Clinical Trial Protocol
Iranian Registry of Clinical Trials

20 Jun 2026

The Effects of Probiotic Supplementation on disease progression and serum levels of inflammatory biomarkers in Patients With Multiple Sclerosis

Protocol summary

Study aim
Comparison of serum level of (hs-CRP ، IL-17 ، IL-35 ، TGF-β و FOXP3) between two groups of MS patients receiving probiotic supplements and placebo and in each group before and after intervention Comparison of the mean number of bifidobacter counts, lactobacillus and fecal chloroform before and after probiotic supplementation, and placebo in patients with MS in each group and between groups

Design
A double-blind, randomized controlled clinical trial with a control group with a sample size of 50 subjects

Settings and conduct
Patients receive supplements and placebo in weeks zero, four and eight . Patients will be advised to take 2 capsules daily after lunch. The duration of the intervention is 12 weeks and all patients are enrolled in the MS Association of Khuzestan Province in Ahvaz Golestan Hospital. Researcher and participants have been blinded to the end of the intervention.

Participants/Inclusion and exclusion criteria
Include criteria: Diagnosis based on Mc Donald and MRI criteria EDSS score is less than 3 exclude criteria: Consumption of any probiotic and prebiotic and antibiotic supplement or supplement in the last 1 month Taking non-steroidal anti-inflammatory drugs NSAIDs, estrogen, progesterone, immunosuppressions, diuretics and corticosteroids

Intervention groups
Group A (probiotic): daily intake of two capsules Group B (placebo): A placebo similar to that of high-quality sacchar from corn starch (prepared by the company Protexin). Each probiotic capsule containing probiotic contains 109 * 2 * CFU /g of each species of Lactobacillus acidophilus, Lactobacillus casei , Bifidobacterium bifidum and Lactobacillus fermentum, Lactobacillus bulgaricus and Streptococcus thermophilus.

Main outcome variables
hs-CRP ، IL-17 ، IL-35 ، TGF-β و FOXP3

General information

Reason for update
Acronym
IRCT registration information
IRCT registration number: **IRCT20181210041918N1**
Registration date: **2018-12-15, 1397/09/24**
Registration timing: **prospective**

Last update: **2018-12-15, 1397/09/24**
Update count: **0**

Registration date
2018-12-15, 1397/09/24

Registrant information
Name
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Recruitment status
Recruitment complete
Funding source

Expected recruitment start date
2019-01-04, 1397/10/14
Expected recruitment end date
2019-06-19, 1398/03/29
Actual recruitment start date
empty
Actual recruitment end date

empty

Trial completion date

empty

Scientific title

The Effects of Probiotic Supplementation on disease progression and serum levels of inflammatory biomarkers in Patients With Multiple Sclerosis

Public title

The effect of probiotic supplement on some inflammatory markers in patients with multiple sclerosis

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

Diagnosis based on Mc Donald and MRI criteria EDSS score is less than 3 Clinical status of relapse-remittance

Exclusion criteria:

Unwillingness to continue cooperation Exacerbation of the disease during the study There is a relapse during the intervention History of antibiotic use during 1 month ago Consumption of any probiotic and prebiotic supplement and antibiotic in the last 1 month Consumption supplements containing of vitamin, fiber, omega-3, anti-oxidants during 3 weeks before and during the study. Taking non-steroidal anti-inflammatory drugs (NSAIDs), estrogen, progesterone, immunosuppressions, diuretics and corticosteroids drugs. History of gastroenteritis during the last month History of intestinal surgery during the past month Inflammatory bowel disease (IBD), rheumatoid arthritis, systemic lupus, type 1 diabetes and other autoimmune diseases and pregnancy

Age

From **18 years** old to **55 years** old

Gender

Both

Phase

3

Groups that have been masked

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

Sample size

Target sample size: **50**

Randomization (investigator's opinion)

Randomized

Randomization description

Patients who are eligible for the study are randomly assigned to one of the two groups receiving probiotic supplementation and placebo supplementation. Thus, supplements and placebo from both groups are randomly coded by an individual other than the researcher from No. 1-50 and according to the entry of patients to study, a code is assigned to them. Then The patients are randomly divided into 2 groups of 25 with balanced block method as follows: 1- Group A (probiotic): Daily intake of two capsules 2. Group B (placebo): Placebo, similar to the high sachet made from corn starch (prepared by the company Protexin)

Blinding (investigator's opinion)

Double blinded

Blinding description

None of the patients, as well as the researcher, clinical care, the outcome evaluator and data analyzer will be aware of the group in which the patients are located and the type of intervention received.

