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Diuretics and Diabetes Control: DIaDIC study

Submission date
20/07/2013

Recruitment status
No longer recruiting

Registration date
01/08/2013

Overall study status
Completed

Last Edited
01/08/2013

Condition category
Nutritional, Metabolic, Endocrine

[X] Prospectively registered

[_] Protocol

[_] Statistical analysis plan

[X] Results

[_] Individual participant data

Plain English summary of protocol

Background and study aims
Diuretics are the most commonly used drugs for the treatment of high blood pressure, even in patients with diabetes. It is known that thiazide and loop diuretics have side effects that favour diabetes. They also usually cause an increase in blood levels of uric acid (hyperuricemia). We are carrying out a study to find out if stopping diuretic treatment and changing to a different drug for high blood pressure may improve glucose tolerance in diabetic and non-diabetic patients. If confirmed, this treatment variation could reduce the occurrence of diabetes, hyperuricemia and the resulting risk of heart disease associated with these conditions.

Who can participate?
At least 80 male and female patients with high blood pressure, aged 30-80 years, including non-diabetic, pre-diabetics and diabetics on diuretic treatment.

What does the study involve?
Participants will be randomly divided into two groups: one group will continue the treatment with diuretics, while for the other group the diuretic will be replaced with a drug called amlodipine. Both groups will be followed for about 6 weeks. At the start of the study and at the end of the follow-up all patients will undergo clinical examinations. In addition, every week participants will either be contacted over telephone or they will have to visit the clinic to regulate the treatment.

What are the possible benefits and risks of participating?
Patients may experience an improvement in glucose metabolism, reducing the risk of heart disease. There are no specific risks and patients will be monitored every week for the whole duration of the study.

Where is the study run from?
The study has been set up by the University of Palermo, Biomedic Department of Internal and Specialistic Medicine (DIBIMIS), Italy.

When is the study starting and how long is it expected to run for?
The study is starting in September 2013 and will last until March 2014.

Who is funding the study?
Funding will be provided by the University of Palermo (Italy), the AOU Policlinico Paolo Giaccone and the non-lucrative Association of Nutrition and Health (Associazione Onlus Nutrizione e Salute), Italy.

Who is the main contact?
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Contact information

Type(s)
Scientific

Contact name
Prof Silvio Buscemi

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Additional identifiers

Protocol serial number
2/2013

Study information

Scientific Title
Effects of withdrawing diuretic therapy (thiazide or loop), used for the treatment of hypertension, on glucose metabolism in subjects with normal glucose tolerance, pre-diabetes or type 2 diabetes: a randomized controlled trial

Study objectives
Diuretics (thiazide and loop) have a deleterious effect on glucose tolerance. Discontinuation of anti-hypertensive diuretic treatment may improve glucose tolerance and reduce the hypoglycemic treatment in type 2 diabetics.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Local Ethical Committee of the University Hospital of Palermo (I) approved on the 22th May 2013 (ref. 06/2013)

Study design
Randomized single-blind longitudinal intervention trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Hypertension, diabetes, cardiovascular risk

Interventions
Evaluation at 6 plus or minus 1 week of the cardiovascular and metabolic effects of two different treatments of hypertension: a) continuation of the previous antihypertensive treatment that includes a diuretic vs. b) replacement of the diuretic with the calcium channel blocker amlodipine (according to a pre-specified flow-chart of dose regulation). Study participants will be assigned to one of two treatment groups randomly. The changes of therapy will be decided by investigators not in direct contact with the participants and those who will carry out the investigations will not be aware of the treatment (single-blinded).
Amlodipine 2,5-10 mg orally, once a day vs. hydrochlorotiazide12,5-25 mg or furosemide 10-20 mg orally once a day for 6+/-1 weeks.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Amlodipine, hydrochlorotiazide and furosemide

Primary outcome(s)
1. Effects on carbohydrates and uric acid metabolism:
Fasting plasma glucose; postprandial glycemia, glycated hemoglobin, glycemia 2h after glucose oral load (75g), 7-day mean glycemia and glycemic variability from continuous subcutaneous glucose monitoring, basal insulinemia, HOMA-I (homeostasis model assessment-index), HOMA-beta, QUICKI (quantitative insulin-sensitivity check index), change in hypoglicemic therapy in diabetics, serum uric acid concentrations.

Key secondary outcome(s))
Effects on cardiovascular and renal performances:
1. Endothelial function (measured as "flow-mediated dilation")
2. Urinary isoprostanoids
3. Cardiac function evaluated by means of echocardiography, self-monitoring of blood pressure, 24h ambulatory blood pressure monitoring
4. Intra-renal resistances by means of echo-doppler RI (resistance index) and PI (pulsatility index)
5. Creatinine concentrations, calculated Glomerular filtration rate (GFR) [MDRD, Modification of Diet in Renal Disease; CKEPI, Kidney Disease Outcomes Quality Initiative; KDOQI, Chronic Kidney

Disease Epidemiology Collaboration]
6. Serum cholesterol, HDL-cholesterol, triglycerides concentrations
Outcomes are measured before and 6+/-1 weeks after randomization

Completion date
31/03/2014

Eligibility

Key inclusion criteria
1. Male and female subjects
2. Aged 30-80 years
3. Having hypertension for less than 15 years
4. Basal blood pressure <140/90 mmHg
5. Non diabetics or having diabetes for less than 15 years
6. Using at least one of the following diuretics for more than 6 months: furosemide, torasemide, hydrochlorothiazide, chlorthalidone

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Average 24 hour blood pressure from ambulatory blood pressure monitoring > 160/90 mmHg
2. Concomitant use of >3 anti-hypertensives
3. Habitual use of indapamide, spironolactone, calcium channel blockers
4. Habitual use of FANS, corticosteroids, litium salts
5. Allergy or intolerance versus calcium-channel blockers
6. Self monitoring average glycemia > 250 mg/dl
7. Glycated hemoglobin > 86 mol/mol
8. Habitual smokers: more than 10 cigarette/day
9. Habitual use of super-alcoholics or wine more than 1 glass/day
10. Secondary hypertension, congestive heart failure, liver cirrhosis, chronic renal failure (calculated -CKEPI, MDRD - GFR< 40 ml/min/1.73 m2)
11. Connective diseases
12. Severe gastro-oesophageal reflux with Barrett's esofagus
13. Atrioventricular conduction defects
14. Pregnancy or lactation in the last six months
15. Denial of informed consent

Date of first enrolment
01/09/2013

Date of final enrolment
31/03/2014

Locations

Countries of recruitment
Italy

Study participating centre
Dipartimento Biomedico di medicina Interna e Specialistica (DIBIMIS)
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Sponsor information

Organisation
University of Palermo (Italy)

ROR
https://ror.org/044k9ta02

Funder(s)

Funder type
University/education

Funder Name
University of Palermo (Italy)

Funder Name
Policlinico "P. Giaccone" - Palermo (Italy)

Funder Name
Onlus Nutrition and Health (Associazione Onlus Nutrizione e Salute) (Italy)

Results and Publications

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	01/12/2013		Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes