Clinical Trial Protocol
Iranian Registry of Clinical Trials

16 Sep 2026

Study of the effects of melatonin supplementation on clinical status and metabolic profiles in patients with rheumatoid arthritis

Protocol summary

Study aim

Objective: The aim of this study is to determine the effects of melatonin supplementation on clinical status and metabolic profiles in patients with rheumatoid arthritis.

Design

Study design: randomized double-blind placebo-controlled trial. Patients will be assigned into two groups to receive melatonin supplement (n=33) or placebo (n=33).

Settings and conduct

Among patients with rheumatoid arthritis referred to Beheshti Clinic, 66 patients will be selected according to inclusion and exclusion criteria. Participants, investigators or the assessors of the outcomes are unaware of the study groups. Supplements and placebos are similar in shape and size. Fasting blood samples will be taken at baseline and end of the intervention. intervention: 12 weeks.

Participants/Inclusion and exclusion criteria

Inclusion criteria: patients with rheumatoid arthritis.; aged 20 to 80 years. Exclusion criteria: Patients with infectious, malignant and other inflammatory diseases, those taking melatonin supplements or antioxidant supplements within 3 months prior to enrollment in the study, the night shift workers, subjects taking antibiotics medications, patients with thyroid diseases, current smokers, rheumatoid arthritis patients who were diagnosed less than 1 year before the start of the study, and unwillingness to cooperate

Intervention groups

Intervention group: 6 mg/day Melatonin (RAZAK, Iran), one hour before bedtime for 12 weeks. Control group: Placebo (Barij Essence, Iran), one hour before bedtime for 12 weeks.

Main outcome variables

Outcomes: DAS28, serum CRP and ESR (primary outcomes) and metabolic profiles, biomarkers of oxidative damage (secondary outcomes) will be quantified at study baseline and end-of-trial.

General information

Reason for update

The updating process was done before publishing the paper to correct the registration information. After the initial registration of IRCT and before the start of the study and before patients recruitment, according to the project investigators, it was decided that criteria such as smoking or thyroid disease that can play a role in the rate of metabolism or exacerbation of rheumatoid arthritis should be added to exclusion criteria. Also, given that it is difficult to differentiate rheumatoid arthritis from other similar diseases at the onset of the RA because the initial manifestations may not be typical (polyarticular involvement), it was decided to exclude patients who have been diagnosed over the past year before the start of the study. In addition, since a large proportion of patients with rheumatoid arthritis mention the use of anti-inflammatory drugs such as NSAIDs in their history and the removal of a drug from the patient's drugs is not ethically correct. Also, if the patients currently using NSAIDs were excluded from the study, we lost a large part of the available samples. To solve the mentioned issue it was decided that patients in the two arms of the study be compared statistically at the end of the study in terms of drugs associated with RA to find out that is it a significant differences between the two groups or not. Regarding updating of some outcomes, before the patients entered the study, it was decided that since the clinical signs in patients with rheumatoid arthritis are very important in the diagnosis, a criterion for the severity of the disease, which includes clinical examinations of 28 important joints in this disease (DAS28-ESR) should also be included in the main outcomes, and since the ESR was required to calculate it, this variable was also added. Unfortunately, in the case of CRP, the goal was to measure quantitatively (hs-CRP) at first, but due to an error and lack of coordination with the laboratory, patients' CRP was measured qualitatively

and when the investigators realized this error, it was not possible to correct it. As a result, CRP of all patients was measured qualitatively. Also in the case of LDL, since other items in the patients' lipid profile were to be measured, LDL, which was omitted in the initial recording, was added.

Acronym

IRCT registration information

IRCT registration number: **IRCT20170513033941N67**
Registration date: **2019-11-30, 1398/09/09**
Registration timing: **registered_while_recruiting**

Last update: **2020-11-23, 1399/09/03**
Update count: **2**

Registration date

2019-11-30, 1398/09/09

Registrant information

Name

Mohammadreza Sharif

Name of organization / entity

Country

Iran (Islamic Republic of)

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+98 31 5546 3378

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ostadmohammadi-vr@kaums.ac.ir

Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2019-10-23, 1398/08/01

Expected recruitment end date

2019-12-21, 1398/09/30

Actual recruitment start date

2019-11-20, 1398/08/29

Actual recruitment end date

2020-02-26, 1398/12/07

Trial completion date

2020-05-20, 1399/02/31

Scientific title

Study of the effects of melatonin supplementation on clinical status and metabolic profiles in patients with rheumatoid arthritis

Public title

The effects of melatonin supplementation in the treatment of rheumatoid arthritis

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

Patients diagnosed with rheumatoid arthritis Individuals aged 20-80 years old

Exclusion criteria:

Patients with infectious, malignant and other inflammatory diseases those taking melatonin supplements or antioxidant supplements within 3 months prior to enrollment in the study the night shift workers subjects taking antibiotics medications unwillingness to cooperate Patients with thyroid diseases Current smokers Rheumatoid arthritis patients who were diagnosed less than on 1 year before the start of the study

Age

From **20 years** old to **80 years** old

Gender

Both

Phase

3

Groups that have been masked

- Participant
- Investigator
- Outcome assessor

Sample size

Target sample size: **66**
Actual sample size reached: **64**

Randomization (investigator's opinion)

Randomized

Randomization description

Patients will be randomly assigned into two groups. A randomization list will be generated from 1 to 66 by a random number generator (https://stattrek.com/statistics/random-number-generator.aspx) and patients were randomly assigned into each intervention group by their numbers. The block randomization technique with 1:1 ratio will be used to achieve balanced group sizes. Supplements and placebos are in the same packaging at the Pharmaceutical company. Only the code is written on the packages. Patients and researchers do not know the type of intervention and after analyzing the data, packet codes are decoded.

Blinding (investigator's opinion)

Double blinded

Blinding description

Participants, investigators or the assessors of the outcomes are unaware of the study groups.

Placebo

Used

Assignment

Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Ethics committee of Kashan University of Medical Sciences

Street address

Ghotbe Ravandi Boulevard, Kashan

City

Kashan

Province
Isfehan
Postal code
8115187159
Approval date
2019-10-21, 1398/07/29
Ethics committee reference number
IR.KAUMS.MEDNT.REC.1398.078

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
CRP
Timepoint
At the beginning of the study and after 12 weeks of intervention
Method of measurement
Qualitative (Negative, +1, +2 and +3)

2

Description
ESR
Timepoint
At the beginning of the study and after 12 weeks of intervention
Method of measurement
mm/h

3

Description
Disease activity
Timepoint
At the beginning of the study and after 12 weeks of intervention
Method of measurement
DAS28-ESR (using a questionnaire for VAS and a checklist to note physical examination results)

Secondary outcomes

1

Description
Malondialdehyde
Timepoint
At the beginning of the study and after 12 weeks of intervention
Method of measurement
Spectrophotometry

2

Description
Glutathione peroxidase
Timepoint
At the beginning of the study and after 12 weeks of intervention
Method of measurement
Spectrophotometry

3

Description
Total antioxidant capacity
Timepoint
At the beginning of the study and after 12 weeks of intervention
Method of measurement
Spectrophotometry

4

Description
Triglycerides
Timepoint
At the beginning of the study and after 12 weeks of intervention
Method of measurement
Enzymatic kit

5

Description
Total cholesterol
Timepoint
At the beginning of the study and after 12 weeks of intervention
Method of measurement
Enzymatic kit

6

Description
HDL
Timepoint
At the beginning of the study and after 12 weeks of intervention
Method of measurement
Enzymatic kit

7

Description
Insulin
Timepoint
At the beginning of the study and after 12 weeks of intervention
Method of measurement
Elisa kit

8

Description
Fasting plasma glucose
Timepoint
At the beginning of the study and after 12 weeks of intervention
Method of measurement
Enzymatic kit

9

Description
LDL
Timepoint
At the beginning of the study and after 12 weeks of intervention
Method of measurement
Enzymatic kit

Intervention groups

1

Description
Intervention group: 6 mg/day Melatonin (RAZAK, Iran), one hour before bedtime for 12 weeks.
Category
Treatment - Drugs

2

Description
Control group: Placebo (Barij Essence, Iran), one hour before bedtime for 12 weeks.
Category
Placebo

Recruitment centers

1

Recruitment center
Name of recruitment center
Beheshti Clinic
Full name of responsible person
Dr. Kamal Esalatmanesh
Street address
Ghotbe Ravandi Boulevard, Kashan
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Sponsors / Funding sources

1

Sponsor
Name of organization / entity
Vice chancellor for research, Kashan University of Medical Sciences
Full name of responsible person
Dr. Hamidreza Banafsheh
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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
Vice chancellor for research, Kashan 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
Kashan University of Medical Sciences
Full name of responsible person
Amirhossein Loghman
Position
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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