Clinical Trial Protocol
Iranian Registry of Clinical Trials

07 Nov 2026

Evaluation of symbiotic supplementation on the disease activity in rheumatoid arthritis

Protocol summary

Study aim
The effect of adding synbiotic supplement to the regimen of treating patients with rheumatoid arthritis for 3 months on the severity of the disease

Design
Two arm parallel group (1 synbiotic group and another placebo control group) randomised trial with blinded post-therapeutic care and outcome assessment.

Settings and conduct
Patients who attended Isfahan Al Zahra hospital Rheumatology clinic with RA

Participants/Inclusion and exclusion criteria
INCLUSION criteria: patients who diagnosed with RA based on ACR criteria; at least 3 months passed from diagnosis; Age 18 to 80 years ; At least 4 swollen joints which were stable for at least 1 month with corticosteroids & methotrexate (DMARD); EXCLUSION criteria: No willingness to give informed consent; Allergic to probiotics; probiotic use (food or drug) in the last 2 weeks; IBD; perforated bowel; existence of surgical plan in the study time course; renal or hepatic disease, Cushing, DM, thyroid disease,; use of antibiotics in the last month; weight loss regimen; smoking; antioxidant user; participating in any other clinical trial; biologic agents user; discontinuation of participation by the patient.

Intervention groups
Two groups, in addition to corticosteroids and methotrexate that were given to all patients (standard therapy of RA) synbiotic for group 1 and placebo for group 2 were prescribed.

Main outcome variables
RA severity; RA activity

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20121216011763N37**
Registration date: **2019-06-25, 1398/04/04**
Registration timing: **retrospective**

Last update: **2019-06-25, 1398/04/04**
Update count: **0**

Registration date
2019-06-25, 1398/04/04

Registrant information

Name
Gholamreza Askari

Name of organization / entity
Isfahan University of Medical Sciences

Country
Iran (Islamic Republic of)

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Recruitment status
Recruitment complete

Funding source

Expected recruitment start date
2019-03-02, 1397/12/11

Expected recruitment end date
2019-06-01, 1398/03/11

Actual recruitment start date
empty

Actual recruitment end date
empty

Trial completion date
empty

Scientific title
Evaluation of symbiotic supplementation on the disease activity in rheumatoid arthritis

Public title

Effect of symbiotic supplementation in rheumatoid arthritis

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

Rheumatoid arthritis patients (based on ACR criteria) At least 3 months after the diagnosis of RA. At least 4 swollen joints which were in a stable status for at least 1 month, on MTX and prednisolone

Exclusion criteria:

Drug reaction and hypersensitivity patient dissatisfaction consumption of probiotic oral or medical in the last 2 weeks IBD intestinal perforation creatinine clearance by using the CKD-EPI equation of less than 40 mL/min per 1.73 m2 aspartate and alanine aminotransferase levels greater than twice the upper limit of normal active or recent hepatitis or cirrhosis plan for surgery in the next 3 months thyroid disorders Cushing's disease or syndrome malignant tumors, inadequately controlled diabetes mellitus or arterial hypertension serious infections, serious cardiac or respiratory diseases, leukopenia or thrombocytopenia, inadequate contraception, pregnancy or a plan for it in the next 3 months, breastfeeding, osteoporosis, use of cytotoxic or immunosuppressive drugs for 3 months before inclusion, current or past substance abuse (including tobacco) or alcohol use greater than 2 U/d and psychological illnesses or intellectual disorders that would preclude adherence to the study protocol

Age

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

Gender

Both

Phase

N/A

Groups that have been masked

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

Sample size

Target sample size: **200**

Randomization (investigator's opinion)

