Clinical Trial Protocol
Iranian Registry of Clinical Trials

27 Oct 2026

Comparison of the Effectiveness of Magnesium Supplement with not Taking of Magnesium Supplement on Doxorubicin- Induced Cardiotoxicity in Breast Cancer Patients

Protocol summary

Study aim

Determination of the effect of magnesium against doxorubicin-induced cardiotoxicity .

Design

This clinical trial has a control group. The study is a phase 2-3, prospective, randomized, open-label trial planned for 80 patients

Settings and conduct

This study will be conducted as a two-group randomized clinical trial at the Cancer Institute of Imam Khomeini Hospital. Eligible patients, after referral by an oncologist and obtaining informed consent, will be randomly assigned to one of two intervention groups (receiving magnesium citrate supplementation along with standard chemotherapy regimen) or control (receiving only standard chemotherapy regimen). The sampling process, intervention prescription, and patient follow-up will be performed at the oncology clinic of the aforementioned hospital. Since patients are aware of their group, blinding was not performed.

Participants/Inclusion and exclusion criteria

Inclusion criteria: Histopathologically confirmed breast adenocarcinoma, HER2-negative, grade 1–2, stage 1–2, candidates for doxorubicin/cyclophosphamide chemotherapy, age 18–65 years, normal cardiac, renal, and hepatic function. Exclusion criteria: Hypermagnesemia, hypomagnesemia, oral magnesium supplementation within the previous 21 days

Intervention groups

Intervention: Oral magnesium citrate 420 mg every 12 h for 4 chemotherapy cycles (8 weeks), manufactured by Ofogh Tolid Darou Pars, plus standard doxorubicin/cyclophosphamide chemotherapy. Control: Standard doxorubicin/cyclophosphamide chemotherapy only.

Main outcome variables

Plasma magnesium, red blood cell magnesium, left ventricular ejection fraction, electrocardiographic findings, serum troponin, serum albumin, serum lactate, plasma fibrinogen, erythrocyte sedimentation rate, C-reactive protein, neutrophil-to-lymphocyte ratio.

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20251210068277N1**
Registration date: **2026-07-14, 1405/04/23**
Registration timing: **prospective**

Last update: **2026-07-14, 1405/04/23**
Update count: **0**

Registration date

2026-07-14, 1405/04/23

Registrant information

Name

Sara Assadi Eydivand

Name of organization / entity

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Iran (Islamic Republic of)

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Recruitment status

recruiting

Funding source

Expected recruitment start date

2026-07-23, 1405/05/01

Expected recruitment end date

2026-12-22, 1405/10/01

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date

empty

Scientific title

Comparison of the Effectiveness of Magnesium Supplement with not Taking of Magnesium Supplement on Doxorubicin- Induced Cardiotoxicity in Breast Cancer Patients

Public title

Investigation the protective role of oral magnesium supplementation on Doxorubicin- induced cardiotoxicity

Purpose

Prevention

Inclusion/Exclusion criteria

Inclusion criteria:

Patients who are being treated with a doxorubicin-containing drug regimen for the first time will be selected. All patients that breast adenocarcinoma is confirmed histopathologically in them and have negative human epidermal growth factor receptor 2 , grade 1 or 2 and stage 1 or 2 will undergo a chemotherapy regimen containing doxorubicin and cyclophosphamide (AC) will be included in the study. In order to control for confounding factors and reduce heterogeneity due to differences in treatment history and type of chemotherapy regimen, only patients with breast adenocarcinoma who had no history of chemotherapy and would be candidates for AC regimen were included in the study All patients will receive the standard AC chemotherapy regimen including: Doxorubicin (Adriamycin) 60mg/m2 and Cyclophosphamide 600mg/m2 each 2 weeks 4 times Normal kidney function (Glomerular filtration rate (GFR) > 60 milliliter in minute(ml/min), normal serum level of Blood urea nitrogen and creatinine (Bun and Cr)) Normal liver function (given that liver function tests (LFT) are normal).

Exclusion criteria:

Underlying heart disease such as heart failure, arrhythmia, ischemic heart disease Age over 65 years Pre-existing hypermagnesemia hypomagnesemia Taking magnesium supplements within the past 21 days

Age

From **18 years** old to **65 years** old

Gender

Female

Phase

2-3

Groups that have been masked

No information

Sample size

Target sample size: **80**

Randomization (investigator's opinion)

Randomized

Randomization description

After meeting the inclusion criteria and obtaining informed consent, participants will be allocated in a 1:1 ratio to the intervention and control groups. The random sequence will be created using SPSS version 26 software and through the generation of random numbers (Random Number Generator). In order to maintain a balance in the number of people in the two groups during the study, a random block method with a block size of 4 will be used. 20 blocks of 4 will be formed, and each patient will receive a code in the order of entry. The allocation list will be prepared by someone outside the outcome assessment team and will be kept in opaque, sealed, numbered envelopes and sequentially stored. After each participant enters the study, the relevant envelope will be opened in numerical order and the allocation group will be determined. The cardiac outcome assessor (ECG and echocardiography) will not be aware of the group allocation of the patients

