# Clinical Trial Protocol
# Iranian Registry of Clinical Trials

25 Jun 2026

## Effect of synbiotics supplementation and anti-inflammatory-antioxidant rich diet on inflammatory marker and clinical manifestations in patients with progressive forms of Multiple Sclerosis

## Protocol summary

**Study aim**

To assess the effects of synbiotics supplementation and anti-inflammatory-antioxidant-rich diet on the inflammatory marker and clinical manifestations in patients with progressive forms of Multiple Sclerosis (MS).

**Design**

A randomized double-blind controlled clinical trial with two-arm parallel groups on 70 eligible patients (n of intevention= 35; n of control= 35).

**Settings and conduct**

The present study will be conducted in Isfahan MS center. An anti-inflammatory-antioxidant-rich diet, based on Dietary Inflammatory Index (DII) and Oxygen Radical Absorbance Capacity (ORAC), co-intervented by synbiotic supplement will be prescribed for 4 months. The severity of clinical manifestations and the fecal level of calprotectin will be measured before and after the intervention.

**Participants/Inclusion and exclusion criteria**

Inclusion criteria: progressive MS patients (diagnosed by a neurologist according to expanded disability status scale) who agree to participate in the study, aged between 20-60 years old. Exclusion criteria: non-compliance with diets and supplements (adherence less than 80%), participation in the other clinical trials, the occurrence of acute medical conditions 6 months before and during the study period.

**Intervention groups**

Intervention group 1: synbiotic supplement (one capsule contains lactobacillus casei, lactobacillus acidophilus, lactobacillus plantarum, lactobacillus bulgaricus, bifidobacterium breve, bifidobacterium infantis, bifidobacterium longum, streptococcus thermophilus) in dose of 4.5* 10^11 per day and fructooligosaccharide 100 mg plus anti-inflammatory-antioxidant-rich diet. Intervention group 2: placebo capsule (contains starch) plus dietary recommendations.

**Main outcome variables**

DII; ORAC; fecal calprotectin; quality of life; fatigue; pain; disease activity; visual impairment; depression; anxiety; anthropometric indices

## General information

**Reason for update**

**Acronym**

**IRCT registration information**

IRCT registration number: **IRCT20141108019853N7**
Registration date: **2021-08-15, 1400/05/24**
Registration timing: **registered_while_recruiting**

Last update: **2021-08-15, 1400/05/24**
Update count: **0**

**Registration date**

2021-08-15, 1400/05/24

**Registrant information**

**Name**

Zamzam Paknahad

**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**

2021-08-13, 1400/05/22

**Expected recruitment end date**

2021-12-16, 1400/09/25

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

**Scientific title**
Effect of synbiotics supplementation and anti-inflammatory-antioxidant rich diet on inflammatory marker and clinical manifestations in patients with progressive forms of Multiple Sclerosis

**Public title**
Effect of synbiotic and anti-inflammatory-antioxidant rich diet in progressive multiple sclerosis
**Purpose**
Treatment
**Inclusion/Exclusion criteria**
**Inclusion criteria:**
Progressive MS Patients based on EDSS criteria (RRMS, PPMS, PRMS), who agree to participate in the study. Aged between 20-60 years old Having basic literacy Mental acceptance for participation and compliance
**Exclusion criteria:**
Non-compliance with diet and supplement (adherence rate below 80 %) participation in other clinical trials at one time The occurrence of acute & serious medical conditions (urgent surgeries, accidents) COVID-19 infection (during the study) Taking immunomodulatory drugs - commons in relapsing-remitting MS- during and 6 months before the intervention (such as interferons, Sphingosine-1-phosphate receptor modulators, monoclonal antibodies, dimethyl fumarate) Regular consumption of anti-anxiety and anti-depressant drugs during and six months before the intervention Taking the other forms of synbiotic, probiotic, prebiotic, and postbiotic supplements during and 6 months before the intervention Taking antibiotics during and 2 months before the intervention Taking corticosteroids (for example methylprednisolone in doses more than 30 mg/day) and adrenocorticotropin hormone as full doses during and 6 months before the intervention Regular smoking (at least two cigarettes per day) Patients with pancreatitis, sepsis, dialysis, chronic diarrhea, and inpatient individuals with or without central venous catheter Patients who are waiting for abdominal surgeries Patients with acute immune deficiencies such as AIDS and cancers Patients with short bowel syndrome or at risk for mesenteric ischemia Patients who are in pregnancy or breastfeeding period or those with pregnancy attempt The unwillingness to cooperate
**Age**
From **20 years** old to **60 years** old
**Gender**
Both

