The peritoneal microvascular endothelial glycocalyx in peritoneal dialysis patients

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Ethical review	Approved WMO
Status	Pending
Health condition type	Nephropathies
Study type	Observational invasive

Summary

ID

NL-OMON34683

Source
ToetsingOnline

Brief title
Peritoneal endothelial glycocalyx in PD

Condition

- Nephropathies
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
peritoneal dialysis, peritoneal vascular abnormalities

Research involving
Human

Sponsors and support

Primary sponsor: AMC
Source(s) of monetary or material Support: Baxter Renal Discoveries Extramural Grant Program,Drs. C.A. Vlahu;MD;is funded by a grant from Baxter Renal Discoveries Extramural Grant Program

Intervention

Keyword: Peritoneal dialysis, Peritoneal glycocalyx, Peritoneal membrane, Peritoneal transport

Outcome measures

Primary outcome

1) The thickness of the peritoneal endothelial glycocalyx (as measured by

Orthogonal Polarization Spectroscopy)

2) The thickness of the sublingual endothelial glycocalyx (as measured by

Orthogonal Polarization Spectroscopy)

Secondary outcome

1) Parameters of peritoneal transport in PD patients

2) Morphological alterations of the peritoneal membrane

3) Glycocalyx constituents (hyaluronan, heparansulphate and syndecan-1) and

their regulating enzymes (hyaluronidase and heparanase) in plasma and dialysate

Study description

Background summary

Patients treated with chronic peritoneal dialysis (PD) develop alterations in peritoneal transport rates and ultrafiltration failure. Morphologically these are associated with vascular alterations that are partly diabetiform and partly atherosclerotic. The glycocalyx is a negatively charged mesh of membranous glycoproteins, proteoglycans and glycosaminoglycans situated at the luminal side of all blood vessels. It exerts a wide range of vasculoprotective effects like inhibition of coagulation, inhibition of leucocyte and platelet adhesion, regulation of redox state, shear-induced release of NO, regulation of endothelial permeability, being an important factor in vascular homeostasis. The glycocalyx is very sensitive to inflammatory mediators and hyperglycaemia, which alter the transendothelial permeability, probably leading to changes in the underlying cell-interstitial matrix, which in turn affects peritoneal transport. No information is available on the peritoneal microcirculatory

glycocalyx and its evolution in time during PD. Since this entity appears to influence transendothelial solute and water transport in many tissues throughout the body, it will be important to include the glycocalyx in studies of the peritoneal barrier and its pathophysiology.

Study objective

The aim of the study is to investigate the changes in peritoneal endothelial glycocalyx in end-stage renal disease (ESRD), with the duration of peritoneal dialysis, and relate these changes to alterations in peritoneal transport and morphology. Defining the role of the glycocalyx in this condition will guide further strategies on its preservation. The changes in the sublingual endothelial glycocalyx with time on renal replacement therapy (PD and transplantation) will also be investigated.

Study design

We will perform a cross-sectional observational study with invasive measurements.
Measurements of the peritoneal microvascular glycocalyx thickness will be done in:
- patients with ESRD starting PD or undergoing preemptive kidney transplantation,
- stable, prevalent PD patients free of acute inflammatory conditions and malignancy, undergoing any procedure involving the opening of the peritoneal cavity (kidney transplantation, incidental abdominal condition, PD related problems (excluding recent peritonitis), e.g. catheter replacement, catheter removal because of membrane failure),
- sex and age matched controls with normal renal function.
In incident peritoneal dialysis patients, OPS imaging of the peritoneal microvasculature will be done during the implantation of the peritoneal catheter by laparotomy. This will be repeated at the time of transplantation.
In addition, in prevalent peritoneal dialysis patients measurements of the peritoneal microvascular glycocalyx will be performed at the time of transplantation. Peritoneal transport function is assessed on a yearly basis using the Standard Peritoneal permeability Analysis (SPA) as part of regular follow-up of patients. Peritoneal biopsies will be performed in all participants except the PD patients undergoing a cadaveric kidney transplantation, at the time of surgery.
Relationships between peritoneal microvascular glycocalyx and parameters of peritoneal transport and morphology will be investigated.
For reference data on peritoneal glycocalyx, we will do measurements in otherwise healthy individuals, kidney donors undergoing nephrectomy.
All participants will undergo OPS imaging of sublingual microvasculature before surgery. In patients, this will be repeated at 3 and 12 months.
Furthermore, measurements of glycocalyx constituents (hyaluronan,

heparansulphate) and their regulating enzymes (hyaluronidase, heparanase), will be done in plasma and dialysate (when applicable).

Study burden and risks

The study consists of the following measurements which will all take place during the admission in the hospital: measurements of the sublingual endothelial glycocalyx, measurements of the peritoneal endothelial glycocalyx, body weight, blood pressure and blood sampling. The inform consent will be signed during a previous visit at the outpatient clinic.
Measurements of the sublingual endothelial glycocalyx will be repeated in patients during future visits at the outpatient (at 3months and 1year).
In all participants, in addition to the regular blood samples which are taken during their hospital admission or outpatient clinic visit, 20.5 ml of extra blood will be drawn once via vena puncture, and stored for analysis.
All PD patients will undergo a Standard Peritoneal permeability Analysis test (SPA). This test is performed in the AMC on a yearly basis as part of the regular follow-up of PD patients. It allows measurements of small solute transport, transport of proteins, and fluid kinetics. The methodology is well established. In patients who receive a kidney transplant and do not have a SPA performed in the last 3 months before the intervention, a SPA will be performed one week before surgery. PD patients coming from other hospitals for transplantation will also be invited to undergo a SPA one week before surgery. Since its introduction in the mid nineties more than 800 SPAs have been performed without problems, especially no anaphylactic reactions have occurred.
Peritoneal biopsy will be performed during surgery. There is a small risk of bleeding after biopsy but local hemostasis is applied. There is also a risk of leakage. As the chances of primary graft function in living-related transplant recipients are very high (more than 90%), and PD is discontinued immediately, the risk of leakage is acceptable. Above all, in most of these cases the peritoneal catheter is removed during transplantation. In the case of post-mortal transplantation, a peritoneal biopsy will not be performed due to the risk of delayed graft function, necessitating the continuation of PD postoperatively.

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

1. Patients with end stage renal disease starting peritoneal dialysis (PD) (at the moment of catheter implantation) or undergoing preemptive kidney transplantation;
2. Stable prevalent PD patients, free of acute inflammatory conditions and malignancy, undergoing any procedure involving the opening of the peritoneal cavity (kidney transplantation, incidental abdominal condition, PD related problems excluding recent peritonitis (4weeks prior to the measurements), e.g. catheter replacement, catheter removal because of membrane failure);
3. A control group: kidney donors undergoing nephrectomy;
4. Age: 18-60 years

Exclusion criteria

1. unstable clinical condition
2. smoking
3. recent history of peritonitis (peritonitis less than 4weeks prior to the measurement)
4. use of antioxidants

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-05-2010
Enrollment:	80
Type:	Anticipated

Ethics review

Approved WMO

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	NL30759.018.10