Clinical Trial Protocol
Iranian Registry of Clinical Trials

26 Jun 2026

Survey the effect of probiotic supplementation on the intestinal metabolites, some oxidative stress indicators, fatigue, pain and depression in patients with Multiple Sclerosis

Protocol summary

Study aim
Comparison of changes in intestinal microbiome, oxidative stress indices, pain intensity, fatigue severity and depression between two groups of MS patients receiving probiotic supplement and placebo and within each group before and after the intervention

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
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
Intensity of pain, fatigue, depression and intestinal microbiome

General information

Reason for update

Acronym
Jl

IRCT registration information
IRCT registration number: **IRCT20181210041918N2**
Registration date: **2020-08-21, 1399/05/31**
Registration timing: **retrospective**

Last update: **2020-08-21, 1399/05/31**
Update count: **0**

Registration date
2020-08-21, 1399/05/31

Registrant information

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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
2019-01-04, 1397/10/14

Expected recruitment end date
2019-06-19, 1398/03/29

Actual recruitment start date
2019-01-10, 1397/10/20

Actual recruitment end date
2019-09-09, 1398/06/18

Trial completion date

2019-12-21, 1398/09/30

Scientific title
Survey the effect of probiotic supplementation on the intestinal metabolites, some oxidative stress indicators, fatigue, pain and depression in patients with Multiple Sclerosis

Public title
Effect of probiotic in patients with Multiple Sclerosis

Purpose
Treatment

Inclusion/Exclusion criteria

Inclusion criteria:
Selection based on revised Mc Donald criteria a relapsing–remitting course one or more documented relapses in the previous year or two or more in the previous 2 years a score of 0 to 5.5 on the EDSS Age range between 18 to 55

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
- Investigator
- Data analyser

Sample size
Target sample size: **50**
Actual sample size reached: **38**

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) Block randomization method has been used for randomization. Blocks size of 4 are generated using www.sealedenvelope.com.

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. In order to conceal the randomization process, individual codes have been on the medicine boxes, which are produced by the software.

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

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Ahwaz

Province
Khouzestan

Postal code
6135715794

Approval date
2020-02-08, 1398/11/19

Ethics committee reference number
IR.AJUMS.REC.1398.865

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
Antioxidant index levels (malondialdehyde and total antioxidant capacity)

Timepoint
Before the intervention and after the end of the 12-week intervention period
Method of measurement
Serum samples will be stored for measuring antioxidant index values up to 80 ° C in the freezer. Measuring serum levels of malondialdehyde and total antioxidant capacity 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
Fatigue Assessment
Timepoint
Before the intervention and after the end of the 12-week intervention period
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.

3

Description
changes in pain intensity
Timepoint
Before the intervention and after the end of the 12-week intervention period
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

4

Description
severity of depression
Timepoint
Before the intervention and after the end of the 12-week intervention period
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.

Secondary outcomes

1

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.

Intervention groups

1

Description
Intervention group: 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: 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
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Sponsors / Funding sources

1

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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)
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
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