

Colchicine for the prevention of postoperative atrial fibrillation in patients undergoing Coronary Artery By-pass Grafting

Submission date 26/06/2013	Recruitment status No longer recruiting	☐ Prospectively registered ☐ Protocol
Registration date 10/07/2013	Overall study status Completed	☐ Statistical analysis plan ☐ Results
Last Edited 10/07/2013	Condition category Circulatory System	☐ Individual participant data ☐ Record updated in last year

Plain English summary of protocol

Background and study aims

Postoperative atrial fibrillation (POAF) (irregular heart beat) is the most common complication after a heart surgery, affecting 20-30% of patients after coronary artery bypass graft (CABG) surgery and up to 50% after combined CABG/valve surgery. Nowadays, POAF prevention has become important because of its great clinical and economic burden. Indeed, POAF is associated with a worse mid-time and long-time prognosis and also with increased costs. Various different factors are responsible for causing POAF and they are not completely understood yet. Previous research suggests that anti-inflammatory agents (pain killers) may potentially be useful in the treatment methodology. Colchicine, a non-steroid anti-inflammatory agent, reduced complications in patients undergoing heart surgery and was also safe. Further, colchicine was also found to reduce the occurrence of POAF after a heart surgery. The purpose of this study is to find out how well colchicine works in preventing POAF in patients undergoing CABG surgery.

Who can participate?

All patients referred to undergo CABG surgery can participate in the study.

What does the study involve?

Patients are randomly allocated to receive colchicine or a placebo (dummy) starting from the day before the heart surgery until they get discharged from the hospital. They are checked using various tests like, continuous ECG (electrocardiogram) display, telemetry and Holter ECG for the occurrence of irregular heart beat.

What are the possible benefits and risks of participating?

Postoperative atrial fibrillation is the most common complication after heart surgery. There are evidences that it is associated with predicting the likelihood of future diseases and it may lead to extended hospital stay and cost. Reducing its occurrence will prevent all the above. The major risk of the study is the possible occurrence of colchicine toxicity that is rare and usually associated with higher doses in patients with normal kidney and liver function. Some side effects like stomach discomfort or diarrhoea can bother some patients.

Where is the study run from?

The study is run from the the Cardiac Surgery Unit , the Catholic University of the Sacred Heart, Rome, Italy.

When is the study starting and how long is it expected to run for?

The study starts to enroll participants from July 2013. Given the number of patients, it is expected to last for at least 12 months.

Who is funding the study?

The Catholic University of the Sacred Heart, Rome, Italy.

Who is the main contact?

Prof Claudio Pragliola

cpragliola@rm.unicatt.it

Contact information

Type(s)

Scientific

Contact name

Prof Claudio Pragliola

Contact details

Catholic University of the Sacred Heart

(Università Cattolica S. Cuore Roma)

Dept of Cardiovascular Sciences Unit of Cardiac Surgery

Policlinico A. Gemelli

L.go Gemelli 8

Rome

Italy

00168

Additional identifiers

Protocol serial number

AF2/2013

Study information

Scientific Title

A randomized double blind controlled study to determine whether the use of colchicine is effective in reducing the incidence of atrial fibrillation after coronary artery by-pass grafting

Acronym

COVER CABG

Study objectives

We are verifying the hypothesis that the use of colchicine (1 mg bid) started 24 hrs before surgery and administered postoperatively (0.5mg bid) until hospital discharge (or for a maximum

of 10 days) will significantly reduce the incidence of postoperative atrial fibrillation in the patients submitted to coronary artery by-pass surgery

Ethics approval required

Old ethics approval format

Ethics approval(s)

Ethics Commission of Catholic University of the Sacred Heart Roma May 2013

Primary study design

Interventional

Study design

Controlled randomized double blind

Study type(s)

Prevention

Health condition(s) or problem(s) studied

Coronary Artery Disease Coronary Artery Surgery Atrial Fibrillation

Interventions

Patients will be randomized to receive placebo or colchicine, in addition to standard therapy, using a computer generated table of casual numbers. A separate randomization will be followed for patients with a history of previous paroxysmal atrial fibrillation.

Treatment will be started on day -1 (i.e., the day before CABG surgery) and continued until hospital discharge. Patients randomized to colchicine will receive 1 mg bid on day -1 and then 0.5 mg twice a day until discharge or for a maximum of 10 days. A half dose will be administered in patients <70 kg. All patients will give informed written consent to participation in the study, which will comply with the Declaration of Helsinki.

Clinical assessment

For each patient demographic data and clinical history, including drug therapy, coronary angiography and significant comorbidities will be collected.

Assessment of atrial fibrillation

The occurrence of AF during hospital stay will be assessed through the following methods:

1. continuous ECG monitoring in ICCU (Intensive Cardio-surgical Care Unit)
2. forty-eight-hour ECG Holter monitoring in the first two days after ICCU discharge
3. Two standard ECG recordings (in the morning and in the evening) from the third day after ICCU discharge until the end of the study
4. Immediate ECG recording in case of arrhythmic symptoms

Holter ECG monitoring

Holter ECG recordings will be done using 3-channel recorders. Detailed analysis of arrhythmias will be performed. Furthermore, heart rate variability (HRV) will be analysed, both in the time-domain and in the frequency-domain, in order to assess the possible relation of cardiac autonomic imbalance with the occurrence of post-operative atrial fibrillation (POAF).

Echocardiography

A two-dimensional echocardiographic Doppler examination will be performed before CABG

surgery and at discharge, in order to assess atrial/ventricular dimensions, valvular defects and the occurrence of pericardial effusion.

Blood markers of inflammation

A venous blood sample will be collected before CABG surgery, on first day of Holter monitoring and at discharge to assess inflammatory state by measuring white cells count, C-reactive protein, VES, interleukin-6 (IL-6) and fibrinogen serum levels.

Intervention Type

Drug

Phase

Not Specified

Drug/device/biological/vaccine name(s)

Colchicine

Primary outcome(s)

Postoperative Atrial Fibrillation as defined by the 2010 ESC Guideline for the treatment of Atrial Fibrillation occurring at any time during the postoperative period . The arrhythmia may be detected by any of the following postoperative exams a) ECG monitoring in the ICU; b) 48 hrs Holter ECG thereafter ; c) 12 Leads ECG twice a day until hospital discharge

Key secondary outcome(s)

Occurrence of any atrial arrhythmia

Occurrence of any arrhythmia necessitating drug suspension

Occurrence of any complication or major side effect of Colchicine

Completion date

31/07/2014

Eligibility

Key inclusion criteria

All the patients electively submitted to coronary artery by-pass grafting with arterial conduits and without contraindications to colchicine

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Not Specified

Sex

All

Key exclusion criteria

1. Patients with preoperative atrial fibrillation
2. Known contraindication to Colchicine
3. Transaminases on admission more than 1.5 times the normal values
4. Creatinine clearance less than 30 ml/min
5. History of myopathy or elevated creatinine kinase
6. Hematologic disease
7. Gastrointestinal disease
8. Presence of systemic inflammatory or autoimmune disease

Date of first enrolment

01/07/2013

Date of final enrolment

31/07/2014

Locations

Countries of recruitment

Italy

Study participating centre

Catholic University of the Sacred Heart

Rome

Italy

00168

Sponsor information

Organisation

Catholic University of the Sacred Heart-Rome (Italy)

ROR

<https://ror.org/03h7r5v07>

Funder(s)

Funder type

University/education

Funder Name

Catholic University of the Sacred Heart (Italy)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration