD is also effective in specific epilepsy forms, such as GLUT1 deficiency syndrome and West syndrome, as confirmed by national and international guidelines [15]. Despite the proven efficacy of KD in children with pharmacoresistant epilepsy, its implementation and sustainable use in clinical rehabilitation settings remain an open question, especially in patients with severe neurological and cognitive impairments. Most randomized and controlled trials have been conducted in specialized epilepsy centers with high resource availability, whereas implementing KD in routine practice, including rehabilitation facilities, faces multiple barriers – from low parental awareness to limited access to nutritionists and outpatient follow-up [16]. Particularly challenging is the organization of KD in patients with comorbidities: cerebral palsy, speech development delay, autism, or congenital malformations of the central nervous system. These children require not only diet therapy but also comprehensive multidisciplinary support,

including neurologists, rehabilitation specialists, dietitians, speech therapists, and social adaptation experts.

Long-term tolerability of the diet, frequency and structure of side effects, adherence in real-world clinical settings, and sustainability of positive outcomes after therapy discontinuation remain insufficiently studied. To date, only a limited number of studies have evaluated KD use in inpatient and outpatient rehabilitation, emphasizing the need to accumulate clinical data from everyday practice.

Thus, conducting observational studies on the use of KD in pediatric rehabilitation, especially in patients with a high degree of neuropsychological comorbidity, is a relevant and highly demanded direction of modern neurology and nutritional science.

### **Materials and Methods.**

#### *Ethical Issues*

The study was approved by the local ethics committee of NJSC «National Center for Children's Rehabilitation», Astana, Kazakhstan (protocol No. 1 dated February 22, 2022). All parents or legal representatives of the patients gave written informed consent to participate in the ketogenic therapy program and to the processing of medical information in a generalized form. The therapy and follow-up protocol complied with national standards and the principles of the Declaration of Helsinki.

#### *Study type*

This study is a prospective series of clinical observations conducted at the National Center for Children's Rehabilitation (NCCR), Astana, Republic of Kazakhstan, from March 2022 to March 2025. The aim of the work was to study the effectiveness and tolerability of the ketogenic diet in patients with pharmacoresistant epilepsy and epileptic syndromes of various etiologies.

#### *Participants*

The study included patients aged 1 to 18 years (median age – 8 years) with an established diagnosis of pharmacoresistant epilepsy or confirmed epileptic syndromes on the background of various neurological diseases. The diagnosis was established on the basis of clinical presentation, electroencephalography (EEG-video monitoring), neuroimaging (MRI, if available), medical history, and previous therapy. A mandatory inclusion criterion was the absence of sustained effect from at least two antiepileptic drugs (AEDs) administered in adequate dosage. Exclusion criteria were: decompensated somatic conditions, severe metabolic disorders, parental refusal to follow the ketogenic diet, or intolerance of the main dietary components. All patients were hospitalized and monitored by a multidisciplinary team, including a neurologist, dietitian, clinical pharmacologist, and epileptologist.

#### *Intervention*

The ketogenic diet was prescribed while maintaining previously selected antiepileptic therapy. The ratio of fats to proteins and carbohydrates was selected individually, depending on age, body weight, metabolic tolerance, and clinical presentation. Classical KD regimens with ratios of 2:1, 3:1, and 4:1 were used. The diet was designed according to physiological caloric intake and daily fluid requirements. The diet was based on high-fat foods (cream, oils, fatty meats and fish), proteins (eggs, meat, cheese), and a limited amount of carbohydrates (vegetables, fruits with a low glycemic index). All patients received vitamin and mineral supplements (calcium, magnesium, carnitine, multivitamins) as indicated. Ketone levels in urine and blood glucose were monitored 2–3 times per day. Patients and their families received instructions on dietary adherence, maintaining a food diary, and monitoring side effects. Patients were followed up throughout the KD period (from 4 to 18 months).

