Clinical Trial Protocol
Iranian Registry of Clinical Trials

27 Jun 2026

Efficacy of combination therapy of L-glutamine and Hydroxyurea in comparison with Hydroxyurea alone in patients with sickle cell anemia: a randomized, double-blinded clinical trial

Protocol summary

Study aim
Comparison of combination therapy of L-glutamine and hydroxyurea compared with hydroxyurea alone in patients with sickle cell anemia

Design
The final sample size is 126 people in total (63 people in each group) This study is a randomized, controlled, parallel clinical trial in which all patients are examined in two groups. Intervention group A will receive L-glutamine and hydroxyurea combination therapy, and group B will receive hydroxyurea treatment alone (control group).

Settings and conduct
This study is a randomized, controlled trial (standard treatment of hydroxyurea), double-blind and 6-month parallel group. The allocation of two randomized block blinds is encoded in numbered envelopes and is prepared according to the sample size and will be provided to the patient's attending physician.

Participants/Inclusion and exclusion criteria
Patients who are at least 5 years old; diagnosed with sickle cell anemia, and have documented at least two pain crises in the past year are eligible to enter the study. Patients who receive hydroxyurea treatment at a dose that is constant for at least 3 months prior to screening and intend to continue that treatment are eligible to participate. Exclusion criteria are: Patients admitted for non-sickle cell disease within 2 months prior to screening, normalized international prothrombin time ratio greater than 2.0, serum albumin level less than 3.0 g / dL, Each blood product is taken 3 weeks before screening and has clinically significant kidney or liver disease, treated with L-glutamine within 30 days before screening.

Intervention groups
Receive a combination of L-glutamine and hydroxyurea

Main outcome variables
The main outcome variable of the study is the number of pain crises at the end of 6 months.

General information

Reason for update
I would like to designate the acronym "GLOBE Trial" (Glutamine and Hydroxyurea Benefit Evaluation in Sickle Cell Anemia) for this study.

Acronym
GLOBE Trial

IRCT registration information
IRCT registration number: **IRCT20210715051904N1**
Registration date: **2022-02-19, 1400/11/30**
Registration timing: **registered_while_recruiting**

Last update: **2025-08-04, 1404/05/13**
Update count: **1**

Registration date
2022-02-19, 1400/11/30

Registrant information

Name
Nader Shakibazad

Name of organization / entity

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Iran (Islamic Republic of)

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Recruitment status
Recruitment complete

Funding source

Expected recruitment start date
2022-02-14, 1400/11/25

Expected recruitment end date
2022-10-17, 1401/07/25

Actual recruitment start date
empty
Actual recruitment end date
empty
Trial completion date
empty

Scientific title
Efficacy of combination therapy of L-glutamine and Hydroxyurea in comparison with Hydroxyurea alone in patients with sickle cell anemia: a randomized, double-blinded clinical trial

Public title
The effect of combination therapy of L-glutamine and hydroxyurea in patients with sickle cell anemia
Purpose
Treatment
Inclusion/Exclusion criteria
Inclusion criteria:
Patients with sickle-cell syndrome Age more than five-year-old No other accompanying hematologic diseases All patients should be on Hydroxyurea At least two (extreme) pain crises have been documented in the past year (defining a pain crisis as pain that results from treatment with a drug or injectable ketorolac in the emergency department (ED) (or outpatient treatment center) or during hospitalization. Becomes)
Exclusion criteria:
Occurrence of life-threatening events not related to SCD during treatment Patient dissatisfaction with participation in the study Serum albumin levels are less than 3 g / dL Internationally normalized ratios of prothrombin time are higher than 2.0 The treated with L-glutamine within 30 days prior to screening.
Age
From **5 years** old
Gender
Both

Phase
3
Groups that have been masked

- Participant
- Care provider
- Investigator
- Outcome assessor
- Data analyser

Sample size
Target sample size: **126**
Randomization (investigator's opinion)
Randomized
Randomization description
This study is a randomized controlled clinical trial in which all patients are examined in two groups, which we represent with two symbols A and B. Group A will receive L-glutamine and hydroxyurea combination therapy in the intervention (intervention group) and group B will receive hydroxyurea treatment alone (control group). Participants in the study will be randomly divided into two groups A and B equal to .... individual. In order to randomly assign individuals to two equal groups to receive the intervention, the Permuted Block Randomization method with a block size of 6 has been used. The block randomization scheme was created using the free Randomization.com website (http://randomization.com). From the order of the Permuted Block Randomization table, the allocator and evaluator should not be aware of the type of intervention being performed on the individual and the size of the block. Thus, it can be said that the data allocation will remain hidden until the end of the study. Thus, each participant will be assigned to intervention or control groups and will enter the study. 1.
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A 121.
A 122.
B 123.
B 124.
A 125.
B 126.
A

Blinding (investigator's opinion)
Double blinded

Blinding description
From the order of the Permuted Block Randomizotion table, the allocator and evaluator should not be aware of the type of intervention being performed on the individual and the size of the block. Thus, it can be said that the data allocation will remain hidden until the end of the study. In this way, each participant will be assigned to intervention or control groups and will be included in the study. Pain Crisis Judgment and Laboratory Tests: All pain crises reported in the case report forms will be recorded by the researchers. An independent judging panel consisting of two hematologists-oncologists who are unaware of the assignment of the trial team will evaluate each episode to determine whether the event meets the definition of a pain crisis for performance evaluation.

