Clinical Trial Protocol
Iranian Registry of Clinical Trials

22 Nov 2026

Comparison of the Efficacy of Phenytoin and Levetiracetam in Children with Benzodiazepine-Resistant Status Epilepticus: A Randomized Controlled Clinical Trial

Protocol summary

Study aim

Comparison of the efficacy of Phenytoin and Levetiracetam in children with benzodiazepine-resistant status epilepticus.

Design

Study Type: Randomized Controlled Trial (RCT). Randomization: Block randomization using blocks of 2, 4, and 8. Blinding: Double-blinding is not feasible due to differences in infusion durations.

Settings and conduct

Location: Mofid Hospital, Tehran. Procedure: Patients with persistent status epilepticus after two doses of benzodiazepines are randomized into one of the two treatment groups

Participants/Inclusion and exclusion criteria

Inclusion Criteria: Boys or girls aged 6 months to 17 years and 11 months. Benzodiazepine-resistant status epilepticus (BRSE) after two doses of benzodiazepines. Exclusion Criteria: Known or suspected pregnancy. Allergy or contraindication to Levetiracetam or Phenytoin. Known renal failure (renal function below 50% of the expected for age). Prior administration of a second-line antiepileptic drug before emergency department admission. Seizures following head trauma. Underlying heart disease.

Intervention groups

Group 1: Intravenous Levetiracetam at a dose of 40 mg/kg over 5 minutes (maximum dose 2.5 g). Group 2: Intravenous Phenytoin at a dose of 20 mg/kg over at least 20 minutes (maximum dose 2 g at a maximum infusion rate of 1 mg/kg/min).

Main outcome variables

Primary Outcome: Time from the start of drug infusion to the cessation of all observable seizure activity. Secondary Outcomes: Requirement for additional antiepileptic drugs, ICU admission, and occurrence of serious adverse events (death, respiratory depression, cardiovascular instability).

General information

Reason for update

Dear IRCT Reviewer/Expert, With due respect, following the progress of our research project and a re-evaluation of the study methodology, we hereby request an adjustment of the sample size from 128 to 78 patients. This reduction in sample size accounts for project time constraints and operational challenges in enrolling eligible patients (due to strict inclusion and exclusion criteria maintained to uphold scientific rigor), aimed at avoiding unnecessary delays in completing the study. Please note that a post-hoc power analysis was re-calculated, confirming that a sample size of 78 provides adequate statistical power and validity to evaluate the primary outcomes of the study. Thank you very much in advance for your time, consideration, and assistance.

Acronym

IRCT registration information

IRCT registration number: **IRCT20241019063425N1**
Registration date: **2025-01-02, 1403/10/13**
Registration timing: **registered_while_recruiting**

Last update: **2026-09-12, 1405/06/21**
Update count: **1**

Registration date

2025-01-02, 1403/10/13

Registrant information

Name

Seyed Amin Jazayeri

Name of organization / entity

Country

Iran (Islamic Republic of)

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Email address

aminjaz430@yahoo.com

Recruitment status
Recruitment complete
Funding source

Expected recruitment start date
2024-12-30, 1403/10/10
Expected recruitment end date
2025-12-22, 1404/10/01
Actual recruitment start date
empty
Actual recruitment end date
empty
Trial completion date
empty

Scientific title
Comparison of the Efficacy of Phenytoin and Levetiracetam in Children with Benzodiazepine-Resistant Status Epilepticus: A Randomized Controlled Clinical Trial

Public title
Trial of Phenytoin and Levetiracetam in Children with Resistant Status Epilepticus
Purpose
Treatment
Inclusion/Exclusion criteria
Inclusion criteria:
Boys or girls aged 6 months to 17 years and 11 months The patient has received two consecutive doses of first-line treatment but continues to experience ongoing status epilepticus.
Exclusion criteria:
Patients with known or suspected pregnancy Patients with a known contraindication or allergy to Levetiracetam or Phenytoin Patients with known renal failure (patients undergoing hemodialysis or with renal function below 50% of the expected for their age) Prior administration of a second-line antiepileptic drug before admission to the emergency department Seizures following head trauma Individuals with underlying heart disease
Age
From **6 months** old to **18 years** old
Gender
Both