#### *Outcome assessment methods*

The primary criterion of therapy effectiveness was a reduction in seizure frequency compared to baseline. Changes were evaluated according to the following categories: complete

seizure remission,  $\geq 50\%$  reduction,  $< 50\%$  reduction, and no effect. Additional observed parameters included EEG changes (if available), improvement in cognitive and behavioral status (as assessed by physicians and parents), and presence and severity of side effects. Data were recorded in medical documentation and observational protocols. Time points of observation: 4 months, 6 months, 12 months, and 12–18 months after initiation of KD.

#### *Methods of controlling confounding factors*

All participants had equal access to dietary support in inpatient settings. However, after discharge, diet adherence at home was carried out either under remote supervision (if contact with NCCR was maintained) or without systematic monitoring. The volume and quality of home support could vary. Parents were provided with guidelines and recommendations, but comprehensive multidisciplinary monitoring at the place of residence was not available.

#### *Statistical analysis*

Statistical data analysis was carried out using IBM SPSS Statistics version 25. All variables were preliminarily checked for completeness and distribution. For descriptive statistics, quantitative variables were presented as mean and standard deviation ( $M \pm SD$ ) or median with range (min–max), depending on the type of distribution. Categorical variables were described in absolute numbers and percentages.

To assess the association between clinical characteristics and the response to the ketogenic diet, non-parametric tests were applied. Comparison of frequencies in independent groups (e.g., by sex, epilepsy type, presence of side effects) was performed using Pearson's  $\chi^2$  test; in cases of expected counts  $< 5$ , Fisher's exact test was applied. To compare quantitative variables between two independent samples (e.g., age, epilepsy duration before therapy initiation), Student's t-test was used for normally distributed variables, or the Mann–Whitney U test in case of non-normal distribution (normality assessed by the Shapiro–Wilk test).

To evaluate the dynamics of clinical response to the ketogenic diet at different time points (4, 6, 12, and 12–18 months),  $\chi^2$  test was used with calculation of degrees of freedom and corresponding p-value. The statistical significance level was set at  $p < 0.05$ . No correction for multiple comparisons was applied, since the main purpose of the analysis was to evaluate the general trend of associations in the context of a limited sample.

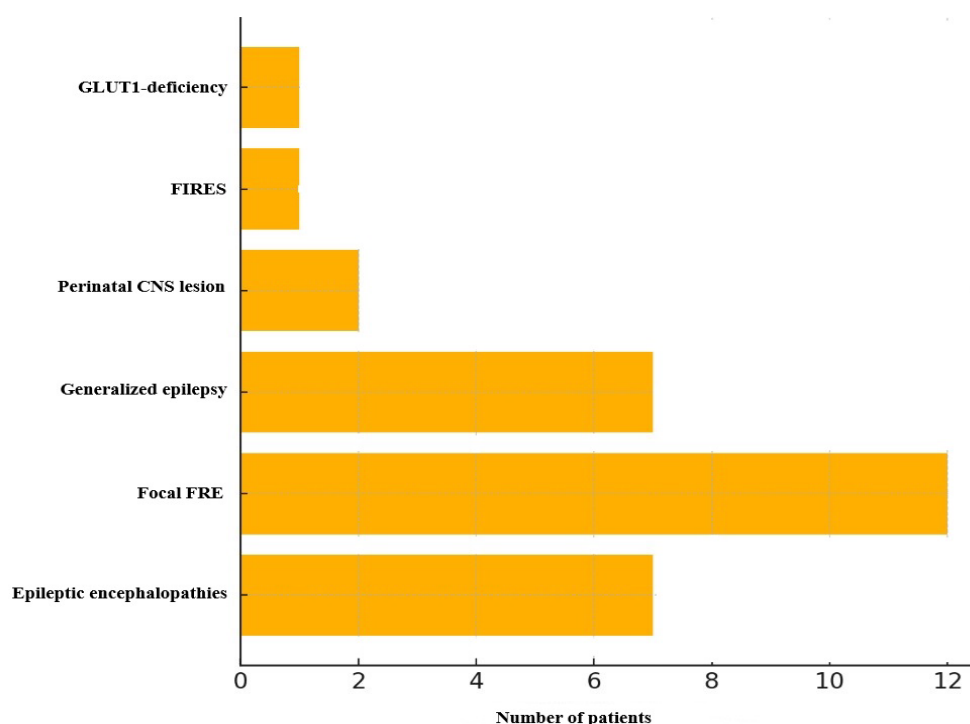
**Results.** Thirty patients were included in the study, with a median age of 8 years (range: 1–27) (Table 1). There were 16 males (53.3%) and 14 females (46.7%). The mean duration of adherence to the ketogenic diet was 10 months. Concomitant neurological disorders were identified in 22 patients (73.3%). The mean duration of epilepsy prior to initiation of the ketogenic diet was  $3.6 \pm 2.0$  years. The mean number of previously tried antiepileptic drugs was  $3.4 \pm 1.1$ . The mean body mass index was  $17.2 \pm 2.5$ . Cognitive status: normal – in 6 patients (20%), developmental delay – in 12 (40%), intellectual disability – in 12 (40%).