Placebo
Used

Assignment
Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee
Research Ethics Committees of Bushehr province university of medical sciences

Street address
BPUMS Vice chancellery for Education, Bushehr University of Medical Sciences, Salman Farsi St, Alamdar St, Bushehr, Iran.

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Approval date
2021-09-19, 1400/06/28

Ethics committee reference number
IR.BPUMS.REC.1400.107

Health conditions studied

1

Description of health condition studied
Sickle cell anemia, L-glutamine, hydroxyurea, pain crisis
ICD-10 code
D57
ICD-10 code description
Sickle-cell disorders, Sickle-cell anaemia with crisis, Sickle-cell anaemia without crisis, Double heterozygous sickling disorders, Sickle-cell trait, Other sickle-cell disorders

Primary outcomes

1

Description
Number of pain crisis
Timepoint
Before intervention and 6 months after intervention
Method of measurement
Clinical examination by a pediatric hematologist and oncologist

2

Description
Number of hospitalizations for pain associated with sickle cell anemia
Timepoint
Before intervention and 6 months after intervention
Method of measurement
Clinical examination by a pediatric hematologist and oncologist

Secondary outcomes

1

Description
Number of Priapism event
Timepoint
Before intervention and 6 months after intervention
Method of measurement
Clinical examination by a pediatric hematologist and oncologist

2

Description
Number of acute chest syndrome
Timepoint
Before intervention and 6 months after intervention
Method of measurement
Clinical examination by a pediatric hematologist and oncologist

3

Description
Number of splenic sequestration events
Timepoint
Before intervention and 6 months after intervention
Method of measurement
Clinical examination by a pediatric hematologist and oncologist

Intervention groups

1

Description
Intervention group: Intervention group: The allocation of two randomized block blinds is encoded in numbered envelopes and is prepared according to the number of samples and will be provided to the patient's attending physician. Therefore, eligible patients will be randomly divided into a 1: 1 ratio for L-glutamine and hydroxyurea combination therapy or hydroxyurea alone, with randomized block allocation. The planned treatment period will be 6 months, during which patients, in addition to consuming hydroxyurea, take L-glutamine powder orally twice a day at a dose of approximately 0.3 g / kg body weight per dose (10 g, 20 g). Grams or 30 grams [maximum dose] per day). The contents of the package will be mixed with an unheated drink or food and consumed immediately. Patients will be contacted by telephone each week between monthly visits to encourage adherence. The validity of the test group assignment and the correct supply of L-glutamine or placebo for each patient will be verified by an independent research drug service. Patients can receive blood transfusions and other necessary clinical treatments if needed.
Category
Treatment - Drugs

2

Description
Control group: The allocation of two randomized block blinds is encoded in numbered envelopes and is prepared according to the number of samples and will be provided to the patient's attending physician. Therefore, eligible patients will be randomly divided into a 1: 1 ratio for L-glutamine and hydroxyurea combination therapy or hydroxyurea alone, with randomized block allocation. The planned treatment period will be 6 months, during which the control group will receive placebo powder (100% maltodextrin) orally twice a day. Experimental drug and placebo in individual packages and visually identical contain 5 grams of white powder without taste is provided, and all packages will be returned by patients to assess compliance. The contents of the package will be mixed with an unheated drink or food and consumed immediately. Patients will be contacted by telephone each week between monthly visits to encourage adherence. The validity of the test group assignment and the correct supply of L-glutamine or placebo for each patient will be verified by an independent research drug

service. Patients can receive blood transfusions and other necessary clinical treatments if needed.

Category
Treatment - Drugs

Recruitment centers

1

Recruitment center

Name of recruitment center
Shohadaye Khalij-e-fars hospital

Full name of responsible person
Nader Shakibazad

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Ayatollah Taleghani Boulevard, Shohadaye Khalij-e-fars hospital

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2

Recruitment center

Name of recruitment center
Dr.shakibazad pediatric oncology clinic

Full name of responsible person
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Sponsors / Funding sources

1

Sponsor

Name of organization / entity
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Full name of responsible person
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Grant name
Vice Chancellor for Research, Bushehr University of Medical Sciences

Grant code / Reference number
1755

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

Title of funding source
Boushehr 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
Boushehr University of Medical Sciences

Full name of responsible person
Nader Shakibazad

Position
Assistant Professor

Latest degree
Subspecialist

Other areas of specialty/work
Pediatric hematology annd oncology

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Position
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Latest degree
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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
Not applicable

Data Dictionary
Not applicable