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Increasing dialysate magnesium (IDM): the effect on blood vessel stiffness, blood pressure, and changes to the functioning of the lining of blood vessels in patients receiving hemodialysis treatment

Submission date	Recruitment status	[_] Prospectively registered
18/06/2020	No longer recruiting	[_] Protocol
Registration date	Overall study status	[_] Statistical analysis plan
22/06/2020	Completed	[X] Results
Last Edited	Condition category	[_] Individual participant data
05/10/2020	Circulatory System	

Plain English summary of protocol

Background and study aims

Hemodialysis is a treatment for patients with end-stage kidney disease where blood is removed from the body (usually via blood vessels of the arm) and filtered through a machine, where products in the blood are exchanged with the dialysis fluid (dialysate) across a membrane, before being returned to the body. It is used to replace the loss of function of the kidneys, to filter wastes and water from the blood, to ensure that these do not build up. Hemodialysis helps to control blood pressure and balance important minerals in the blood.

Cardiovascular diseases are the most frequent cause of death in patients with end-stage kidney disease. Blood vessel stiffness, high blood pressure, and changes to the functioning of the lining of blood vessels are factors involved in the progress of cardiovascular disease in hemodialysis patients. It has previously been shown that using a higher concentration of magnesium in the dialysis fluid during dialysis sessions could reduce the rate at which blood vessel stiffness develops, and may improve the functioning of the lining of blood vessels.

The aim of this study is to examine whether increasing the concentration of magnesium in the dialysate from 0.50 mmol/L to 0.75 mmol/L could affect blood vessel stiffness, high blood pressure, and changes to the functioning of the lining of blood vessels in patients with end-stage kidney disease undergoing hemodialysis. The study also aims to investigate the long-term effect of increased magnesium concentration in the dialysate (to 0.75 mmol/L) on mineral metabolism markers over 6 months.

Who can participate?

All patients with end-stage kidney disease, aged more than 18 years, and undergoing regular hemodialysis will be eligible to participate, excluding critically ill patients and pregnant patients or patients at risk of pregnancy.

What does the study involve?
Participants are assigned to 2 weeks of treatment with either a concentration of magnesium in the dialysis fluid at 0.50 mmol/L or at 0.75 mmol/L. Then they will have 3 days with no hemodialysis, followed by 2 weeks of hemodialysis with the concentration of magnesium that they had not previously recived. At the end of the 4 weeks of treatment participants will be assessed for changes to the blood vessels and blood pressure.

After the 4 weeks of treatment, all participants who will be continuing hemodialysis will receive hemodialysis with a concentration of magnesium in the dialysis fluid of 0.75 mmol/L, as already planned for every patient by the internal guidelines of the network to whom the dialysis center of the study belongs. After a period of 6 months, long term-changes will be assessed.

What are the possible benefits and risks of participating?
It has previously been demonstrated that there could be an overall cardiovascular benefit in using a higher concentration of magnesium in the dialysis fluid. A possible risk is related to a high blood magnesium level causing low blood pressure. The risks of participating in this study are not anticipated to be greater than for routine hemodialysis treatment.

Where is the study run from?
Dialysis center of the Regional Hospital of Bellinzona and Valli (Switzerland)

When is the study starting and how long is it expected to run for?
May 2017 to August 2019

Who is funding the study?
Scientific Research Advisory Board (ABREOC) of the Ente Ospedaliero Cantonale (Switzerland)

Who is the main contact?
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Contact information

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Public

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
Nil known

Study information

Scientific Title
Consequences of supraphysiological dialysate magnesium on arterial stiffness, hemodynamic profile and endothelial function in hemodialysis: observational cross-over study followed by a follow-up phase

Acronym
IDM

Study objectives
Dialysate magnesium at 0.75 mmol/L improves arterial stiffness, blood pressure, and endothelial function when compared to dialysate magnesium at 0.50 mmol/L in hemodialysis patients.

Ethics approval required
Old ethics approval format

Ethics approval(s)

Approved 29/05/2018, the Swiss Ethics Commission (Comitato etico cantonale c/o Ufficio di sanità, Via Orico 5, 6501 Bellinzona, Switzerland; +41 (0) 91 814 30 57; dss-ce@ti.ch), ref: CE3358, BASEC2018-00830.

Study design
Single-centre randomized crossover study followed by an observational follow-up phase

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Arterial stiffness, hemodynamic profile and endothelial function in hemodialysis patients

Interventions
4-week cross-over study aimed at investigating the consequences of increasing dialysate magnesium (D-Mg2+) from 0.50 to 0.75 mmol/L on arterial stiffness, hemodynamic profile, and endothelial function in subjects undergoing hemodialysis (HD).

