Ammendment of protocol: Intravenous iron treatment in iron deficient patients with idiopathic pulmonary arterial hypertension. Title amendment: Skeletal muscle strength in healthy persons and patients with pulmonary hypertension

Published: 09-11-2010
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To evaluate the effects of intravenous iron suppletion in iron deficient PAH patients.Amendment: to compare exercise capacity and isolated muscle strength in IPAH patients and healthy controls

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Muscle disorders
Study type	Interventional

Summary

ID

NL-OMON39402

Source
ToetsingOnline

Brief title
Treating iron deficiency in pulmonary hypertension.

Condition

- Muscle disorders
- Pulmonary vascular disorders
- Vascular hypertensive disorders

Synonym
high blood pressure in the lung vasculature, pulmonary hypertension

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Exercise capacity, Iron deficiency, Muscle strenght, Pulmonary hypertension

Outcome measures

Primary outcome

Six minute walking distance

Amendment: contractile force and structure of single quadriceps muscle fibers

Secondary outcome

cardiopulmonary exercise test (VO2max), myoglobin concentration in quadriceps muscle, serum iron parameters, serum hepcidin and interleukin-6 (IL-6), muscle strength, quality of life (QOL), and NYHA functional class, cardiac function (MRI).

Amendment: Submaximal CPET (75% Wmax)

Study description

Background summary

Patients with pulmonary arterial hypertension (PAH) develop progressive right heart failure which eventually will lead to death. During the progression of the disease the physical performance of these patients deteriorates. Maintaining there exercise capacity is a major goal in PAH treatment. Iron

treatment is known to have a positive effect on physical performance in patients with left heart failure and iron deficiency. Whether this is also effective in patients with right heart failure (PAH) and iron deficiency is until now not investigated.

Amendment: Preliminary results of the iron study (NL33043.029.10) have revealed that administration of iron improves the exercise capacity of iron deficient PAH patients. However, no change in maximal force, calcium sensitivity and passive force was measured in the biopsies of the quadriceps muscle (ex vivo). With the quadriceps biopsies we are the first to measure muscle strength and are able to show that although there
might be atrophy of the muscle, the intrinsic properties of the sarcomeres seems to be intact. The contradiction between exercise capacity and muscle strength is interesting and requires further investigation. Therefore, we would like to include healthy age matched controls to further increase our understanding of the correlation between in vivo exercise capacity and ex vivo muscle strength.

Study objective

To evaluate the effects of intravenous iron suppletion in iron deficient PAH patients.

Amendment: to compare exercise capacity and isolated muscle strength in IPAH patients and healthy controls

Study design

In this study, 30 idiopathic IPAH patients with iron deficiency will be included. The patients must have stable disease for at least 3 months under optimal treatment. At baseline 6MWD, maximal and submaximal (75% Wmax) cardiopulmonary exercise testing (CPET), and a biopsy of the quadriceps muscle are performed. Also blood iron parameters are measured and hepcidin, IL-6 and TNF-* levels are determined, a QOL questionnaire has to be filled in, and NYHA functional class is established. Cardiac function is measured by MRI. Patients receive iron infusions weekly until iron levels are restored (correction phase), followed by monthly infusions to maintain iron levels (maintenance phase). The endpoint is 12 weeks after the iron infusion and all baseline measurements are repeated.

Amendment: 10 healthy control subjects visit the hospital for maximal and submaximal CPET, general lab measurements and quadricepsbiopsy

Intervention

Included patients receive a high dose iron infusion of 1000mg iron in 250 ml

NaCl 0.9%. Before iron infusion, blood samples are drawn to measure iron parameters. Four weeks after iron administration, iron parameters are measured in the general practitioners setting. When iron parameters are still under normal values, a repeat infusion will be given of 500 mg iron (equals 10 ml Ferinject).

Amendment: not applicable

Study burden and risks

The patients will be hospitalised two days at the beginning and two days at the end of the study to perform the exercise and strength tests, six minute walking distance and for biopsy of the quadriceps muscle. Also NYHA functional class will be determined and a QOL questionnaire has to be filled in. Patients then receive a high dose iron infusion (1000mg iron). They will get an intravenous line in the elbow for iron infusion. This intravenous line gives some small discomfort for the patients, however this is a very regularly done procedure. The risks of Ferinject infusion are headache, gastrointestinal complaints (nausea, vomiting), fever, hypotension, muscular pain, paresthesia, urticaria, anaphylactic reactions and phlebitis at injection side or discomfort of the infusion fluid. Around administration, patients are extensively monitored. We hypothesize that iron deficient IPAH patients will benefit from iron treatment with improved exercise capacity.

Amendment: The control patients will be in the hospital for one day in this study to perform the exercise tests, and for biopsy of the quadriceps muscle

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

Idiopathic pulmonary arterial hypertension and iron deficiency
Amendment: Healthy controls

Exclusion criteria

Current or recent iron treatment
Current other research treatment
Known history of anemia of other causes
Chronic (inflammatory) disease other than PAH
Amendment: Current or history of skeletal muscle problems and/or coagulation disturbances

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-01-2011
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Ferinject
Generic name:	Ferric carboxymaltose
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	09-11-2010
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-12-2010
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-02-2011
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-05-2013
Application type:	Amendment
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	EUCTR2010-023233-30-NL
CCMO	NL33043.029.10

Study results

Date completed:	01-03-2013
Actual enrolment:	20