Clinical Trial Protocol
Iranian Registry of Clinical Trials

22 Nov 2026

The Effect of Ketogenic Diet on Seizure Control in Children with Refractory Status Epilepticus: A Clinical Trial

Protocol summary

Study aim

To evaluate the efficacy and safety of the ketogenic diet in controlling seizures in children with refractory status epilepticus through a clinical trial

Design

This study is designed as an interventional clinical trial with a control group. Sampling will be performed on 20 children with refractory status epilepticus hospitalized in the Pediatric Intensive Care Unit (PICU). Eligible children will be randomly allocated into two groups of the intervention group and the control group.

Settings and conduct

The intervention group receives standard treatment + a 4:1 ketogenic diet (≥7 days), while the control group receives standard treatment alone. Both groups are monitored for adverse effects. The primary outcome is assessed on day 7. Study setting: Pediatric Intensive Care Unit (PICU) of Zahra Mardani Azari Children's Hospital, affiliated with Tabriz University of Medical Sciences.

Participants/Inclusion and exclusion criteria

Participants are children aged 1 month to 18 years with a definite diagnosis of refractory status epilepticus (based on ILAE criteria) who, despite receiving first- and second-line treatments, have had persistent seizures for at least 30 minutes, are hospitalized in the PICU, and whose parents have provided written informed consent. Exclusion criteria include absolute contraindications to the diet (fatty acid oxidation defects, pyruvate kinase deficiency, porphyria, primary carnitine deficiency, GLUT1 deficiency), severe liver/renal failure, and inherited metabolic disorders.

Intervention groups

The intervention group (n=10) will receive standard antiseizure treatment plus a ketogenic diet (4:1 ratio). The control group (n=10) will receive standard treatment alone, without the ketogenic diet.

Main outcome variables

Cessation of clinical and electroencephalographic seizures within 7 days of initiating the ketogenic diet

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20240519061838N4**
Registration date: **2026-09-17, 1405/06/26**
Registration timing: **registered_while_recruiting**

Last update: **2026-09-17, 1405/06/26**
Update count: **0**

Registration date

2026-09-17, 1405/06/26

Registrant information

Name

Khatereh Rezazadeh

Name of organization / entity

Country

Iran (Islamic Republic of)

Phone

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Recruitment status

recruiting

Funding source

Expected recruitment start date

2026-09-01, 1405/06/10

Expected recruitment end date

2027-09-01, 1406/06/10

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title
The Effect of Ketogenic Diet on Seizure Control in Children with Refractory Status Epilepticus: A Clinical Trial

Public title
Examination of Ketogenic Diet on Seizure Control in Children with Refractory Status Epilepticus: A Clinical Trial

Purpose
Treatment

Inclusion/Exclusion criteria

Inclusion criteria:
Age between 1 month and 18 years. Definite diagnosis of refractory status epilepticus based on the ILAE definition: failure to respond to two lines of therapy (first-line benzodiazepine and one second-line antiseizure medication, i.e., phenytoin, levetiracetam, or sodium valproate) for refractory status epilepticus; and failure to respond to the third-line therapy along with the induction of pharmacological coma for super-refractory status epilepticus. Persistence of seizure activity (clinical or electroencephalographic) for at least 30 minutes despite receiving the aforementioned treatments. Obtaining written informed consent from the parents or legal guardian of the patient.

Exclusion criteria:
Presence of absolute contraindications to the ketogenic diet: Fatty acid oxidation defects, Pyruvate kinase deficiency, Porphyria, Primary carnitine deficiency, GLUT1 deficiency Severe liver failure (liver enzymes > 3 times the upper limit of normal) or severe renal failure (GFR < 30 ml/min) Inherited congenital metabolic disorders (inborn errors of metabolism) Unwillingness of the parents or legal guardian to continue participation in the study

Age
From **1 month** old to **18 years** old

Gender
Both

Phase
N/A

Groups that have been masked

- Outcome assessor
- Data analyser

Sample size
Target sample size: **20**

Randomization (investigator's opinion)
Randomized

Randomization description
Randomization will be performed using simple randomization on an individual basis. A random number table will be used for this purpose. Initially, each of the 20 eligible patients will be assigned numbers 1 to 20. Then, by referring to a random number table, starting from a specified point, random numbers will be sequentially extracted. Even numbers will be allocated to the intervention group and odd numbers to the control group. In case of encountering duplicate numbers or numbers outside the range, the next number will be used, and this process will continue until 10 patients are allocated to each group. The random sequence will be generated by an individual independent of the implementation team and placed in sequentially numbered, opaque, sealed envelopes (SNOSE). After confirming patient eligibility and obtaining informed consent, the relevant envelope will be opened by the attending nurse or physician (who has no role in outcome assessment) and the patient's group assignment will be revealed. Thus, the principal investigator, outcome assessor, and data collector will remain blinded to the patients' group allocations.

Blinding (investigator's opinion)
Single blinded

Blinding description
Given the overt nature of the intervention (ketogenic diet compared to the standard hospital diet), blinding of patients, parents/legal guardians, and healthcare personnel (attending physicians, nurses, and dietitians) is not feasible, and these individuals will be aware of the patients' group assignments. To minimize bias in the study, the outcome assessor (the pediatric neurologist responsible for interpreting EEG recordings and performing clinical seizure evaluations), data collectors, and the statistical analyst will be kept blinded to the patients' group allocations. This will be achieved as follows: EEG recordings and clinical reports will be provided to the neurologist without any indication of the intervention or control group. Data will be extracted from medical records and checklists by an individual who is not informed of the patient's group assignment. The final data analysis will be performed by the statistician using codes A and B (without revealing the intervention or control group), and the code will be broken only after the completion of the statistical analyses.

