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Effect of hypoglycemic agents on ischemic preconditioning in patients with diabetes and symptomatic coronary artery disease

Submission date
09/03/2012

Recruitment status
No longer recruiting

Registration date
22/05/2012

Overall study status
Completed

Last Edited
19/05/2017

Condition category
Circulatory System

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and aims:
A myocardial ischemia occurs when the blood flow to your heart is reduced, preventing it from receiving enough oxygen. Ischemic preconditioning (IPC) is an experimental technique that promotes resistance to ischemic insult. It seems that the underlying mechanism for this phenomenon involve the KATP (potassium ATP) channels. Some hypoglycemic (low bloof sugar) drugs, like glybenclamide, can eliminate this protective effect, contributing to a worse prognosis. The aim of this study is to evaluate the effects of 2 hypoglycemic agents on myocardial IPC in patients with type 2 diabetes and multivessel coronary disease.

Who can participate?
Patients with type 2 diabetes and multi-vessel coronary disease confirmed by coronary angiography and ischemic exercise test.

What does the study involve?
The study involves two phases. In phase one, (without medication), all participants undergo two consecutive treadmill exercise tests (ET1 and ET2) to demonstrate IPC. After that all patients will receive hypoglycemic drugs for one week and they will undergo to more two sequential ET (ET3 and ET4), in phase II. The time interval between the ET1-2 and ET3-4 will be 30 minutes. Calcium entry blocking agents, b-blockers, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, and sulfonylurea drugs are withdrawn five days before the study. Nitrates are withdrawn 2 days before.

What are the possible benefits and risks of participating?
Preserving the viability of myocardium therefore has been recognized as a major therapeutic target. Classes of pharmacological agents that may be able to mimic or preserve the protection conferred by ischemic preconditioning provide some basis for a possible clinically improvement in patients with coronary artery disease. All patients selected are stable clinically and not demonstrate any potential risk. The participants will receive an individualized follow-up program consisting of specialized medical care in Heart Institute, University of Sao Paulo.

Where is the study run from?
Heart Institute, University of Sao Paulo (Brazil)

When is study starting and how long is it expected to run for?
January 2008 to January 2013

Who is funding the study?
Zerbini Foundation

Who is the main contact?
Dr Whady Hueb
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Contact information

Type(s)
Scientific

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05403000

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
Effect of hypoglycemic agents on ischemic preconditioning in patients with diabetes and symptomatic coronary artery disease

Study objectives
We hypothesized that both glinide and inhibitor of dipeptidyl peptidase-4 (DPP-4) drugs may interfere with ischemic preconditioning cellular mechanism. For this reason we will test this

hypothesis by conducting a prospective study in which individuals with type 2 diabetes and symptomatic coronary artery disease were selected to receive glinide or inhibitor of DPP-4 and we will evaluate their effects on warm-up phenomenon.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Institutional Review Board, Committee for the Analysis of Research Projects [Comissão para Análise de Projetos de Pesquisa, 07 December 2007

Study design
Single-centre prospective study

Primary study design
Interventional

Secondary study design
Non randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Screening

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Type 2 diabetes / coronary artery disease

Interventions
Meglitinide group: Repaglinide 6 mg daily, oral dose, during 1 week
Inhibitor DPP-4 group: Vildagliptin 100 mg daily, oral dose, during 1 week

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
We will evaluate the effect of two hypoglycemic drugs on ischemic preconditioning by two sequential treadmill exercise tests (warm-up phenomenon). The warm-up phenomenon will be analysed by following parameters:
1. The time to onset of 1.0-mm ST-segment depression (the horizontal or downsloping ST-segment depressions were considered)
2. Rate pressure product (heart rate x systolic blood pressure) at the onset of 1.0-mm ST-segment depression

Secondary outcome measures
No secondary outcome measures

Overall study start date
15/01/2008

Completion date
15/01/2013

Eligibility

Key inclusion criteria
1. Patients with type 2 diabetes mellitus under adequate drug treatment and no insulin dependence
2. A positive test for myocardial ischemia during a previous treadmill exercise test (horizontal or downsloping ST-segment depression >=1.0 mm)
3. Multivessel coronary disease confirmed by coronary angiography, and coronary disease with an internal diameter reduction of >=70% of at least two major coronary branches
4. Preserved left ventricular function confirmed by transthoracic echodopplercardiography

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
206

Key exclusion criteria
1. Myocardial infarction during the last 3 month
2. Severely impaired myocardial function (ejection fraction <45%)
3. ECG changes that could interfere with the interpretation of the ST segment
4. Impaired hepatic or renal function
5. Progressive fatal disease
6. Mental disorder

Date of first enrolment
15/01/2008

Date of final enrolment
15/01/2013

Locations

Countries of recruitment

Brazil

Study participating centre
Av Dr Eneas de Carvalho Aguiar
Sao Paulo
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05403000

Sponsor information

Organisation
Zerbini Foundation (Fundação Zerbini) (Brazil)

Sponsor details
Av Dr Eneas de Carvalho Aguiar
44 AB 114 Cerqueira Cesar
Sao Paulo
Brazil
05403000

Sponsor type
Hospital/treatment centre

Website
http://www.incor.usp.br

ROR
https://ror.org/003c2h870

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Zerbini Foundation (Brazil)

Results and Publications

Publication and dissemination plan

Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/06/2013		Yes	No