Blinding (investigator's opinion)

Not blinded

Blinding description

Placebo

Not used

Assignment

Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Imam Khomeini Hospital Ethics Committee

Street address

No.19, Facing the Helicopter Runway, South-West Side, Office of the Vice President for Research in the Vice President for Academic Affairs, Imam Khomeini Hospital, Keshavarz Boulevard

City

Tehran

Province

Tehran

Postal code

3314114197

Approval date

2025-12-02, 1404/09/11

Ethics committee reference number

IR.TUMS.IKHC.REC.1404.404

Health conditions studied

1

Description of health condition studied

breast cancer

ICD-10 code

C50

ICD-10 code description

Malignant neoplasm of breast

Primary outcomes

1

Description
Left ventricular ejection fraction
Timepoint
Measurement of ejection fraction before the intervention and 2 weeks after the completion of the intervention
Method of measurement
Transthoracic echocardiography

2

Description
Nonspecific ST-T changes on ECG
Timepoint
Before the intervention and 2 weeks after the completion of intervention
Method of measurement
Standard twelve-lead ECG recording

3

Description
Plasma Troponin level
Timepoint
Before the intervention and 2 weeks after the completion of intervention
Method of measurement
Serum troponin measurement with a dedicated ELISA kit

4

Description
Serum magnesium level
Timepoint
Before the intervention and 2 weeks after the completion of the intervention
Method of measurement
Measurement of serum magnesium concentration with a biochemistry autoanalyzer

5

Description
Serum albumin level
Timepoint
Before the intervention and 2 weeks after the completion of the intervention
Method of measurement
Serum albumin measurement with an autobiochemistry analyzer

6

Description
Serum lactate level
Timepoint
Before the intervention and 2 weeks after the completion of the intervention
Method of measurement
Serum lactate measurement with an autobiochemistry analyzer

7

Description
Plasma fibrinogen level
Timepoint
Before the intervention and 2 weeks after the completion of the intervention
Method of measurement
Plasma fibrinogen measurement by coagulation method

8

Description
Erythrocyte sedimentation rate(ESR)
Timepoint
Before the intervention and 2 weeks after the completion of the intervention
Method of measurement
Measurement by Westergren method

9

Description
C-reactive protein(CRP)
Timepoint
Before the intervention and 2 weeks after the completion of the intervention
Method of measurement
Measurement with a dedicated kit using the ELISA method

10

Description
Neutrophil to lymphocyte ratio
Timepoint
Before the intervention and 2 weeks after the completion of the intervention
Method of measurement
Calculation of the neutrophil to lymphocyte ratio based on the results of a complete blood cell count

11

Description
Magnesium levels inside red blood cells
Timepoint
Before the intervention and 2 weeks after the completion of the intervention
Method of measurement
Measurement of red blood cell magnesium with a dedicated kit using the ELISA method

Secondary outcomes

empty

Intervention groups

1

Description

Intervention group: Patients with breast adenocarcinoma who have no history of receiving chemotherapy and are candidates for the doxorubicin and cyclophosphamide chemotherapy regimen will receive oral magnesium citrate supplement (product of Ofogh Pharmaceutical Company, Pars Pharmaceutical Manufacturing Company, with a concentration of 420 mg of elemental magnesium per tablet) at the same time as the start of the first cycle of chemotherapy with the standard doxorubicin and cyclophosphamide regimen (standard treatment includes doxorubicin at a dose of 60 mg/m2 and cyclophosphamide at a dose of 600 mg/m2, once every 14 days for a total of 4 cycles) in the amount of one tablet (420 mg) every twelve hours for 4 chemotherapy cycles (equivalent to 8 weeks). The method of administration will be oral, preferably after meals.Also, a 20-30 minute face-to-face educational session will be held for each patient by a member of the research team, which will include the correct way to take the supplement, possible gastrointestinal side effects and warning signs for stopping use, the importance of adhering to daily intake and monitoring cardiac symptoms, and how to contact the research team in case of any complications. Patients in this group will also receive all supportive and standard care in accordance with the department's protocol

Category

Prevention

2

Description

Control group: Patients with breast adenocarcinoma who have no history of chemotherapy and are candidates for the chemotherapy regimen of doxorubicin and cyclophosphamide will receive only standard treatment including doxorubicin and cyclophosphamide according to the center's treatment protocol including doxorubicin at a dose of 60 mg/m2 and cyclophosphamide at a dose of 600 mg/m2, once every 14 days for a total of 4 cycles, and will not receive any magnesium supplements during the study period. A face-to-face educational session for this group will also be held for 15 to 20 minutes by a member of the research team, the content of which will include an explanation of the importance of following up on cardiac symptoms and how to contact the research team in case of any complications. All supportive and standard care will also be provided for this group according to the department's protocol

Category

N/A

Recruitment centers

1

Recruitment center

Name of recruitment center

The Cancer Institute of Imam Khomeini Hospital

Full name of responsible person

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity

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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

Tehran 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

Tehran University of Medical Sciences

Full name of responsible person

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Position
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Latest degree
Ph.D.

Other areas of specialty/work
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Bachelor

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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