Placebo
Not used

Assignment
Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee
Ethics committee of Tabriz University of Medical Science

Street address
Pediatric Health Research Center, Mardani Azar Children Hospital, Mardani Azar Street, Khavaran Town

City
Tabriz

Province
East Azarbaijan

Postal code
5143377505
Approval date
2026-07-01, 1405/04/10
Ethics committee reference number
IR.TBZMED.REC.1405.311

Health conditions studied

1

Description of health condition studied
Refractory Status Epilepticus
ICD-10 code
G40
ICD-10 code description
Epilepsy and recurrent seizures

Primary outcomes

1

Description
Cessation of clinical and electroencephalographic seizures within 7 days of initiating the diet.
Timepoint
Clinical seizures are monitored continuously throughout the 7-day study period, with the final EEG evaluation performed on day 7 to determine the primary outcome.
Method of measurement
Clinically and using electroencephalography (EEG)

Secondary outcomes

1

Description
Time to ketosis
Timepoint
Daily from the start of the diet until day 7
Method of measurement
Urine ketone measurement using ketone strips or urinalysis

2

Description
Metabolic acidosis
Timepoint
Daily during the 7-day study period
Method of measurement
Blood pH and bicarbonate measurement from arterial or venous blood samples

3

Description
Hypoglycemia
Timepoint
Every 6 hours during the 7-day study period
Method of measurement
Blood glucose measurement using a glucometer

4

Description
Hypertriglyceridemia
Timepoint
Daily during the 7-day study period
Method of measurement
Triglyceride measurement from blood samples (lipid profile)

5

Description
Gastrointestinal complications
Timepoint
Daily during the 7-day study period
Method of measurement
Recording in a gastrointestinal symptom checklist by nurses based on clinical observation

6

Description
Urinary stones and hyperuricemia
Timepoint
Upon occurrence of symptoms or clinical need (as per the attending physician's judgment)
Method of measurement
Kidney ultrasound (for stones) and serum uric acid testing

7

Description
Length of stay in PICU
Timepoint
At the time of discharge from PICU (end of study period)
Method of measurement
Extraction from patient medical records (recording admission and discharge dates)

Intervention groups

1

Description
Intervention group: The intervention group consists of 10 children with refractory status epilepticus hospitalized in the PICU who, in addition to standard treatment (antiseizure medications and anesthetics per hospital protocol), will receive a ketogenic diet with a 4:1 ratio (fat to protein + carbohydrates) via a nasogastric (NG) tube. The diet is initiated after an 8- to 12-hour fasting period, with the initial dose set at one-third of the daily caloric requirement, gradually reaching full calories over 3 days. In case of intolerance, the diet ratio will be reduced to 3:1 or 2:1. The intervention will continue for at least 7 days, with adverse effects monitored through blood glucose measurements every 6 hours, daily laboratory tests, and recording of gastrointestinal symptoms. The primary outcome is the cessation of clinical and EEG seizures within 7 days.
Category

Treatment - Other

2

Description
Control group: The control group consists of 10 children with refractory status epilepticus hospitalized in the PICU who will receive only standard treatment (antiseizure medications and anesthetics according to the hospital protocol) and will not receive the ketogenic diet. Their nutrition will be provided according to the standard hospital diet (via nasogastric tube or parenterally).

Category
Treatment - Other

Recruitment centers

1

Recruitment center

Name of recruitment center
Zahra Mardani Azari Children Hospital

Full name of responsible person
Khatereh Rezazadeh

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Zahra Mardani Azari Children Hospital, Mardani Azar street, Khavaran Town

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity
Tabriz University of Medical Sciences

Full name of responsible person
Khosro Adib Kia

Street address
No. 2 Central Building, 3rd Floor, Vice-Chancellor for Research and Technology, Tabriz University of Medical Sciences, Golgasht Street, Tabriz, Iran.

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Grant name

Grant code / Reference number

Is the source of funding the same sponsor organization/entity?
Yes

Title of funding source
Tabriz University of Medical Sciences

Proportion provided by this source
100

Public or private sector
Public

Domestic or foreign origin
Domestic

Category of foreign source of funding
empty

Country of origin

Type of organization providing the funding
Academic

Person responsible for general inquiries

Contact

Name of organization / entity
Tabriz University of Medical Sciences

Full name of responsible person
Khatereh Rezazadeh

Position
Assistant Professor

Latest degree
Medical doctor

Other areas of specialty/work
Nutrition

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Position
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Latest degree
Ph.D.

Other areas of specialty/work
Nutrition

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Sharing plan

Deidentified Individual Participant Data Set (IPD)
Undecided - It is not yet known if there will be a plan to make this available
Study Protocol
Undecided - It is not yet known if there will be a plan to make this available
Statistical Analysis Plan
Undecided - It is not yet known if there will be a plan to make this available
Informed Consent Form
Undecided - It is not yet known if there will be a plan to make this available
Clinical Study Report
Undecided - It is not yet known if there will be a plan to make this available
Analytic Code
Undecided - It is not yet known if there will be a plan to make this available
Data Dictionary
Undecided - It is not yet known if there will be a plan to make this available