Strain-area loop in drug-induced (Selexipag (Uptravi(®))) afterload reduction of the right ventricular in pulmonary arterial hypertension

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Heart failures
Study type	Observational non invasive

Summary

ID

NL-OMON46728

Source
ToetsingOnline

Brief title
SALDIAPAH

Condition

- Heart failures
- Vascular hypertensive disorders

Synonym
pulmonary arterial hypertension, raised blood pressure in the pulmonary artery

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: ACTELION;farmaceutische industrie

Intervention

Keyword: Pulmonary arterial hypertension, Selexipag, Strain-area loop, Strain-volume loop

Outcome measures

Primary outcome

Primary endpoints are characteristics of the strain-area loop; slope systolic

deformation (Sslope), slope diastolic deformation (Dslope).

Secondary outcome

Secondary endpoints

- occurrence of cardiovascular events and hospital admissions in the first two

years after starting selexipag

- characteristics of strain-area loop; intersection with the X-axis (RVEDA),

intersection with the Y-axis (peakstrain)

Study description

Background summary

Pulmonary arterial hypertension (PAH) is a rare, progressive disease with a rather poor prognosis. In PAH patients, there is an increased resistance in the pulmonary artery, forcing the right ventricle to produce increased pressure to circulate the same amount of blood. This influence the right ventricle hemodynamics. Due to the increased pressure, the right ventricle become hypertrophic, thereafter dilated and finally results in right heart failure.
Drug therapy in PAH aims to reduce the pulmonary resistance. Current methods to determine the vascular resistance reliable are invasive and therefore not practical to evaluate therapeutic success.
The introduction of Specke tracking echocardiography provides the opportunity to measure wall deformation (so called strain). By combining concomitant

temporal echocardiographic measures of strain and area of the ventricles a strain-area loop can be constructed. With this strain-area loop it is possible to measure hemodynamical changes in the heart. Previous studies showed that the strain-area loop characteristics changes as the invasive measured pulmonary artery pressure raises.
To explore the usability of this new non-invasive technique, we will examine whether drug-induces afterload reduction with Selexipag, a prostaglandin receptor antagonist, will influence the characteristics of the strain-area loop in PAH patients. In the future, this could be useful to follow-up PAH patients. Besides this, we will examine whether or not changes in characteristics of the strain-area loop have prognostic value.

Study objective

Our primary objective is to determine whether drug-induced reduction in pulmonary afterload causes a change in strain-area loop after 17 weeks of use of selexipag (maximum tolerable dose 2dd 1600 micrograms / day).
Secondary objective is to investigate whether the drug-induced changes of the strain-area loop have prognostic value regarding the occurrence of cardiovascular events (death, hospitalization due to exacerbation of PAH) and disease progression based on NYHA classification and a 6MWD test within two years.

Study design

Explorative prospective study in which 25 PAH patients (WHO 1, NYHA II-III) will undergo a non-invasive echocardiogram before and 17 weeks after the start of selexipag to obtain strain-area loops. The occurrence of clinical cardiovascular events, hospital admissions and disease progression based on functional NYHA classification and the 6 MWD test will be reported for two years.

Study burden and risks

Test subjects will be treated with Selexipag on clinical grounds according to international guidelines and on the advice of the multidisciplinary pulmonary hypertension team of the Radboudumc Expertise center for pulmonary hypertension. Previous studies have shown that PAH patients benefit from this drug, which results of a reduction in mortality and from complications related to PAH. This study also shows that Selexipag is safe whereby the chance of serious adverse events is not increased. A few adverse events, mostly gastrointestinal side effects, occurred more frequently. These complaints outweigh the possible positive effects on health.
Subjects will undergo several echocardiograms. This measurement is non-invasive and does not involve any degree of risk.
This study provides not only more insight into PAH and the effects of drug

treatment, but may also indicate the application of a simple, non-invasive measurement that can be used during the follow-up of PAH patients to determine the effectiveness of the drug. These are potentially important benefits.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- men and female patiënts, aged betweent 18 and 75 years old
- PAH WHO group 1
- NYHA II-III
- decision to start with Selexipag/Uptravi(®) has already been taken
- legally capable, informed consent

Exclusion criteria

- pulmonary hypertension WHO group 2-5
- other prostacyclin usage < 1 month before inclusion
- moderate or severe obstructive lung disease
- severe restrictive lung disease
- moderate to severe liver function failure
- severe kidney failure
- BMI < 18.5
- receiving another study product <1 month before or during study
- life expectancy less than 12 months
- pregnancy during study time
- known sensitivity to study medication

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	19-09-2018
Enrollment:	25
Type:	Actual

Ethics review

Approved WMO

Date:	24-05-2018
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL64665.091.18