# Clinical Trial Protocol
# Iranian Registry of Clinical Trials

06 Nov 2026

## Evaluating the effectiveness of silymarin in preventing vancomycin-induced nephrotoxicity in hospitalized patients

### Protocol summary

**Study aim**
Determining the effectiveness of silymaran in preventing vancomycin-induced nephrotoxicity in patients admitted to Namazi and Shahid Faqihi hospitals in Shiraz

**Design**
The clinical trial has two control and treatment groups, double-blind, randomized by permutation block method.

**Settings and conduct**
A multicenter, randomized, double-blind, placebo-controlled clinical trial in two educational medical centers in Shiraz including Namazi Hospital and Shahid Faqihi Hospital Preparing the placebo as the same as Livergol tablets regarding size, color, and shape The unawareness of the nursing staff about groups The unawareness of the physician and assistant researcher about groups

**Participants/Inclusion and exclusion criteria**
Patients referred to teaching hospitals who have been diagnosed with an indication for the use of systemic (injectable) vancomycin for at least 7 days. The patients are hemodynamically stable, willing to participate in the study, receiving vancomycin injection for at least 7 days, absence of hypersensitivity reaction following silymarin consumption, no confirmed history of acute kidney injury, no confirmed history of chronic kidney disease, no vancomycin use in the past 14 days, no simultaneous use of drugs or compounds with antioxidant effect, no simultaneous use of drugs with prominent nephrotoxicity, and oral tolerance to drugs

**Intervention groups**
The two treatment and control groups will be given vancomycin based on the treatment protocol. However, in the patients of the treatment group, silymarin tablets (Livergol) 140 mg three times a day will be given orally as long as vancomycin is prescribed.

**Main outcome variables**
Increase in serum creatinine level; Development of acute tubular necrosis (ATN); The change in oxidant and antioxidant markers in serum

### General information

**Reason for update**

**Acronym**

**IRCT registration information**
IRCT registration number: **IRCT20161010030246N6**
Registration date: **2023-05-27, 1402/03/06**
Registration timing: **prospective**

Last update: **2023-05-27, 1402/03/06**
Update count: **0**

**Registration date**
2023-05-27, 1402/03/06

**Registrant information**

**Name**
Iman Karimzadeh

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**Recruitment status**
**Recruitment complete**

**Funding source**

**Expected recruitment start date**
2023-06-13, 1402/03/23

**Expected recruitment end date**
2023-12-14, 1402/09/23

**Actual recruitment start date**
empty

**Actual recruitment end date**
empty

**Trial completion date**
empty

**Scientific title**
Evaluating the effectiveness of silymarin in preventing vancomycin-induced nephrotoxicity in hospitalized patients

**Public title**
Evaluating the effectiveness of silymarin in preventing vancomycin nephrotoxicity

**Purpose**
Prevention

**Inclusion/Exclusion criteria**

**Inclusion criteria:**
Hemodynamic stability (mean arterial blood pressure above 70 mmHg and/or systolic blood pressure above 90 mmHg. Willingness to participate in the study Receiving vancomycin intravenously for at least 1 week with the maintenance dosage regimen of 30-45 mg/kg/day or 1-2 g twice a day. Notably, the vancomycin regimen is the same in both hospitals.

**Exclusion criteria:**
Confirmed history of acute kidney injury Confirmed history of chronic kidney disease Taking vancomycin within the last 14 days Taking silymarin orally at least during the past day Confirmed history of hypersensitivity reactions following oral consumption of silymarin Simultaneous use of agents with antioxidant activity such as vitamin C, vitamin E, vitamin A, melatonin Receiving drugs with high nephrotoxicity potential such as aminoglycosides, amphotericin b, colistin Oral intolerance to drugs

**Age**
From **18 years** old

**Gender**
Both

**Phase**
3

**Groups that have been masked**

- Participant
- Care provider
- Investigator
- Data analyser

**Sample size**
Target sample size: **80**
More than 1 sample in each individual
Number of samples in each individual: **40**
Forty patients are in the intervention (Silymarin) and 40 patients in the control group (Placebo).

**Randomization (investigator's opinion)**
Randomized

**Randomization description**
Block randomization (quadruple blocks): All possible blocks are arranged as follows: block 1: ABAB block 2: AABB block 3: ABBA block 4: BBAA block 5: BABA block 6: BAAB. We need 20 blocks to select 80 people. We randomly select these blocks from the numbers 1 to 6. For example, number 6 is chosen as the first block and number 2 as the forth block. The people who enter the study are given B-A-A-B-A-A-B-B, respectively. Finally, group A receives placebo and group B receives silymarin.

**Blinding (investigator's opinion)**
Double blinded

**Blinding description**
The researcher does not know whether the drug he gives to the patient is a placebo or the original drug. On the other hand, the participant (patient) is also unaware of whether the drug given to him is a placebo or the original drug.

**Placebo**
Used

**Assignment**
Parallel

**Other design features**

## Secondary Ids

empty

## Ethics committees

### 1

**Ethics committee**

**Name of ethics committee**
Ethics Committee of Shiraz Medical Sciences

**Street address**
Research and Technology Vice-Chancellor of Shiraz University of Medical Sciences-Shiraz Zand Street-Central Building of Shiraz University of Medical Sciences-7th Floor-Research and Technology Vice-Chancellor

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**Approval date**
2023-05-21, 1402/02/31

**Ethics committee reference number**
IR.SUMS.REC.1402.073

## Health conditions studied

### 1

**Description of health condition studied**
Vancomycin-induced nephrotoxicity in hospitalized patients

**ICD-10 code**
N14

**ICD-10 code description**
Drug- and heavy-metal-induced tubulo-interstitial and tubular conditions

## Primary outcomes

### 1

**Description**
Vancomycin nephrotoxicity as an increase in serum creatinine by ≥ 0.3 mg/dl within 48 hrs or an increase in serum creatinine to ≥ 1.5 times baseline within the previous seven days

**Timepoint**
Sampling of urine and blood (5 ml) of patients will be done before starting the drug (day zero) and on days 1, 2, 3, 5, 7, 10, and 14 of vancomycin treatment
**Method of measurement**
Measurement of serum creatinine is done by using an autoanalyzer instrument.

**2**

**Description**
Acute tubular necrosis is defined as fractional excretion of sodium more than 2% in the absence of diuretic treatment.
**Timepoint**
Sampling of urine and blood (5 ml) of patients will be done before starting the drug (day zero) and on days 1, 2, 3, 5, 7, 10, and 14 of vancomycin
**Method of measurement**
Measurement of serum as well as urine creatinine along with serum as well as urine sodium is done by using an autoanalyzer instrument.

## Secondary outcomes

**1**

**Description**
Serum level of malondialdehyde, total antioxidant capacity, and glutathione
**Timepoint**
At days 0 and 14 of vancomycin treatment
**Method of measurement**
Serum level of malondialdehyde, total antioxidant capacity, and glutathione are measured by the ELISA technique.

## Intervention groups

**1**

**Description**
Intervention group: In this group, as long as vancomycin is received, silymarin tablets from the Gol Daru company (Livergol) are prescribed orally in the amount of 140 mg three times a day orally.
**Category**
Prevention

**2**

**Description**
Control group: In this group, along with vancomycin, placebo tablets 140 mg three times a day are given orally.
**Category**
Prevention

## Recruitment centers

**1**

**Recruitment center**
**Name of recruitment center**
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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**
Shiraz 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