Immunoglobulin therapy for patients with idiopathic cardiomyopathy and endomyocardial parvovirus B19 persistence - a prospective, double-blind, randomized, placebo-controlled clinical trial

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A controlled trial to investigate whether high dose of intravenous immunoglobulin (IVIg) in addition to conventional heart failure therapy in patients with idiopathic cardiomyopathy and PVB19 persistence in the heart achieves improvement of cardiac...

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

Summary

ID

NL-OMON33416

Source
ToetsingOnline

Brief title
IVIg for PVB19 mediated cardiomyopathy

Condition

- Myocardial disorders
- Viral infectious disorders

Synonym
viral mediated heartfailure

Research involving
Human

Sponsors and support

Primary sponsor: Sanquin Plasmaproducten
Source(s) of monetary or material Support: Sanquin Plasmaproducten

Intervention

Keyword: Cardiomyopathies, Human, Immunoglobulins, Intravenous, Parvovirus B19, Therapy

Outcome measures

Primary outcome

The main study parameter is the change in cardiac ejection fraction presence of the heart from baseline to endpoint.

Secondary outcome

Secondary parameters include changes in presence of cardiotrophic viruses (per µg DNA of PVB19, HHV-6, EV, ADV, EBV), inflammation (CD45-staining lymphocytes per/mm2), fibrosis (collageen volume fractie /mm2), cardiac functional capacity (NYHA functional class), patient quality of life (Minnesota Living with Heart Failure Questionnaire), other echocardiographic parameters (LVEDD, LVESD).
Tertiary parameters: The change in antibodies titers against Parvovirus B19 antigens VP1/VP2 and NS1 (non-structural protein). These antibodies will be compared to the antibodies present in the used Nanogam batches and associated with changes in the presence of specific PVB19 subtypes.

Study description

Background summary

Parvovirus B19 (PVB19) persistence in the heart has been associated with progressive cardiac dysfunction and evolution to idiopathic cardiomyopathy.

Study objective

A controlled trial to investigate whether high dose of intravenous immunoglobulin (IVIg) in addition to conventional heart failure therapy in patients with idiopathic cardiomyopathy and PVB19 persistence in the heart achieves improvement of cardiac function in conjunction with virus elimination. Moreover, the titer of B19-antibodies in the serum of the patients will be determined before and after infusion, and in the used IVIg product .

Study design

A prospective, randomized, double-blind, placebo-controlled trail to evaluate the effect of IVIg on virus presence and cardiac functional capacity before and 6 months after IVIg therapy.

Intervention

Intervention: Patients will be randomised into 2 groups. Both groups will continue with their regular heart failure regimen. Group A will receive a total dose of 2 gr/kg bodyweight of intravenous immunoglobulin product Nanogam® administered as 0.5 gr/kg IV over a period of 6 hours on each of 4 consecutive days. Group B will receive placebo, an inactive medication indistinguishable from the interventional drug. As placebo the plasma volume expander G.P.O. (* Gepasteuriseerde Plasma-eiwit Oplossing*) is used.

Study burden and risks

All patients will undergo routine diagnostic work-up, treatment and follow-up for their heart failure. Patients will be randomized to either receive IVIg or placebo, G.P.O., on top of their standard heart failure regimen. Patients receiving IVIg might have benefit from treatment because of elimination of PVB19. During the infusion the patient will be hospitalized for four days. Undesirable side effects from plasma products are usualy mild. After 3 month and 6 months there will be follow-up visits. The visits and investigations are part of the routine check-up, except for the endomyocardial biopsy (EMB) after 6 months. The procedure to obtain EMBs is a safe one, with a very low risk (<0.5 %) of peri-procedure complications.
Before the infusion 1 extra blood sample of 10 ml and 3 of 5 ml will be taken. Moreover, in order to monitor the presence of antibodies against PVB19 and total IgG levels in total 40 ml blood will be taken in 6 months (3 x 10 ml and 2 x 5 ml). Furthermore, 30 ml (3 x 10ml) blood will be used for future research. Moreover, at baseline and after 6 months a questionnaire should be to be filled out.

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

* Symptomatic idiopathic cardiomyopathy >6 months
* Optimal conventional heart failure medication ><=3 months
* PVB19 viral load >200 copies/mcg DNA in endomyocardial biopsies
* Signed informed consent
* Age between 18 and 75 years

Exclusion criteria

* Other causes for heart failure:
o Significant coronary artery disease (lesions >70 % stenosis).
o Significant valvular disease

o Untreated hypertension (blood pressure >140mmHg)
o Substance abuse
o Chemotherapy induced
*Significant titer of other cardiotrophic viruses (EV, ADV, HHV6, EBV)
*Pregnancy or lactation
* Systemic diseases such as sarcoidosis, giant cell myocarditis, hemochromatosis, or systemic autoimmune diseases.
* Treatment with any other investigational drug within 7 days before study entry or previous enrolment in this study
* Known with allergic reactions against human plasma or plasma products
* Having an ongoing progressive terminal disease, including HIV infection
* Having renal insufficiency (plasma creatinin >115µmol/L or creatinin clearance <20 ml/min)
* Having an ongoing active disease causing general symptoms e.g. chronic active hepatitis, persistent enterovirus infection with ongoing systemic complaints.
* Having detectable anti-IgA antibodies
* Active SLE

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	30-10-2009
Enrollment:	50
Type:	Actual

Medical products/devices used

Product type:	Medicine

Brand name:	G.P.O.
Generic name:	Pasteurised plasma protein solution
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Nanogam
Generic name:	human normal intravenous immunoglobulin
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	23-03-2009
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	06-08-2009
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	30-01-2013
Application type:	Amendment
Review commission:	MEC academisch ziekenhuis Maastricht/Universiteit Maastricht, MEC azM/UM (Maastricht)

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	EUCTR2009-009463-61-NL
ClinicalTrials.gov	NCT00892112
CCMO	NL27156.068.09