The Effect of Furosemide on Protein-Bound Uremic Toxin Plasma Levels and Excretion in Patients with Chronic Kidney Disease

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This study aims to examine the effect of furosemide on renal PBUT excretion and PBUT plasma levels in patients with CKD.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Renal disorders (excl nephropathies)
Study type	Observational invasive

Summary

ID

NL-OMON56204

Source
ToetsingOnline

Brief title
Furosemide-PBUT study

Condition

- Renal disorders (excl nephropathies)

Synonym
Chronic Kidney Disease, reduced kidney function

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Onderzoekssubsidie ontvangen door UU

Intervention

Keyword: Chronic Kidney Disease (CKD), Drug-toxin interaction, Furosemide, Protein-Bound Uremic Toxins

Outcome measures

Primary outcome

The main endpoints of this study are PBUT plasma levels (indoxyl sulphate,

p-cresyl sulphate, indole-3-acetic acid, kynurenic acid, L-kynurenine, hippuric

acid en p-cresyl glucuronide) pre- and post-furosemide treatment

Secondary outcome

- Fractional PBUT excretion pre- and post-furosemide administration

- Surrogate PBUT clearance pre- and post-furosemide administration

- PBUT protein binding pre- and post-furosemide administration.

Study description

Background summary

Protein-bound uremic toxins are known to accumulate in chronic kidney disease (CKD) and are associated with increased morbidity and mortality. It is therefore crucial to maintain the PBUT levels low in this patient group. Furosemide is often prescribed to CKD patients. However, based on preclinical data, furosemide could affect the renal excretion of PBUTs, either by competing for the secretory system in the kidney or by competing for binding to albumin. It is important to examine the effect of furosemide on the excretion and plasma concentration PBUTs as this might have harmful consequences for patients with CKD.

Study objective

This study aims to examine the effect of furosemide on renal PBUT excretion and PBUT plasma levels in patients with CKD.

Study design

This study is observational and includes invasive measurements; a prospective repeated measures cohort study design will be used in which PBUT plasma concentration and excretion will be determined before and after the start of furosemide treatment.

Study burden and risks

Participants will only receive furosemide prescribed by their treating physician as part of routine patient care. In addition, three blood sample drawings and collection of two urine samples and two 12-hour urine collections will be needed. Thus, the risk associated with participation is negligibly low and will include two site visits. These visits will be combined with routine check-ups as much as possible. Participants will receive 30 euros as a compensation (based on the expected time investment and minimum wage) and a travel allowance for all additional visits.

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

• An age of 18 years or older
• An eGFR <60 mL/min/1.73m2 for at least three months (diagnosis of CKD stage 3-5)
• An indication for the start of treatment with furosemide as part of routine patient care
• Willingness to participate in the study and a signed informed consent

Exclusion criteria

• Patients who are already on furosemide treatment
• Patients with a liver disease with hyperbilirubinemia
• Patients who receive any type of renal replacement therapy (peritoneal dialysis, haemodialysis)
• Patients with end-stage renal failure without residual diuresis
• Patients who will start with medication simultaneously with start of furosemide treatment that might interfere with PBUT excretion or PBUT protein binding
• Patients who are incapacitated

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	10-06-2024
Enrollment:	34

Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO Date:	11-12-2023
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	30-07-2024
Application type:	Amendment
Review commission:	METC NedMec

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	NL81338.041.23