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A pilot study for performing hemodialysis without heparin using a citrate-containing dialysis fluid. Can the increased bleeding tests of the patient be prevented?

Submission date
30/06/2021

Recruitment status
No longer recruiting

Registration date
01/07/2021

Overall study status
Completed

Last Edited
03/09/2021

Condition category
Circulatory System

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Dialysis is a procedure to remove waste products and excess fluid from the blood when the kidneys stop working properly. It often involves diverting blood to a machine to be cleaned. As blood is pumped through the artificial kidney, clotting can occur. Normally this is controlled using low molecular weight heparin (LMWH), but the disadvantage of this is that clotting is prevented everywhere in the patient and there is a risk of death from bleeding after injury. Another option is to achieve local anticoagulation using citrate.
This study will investigate the optimum way to manage anticoagulation during dialysis using citrate.

Who can participate?
The study will be performed in hemodialysis patients using oral anticoagulation or antiplatelet agents and receiving hemodialysis in the Albert Schweitzer Hospital after informed consent.

What does the study involve?
Two sessions of hemodialysis with LMWH and two sessions with the study RCA. Blood tests will be taken before, during, and after the session. The burden will not be different from that of the regular thrice-weekly hemodialysis. Time expenditure for the patient will be unaltered. There will be no additional punctures of veins or vascular access. In 2 weeks, an extra amount of 120 ml of blood will be taken from the patient.

What are the possible benefits and risks of participating?
The possible benefit is the prevention of systemic anticoagulation and cooperation with a study that will improve patients chances.

The possible side effects are known because citrate is often used as anticoagulant with CVVH at the intensive care departments. It has to be noted that the proposed citrate concentration of 0.83 mmol/l in the dialysis fluid is 30% less than used with CVVH. Excessive administration (more

than 4 times the proposed amount) of citrate can cause metabolic alkalosis and symptoms of hypocalcemia. These symptoms are divided according to their incidence: seldom paresthesia, extremely seldom muscle contractions, carpopedal spasm, insult, laryngospasm, bronchospasm, increased QT interval, hypotension, heart failure, arrhythmia, and papilledema. The chance of these side effects is further diminished by the used concentration of 0.83 mmol/l citrate, the separate administration of calcium and magnesium, and the regular controls of the permanent present dialysis nurse. If by chance the proposed RCA with citrate does not result in sufficient anticoagulant effect, clotting may occur. The results of clotting are minimal. At worst, in case of clotting of the extracorporal system, the patient will lose approximately 200 ml of blood.

Where is the study run from?
Albert Schweitzer Hospital (Netherlands)

When is the study starting and how long is it expected to run for?
August 2015 to January 2019

Who is funding the study?
Investigator initiated and funded

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Nil known

Study information

Scientific Title
A pilot study regarding regional anticoagulation by a citrate containing dialysis fluid

Acronym
Citradial

Study objectives
The study has 3 objectives:
1. Proving that this form of Regional Citrate Anticoagulation (RCA) does not increase the risk of bleeding while achieving a degree of anticoagulation of the extracorporeal system that is similar to that when using the usual LMWH. 2. The simplification of the existing RCA in order to make it available to patients receiving chronic hemodialysis with a moderate increased risk of bleeding i. e. using oral anticoagulation or antiplatelet agents. 3. Investigate whether serum values of Ca and Mg are similar to those during standard anticoagulation with LMWH.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 14/04/2014, The Medical Ethics Committee of the Erasmus Medical Center (Medische Ethische Toetsings Commissie Erasmus MC, PO Box 2040, 3000 CA Rotterdam, The Netherlands; +31 10 7033625; no email provided), ref: MEC-2015-090; NL50418.078.15

Study design
Prospective single-center non-randomized cross-over cohort study

Primary study design
Interventional

Secondary study design
Non-randomized cross-over

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
See additional files (in Dutch)

Health condition(s) or problem(s) studied
Regional anticoagulation in chronic hemodialysis patients with a moderately increased risk of bleeding

Interventions
Each patient will function as its own control and will be treated with both LMWH and citrate-HD. Each patient will be treated with two consecutive citrate dialyses (C1 and C2). These dialyses will be compared to two consecutive standard dialyses with LMWH. (L1 en L2). The citrate- and standard dialyses will be performed on the same day of the week. A possible third dialysis during the week will not be a study session and therefore be a standard dialysis with LMWH.