The long-term effect of higher D-Mg2+ (0.75 mmol/L) on mineral metabolism markers will be investigated in a six-month follow-up.

After enrolment, patients will be randomly assigned to a 2-week treatment (6 HD sessions) with either standard dialysate magnesium (Group 1, who will receive D-Mg 2+ 0.50 mmol/L treatment) or high dialysate magnesium (Group 2, who will receive D-Mg 2+ 0.75 mmol/L treatment). This will be followed by a 3-day washout period (in which HD treatments were not carried out), and then a second 2-week cross-over phase (further 6 HD sessions where the Group 1 participants will receive high dialysate magnesium and the Group 2 participants will receive standard dialysate magnesium). There will be 12 haemodialysis sessions over the course of the 12 weeks. Assessments will be made at the start, at the point of cross over, and at the end of the 4-week period.

After the 4 weeks of cross-over, subjects continuing dialysis will receive D-Mg2+ set at 0.75 mmol /L, as already planned for every patient by the internal guidelines of the network to whom the dialysis center of the study belongs.

Patients will be followed for a further 6 months to explore metabolic long term-changes related to high dialysate magnesium (0.75 mmol/L).

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Dialysate magnesium 0.50 mmol/L and 0.75 mmol/L

Primary outcome(s)
1. Vascular stiffness as estimated by pulse wave velocity (PWV), augmentation index (AI), and pulse pressure (PP) using a conventional brachial cuff for adults with an integrated high-fidelity pressure sensor, Mobil-o-Graph on the non fistula arm to assess systolic blood pressure, diastolic blood pressure, and heart rate which are assessed 3 times (at the beginning, after half of the time and at the end) during each haemodialysis session between baseline and 4 weeks

Key secondary outcome(s))
1. Hemodynamic profile measured using a conventional brachial cuff for adults with an integrated high-fidelity pressure sensor, Mobil-o-Graph on the non fistula arm to assess systolic blood pressure, diastolic blood pressure, and heart rate which are assessed 3 times (at the beginning, after half of the time and at the end) during each haemodialysis session between baseline and 4 weeks.
2. Endothelial function, as measured by the reactive hyperemia index estimated with a validated, non operator-dependent, device for non-invasive measurement of endothelial function (EndoPAT 2000, Itamar Medical Inc., Israel) at baseline and 2 and 4 weeks
3. Incidence of intradialytic hypotension and bradicardia measured using a conventional brachial cuff for adults with an integrated high-fidelity pressure sensor, Mobil-o-Graph on the non fistula arm to assess systolic blood pressure, diastolic blood pressure, and heart rate which are assessed 3 times (at the beginning, after half of the time and at the end) during each haemodialysis session between baseline and 4 weeks. Intradialytic hypotension is defined as a decrease in systolic blood pressure of ≥20 mmHg or a decrease in mean arterial pressure (MAP) of ≥10 mmHg, and intradialytic bradycardia as an heart rate of ≤60 beats/min.
4. Incidence of pre-/post-dialytic hypermagnesaemia or hyper-/hypo-calcemia measured from ionized magnesium and ionized calcium using an ionometer (Microlyte 6 Analyzer, Kone Instruments, Espoo, Finland) pre- and post-haemodialysis at each haemodialysis session between baseline and 4 weeks
5. Changes in mineral and bone metabolism markers over the 6-month follow up period measured using ionized calcium and ionized magnesium assessed at 0, 1, 2, 3, 4, 5, and 6 months of follow up, and intact parathyroid hormone, 25-OH-Vitamin D, ionized magnesium and total magnesium levels assessed at 0, 3 and 6 months of follow up

Completion date
30/07/2019

Eligibility

Key inclusion criteria
1. Receiving treatment in the participating center with maintenance hemodialysis for ≥3 months
2. Aged ≥18 years
3. Able to understand the protocol and to give written informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
39

Key exclusion criteria
1. Acute illness requiring hospitalization
2. Pregnancy or risk of pregnancy

Date of first enrolment
20/08/2018

Date of final enrolment
31/12/2018

Locations

Countries of recruitment
Switzerland

Study participating centre
Dialysis center of the Regional Hospital of Bellinzona and Valli
Via Ospedale 1
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6500

Sponsor information

Organisation
Ente Ospedaliero Cantonale

ROR
https://ror.org/00sh19a92

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Scientific Research Advisory Board (ABREOC) of the Ente Ospedaliero Cantonale

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made publicly available as participant consent forms and ethics approval did not include permission for secondary use, with access to data only approved for researchers involved in the analysis.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/12/2020	05/10/2020	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes