

# Clinical Trial Protocol

## Iranian Registry of Clinical Trials

10 Jul 2026

### The effect of probiotic and zinc combination therapy for the prevention of recurrence of Hepatic encephalopathy (secondary prophylaxis) in cirrhotic patients

#### Protocol summary

##### Study aim

The effect of probiotic and zinc combination therapy for the prevention of recurrence of Hepatic encephalopathy(HE) in cirrhotic patients

##### Design

A randomized, non-blind controlled trial with three intervention groups on 120 cirrhotic patients

##### Settings and conduct

Patients with cirrhosis who had recovered from an episode of HE in both Sina and Emam Reza Hospital were assigned randomly to 4 groups. Before starting the study and at the end, psychometric performance, blood ammonia levels and quality of life, will be measured.

##### Participants/Inclusion and exclusion criteria

Inclusion criteria: Patients between ages 18-80 years, Cirrhotic patients who had recovered from an episode of hepatic HE. Exclusion criteria: Patients on probiotic therapy, history of alcohol intake during the past 6 weeks, Active infection at the time of enrollment in the study, Previous transjugular intrahepatic portosystemic shunt or shunt surgery, Renal failure, Use of psychoactive drugs, such as antidepressants or sedatives, Any neurologic diseases, such as Alzheimer's disease, Parkinson's disease, and Non hepatic metabolic encephalopathies

##### Intervention groups

Intervention group: The first treatment group consists of 30 patients receiving 1 Comflor Probiotic capsule(450 billion CFU) twice a day and 30 mL of Lactulose 4 times a day for 3 months. Intervention group: The second treatment group consists of 30 patients receiving 25 mg Zinc Gluconate per day and 30 mL of Lactulose 4 times a day for 3 months. Intervention group: The third treatment group consists of 30 patients receiving 1 Comflor Probiotic capsule(450 billion CFU) twice a day and 25 mg Zinc Gluconate per day and 30 mL of Lactulose 4 times a day for 3 months. Control group:

Control group consists of 30 patients receiving 30 mL of Lactulose 4 times a day for 3 months.

##### Main outcome variables

Recurrence of HE

#### General information

##### Reason for update

##### Acronym

##### IRCT registration information

IRCT registration number: **IRCT20170609034406N9**

Registration date: **2021-09-01, 1400/06/10**

Registration timing: **prospective**

Last update: **2021-09-01, 1400/06/10**

Update count: **0**

##### Registration date

2021-09-01, 1400/06/10

##### Registrant information

##### Name

Afshin Gharekhani

##### Name of organization / entity

Faculty of Pharmacy/Tabriz University of Medical Sciences

##### Country

Iran (Islamic Republic of)

##### Phone

+98 41 3334 1315

##### Email address

gharekhaniania@tbzmed.ac.ir

##### Recruitment status

**Recruitment complete**

##### Funding source

##### Expected recruitment start date

2021-09-23, 1400/07/01

##### Expected recruitment end date

2022-04-19, 1401/01/30  
**Actual recruitment start date**  
empty  
**Actual recruitment end date**  
empty  
**Trial completion date**  
empty

#### Scientific title

The effect of probiotic and zinc combination therapy for the prevention of recurrence of Hepatic encephalopathy (secondary prophylaxis) in cirrhotic patients

#### Public title

The effect of probiotic and zinc combination therapy for the prevention of recurrence of Hepatic encephalopathy (secondary prophylaxis) in cirrhotic patients

#### Purpose

Prevention

#### Inclusion/Exclusion criteria

##### Inclusion criteria:

Patients between ages 18 and 80 years Cirrhotic patients who had recovered from an episode of overt hepatic encephalopathy

##### Exclusion criteria:

Patients on probiotic therapy History of alcohol intake during the past 6 weeks Active infection at the time of enrollment in the study Previous transjugular intrahepatic portosystemic shunt or shunt surgery Renal failure Use of psychoactive drugs, such as antidepressants or sedatives Any neurologic diseases, such as Alzheimer's disease, Parkinson's disease, and Non hepatic metabolic encephalopathies

#### Age

From **18 years** old to **80 years** old

#### Gender

Both

#### Phase

3

#### Groups that have been masked

*No information*

#### Sample size

Target sample size: **120**

#### Randomization (investigator's opinion)

Randomized

#### Randomization description

In this study, Permuted Block Randomization method will be used for assigning patients with equal ratio to four groups A, B, C, D. There will be 6 blocks of 8 and 6 blocks of 12 patients With different sequences and codes from 1 to 12. In this study random numbers between 1 to 12 will be given using the Excel software to determine blocks randomly and form a random chain of 4 groups.

