The reservecapacity of the peritoneum with the NO donor sodium nitroprusside during peritoneal dialysis

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The objective is to analyze whether a difference in reservecapacity is present between short-term and long-term PD patients. In case the reservecapacity of the peritoneum is significantly lower in the long-term compared to short-term PD patients, a...

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

Summary

ID

NL-OMON30602

Source
ToetsingOnline

Brief title
Peritoneal reservecapacity

Condition

- Other condition

Synonym
peritoneal membrane failure = impairment to remain on a certain dry weight with peritoneal dialysis

Health condition

aandoeningen ten gevolge van behandeling met peritoneale dialyse als nierfunctie vervangende therapie

Research involving

Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Nierstichting

Intervention

Keyword: peritoneal dialysis, peritoneal vascular surface area, vasodilation

Outcome measures

Primary outcome

The main study parameter is the difference in transport of small solutes by means of the mass transfer area coefficient (MTAC) of creatinine between the SPA with and without the addition of the vasodilator sodium nitroprusside. The difference in MTAC-creatinine between these SPAs will be compared between the short-term and the long-term PD group.

Secondary outcome

Secondary study parameters will be differences between the SPA with and without sodium nitroprusside in:

- Peritoneal solute transport of other small solutes: MTACs of the small solutes urea, urate and dialysate over plasma ratios (D/P) of creatinine, urea, urate, peritoneal glucose absorption
- Intrinsic permeability for macromolecules: clearances of *2-Microglobulin, albumin, immunoglobulin-G, *2-macroglobulin
- Peritoneal fluid kinetics
- Pore sizes of the peritoneal membrane

The baseline characteristics (age, gender, PD duration, end stage renal disease), markers for the peritoneal membrane, peritoneal membrane thickness of the patients will be described and analyzed for differences between the 2 groups.

Study description

Background summary

Peritoneal membrane failure is associated with an increase in the effective peritoneal vascular surface area, which is reflected by transport of small solutes. Its efficacy is determined by peritoneal blood volume. Therefore, the effective peritoneal vascular surface area can be influenced by vasoactive substances and the number of vessels perfused. This can be illustrated by the U-shaped time course for peritoneal solute transport, as described previously by Parikova et al. The initial high values suggest the influence of vasoactive substances. The subsequent decrease is followed by an increase, suggesting neoangiogenesis, a more permanent peritoneal membrane alteration. However, neoangiogenesis is not significantly related with the duration of PD, although significantly more vessels are present in patients with membrane failure. Furthermore, an increase in interindividual variability is present in peritoneal solute transport and ultrafiltration capacity with the duration of PD. This makes it rather difficult to predict which patients will develop marked peritoneal membrane failure.
The Peritoneal Biopsy Study Group reported that vasculopathy was positively correlated with the duration of PD. A prevalence of 29% was present in patients less than 2 years on PD and a prevalence of 77% in patients treated with PD between 4 and 6 years. Vasculopathy was defined as the presence of subendothelial hyalinization eventually causing luminal narrowing or obliteration of peritoneal vessels. It is considered a risk factor for neoangiogenesis and fibrosis of the peritoneal membrane. It is also conceivable that it causes an increase in the stiffness of the peritoneal vessels and a decrease in the intraluminal diameter of the vessel. Therefore, it is hypothesized that the presence of vasculopathy results in a decreased capacity of the peritoneal vessels to vasodilate, a so-called decreased *reservecapacity* of the peritoneal membrane. It was observed that intraperitoneal administration of the vasodilator sodium nitroprusside caused an increase in peritoneal transport of small solutes in stable PD patients. This has been shown for intermittent PD and also for continuous ambulatory PD. A difference in peritoneal protein transport was found between short-term and long-term PD patients in a study of Park et al. However, in this study a large

intra-individual variability was present. With the methodology used by Imholz et al., low intra-individual variation coefficients are present.

Study objective

The objective is to analyze whether a difference in reservecapacity is present between short-term and long-term PD patients. In case the reservecapacity of the peritoneum is significantly lower in the long-term compared to short-term PD patients, a peritoneal function test with the addition of sodium nitroprusside can be used as an additional tool in long-term PD patients who are likely to develop marked peritoneal membrane failure.

Study design

It will be an observational open-label study.

2 standardized peritoneal function tests with a maximal interval of 2 weeks will be performed in all patients who are included in the study: one peritoneal function test with the addition of 4.5mg/L sodium nitroprusside and one peritoneal function test without sodium nitroprusside. The sequence of the 2 tests will be randomized, but not blinded. This will be done in patients < 1 year on PD treatment and > 3 years on PD treatment. It will be observed what differences in study parameters are present between the peritoneal function test with and without sodium nitroprusside in both patient groups.

Study burden and risks

The peritoneal function test without the intervention will be part of the regular yearly assessment of the peritoneal function. Patient burden can be considered to be low, as the SPA with the addition of sodium nitroprusside does not differ from the regular SPA in terms of data collection No side effects have been described previously by adding sodium nitroprusside to the SPA. Therefore, the burden for the patient consists of one additional peritoneal function test for which the patient has to visit the Academic Medical Center. At present it is very difficult to predict which patient will develop marked peritoneal membrane failure. With the results of the present study we hypothesize that we gain more insight in the peritoneal pathophysiology. Furthermore, determination of the reservecapacity of the peritoneal membrane by means of a nitroprusside SPA could be a valuable diagnostic tool to predict which patient will develop severe peritoneal membrane failure.

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

Patients > 18 years of age treated with peritoneal dialysis > 1 month and < 1 year
Patients > 18 years of age treated with peritoneal dialysis > 3 years

Exclusion criteria

Patients with peritonitis less than 4 weeks prior the investigation
Severe overhydration
Signs of hypersensitivity for dextrans
Systolic bloodpressure < 120 mmHg en/of diastolic bloodpressure < 80 mmHg
No informed consent

Study design

Design

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

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2007
Enrollment:	20
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	sodium nitroprusside
Generic name:	sodium nitroprusside

Ethics review

Approved WMO Date:	31-07-2007
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
EudraCT	EUCTR2006-005660-38-NL
CCMO	NL13862.018.07