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Inhibition of cardiac fibrosis by colchicine in acute myocardial infarction

Submission date	Recruitment status	[_] Prospectively registered
28/12/2023	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
02/01/2024	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
02/02/2026	Circulatory System	

Plain English summary of protocol

Background and study aims

When your heart is injured due to a serious heart attack, it sets off an immediate inflammatory response. If the blood flow isn't quickly restored, the damaged tissue can turn into scar tissue. In people with a specific kind of heart attack, called STEMI, restoring blood flow promptly is crucial to minimize damage. This can be done either by using a procedure called PCI or by using fibrinolytic therapy.

Sometimes, even when the blood flow is restored, there can be ongoing damage to the heart tissue. This damage involves changes in tiny structures within the cells, leading to inflammation. Certain cells in the immune system, called macrophages, get involved, releasing substances that either promote or reduce inflammation. In this study, we're looking at a drug called colchicine, known for its anti-inflammatory properties. It seems that colchicine may not only reduce inflammation but also prevent the formation of excess scar tissue in the heart.

Our goal is to understand how colchicine affects specific processes in the body after a heart attack, particularly in patients who undergo a procedure to restore blood flow. We're investigating whether colchicine can decrease the harmful effects of inflammation, promote healing, and potentially prevent heart failure from developing. We're also using a substance called NT-proBNP to help us understand the extent of heart damage. By doing this research, we hope to find new ways to improve outcomes for people who experience this type of heart attack.

Who can participate?

Patients aged 30-75 years, diagnosed with acute myocardial infarction, who have undergone reperfusion therapy and are receiving colchicine treatment in addition to the standard of care, and meet the inclusion criteria.

What does the study involve?

The study involves administering colchicine to reduce cardiac fibrosis by increasing levels of IL-10 and galectin-3 and reducing the ratio of collagen I to collagen III and NT-proBNP. The treatment's effectiveness will be assessed using various biomarkers and echocardiography.

What are the possible benefits and risks of participating?
The benefits of participating in this study include the potential reduction of fibrosis and anti-remodeling effects. However, there are risks involved, such as side effects from colchicine, including nausea, diarrhoea, and gastritis.

Where is the study run from?
Ciputra University (Indonesia)

When is the study starting and how long is it expected to run for?
November 2020 to December 2023

Who is funding the study?
Investigator initiated and funded

Who is the main contact?
Dr Saskia Dyah Handari, saskiadyahandari@gmail.com.

Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Protocol serial number
Ethical approval No : 400/K.3/302/2020

Study information

Scientific Title
Inhibition of cardiac fibrosis by colchicine through differential increase in interleukin-10 and galectin-3 expression and decrease in the ratio of collagen I to collagen III and NT-proBNP in acute myocardial infarction (in vivo study on patients with acute myocardial infarction with ST-segment elevation undergoing primary and delayed percutaneous coronary intervention)

Acronym
ICFC-AMI

Study objectives
It is hypothesized that there is a difference in the effect of colchicine administration in inhibiting cardiac fibrosis through an increase in IL-10 and galectin-3 levels, and a decrease in the ratio of collagen I to collagen III, evaluated by PIIINP (Procollagen 3 N-terminal peptide) and NT-proBNP (N-terminal pro b-type natriuretic peptide), in patients with acute myocardial infarction with ST-segment elevation (STEMI) undergoing primary and delayed percutaneous coronary intervention

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 05/11/2020, Health Research Ethics Committee. General Hosptal Dr. Saiful Anwar Malang (Jl. Jaksa Agung Suprapto no 2. Malang, Malang, 65111, Indonesia; +62 (0)341362101; staf-rsu-drsaifulanwar@jatimprov.go.id), ref: 400/K.3/302/2020

Primary study design
Interventional

Study design
Randomized controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Acute myocardial infarction

Interventions
Patients undergoing primary and delayed percutaneous coronary intervention (PCI) are divided into two groups for each PCI type. Sample selection is through consecutive sampling, and randomization is 1:1 with double-blind allocation.

Primary PCI patients:
1. One group receives a loading dose of 1 mg colchicine 1-2 hours before the PCI procedure, followed by 0.5 mg 1 hour afterwards, and a maintenance dose of 0.5 mg daily for 1 month, along with optimal medical therapy.
2. The other group receives a placebo following the same regimen and optimal medical therapy for 1 month.

Delayed PCI Patients:
1. One group receives a loading dose of 1 mg colchicine 1-2 hours before the PCI procedure, followed by 0.5 mg 1 hour afterwards, and a maintenance dose of 0.5 mg daily for 1 month, along with optimal medical therapy.
2. The other group receives a placebo following the same regimen and optimal medical therapy for 1 month.

This design allows the researchers to observe the effects of colchicine in comparison to placebo in patients undergoing different timings of PCI while ensuring that all groups receive the standard care.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Colchicine

Primary outcome(s)
Left ventricular remodelling measured using echocardiography during hospitalization and 1 month post-hospitalization

Key secondary outcome(s)
Biomarkers (Gal3, IL10, PIIINP and NTProBNP) measured during hospitalization and 1 month post-hospitalization

Completion date
20/12/2023

Eligibility

Key inclusion criteria
1. Patients diagnosed with STEMI for the first time, with the following diagnostic criteria: persistent typical chest pain >30 minutes lasting more than 12 hours, accompanied by ST-segment elevation in at least 2 contiguous leads, and an increase in cardiac enzymes, troponin I.
2. Patients who have received information about the study and signed an informed consent.
3. Patients not pregnant, breastfeeding, or planning pregnancy during the study period.
4. Patients without a history of alcohol abuse.
5. Patients not receiving long-term steroid therapy during the study.
6. Patients not currently taking colchicine for other indications (e.g., gout arthritis, familial Mediterranean fever).

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
30 Years

Upper age limit
75 Years

Sex
All

Total final enrolment
200

Key exclusion criteria
1. Patients with poor medication adherence, as evidenced by the number of missed doses during the study.
2. Patients with a history of hypersensitivity to colchicine.
3. Patients with comorbidities such as infections, inflammation, malignancy, for instance, irritable bowel syndrome (Crohn's Disease or ulcerative colitis), severe renal failure (eGFR <30), a history of hepatic cirrhosis, acute exacerbation of hepatitis, or severe liver disease.
4. Laboratory results as follows: Hemoglobin <11.5g/dl, Leukocytes < 3.0 x 10^9/L, Platelets < 110 x 10^9/L, ALT > 3 times the upper normal limit, Total Bilirubin > 2 times the upper normal limit, Creatinine > 2 times the upper normal limit.
5. Patients who have experienced cardiac arrest.
6. Patients with ventricular fibrillation.
7. Patients with cardiogenic shock or unstable hemodynamics.

Date of first enrolment
20/09/2022

Date of final enrolment
20/02/2023

Locations

Countries of recruitment
Indonesia

Study participating centre
Cardiovascular Research Centre Medical Faculty of Brawijaya University
Jl. Veteran, Ketawanggede, Kecamatan Lowokwaru, Kota Malang, Jawa Timur
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Sponsor information

Organisation
University of Brawijaya

ROR
https://ror.org/01wk3d929

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

Individual participant data (IPD) sharing plan
All data generated or analysed during this study will be included in the subsequent results publication

IPD sharing plan summary
Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		20/01/2025	02/02/2026	Yes	No
Results article		06/08/2024	02/02/2026	Yes	No
Preprint results		23/12/2024	02/01/2025	No	No