The effect of intradialytic supplementation in chronic hemodialysis patients; a pilot study

Published: 27-09-2022
Last updated: 19-08-2024

The primary objective of this pilot study is the feasibility of prolonged intra-dialytic creatine supplementation. The secondary objectives of this pilot study are to study the safety of prolonged intra-dialytic creatine supplementation for dialysis...

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

Summary

ID

NL-OMON51287

Source
ToetsingOnline

Brief title
Intradialytic creatine suppletion

Condition

- Renal disorders (excl nephropathies)

Synonym
Renal failure; Hemodialysis

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W,Firma Crearene AG

Intervention

Keyword: Creatine, Hemodialysis, Muscle function, Quality of life

Outcome measures

Primary outcome

The main parameters for the pilot study are the plasma creatine concentration and intra-erythrocytic creatine concentration of both pre- and post-hemodialysis samples. Intra-erythrocytic creatine concentration will be used as a non-invasive proxy for creatine tissue uptake.

Secondary outcome

Secondary study parameters are hand grip strength as a measure of muscle strength, the combined interdialytic urinary and intradialytic dialysate excretion of creatinine as a measure of muscle mass [1], and bioelectrical impedance analysis (BIA) as a measure of body composition and nutritional status.

Other study parameters are N-terminal pro-brain natriuretic peptide (NT-proBNP) as a cardiac function marker, high sensitivity troponin T (hs-TNT) as a cardiac ischaemia marker, C-reactive protein as an inflammation marker, self-reported physical health using the EQ-6D, SF36, and the DSI, fatigue using the CIS and cognitive functions using the CFQ.

Study description

Background summary

Dialysis is a life-saving treatment, but unfortunately health-related quality of life (HRQoL) of dialysis patients is poor and mortality risks are high compared to the general population. Although several potentially modifiable (e.g. pre-dialysis care and nutritional status) and unmodifiable risk factors (e.g. age and genetics) for excess risk of mortality and poor HRQoL have been identified in dialysis-dependent patients with chronic kidney disease (CKD), there is great need for identification of new potentially modifiable risk factors. We hypothesize that creatine deficiency is such a modifiable risk factor, which underlies several important causes for impaired HRQoL hemodialysis patients, such as protein energy wasting (PEW), sarcopenia, fatigue, muscle weakness, depression, cognitive impairment, and increased susceptibility and a higher risk of an adverse course of infectious diseases. We propose that creatine supplementation is particularly important for patients with dialysis-dependent CKD because (1) endogenous synthesis of creatine in these patients is severely impaired due to the virtual absence of kidney function and, consequently, the virtual absence of the first enzymatic step required for endogenous absence of creatine from the amino acids arginine and glycine (2) unopposed losses of creatine to the dialysis fluid during dialysis sessions, and (3) inadequate intake of creatine due to advices towards a primary plant-based diet in these patients. All this comes on top of the normally existing continuous non-enzymatic conversion of approximately 1.6-1.7% of the endogenous creatine pool to creatinine, which necessitates continuous replenishment of creatine by the combination of endogenous synthesis and dietary intake to remain in steady-state. This is a novel understanding because until recently it was not recognized that kidney function is an important contributor to endogenous creatine synthesis, so that the capacity to of patients with dialysis-dependent CKD to maintain creatine homeostasis in the light of ongoing conversion of creatine into creatinine, additional unopposed losses of creatine to the dialysis fluid and an inadequate dietary intake is severely impaired. Patients with dialysis-dependent CKD could benefit from creatine supplementation by allowing for maintenance of their endogenous creatine pools, which would help them to sustain bodily functions which depend on creatine availability, including normal function of muscles, heart, the immune system and brain. Based on these novel/ recent findings, we hypothesize that creatine, intradialytic creatine supplementation may help to maintain creatine homeostasis among dialysis-dependent chronic kidney disease patients, and consequently improve muscle status, nutritional status, neurocognitive status fatigue and HRQoL.

