Effects of dialysis duration on brain perfusion and cognitive function in end-stage renal disease - short vs. long hemodialysis

Published: 14-06-2019
Last updated: 09-04-2024

Primary objective: To test in patients with ESRD whether a longer HD session (8 hours) compared with CHD limits the decline in cerebral blood flow.Secondary objectives: 1) to investigate whether a longer dialysis session is associated with superior...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cognitive and attention disorders and disturbances
Study type	Interventional

Summary

ID

NL-OMON49428

Source
ToetsingOnline

Brief title
BRAIN-HD

Condition

- Cognitive and attention disorders and disturbances
- Renal disorders (excl nephropathies)

Synonym
cerebral perfusion, cognitive function, Endstage renal disease, renal failure

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Cerebral blood flow, Cognition, Hemodialysis, Hemodynamics

Outcome measures

Primary outcome

The primary outcome of the study is the difference in intradialytic

cerebrovascular hemodynamic changes (cerebral blood flow velocity) between the

longer HD (extended HD and NHD; 8 hours) vs. CHD session.

Secondary outcome

Secondary outcomes of the study are the differences between the longer HD vs.

CHD sessions regarding the following parameters:

-Systemic hemodynamic changes (heart rate, stroke volume, cardiac output and BP)

-Cognitive function

-Cerebrovascular autoregulatory capacity

-BP variability, i.e. baroreflex sensitivity (very short-term BP variability),

standard deviation and coefficient of variation of the NIBP values (short-term

BP variability; only for part A)

-Cardiovascular autonomic (parasympathetic and sympathetic) function

Study description

Background summary

Cardiovascular disease, as the leading cause of mortality, and cognitive

decline are common in patients with end-stage renal disease (ESRD) undergoing conventional hemodialysis (CHD), which is usually performed 3 times per week for about 4 hours. A serious side effect is intradialytic hypotension (IDH), which occurs in approximately 20% of the dialysis sessions (1, 2). Recurrent arterial hypotension endangers perfusion of the heart (coronary circulation) and the brain, and is associated with poor survival. A transient reduction in cerebral blood flow (CBF) occurs during hemodialysis (HD), correlating with intradialytic decline in cognitive dysfunction (3). Nocturnal hemodialysis (NHD; 8 hours) is associated with better hemodynamic tolerance and blood pressure (BP) control, with the majority of the patients no longer requiring antihypertensive medication (4). NHD has the advantage of slow ultrafiltration rate with a reduced incidence of IDH, potentially resulting in preserved CBF and cognitive function.
For the brain as a highly metabolic active organ, constancy of oxygen supply by maintaining CBF is a prime requirement. CBF is under tight autoregulatory control and impairment of CBF control exposes the brain to episodic hypoperfusion. A reduction in CBF in itself may contribute to progression of vascular cognitive impairment. Recent data indicate that cerebral ischemia during HD is a common phenomenon (5) and correlates with the decline in executive cognitive function (6). Notably, intradialytic hemodynamic instability was associated with the development of brain white matter lesions after 1 year (7). Whether or not intrinsic CBF control is impaired in patients with ESRD remains to be determined.
Improvement of hemodynamic stability (defined as smaller reduction in BP during dialysis) with NHD vs. CHD has the potential to limit the intradialytic decline in CBF and cognitive function in ESRD patients.

Study objective

Primary objective:
To test in patients with ESRD whether a longer HD session (8 hours) compared with CHD limits the decline in cerebral blood flow.

Secondary objectives:
1) to investigate whether a longer dialysis session is associated with superior hemodynamic stability, defined as a smaller reduction in blood pressure during dialysis (pre-post), compared with CHD.
2) to test whether a longer dialysis session is associated with less intradialytic cognitive decline compared with CHD.
3) to assess cerebrovascular autoregulatory capacity, blood pressure variability and cardiovascular autonomic function during long vs. short HD sessions.

Study design

A cross-over design will be used consisting of 2 parts:

A) CHD vs. extended HD (4 vs. 8 hours at daytime), and B) NHD vs. CHD (8 hours at night vs. 4 hours at daytime).
For each part 8 patients will be enrolled. Patients will be recruited from the dialysis center Diapriva Buitenveldert B.V. The dialysis center has access to a mobile cerebro- and cardiovascular bedside monitoring, recording and storage unit as designed and in use in the Laboratory for Clinical Cardiovascular Physiology (LCCP, Amsterdam UMC, location AMC).

