ISRCTN33941607 https://doi.org/10.1186/ISRCTN33941607

Effects of eplerenone in patients with primary hyperparathyroidism

Submission date
22/09/2011

Recruitment status
No longer recruiting

Registration date
20/02/2012

Overall study status
Completed

Last Edited
18/09/2017

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
Primary hyperparathyroidism (PHPT) occurs when too much of an hormone called parathyroid hormone (PHT) is produced, leading to high levels of calcium in the blood. This may be associated with cardiovascular (heart) problems such as myocardial ischemia (decreased blood flow to the heart), arrhythmia (heart rhythm problems), arterial hypertension (high blood pressure), endothelial dysfunction (problems with the inner lining of blood vessels) and metabolic abnormalities. Increasing evidence suggests a link between PHT and another hormone called aldosterone. Primary aldosteronism occurs when too much aldosterone is produced. It is suggested that the treatment of either disease (primary aldosteronism or PHPT) has a positive effect on the other. The aim of this study is to find out whether aldosterone inhibition by the drug eplerenone has beneficial effects on the cardiovascular system, bone metabolism and kidney function. The expected outcome is that in PHPT patients treatment with eplerenone decreases PTH levels, improves bone metabolism and decreases blood pressure and cardiovascular pathology.

Who can participate?
Male and female patients aged 18 and over, who have asymptomatic PHPT (i.e., without symptoms) and do not meet the guidelines for surgical treatment, or patients with symptomatic PHPT (i.e., with symptoms) in whom surgery is recommended but not performed because of patient and/or physician preference or medical reasons.

What does the study involve?
Participants are randomly allocated to be treated for 8 weeks with either eplerenone or a dummy drug called a placebo.

What are the possible benefits and risks of participating?
Eplerenone may have additional positive health effects (e.g. muscular) which may be of additional benefit for the study participants. Previous studies documented no significant differences in the incidence of severe adverse events in participants receiving eplerenone compared to those on placebo. To minimize potential harm to the patients, there will be several visits taking place more frequently in the early phase of the study, to guarantee timely detection of potential adverse effects.

Where is the study run from?
Medical University of Graz, Department of Internal Medicine, Division of Cardiology and Division of Endocrinology and Metabolism (Austria)

When is the study starting and how long is it expected to run for?
July 2012 to June 2015

Who is funding the study?
Austrian National Bank (Austria)

Who is the main contact?
Dr Andreas Tomaschitz
andreas.tomaschitz@gmx.at

Contact information

Type(s)
Scientific

Contact name
Dr Andreas Tomaschitz

Contact details
Medical University of Graz
Department of Internal Medicine
Divison of Cardiology
Auenbruggerplatz 15
Graz
Austria
8036
+43 (0)316 385 12544
andreas.tomaschitz@gmx.at

Additional identifiers

Clinical Trials Information System (CTIS)
2011-005683-21

Protocol serial number
4.0: 30.01.2012

Study information

Scientific Title
Effects of eplerenone on parathyroid hormone levels in patients with primary hyperparathyroidism: a randomized, double-blind, placebo-controlled trial

Acronym
EPATH

Study objectives
In patients with primary hyperparathyroidism (PHPT) Mineralocorticoid-receptor (MR) blockade with eplerenone improves cardiovascular and bone health.

The trialists propose a randomized controlled trial to test this hypothesis in PHPT patients. The expected outcome is that in PHPT patients inhibition of aldosterone mediated effects by MR-blockade with eplerenone results in:
1. A decrease of PTH levels
2. Positive effects on bone metabolism reflected by markers of bone metabolism
3. Decreased blood pressure and cardiovascular pathology

The majority of studies noted that even mild forms of primary hyperparathyroidism (PHPT) are associated with higher risk of cardiovascular morbidity and mortality. The precise mechanisms underlying these associations in patients with PHPT their potential role as therapeutic targets are currently not fully elucidated.

Increasing evidence suggests a clinically relevant interplay between aldosterone and PTH. Most studies in humans identified a positive correlation between aldosterone and PTH levels particularly in patients with PHPT. Some studies advocated that PTH is a direct or indirect stimulus for of aldosterone synthesis and secretion in the adrenal, This is of utmost clinical importance, as several studies documented that aldosterone is a major cardiovascular risk factor. Given the linkage between aldosterone and PTH it is suggested that treatment of either disease (primary aldosteronism and PHPT) results in positive effects in the other hormone system.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics Committee of Medical University of Graz, Austria, 12/12/2011, ref: 24-032 ex 11/12

Primary study design
Interventional

Study design
Single-center randomized double-blind placebo-controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Primary hyperparathyroidism (PHPT)

Interventions
Overall, 110 participants will be randomized to 8 weeks of double-blind treatment with eplerenone 25mg and 50 mg once daily, respectively.

Eplerenone will be initiated at 25 mg once daily and titrated to 50 mg once daily after 4 weeks as tolerated by the patient. The study consists of a 8-weeks, double-blind, randomized (active) treatment period: after 8 weeks of randomized treatment the primary outcome [mean change of iPTH(1-84) levels] will be evaluated.

Intervention Type
Drug

Phase
Phase III

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

Primary outcome(s)
Mean change of iPTH(1-84) levels from baseline after 8 weeks

Key secondary outcome(s)
1. Mean change of 24-hour systolic and diastolic ambulatory BP levels from baseline after 8 weeks
2. Mean change of NT-pro-BNP and osteoprotegerin from baseline after 8 weeks
3. Mean change of biomarkers of bone metabolism: osteocalcin, β-CrossLaps, bone alkaline phosphatase

Completion date
30/06/2015

Eligibility

Key inclusion criteria
1. Written informed consent
2. Patients with PHPT:
2.1. Asymptomatic PHPT who do not meet guidelines for surgical treatment
2.2. Symptomatic PHPT in whom surgery is recommended, but not performed because of patient and/or physician preference or perceived medical contraindications
3. Age ≥ 18 years

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria

1. 25 - hydroxy vitamin D [25(OH)D] levels < 20 ng/dl (50 nmol/liter)
2. Estimated glomerular filtration rate (eGFR; according to the MDRD formula) ≤ 50 ml/min
3. Serum potassium > 5.0 mEq/L (mmol/L) at baseline or > 5.5 mEq/L (mmol/L) during active study period
4. Pregnancy or lactating women
5. Drug intake as part of another clinical study 4 weeks before enrolment into the EPATH study and/or during the active study period
6. Any disease with an estimated life expectancy below 1 year
7. Chemotherapy or radiation therapy during the study
8. Intolerance to eplerenone or any ingredient occurring in eplerenone
9. Severe acute or chronic liver diseases (Child-Pugh Class C)
10. Concurrent intake of potassium sparing drugs, e.g. diuretics (amiloride and triamterene) or CPY3A4-inhibitors and ongoing potassium supplementation

Date of first enrolment
01/07/2012

Date of final enrolment
30/06/2015

Locations

Countries of recruitment
Austria

Study participating centre
Medical University of Graz
Graz
Austria
8036

Sponsor information

Organisation
Medical University of Graz (Austria)

ROR
https://ror.org/02n0bts35

Funder(s)

Funder type
Government

Funder Name
Austrian National Bank (Austria) (Jubiläumsfond ref: 14621)

Alternative Name(s)
Austrian National Bank, National Bank of Austria, The Oesterreichische Nationalbank (OeNB), Die Oesterreichische Nationalbank (OeNB), OeNB

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Austria

Funder Name
Medical University of Graz (Austria)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/12/2017		Yes	No