**Table 1.** Clinical and demographic data

Variable	Indicator
Total number of patients	30
Age, years (median, range)	8 (1–27)
Male, n (%)	16 (53.3%)
Female, n (%)	14 (46.7%)
Mean duration of KD, months	10 months
Comorbid neurological diagnoses	22 (73.3%)
Duration of epilepsy before KD initiation, years	$3.6 \pm 2.0$
Mean number of AEDs tried before KD	$3.4 \pm 1.1$
BMI (mean $\pm$ SD)	$17.2 \pm 2.5$

Variable	Indicator
Cognitive status	
Normal	6 (20%)
Developmental delay	12 (40%)
Intellectual disability	12 (40%)

The largest proportion of patients receiving the ketogenic diet (Figure 1) belonged to the group with focal drug-resistant epilepsy – 12 individuals (40.0%). Seven patients (23.3%) were observed in the groups with epileptic encephalopathies and generalized epilepsy. Less common were cases of congenital malformations of the central nervous system (2 patients, 6.7%), as well as rare forms – FIRES syndrome and GLUT1 deficiency, each represented by a single case (3.3%).



**Figure 1.** Distribution of patients by nosological categories

Of 30 patients observed during 4 months after the initiation of the ketogenic diet (Table 2), 22 (73.3%) demonstrated a clinically significant response in the form of complete cessation of seizures or their reduction by  $\geq 50\%$ . After 6 months, 23 patients continued therapy, of whom positive dynamics persisted in 13 (56.5%). At 12 months, efficacy  $\geq 50\%$  was noted in 7 out of 15 (46.7%), and at 12–18 months — in 7 out of 17 (41.2%).

The distribution of clinical response across time points was analyzed using the  $\chi^2$  test. The obtained  $\chi^2$  value = 5.67 with 3 degrees of freedom did not reach statistical significance ( $p = 0.129$ ).

**Table 2.** Effectiveness of CD at different time points

Observation period	Total number of patients (n)	Clinical response $\geq 50\%$ n (%)	Response $< 50\%$ or no dynamics n (%)
4 months	30	22 (73.3%)	8 (26.7%)
6 months	23	13 (56.5%)	10 (43.5%)

Observation period	Total number of patients (n)	Clinical response $\geq 50\%$ n (%)	Response $< 50\%$ or no dynamics n (%)
12 months	15	7 (46.7%)	8 (53.3%)
12–18 months	17	7 (41.2%)	10 (58.8%)
$\chi^2$ -test			df = 3 / p = 0,129

Adverse effects of the ketogenic diet were recorded in 11 out of 30 patients (36.7%) (Table 3). The most common were gastrointestinal disorders (nausea, pain, constipation), identified in 3 patients (10.0%), in one case becoming the reason for discontinuation of therapy. General weakness was observed in 2 patients (6.7%), in one case it was a factor leading to withdrawal from KD. One patient (3.3%) experienced paresthesia and burning in the legs, which was accompanied by discontinuation of the diet. Episodes of hypoglycemia were registered in one patient (3.3%) and did not lead to discontinuation of KD.