Part A) Eight patients receiving CHD treatment will be asked to undergo a longer HD session at daytime (extended HD) on the first dialysis day of the week (Monday or Tuesday), extending the HD treatment time to 8 hours. Intradialytic hemodynamic measurements will be performed at both visits in random order (CHD > extended HD or extended HD > CHD) with an interval of 2 weeks.
Part B) Eight patients receiving NHD treatment will be asked to undergo CHD treatment at daytime on the first dialysis day of the week, shortening the HD treatment time to 4 hours. Intradialytic hemodynamic measurements will be performed at both visits in random order (CHD > NHD or NHD > CHD) with an interval of 2 weeks.

The following measurements will be performed during dialysis:
-Systemic hemodynamic variables: Beat-to-beat non-invasive continuous arterial BP monitoring (finger plethysmography contralateral to the AV fistula arm) and automated oscillometric non-invasive BP (NIBP) measurement, heart rate, stroke volume and cardiac output (pulse contour analysis). NIBP measurements will be performed every 30 min during daytime dialysis and only twice during NHD (at the start of dialysis treatment and at the end).
-Cerebrovascular hemodynamic variables: CBF velocity (middle cerebral artery blood flow velocity by transcranial Doppler ultrasonography) and end-tidal CO2 (PETCO2). Static cerebrovascular autoregulation will be assessed in the time domain by relating the changes in CBF velocity to changes in BP during dialysis. Dynamic cerebrovascular autoregulation, measured prior to and after dialysis, will be quantified in the frequency domain expressed as the arterial pressure-to-CBF velocity transfer function coherence, phase shift and gain.
-BP variability: Cardiac baroreflex sensitivity will be evaluated during the first half hour and last half hour of the dialysis session (very short-term BP variability). Also standard deviation (SD) and coefficient of variation (CV) of the BP values from the NIBP measurements will be estimated (short-term BP variability).
-Cardiovascular autonomic function: Cardiovascular sympathetic and parasympathetic function and postural BP response (orthostatic hypotension) will be assessed prior to and after dialysis.
-Cognitive function will be assessed during the last hour of both HD sessions using a validated neuropsychological protocol.
All measurements will be performed on the first dialysis day of the week (Monday or Tuesday after the long interdialytic interval) to account for different interdialytic weight gain, which determines the ultrafiltration rate,

throughout the week.

Intervention

A longer HD session (8 hours) will be compared with a conventional HD session (4 hours)

Study burden and risks

The burden for the subjects will be minimal: Measurement of CBF velocity by transcranial Doppler and continuous non-invasive BP measurement using finger plethysmography are generally well-tolerated. Blood sampling will be performed from the arterial lines of the extracorporeal circuit before and after dialysis (no venipuncture). Evaluation of cognitive functioning (using a test battery) during dialysis is limited to 30-45 min. Patients regularly treated with NHD could encounter an increased prevalence of IDH during CHD, which they would also encounter if one of their dialysis sessions is scheduled at daytime for personal reasons. No extra risks are to be expected with participation. Whereas the benefit for patients is as yet unknown, in terms of cerebral perfusion and cognitive function, improvement of hemodynamic stability with NHD has the potential to limit the intradialytic reduction in CBF with preserved cognitive function in ESRD patients, which will improve the prospects and quality of life in this patient population. This study addresses the underlying mechanism(s) of HD-related brain decay and opens the discussion on preservation of cognitive function as a highly relevant objective in this frail 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

- Conventional HD (for part A): Treatment with conventional HD 3 times per week 4 hours
- Nocturnal HD (for part B): Treatment with nocturnal HD 3 times per week 8 hours
- Age >18 years
- Presence of a well-functioning central venous catheter or AV fistula or graft with a vascular access flow of >400 mL/min

Exclusion criteria

- Unable to obtain an optimal transcranial acoustic window during dialysis
- Severe cognitive impairment
- Medical history of (major) psychiatric illness, such as psychosis, schizophrenia, severe personality disorder or depression with vital signs, that could affect cognitive performance
- Non-adherence to the dialysis procedure
- Insufficient proficiency in the Dutch Language

Study design

Design

Study type:	Interventional
Intervention model:	Crossover

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-06-2019
Enrollment:	16
Type:	Actual

Ethics review

Approved WMO Date:	14-06-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-02-2020
Application type:	Amendment
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	NL69044.029.19