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)

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+98 41 3334 1315

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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 moths.
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
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2

Recruitment center
Name of recruitment center
Emam Reza Hospital
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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

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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Person responsible for updating data

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Position
Pharmacy Student

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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
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