Four patients (13.3%) discontinued the diet due to the difficulty of adherence, another five (16.7%) – by family decision not related to adverse effects. In three patients (10.0%) the reason for withdrawal was the absence of clinical improvement. In 19 patients (63.3%) no adverse effects were observed, therapy continued. The predominant severity level of the recorded effects corresponded to Grade 1–2 according to the CTCAE scale.

**Table 3.** Adverse events and reasons for withdrawal

Adverse event / reason	Number of patients (n)	Share of sample (%)	Severity by CTCAE (predominant grade)	Related to trial completion (yes/no (n))
GI dysfunction (nausea, pain, constipation)	3	10.0%	Grade 2 (moderate)	1 / 2
General weakness	2	6.7%	Grade 1 (mild)	1 / 1
Paresthesia, burning in legs	1	3.3%	Grade 2 (moderate)	1 / 0
Hypoglycemia (episodes by glucometer)	1	3.3%	Grade 1 (mild, no hospitalization)	0 / 1
Difficulty adhering to diet	4	13.3%	Not applicable	4 / 0
Withdrawal by family decision	5	16.7%	Not applicable	5 / 0
Lack of clinical effect	3	10.0%	—	3 / 0
No adverse events	19	63.3%	—	0 / 19

A more detailed description of the clinical cases, including patient characteristics, methods for assessing effectiveness, and side effects, is provided in (Appendix 1).

Of the 30 patients, a positive response to the ketogenic diet (Table 4) (seizure reduction  $\geq 50\%$ ) was recorded in 18 individuals. Among them, the proportion of males was 55.6% (10 of 18), while in the group with  $< 50\%$  effect or no effect (n=12) it was also 50% (6 of 12); the difference by sex was statistically insignificant (p=0.94). The mean age of patients in the effective response group was  $7.5 \pm 2.1$  years, whereas in the ineffective response group it was  $8.3 \pm 3.0$  years (p=0.42). The focal form of epilepsy predominated in both groups but was more pronounced among responders: 12 versus 6 patients, respectively; conversely, generalized

forms were more frequent among non-responders (5 versus 3), but no statistically significant association was found ( $p=0.21$ ).

The mean duration of epilepsy before the initiation of KD was  $3.2 \pm 1.8$  years in the responder group and  $4.1 \pm 2.2$  years in the non-responder group ( $p=0.19$ ). The presence of severe cognitive impairments (intellectual disability) was noted in 10 of 18 in the responder group and in 2 of 12 in the non-responder group; patients with developmental delay predominated in the latter, with the difference being statistically significant ( $p=0.04$ ). Adherence to the diet was higher in the group with a positive effect: 88.9% completed the full course versus 41.7% in the ineffective response group ( $p=0.006$ ).

Side effects were recorded in 4 of 18 patients with  $\geq 50\%$  response and in 7 of 12 with  $<50\%$  response ( $p=0.03$ ), which suggests a possible link between the severity of adverse events and the reduction of effectiveness or adherence to KD.

**Table 4.** Associations between characteristics and response to KD

Variable	Response $\geq 50\%$ n=18 (%)	Response $<50\%$ or no effect n=12 (%)	p-value
Sex			
male	10 (55.6%)	6 (50.0%)	0.94
female	8 (44.4%)	6 (50.0%)	
Age, years (mean $\pm$ SD)	$7.5 \pm 2.1$	$8.3 \pm 3.0$	0.42
Type of epilepsy			
focal	12 (66.7%)	6 (50.0%)	0.21
generalized	3 (16.7%)	5 (41.7%)	
Duration of epilepsy before KD, years	$3.2 \pm 1.8$	$4.1 \pm 2.2$	0.19
Cognitive impairment			
DD	8 (44.4%)	10 (83.3%)	0.04
ID	10 (55.6%)	2 (16.7%)	
Completed KD course fully, n (%)	16 (88.9%)	5 (41.7%)	0.006
Side effects			
present	4 (22.2%)	7 (58.3%)	0.03
absent	14 (77.8%)	5 (41.7%)	