Phase
3
Groups that have been masked
No information
Sample size
Target sample size: **78**
Randomization (investigator's opinion)
Randomized
Randomization description
Double-blinding is not feasible due to the difference in the infusion durations of these two drugs. A random sequence prepared in advance, using blocks of 2, 4, and 8, is generated through simple randomization and used to assign each patient to a treatment. Patients are entered into the random sequence based on the order of their arrival.
Blinding (investigator's opinion)
Not blinded
Blinding description
Placebo
Not used
Assignment
Parallel
Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee
Name of ethics committee
The specialized committee of ethics in biomedical research
Street address
Shahid Beheshti University of Medical Sciences and Health Services, University Headquarters, Building No. 2, 6th Floor, Arabi Street, Yemen Street, Shahid Chamran Highway, Tehran, Iran.
City
Tehran
Province
Tehran
Postal code
1985717444
Approval date
2024-10-12, 1403/07/21
Ethics committee reference number
IR.SBMU.MSP.REC.1403.390

Health conditions studied

1

Description of health condition studied
status epilepticus
ICD-10 code
G40.301
ICD-10 code description
refractory status epilepticus

Primary outcomes

1

Description
The time from the start of drug injection to the cessation of all visible signs of seizure activity, which is defined as the cessation of all rhythmic seizure activity.
Timepoint
From the time of drug injection to the end of epileptic status
Method of measurement
using a stopwatch by the therapist

Secondary outcomes

1

Description
The need for tertiary anticonvulsants to manage seizures after second-line therapy
Timepoint
After failure to respond to second-line therapy
Method of measurement
The number of patients who needed third-line treatment is recorded in each group

Intervention groups

1

Description
Intervention group: Levetiracetam is administered over 5 minutes at a dose of 40 mg/kg, with a maximum dose of 2.5 grams. Following the initiation of injection, the patient is monitored by the resident for the cessation of SE symptoms, and when possible, a video recording is made to document the exact time SE ends. During SE treatment, the APLS algorithm is always followed, and emergency measures (e.g., intubation) are performed if necessary.
Category
Treatment - Drugs

2

Description
Intervention group: Phenytoin is administered over a minimum of 20 minutes at a dose of 20 mg/kg, with a maximum dose of 2 grams and an infusion rate of no more than 1 mg/kg/min. If one medication does not result in a response, the patient is reevaluated, and the persistence of SE is confirmed before initiating another medication. For instance, if the patient does not respond to phenytoin, levetiracetam will be started. The response to phenytoin is assessed up to 25 minutes after initiation, while the response to levetiracetam is evaluated up to 10 minutes after the start of infusion. Patients' outcomes are documented accordingly.
Category
Treatment - Drugs

Recruitment centers

1

Recruitment center
Name of recruitment center
Mofid's children hospital
Full name of responsible person
Farzad Ahmad Abadi
Street address
Mofid children hospital, Shariati Street, above Hosseinieh Ershad, Tehran, Tehran Province, Iran.
City
Tehran
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Sponsors / Funding sources

1

Sponsor
Name of organization / entity
Shahid Beheshti University of Medical Sciences
Full name of responsible person
Farzad Ahmadabadi
Street address
Shahid Shahriari Square, Shahid Shahriari Square, Shahid Beheshti University, Shahid Beheshti University, Building No. 2, Faculty of Health, Neuroscience Research Center (3rd and 4th floor), Evin, Tehran, Iran
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Email
nrciran@sbmu.ac.ir
Web page address
https://nrc.sbmu.ac.ir/
Grant name
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
Shahid Beheshti 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
Shahid Beheshti University of Medical Sciences
Full name of responsible person
Farzad Ahmadabadi

Position
Professor of Shahid Beheshti University of Medical Sciences
Latest degree
Subspecialist
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Neuroscience
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Person responsible for updating data

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Sharing plan

Deidentified Individual Participant Data Set (IPD)
No - There is not a plan to make this available
Justification/reason for indecision/not sharing IPD
There is no further information
Study Protocol
No - There is not a plan to make this available
Statistical Analysis Plan
No - There is not a plan to make this available
Informed Consent Form
No - There is not a plan to make this available
Clinical Study Report
No - There is not a plan to make this available
Analytic Code
No - There is not a plan to make this available
Data Dictionary
No - There is not a plan to make this available