**Phase**
3
**Groups that have been masked**

- Participant
- Outcome assessor
- Data analyser

**Sample size**
Target sample size: **70**
**Randomization (investigator's opinion)**
Randomized
**Randomization description**
Randomization will be conducted based on https://www.sealedenvelope.com/simple-randomiser/v1/lists. Each block has a capacity for 6 subjects. Then, within each block, subjects will be randomly assigned to treatment or placebo. Random assignment will be done using a random chain that will be extracted from the site. Randomization will be stratified based on the type of progressive MS (three types: PPMS, SPMS, PRMS).
**Blinding (investigator's opinion)**
Double blinded
**Blinding description**
Synbiotic supplements and placebo (identical in color, shape, and odor) will be packaged in similar boxes and the researcher and patients will not be informed of the contents of the packs until the end of the study. In addition, the individualized diets and dietary recommendations will be packaged in similar packets. Furthermore, the outcome assessor and data analyzer will be blinded to treatment allocation. HOWEVER, blinding of the investigator is not possible because of obvious differences between the intervention diet (in the intervention group) and dietary recommendations (in the control group).
**Placebo**
Used
**Assignment**
Parallel
**Other design features**
The current study is a co-intervention of Diet & Nutritional Supplement.

## Secondary Ids

empty

## Ethics committees

### 1

**Ethics committee**
**Name of ethics committee**
Ethics committee of Isfahan University of Medical Sciences
**Street address**
Hezar Jerib Ave.
**City**
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**Province**
Isfehan
**Postal code**
8174673461
**Approval date**
2021-07-26, 1400/05/04
**Ethics committee reference number**
IR.MUI.RESEARCH.REC.1400.195

## 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**
Fecal level of calprotectin
**Timepoint**
At baseline and after 16 weeks
**Method of measurement**
Enzyme Linked Immuno Sorbent Assay (ELISA) kits

### 2

**Description**
Disease activity
**Timepoint**
At baseline and after 16 weeks
**Method of measurement**
scoring form of Expanded Disability Status Scale (EDSS)

### 3

**Description**
Fatigue severity
**Timepoint**
At baseline and after 16 weeks
**Method of measurement**
Modified Fatigue Impact Scale 21 items (MFIS) questionnaire

## Secondary outcomes

### 1

**Description**
The inflammatory status of diet
**Timepoint**
At baseline and after 16 weeks
**Method of measurement**
Calculation of Dietary Inflammatory Index (DII) score

### 2

**Description**
The antioxidant level of diet
**Timepoint**
At baseline and after 16 weeks
**Method of measurement**
Calculation of Oxygen Radical Absorbance Capacity (ORAC) score

### 3

**Description**
Quality of life
**Timepoint**
At baseline and after 16 weeks
**Method of measurement**
Multiple Sclerosis Quality of Life (MSQOL-54) 54 items

### 4

**Description**
Pain severity
**Timepoint**
At baseline and after 16 weeks
**Method of measurement**
Global Pain Scale (GPS)

### 5

**Description**
Sexual satisfaction level
**Timepoint**
At baseline and after 16 weeks
**Method of measurement**
Sexual Satisfaction Scale (SSS)

### 6

**Description**
Bladder control evaluation
**Timepoint**
At baseline and after 16 weeks
**Method of measurement**
Bladder Control Scale (BLCS) 4 items

### 7

**Description**
Bowl control evaluation
**Timepoint**
At baseline and after 16 weeks
**Method of measurement**
Bowel Control Scale (BWCS) 5 items

### 8

**Description**
Impact of Vision Impairment evaluation
**Timepoint**
At baseline and after 16 weeks
**Method of measurement**
Impact of Vision Impairment (IVI) 32 items