**Discussion.** The study included 30 patients, with a median age of 8 years (range 1–27 years), which is comparable to the characteristics of large cohorts, where the mean age of children at the initiation of KD is between 5 and 8 years [9, 17]. The gender ratio (males – 53.3%, females – 46.7%) also corresponds to the proportions noted in similar studies, where a slight male predominance is more commonly observed.

The mean duration of epilepsy prior to the initiation of KD was  $3.6 \pm 2.0$  years, and the mean number of previously tried antiepileptic drugs (AEDs) was  $3.4 \pm 1.1$ . This reflects the nature of the sample—patients with pronounced drug resistance: in the trajectories of large studies, similar figures reach 6 or more AEDs by the time KD is initiated [17]. The presence of concomitant neurological disorders in 73.3% of patients (cerebral palsy, developmental delay, intellectual disability) is also typical for trained samples, highlighting the complexity of the clinical picture and the need for a comprehensive approach.

The average body mass index (BMI) was  $17.2 \pm 2.5$ , indicating a normal nutritional status, which is characteristic of children who began KD in a timely manner and received specialist

monitoring [15]. The distribution of cognitive status (normal – 20%, developmental delay – 40%, intellectual disability – 40%) demonstrates a significant proportion of patients with neuropsychological disorders, which is typical for a pharmacoresistant pediatric epilepsy cohort.

After 4 months of therapy, 22 out of 30 patients (73.3%) demonstrated a clinically significant response ( $\geq 50\%$  seizure reduction or complete seizure freedom), which is comparable to the results of large meta-analyses:  $\geq 50\%$  reduction was observed in 56–65% of children at 3–4 months of therapy [9, 10].

With continued follow-up, the proportion of responders decreased: 13 out of 23 (56.5%) at 6 months, 7 out of 15 (46.7%) at 12 months, and 7 out of 17 (41.2%) at 12–18 months. A decline in efficacy over time has been described in several cohorts: from 75% at 3–6 months to 40–50% by 1 year [16]. Reasons for the decline may include reduced adherence, physiological adaptation, and increased metabolic mass.

Statistical analysis of dynamics using the  $\chi^2$ -test did not reveal a significant difference between time points of efficacy ( $\chi^2 = 5.67$ ,  $df = 3$ ,  $p = 0.129$ ), which corresponds to the trend of gradual reduction without sharp fluctuations. A similar pattern is described in cohorts where the response rate stabilizes after 6–12 months at 40–50% [18].

Among the 18 patients with a clinical response ( $\geq 50\%$ ), focal epilepsy was found in 12 individuals (66.7%), whereas among the 12 non-responders only 6 (50%) had focal epilepsy. In the generalized epilepsy group – 3 (16.7%) versus 5 (41.7%). The observed difference did not reach statistical significance ( $p = 0.21$ ), which is consistent with reports that focal epilepsy tends to show better response to KD, but without consistent evidence [19].

The success rate of KD in focal versus generalized epilepsy usually ranges around 60% and 40%, respectively, according to a meta-analysis of neurocognitive and clinical outcomes [20]. Our results, showing 66.7% versus 41.7%, fall within this range and do not contradict the global trend.

Among rare forms – encephalopathies, KD also demonstrates efficacy in 45–75% of cases [21], which corresponds to our sample and supports the interpretation of KD's success in the diversity of epilepsy types.

In the group with a clinical response to the diet ( $\geq 50\%$  seizure reduction), 10 out of 18 patients (55.6%) had intellectual disability, and 8 (44.4%) had speech and psychomotor developmental delay; among the 12 non-responders, the figures were 2 (16.7%) and 10 (83.3%), respectively. The difference reached statistical significance ( $p = 0.04$ ), indicating a more pronounced response in children with severe cognitive dysfunction.

