Microcirculatory dysfunction plays a key role in uremic vasculopathy

Published: 08-06-2007
Last updated: 30-11-2024

In this trial we will investigate the following hypothesis:- Uremic vasculopathy develops, not only in large and medium sized conduit vessels, but also in the microcirculation.- There is a relationship between the rate of microcirculatory…

Ethical review	Approved WMO
Status	Will not start
Health condition type	Nephropathies
Study type	Observational non invasive

Summary

ID

NL-OMON30604

Source
ToetsingOnline

Brief title
ADMIRED = A'Dam Microcirculatory Insufficiency in REnal Disease

Condition

- Nephropathies
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
kidney disease, renal failure

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Baxter,firma dialyse-materialen

Intervention

Keyword: Endothelial dysfunction, Microcirculation, renal insufficiency, uremic vasculopathy

Outcome measures

Primary outcome

The microcirculation is disturbed in renal patients proportionally to the degree of renal failure. Pathophysiological insight into this phenomenon might show the way towards new treatment strategies.

Secondary outcome

Secondary markers of endothelial dysfunction (vWF, ICAM, etc), inflammation (CRP, cytokines) and insulin resistence (HOMA-IR) will be correlated with the primary study parameters.

Study description

Background summary

In the early stages of CRF (stage I) the risk on cardiovascular disease (CVD) is mainly determined by traditional risk factors, including hypertension, hypercholesterolemia and obesity. Both modifications in lifestyle and pharmacological treatment lower the risk on CVD analogous to non-renal patients. As renal function deteriorates (stages II and III), mild uremic vasculopathy develops, not only in large and medium size conduit vessels, but also in the microcirculation. As severe CRF (stage IV) progresses to end stage renal disease (ESRD, stage V), advanced uremic vasculopathy develops, which appears almost completely resistant to current treatment strategies. Reverse epidemiology emerges when traditional risk factors for CVD are overridden by other factors, such as a derangement of mineral metabolism, which is a characteristic feature of CRF. As a consequence, classical atherosclerosis is converted gradually in the syndrome of uremic vasculopathy, which is a distinct pathological entity consisting of both classical atherosclerosis and osteogenic calcifications in the intimal and medial layers of large and medium size conduit arteries, as well as in small resistance vessels. These alterations result in malnutrition, insulin resistance and catabolism of varies tissues. As uremic vasculopathy is different from classical atherosclerosis, conventional

anti-atherosclerotic therapy is less effective or not effective at all. Hence, it is of paramount importance to determine and characterize the underlying factors, in order to prevent or postpone the occurrence of uremic vasculopathy in patients with ESRD.

Study objective

In this trial we will investigate the following hypothesis:
- Uremic vasculopathy develops, not only in large and medium sized conduit vessels, but also in the microcirculation.
- There is a relationship between the rate of microcirculatory dysfunction [measured by capillary microscopy of the nailfold, laser Doppler flux metry, the sublingual Side-stream Darkfield (SDF) microscopy] and the vascular stiffness of the large vessels, as reflected in the increased pulse wave velocity.
- As medial calcification affects arterioles, we suppose that both the endothelium-dependent and endothelium-independent vasodilatation of the microcirculation will be disturbed.
- The rate of microcirculatory dysfunction correlates with the progression in renal failure. The microcirculatory dysfunction depends on renal function.
- Microcirculatory dysfunction sublingually (the tongue is the proximal part of the gastrointestinal tract) represents the disturbed microcirculation in other vital organs.
- So during a dialysis treatment the microcirculation could be visualised with the small and handy-sized SDF microscopy.

Study design

Uremic vasculopathy will be studied cross-sectional in 120 patients with various stages of CRF (grades I-V). CRF stage V will consist of 20 chronic hemodialysis and 20 chronic ambulant peritoneal patients. Both macro- and microcirculatory changes will be assessed and correlated with various laboratory parameters of endothelial activation. In addition, circulating endothelial cells as well as circulating endothelial progenitor cells will be assessed. With respect to mineral and lipid metabolism, at regular intervals various parameters will be measured, including calcium, phosphate, 1,25(OH)2 vit D, PTH and total chol/HDL/LDL/triglyceride. All medication prescribed will be recorded.
The insulin resistance index by homeostasis model assessment (HOMA-IR) will be used as an alternative method to assess insulin resistance in patients by measuring fasting glucose and fasting insulin.
In the prospective observational part of the study these parameters will be assessed annually within a follow-up period of 2 years in patients with CRF stage III with MDRD clearance < 35 ml/min and CRF stage IV. When dialysis will be started within these 2 years an extra vascular and blood measurement will be done at the start of renal replacement therapy.

Study burden and risks

In the cross sectional part of the study patients will participate in the study for a total of 4 hours. For the prospective observational part of the study, this will consist of patients with CRF stage III with MDRD clearance < 35 ml/min and CRF stage IV. This part of the study will consist 3 x 4 hours individually.
The sublingual microcirculation will be assessed by Sidestream Darkfield Imaging in combination with nitroglycerin. The nitroglycerin given sublingually can shortly cause headache and hypotension.
With the Laser Doppler Flowmetry in combination with iontophoresis some people will experience a feeling of numbness of the local skin. This is not painful or dangerous and is usually well tolerated.

Contacts

Public
Vrije Universiteit Medisch Centrum

De Boelelaan 1117
1081HV Amsterdam
NL
Scientific
Vrije Universiteit Medisch Centrum

De Boelelaan 1117
1081HV Amsterdam
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Patients > 18 years with chronic renal failure stages I-V.

Exclusion criteria

Patients < 18 years, life expectancy < 3 months due to non-renal disease. Diabetic patients and patients with autoimmune disease.

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Will not start
Start date (anticipated):	01-04-2007
Enrollment:	120
Type:	Anticipated

Ethics review

Approved WMO

Date:	08-06-2007
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
CCMO	NL14865.029.07