Study objective

The primary objective of this pilot study is the feasibility of prolonged intra-dialytic creatine supplementation.

The secondary objectives of this pilot study are to study the safety of prolonged intra-dialytic creatine supplementation for dialysis patients and finding the optimal dosage to replenish the creatine pool. To this end we will

step wisely increase creatine concentrations of the dialysis solution (in the range of 0.5 mM to a maximum of 2mM, with the latter reflecting the concentration that can be reached after an oral bolus of creatine).

The third objective is to obtain pilot data on the effect of intradialytic creatine supplementation on muscle status, nutritional status, neurocognitive status fatigue and HRQoL to allow for calculation of the power for a lager intervention study.

Study design

Block-randomized double-blind placebo-controlled pilot study in 16 hemodialysis patients (which will be divided into four groups (0.5mM, 1.0mM, 1.5mM, 2.0mM) each consisting of three patients receiving creatine and one receiving placebo). The total study duration is 8 weeks with 6 weeks of active treatment and 2 weeks of wash-out.

Intervention

Creatine will be added to the dialysis fluid and will thus be continuously administered during the whole hemodialysis session. We will study the effect of four increasing dosages of creatine (3 out of 4 patients per block) or placebo (1 out of 4 patients per block) in four groups of four patients: 0.5mM, 1.0mM, 1.5mM, or 2.0mM of creatine. The patients will receive creatine supplementation or placebo (sterile water with the same composition as the dialysate) during each hemodialysis session during a total period of 6 weeks. Creatine-monohydrate, Creapure® "Pharma Quality" (not GMP), produced by AlzChem Trostberg, Germany will be used for preparation of a 50 mmol/L stock solution of creatine which will be added to the dialysis fluid to reach the projected dialysate concentrations.

Study burden and risks

Patients with dialysis-dependent CKD chronically suffer from multiple severe, currently unresolved health problems and complaints, which together severely impair HRQoL. Patients with dialysis-dependent CKD cannot endogenously synthesize creatine and at the same time suffer from unopposed losses of creatine to the dialysis fluid. The ensuing creatine deficiency may explain an important part of the currently unresolved health problems and complaints from which the patients with dialysis-dependent CKD suffer. The prevention of occurrence of unopposed losses of creatine to the dialysis fluid may therefore be of great benefit for the patients, while the burden and risks of participation are negligible. The burden of participation is negligible because the patients will anyway undergo a 4h dialysis session 3 times per week. Addition of creatine to the dialysis fluid will not change this. Also the blood sampling required for the study will not give any extra burden, because the

sampling will be performed via the connection with the bloodstream that has been made to make the dialysis session possible. The only burden of participation will come from the tests that will be performed and the questionnaires that will be taken. The risks are also negligible because creatine is a natural substance required for normal metabolism that will be added to the dialysis fluid like now e.g. sodium, potassium, magnesium and calcium as natural substances that are required for normal metabolism that are already added to the dialysis fluid, also in order to prevent unopposed losses to the dialysis fluid.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713GZ
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713GZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- Age >=18 years.
- Hemodialysis treatment in the University Medical Centrer MCG or Dialysis

Center Groningen.
- Dialysis vintage >=2 months.
- Conventional hemodialysis, thrice weekly treatment with 3 to 5 hours per dialysis session.
- Hemoglobin at previous routine monthly assessment greater than or equal to 6.5 mmol/l;
- Signed informed consent.

Exclusion criteria

- Pregnancy.
- Presence of clinical signs of infection.
- Confirmed diagnosis of malignancies.
- Incapacity of the Dutch language.
- Inability to complete questionnaires.
- Short life expectancy.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	03-08-2023
Enrollment:	16
Type:	Actual

Ethics review

Approved WMO Date:	27-09-2022
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	29-12-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-03-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	26-02-2024
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL79248.042.22