# Oral COX-2 inhibitor Celecoxib in Peritoneal Dialysis Patients: effects on peritoneal transport and peritoneal defence.

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Based on the positive effects of Celecoxib on ultrafiltration and peritoneal injury during PD in rats, we would like to propose a pilot study using Celecoxib in PD-patients. In this pilot study we will investigate whether the Cox2 inhibitor…

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| **Ethical review** | Approved WMO |
| **Status** | Will not start |
| **Health condition type** | Nephropathies |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON35652

**Source**
ToetsingOnline

**Brief title**
COXPD

### Condition

- Nephropathies

**Synonym**
chronic kidney disease

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Vrije Universiteit Medisch Centrum

**Source(s) of monetary or material Support:** vierde geldstroom Divisie I Beheer BV van VUmc

## Intervention

**Keyword:** COX-2 inhibitor, peritoneal defence, Peritoneal Dialysis, peritoneal transport

## Outcome measures

### Primary outcome

Primary endpoint is amelioration of ultrafiltration after three months of

treatment with Celecoxib.

### Secondary outcome

Secondary endpoints are differences in markers of inflammation(Ca125, Il-6,

TNF, VEGF, hyaluronan, Il-1, Il-8 and MCP-1) and peritoneal transport (D/P

creatinine, D/P urea, Kt/V) after three months of treatment with Celecoxib.

# Study description

### Background summary

Peritoneal dialysis (PD) is a well accepted dialysis technique for patients with end stage renal failure. Currently peritoneal dialysis has been considered as equal renal replacement modality compared to haemodialysis. Compared to haemodialysis, peritoneal dialysis is even more advantageous in the protection of the patients' residual renal function, morbidity-mortality indices, and quality of life in the first two years of treatment. Despite the benefits of this treatment modality, chronic instillation of peritoneal dialysis fluid (PDF) creates an intraperitoneal non-physiological environment that sustains low-grade inflammation, associated with morphological changes. Peritoneal fibrosis and new vessel formation are well-described PD side effects and are thought to be major causes of ultrafiltration (UF) failure and discontinuation of PD therapy.Cyclooxygenase-2 (COX-2) is the inducible isoform of cyclooxygenase. In cancer, COX-2 downstream products (mainly prostaglandin E2 (PGE2) and prostaglandin I2 (PGI2)) seem to mediate an angiogenic process through several mechanisms including vascular endothelial growth factor (VEGF) production and enhanced endothelial cell survival. COX-2 inhibitors are commercially available, among them Celecoxib has shown a positive effect on

inhibition of angiogenesis in several in vitro assays and in vivo cancer models. Celecoxib treatment has beneficial effects on angiogenesis and inflammation. In vitro experiments have demonstrated that under PD or PD-like conditions mesothelial and inflammatory cells express COX-2, as do fibroblasts involved in peritoneal healing after abdominal surgery. A rat peritoneal exposure model, daily treatment with Celecoxib for 5 weeks completely prevented ultrafiltration failure which is a dominant factor for treatment failure and discontinuation of the treatment. It is known that ultrafiltration failure leading to fluid overload is common in PD-patients. The high prevalence of fluid overload may partly explain why cardiovascular disease is still the major cause of mortality (accounting over 40% of all causes of death) in PD-patients. Since Celecoxib showed in vivo very positive effects on the ultrafiltration capacity in vivo, this compound may also show positive effects on cardiovascular diseases as a result of fluid overload might be prevented. Besides the prevention of ultrafiltration failure, Celecoxib partly reduced angiogenesis and fibrosis in the rat model for peritoneal dialysis.

**Study objective**

Based on the positive effects of Celecoxib on ultrafiltration and peritoneal injury during PD in rats, we would like to propose a pilot study using Celecoxib in PD-patients. In this pilot study we will investigate whether the Cox2 inhibitor Celecoxib can improve peritoneal transport, inflammation and defence parameters (Ca125, Il-6, TNF, VEGF, hyaluronan, Il-1, Il-8 and MCP-1 levels) during PD.

**Study design**

The study is designed as a pilot study. Eligible patients will be informed about the study by their physician and will be invited for a screening visit. At the start of the study the peritoneal function of each patient will be determined by a peritoneal membrane and effluent test (PET 3.86%). Group 1: patients will be treated with Celecoxib for a period of three months (2*200 mg/day) after which a second PET is performed. In the following three months, these patients will not be treated with Celecoxib, after which a third PET will be performed.
Group 2: patients will not be treated with celecoxib in the first three months. They will start the celecoxib treatment the second three months. The PET will be performed similarly to group 1. During the PET visits the docter will perform physical examination. Patients are asked to bring the last overnight effluent before coming to the hospital for a PET or a physical visit. The PET and the overnight effluents are collected for determination of peritoneal function (ultrafiltration and transport parameters) and peritoneal defence (Ca125, Il-6, TNF, VEGF, hyaluronan, Il-1, Il-8 and MCP-1). Each subject*s data will be coded with a unique study number and stored on computer file. Changes in fluidtypes will be done according to medical insight .

**Intervention**

giving Celecoxib

**Study burden and risks**

Patients have to use the celebrex pils as extra medication.
Patients need to come t the outpatient clinic for PETs, 3 times (for 4 hrs) in 6 months. The burden is mostly extra time in hospital.

# 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

The patient must provide written consent prior to starting the study
Patients must be over 18 years of age
Patients must have CKD stage 5 and treatment with automated peritoneal dialysis; (APD) using a biocompatible PD fluid
Not expected to receive a living donor transplant < 6 months

### Exclusion criteria

Patients who do not meet the specific inclusion criteria.
UF < 1000 ml/24h at last PET
Urineproduction over 300ml/day
Current use or use of COX-2 inhibitors during the past six months
Allergy for NSAID*s
All infections within the past 6 weeks

## Study design

### Design

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| Study type: | Interventional |
| Intervention model: | Crossover |
| Allocation: | Randomized controlled trial |
| Masking: | Open (masking not used) |

**Primary purpose:** Treatment

### Recruitment

NL

| | |
|---|---|
| Recruitment status: | Will not start |
| Start date (anticipated): | 01-06-2010 |
| Enrollment: | 16 |
| Type: | Anticipated |

### Medical products/devices used

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|---|---|
| Product type: | Medicine |
| Brand name: | Prostaglandinesynthesisinhibitors |
| Generic name: | Celecoxib |

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| Registration: | Yes - NL intended use |

## Ethics review

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| Approved WMO Date: | 08-06-2010 |
| 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 | EUCTR2009-012959-21-NL |
| CCMO | NL26367.029.10 |