### 9

**Description**
Cognitive impairment/depression evaluation
**Timepoint**
At baseline and after 16 weeks
**Method of measurement**
Perceived Deficits Questionnaire-Depression (PDQ-D) 20 items

### 10

**Description**
Anxiety severity
**Timepoint**
At baseline and after 16 weeks
**Method of measurement**
State-Trait Anxiety Inventory (STAI 1 and 2) 20 items

### 11

**Description**
Gastrointestinal evaluation
**Timepoint**
At baseline and after 16 weeks
**Method of measurement**
Gastrointestinal Symptom Rating Scale (GSRS) 15 items

### 12

**Description**
Body weight
**Timepoint**
At baseline and after 16 weeks
**Method of measurement**
SECA digital scale

### 13

**Description**
Body mass index
**Timepoint**
At baseline and after 16 weeks
**Method of measurement**
weight (in kilograms) divided by the square of height (in metres)

### 14

**Description**
Percent of body fat
**Timepoint**
At baseline and after 16 weeks
**Method of measurement**
Deurenberg equation

### 15

**Description**
Waist circumference
**Timepoint**
At baseline and after 16 weeks
**Method of measurement**
tape

### 16

**Description**
Hip circumference
**Timepoint**
At baseline and after 16 weeks
**Method of measurement**
tape

### 17

**Description**
Waist-to-hip ratio
**Timepoint**
At baseline and after 16 weeks
**Method of measurement**
ratio calculation

### 18

**Description**
Triceps Skinfold thickness
**Timepoint**
At baseline and after 16 weeks
**Method of measurement**
Skinfold Caliper

### 19

**Description**
Mid-Arm Circumference (MAC)
**Timepoint**
At baseline and after 16 weeks
**Method of measurement**
tape

### 20

**Description**
corrected mid-Arm Muscle Area (cAMA)
**Timepoint**
At baseline and after 16 weeks
**Method of measurement**
cAMA equation

### 21

**Description**
Physical activity
**Timepoint**
At baseline and after 16 weeks
**Method of measurement**
three-day record

## Intervention groups

### 1

**Description**
Intervention group: administration of synbiotic supplement (one capsule contains Lactobacillus casei, Lactobacillus acidophilus, Lactobacillus plantarum, Lactobacillus bulgaricus, Bifidobacterium breve, Bifidobacterium infantis, Bifidobacterium longum, Streptococcus thermophilus) in dose of 4.5* 10^11 per day and FOS 100 mg/day plus anti-inflammatory-antioxidant rich diet for 4 months (16 weeks)
**Category**
Treatment - Other

**2**

**Description**
Control group: one placebo capsule per day (contains starch) plus dietary recommendations and energy adjustment for 4 months (16 weeks)
**Category**
Placebo

## Recruitment centers

**1**

**Recruitment center**
**Name of recruitment center**
M.S Isfahan Center
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Ahmad Chitsaz
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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**
Esfahan 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**
Esfahan University of Medical Sciences
**Full name of responsible person**
Amir Reza Moravejolahkami
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## Sharing plan

**Deidentified Individual Participant Data Set (IPD)**
Yes - There is a plan to make this available

**Study Protocol**
No - There is not a plan to make this available

**Statistical Analysis Plan**
No - There is not a plan to make this available

**Informed Consent Form**
No - There is not a plan to make this available

**Clinical Study Report**
Yes - There is a plan to make this available

**Analytic Code**
No - There is not a plan to make this available

**Data Dictionary**
Undecided - It is not yet known if there will be a plan to make this available

**Title and more details about the data/document**
The major part of results will be available for individuals. Moreover, the datasets used and/or analyzed during the current study are available from the investigators, on reasonable request.

**When the data will become available and for how long**
The data will become available 12 months after the results' publication.

**To whom data/document is available**
The data/document is available for all individuals, on reasonable request.

**Under which criteria data/document could be used**
The data/document must be used for conducting similar studies and therapeutic approaches, on reasonable request from the investigators.

**From where data/document is obtainable**
mail to paknahad@hlth.mui.ac.ir or a.moravej@mail.mui.ac.ir

**What processes are involved for a request to access data/document**
The data will be sent as soon as possible, after receiving the request.

**Comments**