Randomized

Randomization description

Randomization sequence was generated using STATA 14 statistical software and was stratified with a 1:1 allocation using random block size of 2. Sex, MTX and prednisolone doses were involved in stratification. The Pts were assigned to the MTX-prednisolone based treatment strategy combined with either 1000 mg/day symbiotic supplement (MTX and prednisone PLUS symbiotic group), or placebo (MTX and prednisolone PLUS placebo group) groups following stratified randomization procedures. The symbiotic and placebo were in capsule forms and identical in shape, size, count and also, similar in the appearance of the opaque bottles in which drugs were prepared and numbered, by computer, for each patient. Then bottles were put in 2 black boxes by a "research-blinded rheumatology clinic secretary" to hide the sequence from the main researchers (Esmaili F. and Salesi M.) enrolling and assessing participants. To ensure adequate concealment from the researchers, drugs were administered to the patients by another "research-blinded rheumatology clinic secretary", after the subjects completed all baseline assessments and also, after they signed the informed consent. The statistical sequence of the classified blocks was prepared for the participants by Professor Merasi. The details of the series were unknown to the main investigators (Dr. Esmaili and Dr. Salesi). Main investigators enrolled the participants with ignorance to the allocation sequence and the drugs were put in to two boxes by a secretary and were administered by another.

Blinding (investigator's opinion)

Double blinded

Blinding description

This study was a double-blind clinical trial (participant, researcher). The lactocare synbiotic supplement and its placebo, were produced by Zist takhmir company. Synbiotic supplement and its placebos were put in the same form of package and the patients and researcher were not aware of the content of the package until the end of trial.

Placebo

Used

Assignment

Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Isfahan univesity of medical sciences

Street address

Isfahan, Hezarjirib street

City

Isfahan

Province

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Postal code

8174673461

Approval date

2019-03-02, 1397/12/11

Ethics committee reference number

IR.MUI.MED.REC.1397.281

Health conditions studied

1

Description of health condition studied

Rheumatoid Arthritis

ICD-10 code

M05

ICD-10 code description

Rheumatoid arthritis with rheumatoid factor

Primary outcomes

1

Description

Severity of disease activity

Timepoint

At the beginning of the study and 3 months after starting the drug

Method of measurement

Physical examination for the number of tender joint (T1) and swellen j (S1) and blood tests (ESR, CRP, ALT, Cr), calculate DAS28 according to ESR, Tender Joint, Sowllen joint and VAS dat

Secondary outcomes

empty

Intervention groups

1

Description

Intervention group During the 3 months of our study, we used steroid and DMARD (methotrexate) and synbiotic. This supplement made by the Lactocare brand was made by the biomarker knowledge-based company. In the form of capsules of 500 mg contains 7 probiotic strains with a dose of one billion CFUs and prebiotic fructooligosaccharide. All probiotic strains of this supplement had positive effects on inflammatory control: Lacobacillus casei, Lacobacillus asidophilus, Lacobacillus rhmnosus, Lacobacillus bugaricus, Bifidobacterium breve, Bifidobacterium longun, Streptococcus thermophiles. How to administer supplements was that in 3 months Intervention: Two capsules were consumed every day after lunch

Category

Treatment - Other

2

Description

Control group: Individuals over the course of 3 months, our study of steroids and DMARD (methotrexate) and placebo (containing starch) received two capsules daily after lunch. The placebo is made in the biomarker company and were be available to patients in the form of capsules of the same type as synbiotic.

Category

Placebo

Recruitment centers

1

Recruitment center

Name of recruitment center

Alzahra hospital

Full name of responsible person

Mansour Salesi

Street address

Shohadaie Sofeh Ave.

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8158168131

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity

the University of medical sciences Esfahan

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

the University of medical sciences Esfahan

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
فرح اسماعیلی

Position
Associate professor

Latest degree
Specialist

Other areas of specialty/work
Internal Medicine

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Person responsible for scientific inquiries

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Position
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Person responsible for updating data

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Sharing plan

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

Study Protocol
Yes - There is 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
Yes - There is a plan to make this available

Clinical Study Report
Yes - There is 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

Title and more details about the data/document
The collected identified for the primary outcome measure only will be shared.

When the data will become available and for how long
starting 12 months after publication

To whom data/document is available
En Available for people working in academic institutions

Under which criteria data/document could be used
En The data will provide for educational use

From where data/document is obtainable
Dr.mansour salesi mansour1380@yahoo.com

What processes are involved for a request to access data/document
En The data will send as soon as possible, after receiving the request

Comments