Right ventricular contractile reserve and oxygen consumption in pulmonary arterial hypertension

Published: 11-05-2020
Last updated: 10-04-2024

To investigate the effects of Dobutamine on RV contractility and oxygen consumption in patients with pulmonary arterial hypertension (PAH).

Ethical review	Approved WMO
Status	Pending
Health condition type	Heart failures
Study type	Interventional

Summary

ID

NL-OMON50331

Source
ToetsingOnline

Brief title
RV contractile reserve and oxygen consumption in PAH

Condition

- Heart failures

Synonym
Pulmonary arterial hypertension

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: VICI beurs A Vonk Noordegraaf

Intervention

Keyword: Dobutamine, Pulmonary arterial hypertension, Right heart failure

Outcome measures

Primary outcome

Main study parameters will be:

• Myocardial oxygen consumption (kmono [C11]-acetate)

• Contractility measured as end-systolic elastance (Ees). Which is calculated

using the single beat method

Secondary outcome

Secondary study parameters are:

• Serum dihydroxyphenylacetic acid (DOPAC), dihydroxyphenylglycol (DHPG),

norepinephrine (NE), normetanephrine (NMN), methoxyhydroxyphenylglycol (MHPG)

which are metabolites of catecholamine degradation by monoamine oxidase (MAO).

• Heart rate

Study description

Background summary

In the pulmonary hypertension (PH) guidelines inotropic support with dobutamine is the recommended treatment in patients with decompensated right heart failure due to PH. However recent research has shown that during exercise RV contractile reserve is diminished in PH patients. In addition, Dobutamine is known to increase myocardial oxygen consumption. Hence, the efficacy of Dobutamine administration in patients with severe right heart failure could be questioned. Therefore we aim to study the effects of Dobutamine on RV contractility and oxygen consumption.

Study objective

To investigate the effects of Dobutamine on RV contractility and oxygen

consumption in patients with pulmonary arterial hypertension (PAH).

Study design

This is a prospective non-blinded, non-randomized interventional study. We will prospectively include 16 PAH or CTEPH patients in New York Health Association (NYHA) functional class III or IV.

To be able to correct for the impact of perfusion on the uptake patterns of the [11C]-acetate
tracer, a [15]-H2O scan will be performed first at both days. Subsequently, the [11C]-acetate scan will be performed. Low-dose CT-scans will be performed for attenuation correction. During the PET-procedures, venous samples will be collected at different time points.

On day 1 a CMRI and PET-scan will be performed in resting conditions. On day 2, patients will undergo a right heart catheterization. During RHC blood samples are withdrawn for catecholamine levels before and after initiation of dobutamine infusion. Dobutamine infusion is started after baseline measurements. After 10 minutes of infusion peak plasma concentrations and peak effects occur. Dobutamine infusion is discontinued when the second PET-scan and CMR are obtained.

Abbreviations: CMRI = cardiac magnetic resonance imaging, CT = computed tomography, RHC = right heart catheterization.

Intervention

Not applicable

Study burden and risks

Extensive study protocol where patients are scanned (PET + CMR) on two consecutive days and will undergo a right heart catheterization. The tracers are given through one intravenous (iv) line in a peripheral vein. Blood samples are withdrawn from the same iv-line. The total amount of blood is 120 ml during the entire protocol. The radiation dose of 7.0 mSv remains below the allowed maximum radiation dose of 10 mSv. The right hearth catheterization and one CMR in the protocol are standard follow up procedures. Dobutamine dosage is low; 10 µg.kg-1.min-1, which was well tolerated by PAH patients in earlier studies.

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

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
• Age >18 years
• Patients have to be diagnosed with idiopathic -, hereditary -, or drug- and toxins induced PAH or chronic thrombo-embolic pulmonary hypertension (CTEPH) conform ESC/ERS guidelines. PAH is diagnosed when the following criteria are met:
o Mean Pulmonary Artery Pressure (mPAP) >= 25 mmHg
o Pulmonary Arterial Wedge Pressure (PAWP) > 15 mmHg
o Other possible causes of PAH are excluded

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:

• <1 year since last participation in research that included nuclear imaging
• Congenital heart disease
• Left sided heart disease
• Pulmonary Hypertension other than idiopathic -, hereditary -, or drug- and toxins induced PAH or CTEPH
• Known coronary artery disease
• Pregnancy
• Malignancies
• Kidney failure
• Anemia (Hb < 8.0)
• Atrial fibrillation
• Use of β-blockers or α-blockers
• Use of ACE-inhibitors
• Age > 70 years

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2020
Enrollment:	15
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Dobutamine
Generic name:	Dobutamine
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	11-05-2020
Application type:	First submission
Review commission:	METC Amsterdam UMC

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
EudraCT	EUCTR2017-004844-40-NL
CCMO	NL64257.029.18