The obtained data confirm the presence of some correlation between the severity of neurodevelopmental impairment and KD outcomes—both negative and positive. The efficacy of KD in severe forms of epilepsy, including Lennox–Gastaut syndrome, has been confirmed in several clinical series and reviews. At the same time, the severity of cognitive impairment is not a factor reducing the response to therapy: in patients with intellectual disability and epileptic encephalopathies, the rate of clinical response reaches 45–70% [22].

In our study, the predominance of children with intellectual disability among responders may reflect well-organized dispensary care and high motivation of families of such children. This is confirmed by literature sources: with appropriate support, KD outcomes remain stable regardless of the severity of initial cognitive impairment [23].

Adverse effects of KD were noted in 11 out of 30 patients (36.7%). The largest share consisted of gastrointestinal disorders (3 patients, 10.0%), of whom one developed severe symptoms leading to discontinuation of therapy. General weakness was observed in 2 patients (6.7%), with one case resulting in withdrawal from the diet. Another patient (3.3%) developed

paresthesias and burning sensations in the legs, also leading to discontinuation. Hypoglycemia was recorded in one child (3.3%), but without requiring cessation of KD.

Discontinuation of KD due to reasons not related to adverse effects occurred in 4 patients (13.3%) because of difficulties in maintaining the diet, and in 5 patients (16.7%) for family reasons. In 3 patients (10.0%), the diet was discontinued due to lack of clinical effect, while no adverse reactions were observed. Among all patients, 19 (63.3%) experienced no adverse effects and continued therapy.

This structure of adverse events corresponds to literature data: the frequency of GI syndromes with KD is 10–15%, and general weakness about 5–8% [24]. Discontinuation of the diet is mainly associated with side effects and organizational issues, rather than dietary toxicity.

Comparison of «responders» and «non-responders» revealed a statistically significant association between the presence of side effects and discontinuation of therapy ( $p = 0.03$ ), consistent with data indicating reduced adherence when discomfort arises [25].

Among 18 patients with a clinical response  $\geq 50\%$ , 16 (88.9%) completed the KD course fully, compared to 5 out of 12 (41.7%) in the group without a significant response ( $p = 0.006$ ). This demonstrates a clear statistical relationship between higher adherence and therapy efficacy in our cohort.

The literature confirms the importance of adherence to KD as a key factor for sustained response: in a large cohort, more than 70% of children with good adherence had  $\geq 50\%$  seizure reduction, whereas among those unable to maintain the diet, the figure was no more than 35% [26].

Difficulties in implementing KD – strict restrictions, increased time for meal preparation, and the need for frequent biochemical monitoring – often lead to decreased adherence. This is reflected in a meta-analysis: up to 25% of families discontinue the diet due to inconvenience, despite initial benefit [25].

Consistent family and medical support facilitates adherence: with the involvement of a dietitian, frequent consultations, and regular feedback, adherence levels increase to 80–90% [27].

In our study, groups receiving higher levels of support (in a rehabilitation center setting) showed significantly better response. This underscores the importance of a specialized team and family support as a key component of successful dietary therapy.

**Conclusion.** The use of the ketogenic diet in children with pharmaco-resistant epilepsy in a specialized center demonstrated moderate but clinically significant efficacy: after 4 months from the start of the diet, 73.3% of patients had a response of  $\geq 50\%$ , while after one year the positive effect persisted in 46.7%. Long-term adherence to the diet proved challenging: only half of the patients continued KD after 12 months.

The highest efficacy was observed in focal forms of epilepsy and in patients without pronounced cognitive impairments. High adherence to the diet directly correlated with therapeutic effect ( $p = 0.006$ ), whereas the presence of side effects was associated with lower adherence and worse outcomes ( $p = 0.03$ ).