Placebo

Used

Assignment

Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Ethics committee of Ahwaz Jundishapur University of Medical Sciences

Street address

Golestan Highway

City

Ahwaz

Province

Khouzestan

Postal code

6135715794

Approval date

2018-12-08, 1397/09/17

Ethics committee reference number

IR.AJUMS.REC.1397.679

Health conditions studied

1

Description of health condition studied

Multiple Sclerosis

ICD-10 code

G35

ICD-10 code description

Multiple sclerosis

Primary outcomes

1

Description

Serum level of TGF-β

Timepoint

Before the intervention and after the end of the 12-week intervention period

Method of measurement

Serum samples will be stored for measuring TGF-β values

up to 80 ° C in the freezer. Measuring serum levels of TGF-β using ELISA kit produced by Zellbio Germany will be carried out in accordance with the instructions contained in the kits of the Guideline.

2

Description
Serum level of IL-17
Timepoint
Before the intervention and after the end of the 12-week intervention
Method of measurement
Serum samples will be stored for measuring IL-17 values up to 80 ° C in the freezer. Measuring serum levels of IL-17 using ELISA kit produced by Zellbio Germany will be carried out in accordance with the instructions contained in the kits of the Guideline.

3

Description
Serum level of hs-CRP
Timepoint
Before the intervention and after the end of the 12-week intervention
Method of measurement
Serum samples will be stored for measuring hs-CRP values up to 80 ° C in the freezer. Measuring serum levels of hs-CRP using ELISA kit produced by Zellbio Germany will be carried out in accordance with the instructions contained in the kits of the Guideline.

4

Description
Serum level of FOXP3
Timepoint
Before the intervention and after the end of the 12-week intervention
Method of measurement
Serum samples will be stored for measuring FOXP3 values up to 80 ° C in the freezer. Measuring serum levels of FOXP3 using ELISA kit produced by Zellbio Germany will be carried out in accordance with the instructions contained in the kits of the Guideline.

Secondary outcomes

1

Description
Number of bifidobacter colonies
Timepoint
In the first three days of the study and the last 3 days of study
Method of measurement
Stool samples from each patient were taken in the first 3 days of the study, as well as the last 3 days of study in the sterile plastic container, and the transfer to sterile tubes will be maintained to evaluate the changes in the gastrointestinal flora within the 80-oz. By using bacterial culture, the number of colonies associated with lactobacillus, bifidobacter and chloroform is measured.

2

Description
Number of lactobacillus colonies
Timepoint
In the first three days of the study and the last 3 days of study
Method of measurement
Stool samples from each patient were taken in the first 3 days of the study, as well as the last 3 days of study in the sterile plastic container, and the transfer to sterile tubes will be maintained to evaluate the changes in the gastrointestinal flora within the 80-oz. By using bacterial culture, the number of colonies associated with lactobacillus, bifidobacter and chloroform is measured.

3

Description
fecal chloroform
Timepoint
In the first three days of the study and the last 3 days of study
Method of measurement
Stool samples from each patient were taken in the first 3 days of the study, as well as the last 3 days of study in the sterile plastic container, and the transfer to sterile tubes will be maintained to evaluate the changes in the gastrointestinal flora within the 80-oz. By using bacterial culture, the number of colonies associated with lactobacillus, bifidobacter and chloroform is measured.

4

Description
changes in pain intensity
Timepoint
The beginning and the end of the study
Method of measurement
Pain intensity (NRS) was assessed with a numerical rating scale (scaled from 0 to 10) addressing the average pain, which is associated with MS according to the patient’s point of view. Thereby, 0 represents no pain and 10 the most painful sensation imaginable. Quality of pain (SES) was measured by the pain sensation scale. This tool contains 24 adjectives of pain sensation in a questionnaire; each of them is scaled from 1 to 4. Fourteen items comprise the affective dimension, and ten items contribute to the sensory dimension

5

Description
severity of depression
Timepoint
The beginning and the end of the study
Method of measurement
The Beck Depression Inventory-II (BDI-II) questionnaire included 21 questions to assess depression in patients. Each questionnaire takes a score from 0 to 3. The high score indicates high symptoms of depression.

6

Description
Fatigue Assessment
Timepoint
The beginning and the end of the study
Method of measurement
Fatigue inventory (MFI-20) will be used at the beginning and end of the study to assess fatigue in patients. The questionnaire has three sub-sections, including physical, cognitive and psychological evaluation of fatigue, and ultimately gives a score of 0 to 84 for fatigue. The above is a sign of high fatigue severity.

Intervention groups

1

Description
Supplements used in this study include probiotic capsules prepared by the company Protexin (UK) or placebo (starch). Each probiotic capsule containing probiotic contains 109 * 2 * CFU / g of each species of Lactobacillus acidophilus, Lactobacillus casei , Bifidobacterium bifidum and Lactobacillus fermentum, Lactobacillus bulgaricus and Streptococcus thermophilus.
Category
Treatment - Drugs

2

Description
Control group:Placebo in similar packages with probiotic supplementation from corn starch (prepared by the company Protexin)
Category
Placebo

Recruitment centers

1

Recruitment center
Name of recruitment center
Multiple sclerosis Society of Khoozestan
Full name of responsible person
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Sponsors / Funding sources

1

Sponsor
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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
Ahvaz 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

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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
it is not the objective of this study.
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