Uremic Toxin Removal and Hemodynamics in Long-Hour Hemodialysis and Hemodiafiltration; A Randomized Cross-Over Study

Published: 11-04-2011
Last updated: 10-08-2024

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Nephropathies
Study type	Interventional

Summary

ID

NL-OMON38305

Source
ToetsingOnline

Brief title
Acute effects of long-hour dialysis

Condition

- Nephropathies

Synonym
end-stage renal disease

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht

Source(s) of monetary or material Support: Ministerie van OC&W,Fresenius MC

Intervention

Keyword: dialysis, hemodiafiltration, hemodynamics, uremic toxins

Outcome measures

Primary outcome

The primary outcome of this study is the removal of (especially protein-bound)

uremic toxins.

Secondary outcome

Microcirculation measured by capillaroscopy

Study description

Background summary

Overall survival of patients on renal replacement treatment (RRT) remains low, although many efforts have been made in the past decades to improve the outcome of the dialysis population e.g. by increasing the removal of uremic toxins. Especially protein-bound solutes and peptides are difficult to remove by conventional dialysis treatments, and exactly these particular uremic toxins (mainly p-cresol and indoxyl sulphate) are associated with cardiovascular morbidity and mortality in patients with chronic kidney disease (CKD) and in dialysis patients. Also at the cellular level, multiple adverse effects of (protein-bound) uremic toxins have been described.
Intensive haemodialysis (HD) [short-daily haemodialysis, in-centre nocturnal haemodialysis (NHD) and nocturnal home haemodialysis] is associated with significant improvement of several clinical (e.g. blood pressure, left ventricular hypertrophy, coronary calcification, sleep apnoea, quality of life, fertility), biochemical (e.g. phosphate control, anemia) and biological (e.g. endothelial function, inflammation) parameters . A potential explanation for these observed results is the increased clearance of uremic toxins due to the increased duration and/or frequency of haemodialysis. The kinetics of (protein-bound) uremic toxins in nocturnal haemodialysis has not been studied yet extensively.
Convective strategies, especially online haemodiafiltration (HDF), may further increase uremic toxin removal. This has especially been shown for small uremic retention solutes, phosphate, beta2-microglobulin and cytokines, but it is

uncertain whether online HDF also increases the removal of protein-bound uremic toxins.
We hypothesize that increasing the duration of haemodialysis together with augmentation of convection leads to further increase of (especially protein-bound) uremic toxin removal, which may ultimately lead to improvement of cell biology and eventually of clinical parameters.
Next to the possible improvements in uremic toxin removal, long dialysis also was shown to result in better hemodynamic stability. This is likely due to a more physiologic fluid removal due to long treatment times. This may reduce myocardial stunning which is associated with increased cardiovascular morbidity and mortality. However, also beneficial effects of long dialysis on the functioning of the autonomic nervous system, which is often disturbed during dialysis, might be involved and may lead to improved hemodynamic stability. There is circumstantial evidence that also HDF has beneficial effects on the autonomic nervous system, even in short term, such as during a single dialysis session. The effects of a combination of increasing the dialysis duration and adding convection on hemodynamic stability and autonomous nervous system function have not been studied yet.

Study objective

The primary aim of this study is to compare the removal of (especially protein-bound) uremic toxins between 4-hour and 8-hour HD and HDF in order to evaluate the influence of dialysis duration and of convection on the removal of uremic toxins.
A secondary aim is to compare the haemodynamic response and autonomic nervous system functioning [blood pressure (BP), heart rate, heart rate variability, cardiac output, relative (RBV) and central blood volume (CBV), and peripheral microcirculation with capillaroscopy] between 4-hour and 8-hour HD and HDF.

Study design

Twenty prevalent conventional hemodialysis (CHD) patients (dialysing 3 days a week during 4 hours per dialysis session) will undergo, in random order, a mid-week 4-hour HD session, a mid-week 4-hour HDF session, a mid-week 8-hour HD session, and a mid-week 8-hour HDF session with a 2-week interval between every session to assess the influence of treatment duration and of convection on the removal of uremic toxins and on the haemodynamic responses and autonomic nervous regulation. In between the study dialysis sessions these patients will receive routine CHD treatments. Ten non-participating hemodialysis patients with significant residual urine production (and therefore the absence of significant ultrafiltration during hemodialysis) will undergo the same measurement during one conventional 4-hour hemodialysis session to study the effects of hemodialysis without ultrafiltration on microcirculation and endothelial function. Fifteen other non-participating patients without significant residual urine output and therefore the need for ultrafiltration

during hemodialysis will also undergo the same measurement during one standard dialysis treatment. In this last patient group, bio-impedance will also be performed with the BCM (Body Composition Monitor) before and after the study session. Also, twenty non-participating hemodialysis patients will undergo capillaroscopy at times 0, 30, 60, 120, (150) and 240 minutes when blood samples will be drawn to check the levels of several inflammatory and endothelial markers, in an attempt to correlate observed glycocalyx changes with inflammation. These patients will be studied twice, the first time when Low Molecular Weight Heparin (LMWH) is given at the start of the treatment and the second time when LMWH is given 120 minutes after the start of the treatment, in order to evaluate the potential effect of LMWH on the endothelial glycocalyx.

Intervention

Prevalent conventional hemodialysis patients will undergo a conventional hemodialysis session to study the baseline kinetics and hemodynamics and will subsequently undergo, in a random way, a 4-hour hemodiafiltration session and an 8-hour hemodialysis and hemodiafiltration session, each session separated from the other by a 2-week interval.

Study burden and risks

In this study, only non-invasive techniques which pose a minimal burden to the patient will be used. Blood sampling will coincide with the dialysis sessions. The study will not have direct benefit for the participants. The study can only be performed with this specific patient group.

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

-prevalent stable CHD patients with insignificant residual urine production
-AV-fistula enabling double-needle vascular access with blood flow rate of at least 350 ml/min
-informed consent
-age more than 18 years

Exclusion criteria

-withdrawal of consent
-acute intercurrent illness (infection, malignancy, cardiovascular event, uncontrolled diabetes)

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-10-2011
Enrollment:	65
Type:	Actual

Ethics review

Approved WMO Date:	11-04-2011
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	27-07-2011
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	16-11-2011
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	30-11-2011
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	23-04-2012
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	06-08-2012

Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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
Other	ClinicalTrials.gov Protocol Record NL 34908.068.10
CCMO	NL34908.068.10