However, efficacy may decrease in cases of poor adherence or the presence of concomitant neurological and cognitive impairments. These factors should be taken into account when selecting patients and planning management.

**Appendix 1.** Individual clinical cases of patients receiving the ketogenic diet

<b>Patient</b>	<b>Age</b>	<b>Diagnosis</b>	<b>Cognitive Status</b>	<b>Comorbidities</b>	<b>Duration of KD</b>	<b>Seizure Dynamics</b>	<b>Assessment Method</b>	<b>Side Effects</b>	<b>Completed KD</b>	<b>Notes</b>
m-1	3	West syndrome	severe deficit	—	6 months	no effect	clinical assessment + EEG	gastrointestinal dysfunction	No	Hormone therapy ineffective
f-2	6	CP + focal FRES	moderate developmental delay	pituitary adenoma	12 months	complete remission	diary + EEG	—	Yes	Reduction of pituitary adenoma
m-3	11	GLUT1 deficiency	moderate developmental delay	—	4 months	decrease in EEG discharges	EEG	—	No	No clinical effect
f-4	14	Rolandic epilepsy	normal	—	6 months	50% reduction	diary	paresthesia	No	Discontinued KD due to regimen

**Conflict of interest.**

We declare no conflict of interest.

**Authors' contribution.**

Zh.A. Medetbekova – research concept, patient observation, data collection, statistical processing, drafting the first version of the manuscript.

A. Giniyat – strategic support, coordination of administrative activities, participation in data interpretation.

S. Amangeldikyzy – organizational support, control of the ethical and procedural aspects of the project.

A.S. Kudaibergenov – clinical management of patients, expertise in neurorehabilitation, consultation on side effects.

D.A. Yerezhpov – statistical analysis, consultation on biomedical aspects, editing of the final text.

A.K. Gabdulqaium – assistance in statistical verification, preparation of tables, and literature compilation. Authors declare that this material has not been previously published and is not under consideration by other publishers.

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## ЭПИЛЕПСИЯСЫ БАР БАЛАЛАРДЫ ЕМДЕУ ЖӘНЕ РЕАБИЛИТАЦИЯЛАУДАҒЫ КЕТОГЕНДІ ДИЕТА

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### Түйіндеме

**Кіріспе.** Фармакорезистентті эпилепсия және балалардағы эпилепсиялық синдромдар өзекті клиникалық мәселе болып қала береді. Кетогенді диета (КД) – жоғары майлы және төмен көмірсулы метаболикалық араласу, ол ұстамалардың жиілігін азайту және нейрокогнитивті жағдайды жақсарту үшін тиімді әдіс ретінде қарастырылады.

**Мақсаты.** Бұл зерттеудің мақсаты – оңалту мекемесінде фармакорезистентті эпилепсиясы бар балаларда КД-ның тиімділігін және көтерімділігін бағалау.

**Материалдар мен әдістер.** Проспективті обсервациялық зерттеу Ұлттық балаларды оңалту орталығында (Астана қ., Қазақстан) 2022 жылғы қаңтардан 2025 жылғы наурызға дейін жүргізілді. Зерттеуге 1 жастан 27 жасқа дейінгі (медиана – 8 жас) 30 пациент енгізілді, олардың фармакорезистентті эпилепсиясы немесе эпилепсиялық синдромдары расталған. КД классикалық арақатынаста (2:1, 3:1 және 4:1) антиэпилептикалық терапия аясында қолданылды. Тиімділік 4, 6, 12 және 12–18 айлық

терапия кезеңінде ұстамалар жиілігінің төмендеуі бойынша бағаланды. Қосымша ЭЭГ динамикасы, когнитивті статус және жанама әсерлер ескерілді. Статистикалық талдау SPSS 25 бағдарламасында орындалды.

