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Low-density lipoprotein receptor-related protein 1 (LRP1) expression in Mexican hypertensive patients

Submission date
09/11/2016

Recruitment status
No longer recruiting

Registration date
12/12/2016

Overall study status
Completed

Last Edited
24/04/2019

Condition category
Circulatory System

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

Plain English summary of protocol

Background and study aims
Arterial hypertension (HTA) is high blood pressure in the vessels that carry blood from the heart to the body's tissues. It is a serious public health problem and is a major risk factor for cardiovascular (heart) disease, cerebrovascular disease (e.g., stroke) and kidney failure, which are major causes of death. Studies have found that there is a relationship between high blood pressure and atherosclerosis (the build-up of fatty material inside the arteries). This situation highlights the need to develop useful and easily accessible diagnostic tools for clinical practice. The intima/media thickness (IMT) is a measurement of the innermost two layers of carotid artery wall. It is an excellent marker for atherosclerosis and cardiovascular disease. The aims of this study are to compare the levels of LRP1 protein in circulating monocytes (white blood cells) from patients with high or normal blood pressure, to determine the relationship between LRP1 levels and IMT, and to find out whether LRP1 levels can be used as a marker for atherosclerosis.

Who can participate?
Mexicans age 40-70 with high or normal blood pressure

What does the study involve?
Participants' body measurements are taken, including their height and weight, and their blood pressure is measured. Their IMT is measured with an ultrasound device. Blood samples are collected after fasting for 12 hours to measure LRP1 levels.

What are the possible benefits and risks of participating?
If a participant is found to have hypertension, increased IMT, high blood cholesterol and high LRP1 levels, they may have atherosclerosis. Knowing these results the doctor can give a preventive treatment to avoid cardiovascular and cerebrovascular disease. IMT is assessed with ultrasound, which does not expose the patient to any risk.

Where is the study run from?
National Institute of Cardiology "Ignacio Chavez" (Mexico)

When is the study starting and how long is it expected to run for?
October 2011 to July 2014

Who is funding the study?
National Council of Science and Technology (Mexico)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
JTRM-D-16-00728

Study information

Scientific Title
Monocyte low-density lipoprotein receptor-related protein 1 (LRP1) expression correlates with intima-media thickening in Mexican hypertensive patients

Acronym
LRP1 hypertensive

Study objectives
Arterial hypertension, one of major risk factors for atherosclerosis, contributes to foam cell formation in the vasculature though low-density lipoprotein receptor-related protein 1 (LRP1)

upregulation. The purpose of this work was to study the association between monocyte LRP1 mRNA expression and LRP1 protein levels and intima/media thickness in the carotid artery (IMT) of patients with essential hypertension

If the LRP1 receptor modulates the uptake of c-LDL associated with hypertension, an increased IMT is expected to be found in hypertensive patients along with an overexpression of LRP1 in peripheral blood monocytes

The aims of this study were:
1. To compare LRP1 expression levels in circulating monocytes from patients with essential hypertension against normotensive patients
2. To determine the relationship between LRP1 overexpression and arterial intima/media thickening to assess if monocyte LRP1 expression is a potential biomarker for atherosclerosis

Ethics approval required
Old ethics approval format

Ethics approval(s)
Commission of bioethics of the INC Ignacio Chavez, 16/03/2010, ref: 10-665

Primary study design
Observational

Study design
Single-center observational case-control study

Study type(s)
Screening

Health condition(s) or problem(s) studied
Arterial hypertension

Interventions
The population is recruited from the outpatient Service of the National Institute of Cardiology "Ignacio Chavez", where the hypertension diagnosis was made by a medical specialist. The subjects underwent anthropometric measurements determining their height in meters (m) weight in kilograms (kg). Blood pressure is measured using a mercury sphygmomanometer following the recommendations of the VII Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC VII). Systolic and diastolic blood pressures are measured after rest for at least 10 min, and the average of the second and third measurements is recorded for analysis. Hypertension is defined as systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg or a previous clinical diagnosis of essential hypertension.

A specialist in sonography resolution assesses the intima/media thickness in the carotid artery, all measurements are performed with a Sonosite Micromax ultrasound device coupled to a 13 MHz multifrequency high-resolution linear transducer.

Blood samples were collected after a fasting period of 12 hours. Commercial enzymatic methods were used to determine circulating TC and TG, HDL-C, LDL-C. Angiotensin II was determined by capillary electrophoresis and C-reactive protein was determined by nephelometry. Peripheral

blood mononuclear cell (PBMCs) are isolated from blood collected in EDTA using the Ficoll separation method.

Total RNA was extracted using monocyte TripureTM isolation reagent (Roche Molecular Biochemicals) followed by a reverse transcription reaction.

LRP1 gene expression and HPRT (endogenous gene) were quantified using a commercial kits "TaqMan Gene Expression" employing 7300 Real Time PCR System (Applied Biosystems) equipment. Total protein was extracted from monocytes using TriPureTM reagent (Roche Molecular Biochemicals). Membranes were incubated with monoclonal antibody against human LRP1 (85kDa β-chain). The QuantityOne program was used to quantify the bands present in the membranes.

Intervention Type
Other

Primary outcome(s)
1. Blood pressure (normotensive or hypertensive), measured using a mercury sphygmomanometer at 10 months
2. LRP1 gene expression, quantified using a "TaqMan Gene Expression" commercial kit and 7300 Real Time PCR System at 3 months
3. LRP1 protein, analyzed by western blot at 6 months
4. The intima/media thickness in the carotid artery, assessed with a Sonosite Micromax ultrasound device coupled to a 13 MHz multifrequency high-resolution linear transducer at 10 months

Key secondary outcome(s)
N/A

Completion date
25/07/2014

Eligibility

Key inclusion criteria
Control group:
1. Normal pressure up to 120/80 mmHg
2. Mexican by birth, with at least two previous generations of Mexican origin
3. Agree to participate in the research protocol
4. Age 40-70 years

Hypertensive group:
1. Blood pressure > 140/90mmHg
2. Mexican by birth, with at least two previous generations of Mexican origin
3. Agree to participate in the research protocol

Participant type(s)
Mixed

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
Control group:
1. Have a history of cardiovascular disease
2. Have type 1 or 2 diabetes.
3. Have a chronic degenerative disease
4. Treatment with lipid-lowering medications

Hypertensive group:
1. Treatment with lipid-lowering medications
2. Have type 1 or 2 diabetes
3. Have a chronic degenerative disease

Date of first enrolment
24/07/2013

Date of final enrolment
27/02/2014

Locations

Countries of recruitment
Mexico

Study participating centre
National Institute of Cardiology "Ignacio Chavez"
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Sponsor information

Organisation
National Institute of Cardiology "Ignacio Chavez"

ROR
https://ror.org/046e90j34

Funder(s)

Funder type
Government

Funder Name
Consejo Nacional de Ciencia y Tecnología

Alternative Name(s)
Secretariat of Science, Humanities, Technology, and Innovation, SECIHTI

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Mexico

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from Dr Claudia Huesca-Gomez (c_huesca@yahoo.com).

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results		05/12/2016	24/04/2019	No	No