Immunoadsorption in anti-glomerular basement membrane glomerulonephritis, a pilot study.

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To study the efficacy, adverse events, logistic feasibility and costs of immunoadsorption for the removal of anti-GBM antibodies in patients with acute renal failure due to anti-GBM glomerulonephritis.

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

Summary

ID

NL-OMON41748

Source
ToetsingOnline

Brief title
Immunoadsorption in anti-GBM glomerulonephritis.

Condition

- Autoimmune disorders
- Nephropathies

Synonym
Anti-GBM disease; in combination with pulmonary involvement: Goodpasture's disease.

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W,Fresenius Medical

Care

Intervention

Keyword: GBM, Glomerulonephritis, Immunoadsorption, Renal failure

Outcome measures

Primary outcome

Plasma levels of anti-GBM before and after each immunoadsorption treatment. The main study parameter is the number of days that anti-GBM antibody titre is above a toxic level, defined as >30 ELISA units. Courses of anti-GBM titres will be compared with an historical cohort of patients with anti-GBM disease treated with plasma exchange.

Secondary outcome

1. Tolerability and adverse events of immunoadsorption.

2. Logistic feasibility. We will specifically assess the time between diagnosis and start of the first immunoadsorption treatment.

3. Costs: both personnel requirements and material costs.

Study description

Background summary

Anti-glomerular basement membrane (anti-GBM) glomerulonephritis is a rare organ-specific autoimmune disease that is mediated by anti-GBM antibodies. It is characterized by acute renal failure due to diffuse crescentic glomerulonephritis, often accompanied by pulmonary hemorrhage. Established treatment is cyclophosphamide and corticosteroids to suppress anti-GBM production and daily plasma exchange to remove circulating anti-GBM antibodies. The vast majority of patients with anti-GBM glomerulonephritis present at relatively late stages of the disease and develop irreversible end-stage renal failure despite treatment.

The treatment goal in anti-GBM glomerulonephritis is to achieve undetectable anti-GBM titres as rapid as possible. Immunoadsorption is an extracorporeal technique that may lower anti-GBM titres more effectively than plasma exchange. With this technique the patient*s plasma is passed through an immunoadsorption column that contains protein A that binds antibodies like anti-GBM antibodies. However, data on the efficacy of anti-GBM removal by immunoadsorption compared with plasma exchange are scarce. In the literature, there are only a few case descriptions of the clinical effect of immunoadsorption in patients with anti-GBM disease with some cases showing recovery of renal function despite unfavorable prognosis (serum creatinine >500 µmol/l and/or high percentage of crescents on renal biopsy).

Immunoadsorption is presently not used in the Netherlands for anti-GBM disease. Given the dismal renal prognosis of current standard therapy and the potentially higher efficacy for anti-GBM removal of immunoadsorption, it is justified to treat a cohort of patients with anti-GBM glomerulonephritis with immunoadsorption instead of plasma exchange in an open, non-randomized study using a strict protocol. We will specifically study the efficacy of immunoadsorption for the dynamics of anti-GBM removal, its tolerability and side effects, and the logistic feasibility and costs.

Study objective

To study the efficacy, adverse events, logistic feasibility and costs of immunoadsorption for the removal of anti-GBM antibodies in patients with acute renal failure due to anti-GBM glomerulonephritis.

Study design

Interventional, open, non-randomized, pilot study. After informed consent, patients will be treated according to the current treatment protocol with the exception of daily immunoadsorption instead of daily plasma exchange.

Intervention

Participating patients will be treated with daily immunoadsorption, instead of plasma exchange, until anti-GBM titres are undetectable. All other aspects of the treatment (e.g. immunosuppressive treatment, renal replacement therapy) will be standard.

Study burden and risks

From a patient*s perspective, the burden of daily immunoadsorption is comparable with that of daily plasma exchange with regard to vascular access (central venous catheter) and blood sampling to monitor treatment response. The treament time of one immunoadsorption treament is 1 hour longer compared with

the treatment time of plasma exchange. Possible adverse effects of immunoadsorption are part of the current study proposal but previous studies in other patient groups suggest that frequency and severity of adverse effects of immunoadsorption are comparable with plasma exchange. Therefore, it is justified to treat patients with anti-GBM glomerulonephritis with immunoadsorption instead of plasma exchange under study conditions because of the potential of immunoadsorption for a more effective removal of anti-GBM and the dismal renal prognosis of current treatment. Results of this study will provide the basis for a larger randomised trial to compare plasma exchange and immunoadsorption with regard to renal outcome. The results of that study will potentially benefit future patients with anti-GBM disease.

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

Acute renal failure due to anti-GBM glomerulonephritis with or without accompanying pulmonary involvement. Eligible patients must have a clinical picture met rapidly progressive glomerulonephritis in combination with one of the following: 1. serological evidence of circulating anti-GMB antibodies (Dotblot, Phadia, ELISA); 2. Renal biopsy with necrotising glomerulonephritis with linear fluorescence for IgG along the GBM. Notably, in case of serological evidence of circulating anti-GBM antibodies, a renal biopsy is not mandatory for inclusion in this study.

Exclusion criteria

There are no exclusion criteria. Because of the severity of the disease also patients with a short life expectancy will be included.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	11-05-2017
Enrollment:	8
Type:	Actual

Medical products/devices used

Generic name:	Immunoadsorption with Immunosorba column.
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	07-09-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	22-02-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL52379.042.15