The microcirculation, dialysis modality and sequestered salt (the MIMOSA study)

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Ethical review	Approved WMO
Status	Pending
Health condition type	Renal disorders (excl nephropathies)
Study type	Interventional

Summary

ID

NL-OMON57580

Source
ToetsingOnline

Brief title
The MIMOSA study

Condition

- Renal disorders (excl nephropathies)
- Decreased and nonspecific blood pressure disorders and shock

Synonym
Microcirculatory dysfunction and sequestered salt content in dialysis patients

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC
Source(s) of monetary or material Support: 1. de Nierstichting (Nederland);2. Niercentrum aan de Amstel (Nederland);3. B. Braun Avitum AG (Duitsland),B Braun Avitum AG (Duitsland),de Nierstichting,Niercentrum aan de Amstel

Intervention

Keyword: Hemodiafiltration, Hemodialysis, Microcirculation, Sequestered salt content

Outcome measures

Primary outcome

The SSC (sequestered sodium content) in muscle, as assessed by 23Na-MRI, after 4 weeks of treatment.

Secondary outcome

- The predialytic SSC (sequestered sodium content) in the skin, as assessed by 23Na-MRI, after 4 weeks of treatment.

- Microcirculation, as assessed by skin perfusion/reactivity, after 4 weeks of treatment

- Hemodynamics: peri- and intradialytic blood pressure (BP), BP variability and IDH will be assessed by automatic arm-cuff measurements attached to the dialysis machine (4x per hour). In addition, interdialytic blood pressure will be evaluated. Patients will be asked to measure their blood pressure thrice a day between the second-last and the last dialysis session of each treatment period.

- Patient experience: patient reported outcome measures (PROMs) as indicated by the Dialysis Symptom Index and the EQ-5D-5L visual analogue scale and thirst measured by the Thirst Distress Scale.

- Markers of cardiac damage measured pre- and post treatment in blood drawn from the arterial line of the extracorporeal circuit

- Markers of endothelial damage measured pre- and post treatment in blood drawn from the arterial line of the extracorporeal circuit

- Markers of inflammation: high sensitive C-reactive protein (hsCRP), interleukin-6 receptor (IL-6R), soluble CD 163 and soluble intercellular adhesion molecule-1 (sICAM-1) will be measured pre- and post treatment using blood from the arterial line of the extracorporeal circuit.

- Markers related to sequestered sodium content: serum glycosaminoglycans, syndecan-1 and vascular endothelial growth factor C (VEGF-C) will be assessed pre- and post treatment using blood from the arterial line of the extracorporeal circuit

- Depending on a pilot study, extracellular vesicles as markers for organ damage will be assessed pre- and post treatment using blood from the arterial line of the extracorporeal circuit.

Study description

Background summary

Life expectancy of patients with end-stage kidney disease (ESKD) is extremely poor. Post-dilution online hemodiafiltration (HDF) is associated with reduced mortality, if compared to conventional hemodialysis (HD), especially when high convection volumes are achieved (high-volume HDF; hvHDF). It is unclear, however, why (hv)HDF improves outcomes. Neither increased clearance of middle-molecular weight uremic toxins nor improved bio-incompatibility seems to explain the difference. As the effects are already observed within 2.5 years of treatment, improvement of a functional disorder is more likely than restoration of structural alterations. Possibly, improvement of vascular dysfunction is the missing piece of the puzzle. Previous literature showed that (1) the microcirculation (MC) is severely disturbed in dialysis patients, (2) sodium is a potentially dangerous uremic toxin and can bind to glycosaminoglycans without commensurate water retention (sequestered sodium content [SSC]) and (3) in patients with non-dialysis dependent chronic kidney disease (CKD), a disturbed SSC is related to capillary rarefaction. We hypothesize that (1 and 2) the SSC and the MC are better preserved in hvHDF than in HD, (3) a lower dialysate sodium content leads to a reduced loading of the SSC and (4) the SSC and MC

function are interrelated.

Study objective

Four hypotheses will be investigated. First and second, we will evaluate whether treatment with hvHDF has dissimilar effects on the SSC and MC function, if compared to HD. Next, we will assess whether disorders of the SSC and the MC are influenced by the sodium balance, estimated as *dialysate sodium [DNa] minus plasma sodium [PNa]*. Lastly, we will investigate whether the SSC and MC are interrelated in this patient group.

Study design

Randomized cross-over intervention trial

Intervention

Participants will be subjected to 5 dialysis treatments in random order:
1. Hemodialysis (HD) with net sodium balance: (Dialysate sodium (DNa)= Plasma sodium (PNa))
2. HD with net sodium efflux (DNa < PNa, difference -3 mmol/L);
3. HD after isolated ultrafiltration (DNa = PNa);
4. High-volume HDF (hvHDF) with net sodium balance (DNa = PNa);
5. hvHDF with net sodium efflux (DNa < PNa, difference -3 mmol/L).

Study burden and risks

Study treatments will be performed instead of regular dialysis treatments. These are established treatment modalities. However, a lower DNa has been associated with more intradialytic hypotension. Furthermore, a higher DNa has been associated with increased ultrafiltration (UF) need. The extra burden for patients encompasses 5 MRIs to assess SSC before dialysis (for which they need to visit the Spinoza Center in Amsterdam Zuidoost) and in 5 patients, both before and after dialysis an MRI will be performed (so 10 MRIs); the MC function will be evaluated at the same time points and for these measurements, acethylcholine (Ach) and sodium nitroprusside (SNP) will be administered through iontopheresis (considered non-invasive); at baseline blood will be drawn once before dialysis and at 5 time points, blood will be drawn both before and after dialysis from the extracorporeal circuit (thus no venepuncture is necessary, total required blood volume= 181 ml); blood pressure measurements will be performed 4 times per hour during dialysis treatments and patients are requested to measure their blood pressure at home three times daily for 1 day per treatment period; lastly, participants will be asked to fill in 3 questionnaires at 5 time points.

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

- Age >=18 years
- Treatment with hemodialysis or hemodiafiltration 3x per week during at least 4 hours for at least 3 months
- Blood flow rate feasiblity of >=350 ml/min
- Residual diuresis <200 ml/day
- Plasma sodium before dialysis 137-145 mmol/L at baseline
- spKt/Vurea >= 1.2
- Ability to understand study procedures and willingness to provide informed consent

Exclusion criteria

- Severe incompliance to dialysis procedure and accompanying prescriptions, especially frequency and duration of dialysis treatment
- Life expectancy < 3 months due to non-renal disease
- Expected transplantation within 6 months
- Access recirculation > 10%
- Participation in another clinical intervention trial
- Metal implants (e.g. implantable cardioverter defibrillators)
- Severe obesity (abdominal width >= 188 cm)
- Claustrophobia

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-04-2025
Enrollment:	23
Type:	Anticipated

Medical products/devices used

Registration:	No

Ethics review

Approved WMO

Date:	28-03-2025

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
ClinicalTrials.gov	NCT06327750
CCMO	NL83566.018.24