**Нәтижелер.** 4 айлық терапиядан кейін клиникалық маңызды жауап (ұстамалардың  $\geq 50\%$  төмендеуі немесе ремиссия) 22 пациентте (73,3%) байқалды. 6-айда оң динамика 13 пациентте (56,5%), 12-айда – 15 пациенттің 7-інде (46,7%), 12–18 айда – 17 пациенттің 7-інде (41,2%) сақталды. Айқын когнитивті бұзылыстар КД тиімділігінің төмендігімен ассоциацияланды ( $p=0,04$ ). Диетаның толық курсы аяқтау оң нәтижеге қол жеткізген пациенттерде жиірек байқалды ( $p=0,006$ ). Жанама әсерлер көбінесе жауап болмаған топта тіркелді ( $p=0,03$ ), ауыр асқынулар анықталған жоқ.

**Қорытынды.** COVID-19 инфекциясы ұзақ мерзімді өлім-жітім, инсульт немесе миокард инфарктісі деңгейіне айтарлықтай әсер етпегенімен, артериялық гипертензия, темекі шегу және созылмалы стресс нашар нәтижелермен байланысты болды. Бұл нәтижелер эндоваскулярлық стенттеуден өткен науқастарда жүрек-қантамырлық қауіп факторларын басқарудың маңыздылығын көрсетеді.

**Түйінді сөздер:** кетогенді диета, эпилепсия, резистенттілік, балалар, оңалту, диетотерапия.

## КЕТОГЕННАЯ ДИЕТА В ЛЕЧЕНИИ И РЕАБИЛИТАЦИИ ДЕТЕЙ С ЭПИЛЕПСИЕЙ

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### Аннотация

**Введение.** Фармакорезистентная эпилепсия и эпилептические синдромы у детей остаются актуальной клинической проблемой. Кетогенная диета (КД), представляющая собой высокожировое и низкоуглеводное метаболическое вмешательство, рассматривается как эффективный метод снижения частоты приступов и улучшения нейрокогнитивного статуса.

**Цель.** Целью настоящего исследования была оценка эффективности и переносимости КД у детей с фармакорезистентной эпилепсией в условиях реабилитационного учреждения.

**Материалы и методы.** Проспективное наблюдательное исследование проведено в Национальном центре детской реабилитации (г. Астана, Казахстан) в период с января 2022 года по март 2025 года. В исследование включены 30 пациентов в возрасте от 1 до 27 лет (медиана – 8 лет) с подтвержденной фармакорезистентной эпилепсией либо эпилептическими синдромами. КД применялась в классическом соотношении 2:1, 3:1 и 4:1 на фоне противоэпилептической терапии. Эффективность оценивалась по снижению частоты судорог на 4, 6, 12 и 12–18 месяце терапии. Дополнительно учитывались динамика ЭЭГ, когнитивный статус и побочные эффекты. Статистический анализ выполнен в SPSS 25.

**Результаты.** Через 4 месяца терапии клинически значимый ответ ( $\geq 50\%$  снижение частоты приступов или ремиссия) отмечен у 22 пациентов (73,3%). На 6-м месяце положительная динамика сохранялась у 13 (56,5%), на 12-м – у 7 из 15 (46,7%), на 12–18 месяце – у 7 из 17 (41,2%). Наличие выраженных когнитивных нарушений было

ассоциировано с меньшей эффективностью КД ( $p=0,04$ ). Завершение полного курса диеты достоверно чаще наблюдалось у пациентов с положительным эффектом ( $p=0,006$ ). Побочные эффекты чаще встречались в группе без ответа на терапию ( $p=0,03$ ), тяжёлых осложнений не зафиксировано.

**Заключение.** Кетогенная диета представляет собой эффективный и безопасный метод лечения фармакорезистентной эпилепсии у детей, включая пациентов с тяжёлыми нейроразвивающими нарушениями. Высокая приверженность и междисциплинарная поддержка способствуют клиническому улучшению. Для подтверждения долгосрочной эффективности необходимы контролируемые исследования на более широких выборках.

**Ключевые слова:** кетогенная диета, эпилепсия, резистентность, дети, реабилитация, диетотерапия.