#### 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

Ethics Committee of Tabriz University of Medical Sciences

##### Street address

No 2 central building , Tabriz University of Medical sciences , Golgasht Street , Tabriz

##### City

Tabriz

##### Province

East Azarbaijan

##### Postal code

5165665931

#### Approval date

2021-03-01, 1399/12/11

#### Ethics committee reference number

IR.TBZMED.REC.1399.1144

## Health conditions studied

### 1

#### Description of health condition studied

Chronic hepatic failure

#### ICD-10 code

K72.1

#### ICD-10 code description

Chronic hepatic failure

### 2

#### Description of health condition studied

Hepatic Encephalopathy

#### ICD-10 code

G94.3

#### ICD-10 code description

Encephalopathy in diseases classified elsewhere

## Primary outcomes

### 1

#### Description

Blood ammonia levels

#### Timepoint

Immediately before intervention, At the end of the intervention (3 months from baseline)

#### Method of measurement

Pathobiology laboratory

### 2

#### Description

Psychometric performance

### **Timepoint**

Immediately before intervention, At the end of the intervention (3 months from baseline)

### **Method of measurement**

Trail making task A, Trail making task B, Symbol digit modality task

## **3**

### **Description**

Recurrence of Hepatic Encephalopathy

### **Timepoint**

At the end of the intervention (3 months from baseline)

### **Method of measurement**

Patient medical file

## **Secondary outcomes**

## **1**

### **Description**

Quality of life

### **Timepoint**

Immediately before intervention, At the end of the intervention (3 months from baseline)

### **Method of measurement**

SF36 health survey questionnaire

## **Intervention groups**

## **1**

### **Description**

First Intervention group: consists of 30 patients receiving 1 Comflor Probiotic capsule(450 billion CFU) twice a day and 30 mL of Lactulose 4 times a day for 3 months.

### **Category**

Treatment - Drugs

## **2**

### **Description**

Second intervention group: consists of 30 patients receiving 25 mg Zinc Gluconate per day and 30 mL of Lactulose 4 times a day for 3 months.

### **Category**

Treatment - Drugs

## **3**

### **Description**

Third intervention group: consists of 30 patients receiving 1 Comflor Probiotic capsule(450 billion CFU) twice a day and 25 mg Zinc Gluconate per day and 30 mL of Lactulose 4 times a day for 3 months.

### **Category**

Treatment - Drugs

## **4**

### **Description**

Control group: consists of 30 patients receiving 30 mL of

Lactulose 4 times a day to produce 2 to 3 soft stools per day for 3 months.

### **Category**

Treatment - Drugs

## **Recruitment centers**

## **1**

### **Recruitment center**

#### **Name of recruitment center**

Sina Hospital

#### **Full name of responsible person**

Afshin Gharekhani

#### **Street address**

Sina Medical Research and Training Hospital Shahid Montazeri and Hafez squares Azadi Street Tabriz

#### **City**

Tabriz

#### **Province**

East Azarbaijan

#### **Postal code**

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#### **Phone**

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#### **Email**

gharekhanian@yahoo.com

## **2**

### **Recruitment center**

#### **Name of recruitment center**

Emam Reza Hospital

#### **Full name of responsible person**

Afshin Gharekhani

#### **Street address**

Golgasht street\_ Emam Reza Medical Research and Training Hospital

#### **City**

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#### **Province**

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#### **Postal code**

5147663419

#### **Email**

gharekhanian@yahoo.com

## **Sponsors / Funding sources**

## **1**

### **Sponsor**

#### **Name of organization / entity**

Tabriz University of Medical Sciences

#### **Full name of responsible person**

Dr Afshin Gharekhani

#### **Street address**

No 2 central building, Tabriz University of Medical sciences, Golgasht Street, Tabriz

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gharekhanian@tbzmed.ac.ir

**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**

Afshin Gharekhani

**Position**

Assistant professor

**Latest degree**

Specialist

**Other areas of specialty/work**

Medical Pharmacy

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## Person responsible for scientific inquiries

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**Latest degree**

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## Person responsible for updating data

**Contact**

**Name of organization / entity**

Tabriz University of Medical Sciences

**Full name of responsible person**

Leila amooyi

**Position**

Pharmacy Student

**Latest degree**

Bachelor

**Other areas of specialty/work**

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**Phone**

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**Email**

leila.amooyi.d@gmail.com

## 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**

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