Regional citrate dialysis with calcium- and magnesium-free citrate dialysis fluid:
The dialysis fluid is produced by mixing 9.75 liters of a Ca-, Mg-free, 3,0 mmol/l acetate containing concentrate (Dirinco ACC1208) with 250 ml of a 1500 mmol/l citrate solution (Dirinco Citralock 46.7%, CE 1275). Ca- and Mg-suppletion with a solution containing Ca 54 mmol/100ml, Mg 14 mmol/100ml and 136 ml Cl/100 ml; 35 ml/hour.

LMWH (dalteparin)-HD is the usual standard HD

The treatment lasted for the time of the hemodialysis session being 3.5 to 4.25 hours. The same for both arms. 4 sessions per patient.

Intervention Type
Procedure/Surgery

Primary outcome measure
(Anti)coagulation is measured before, halfway en after the hemodialysis session with non-activated tromboelastometry (NATEM) in whole blood (ROTEM Delta, Tem-innovations München), APTT (Sysmex CS-5100 System, Siemens Healthineers), ionized Ca (ABL90 FLEX, Radiometer).

Secondary outcome measures
1. Clotting phenomena in venous air trap and dialyzer are graded by visual inspection after HD. Venous air trap: 1: no clotting; 2: rim; 3: clot.
Clotting phenomena in the dialyzer: 0: no clotted fibers, 1: <10% of fibers clotted, 2: 10%-50% of fibers clotted, 3: >50% of fibers clotted. Grading is done by a panel of 3 nephrologists and nurses, who are blinded to the method used. Grades are averaged
2. Ionized Ca (ABL90 FLEX, Radiometer), Ca and Mg (Dimension VISTA 1500, Siemens Healthineers), are measured before, halfway en after the hemodialysis session

Overall study start date
16/08/2015

Completion date
29/01/2019

Eligibility

Key inclusion criteria
1. Hemodialysis patients
2. Older than 18 years
3. Cardiovascular stable during and after their hemodialysis sessions
4. Taking acenocoumarol, fenprocoumon, acetylsalicylic acid, dipyridamol, clopidogrel, prasugrel

or a combination here of
5. Good functioning arteriovenous shunt or fistula (blood flow >450 ml/min) for dialysing with two needles or double lumen hemodialysis catheter (blood flow >250ml/min)

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
12

Total final enrolment
12

Key exclusion criteria
1. Unable to give informed consent
2. Unstable during hemodialysis i.e. Drop of blood pressure, muscular cramps
3. With an increased risk of being unstable during hemodialysis
4. With predialysis an ionized calcium <1.0 mmol/l
5. With changes in their dialysis protocol during the study i.e. Change of type and/or size of dialyzer, or change in blood- and/or dialysis fluid flow or change of dialysis modality (hemodialysis, hemofiltration, hemodiafiltration) or change in ultrafiltration
6. With a decrease in Hb >0.5 mmol/l during the study
7. With an increase of erythropoietin dosage >25% during the study
8. With a dysfunctioning arteriovenous shunt or fistula or hemodialysis catheter (see inclusion criteria)
9. With a coagulation defect not to be attributed to the used medication

Date of first enrolment
01/07/2017

Date of final enrolment
01/01/2019

Locations

Countries of recruitment
Netherlands

Study participating centre

Albert Schweitzer Hospital
Albert Schweitzerplaats 25
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Sponsor information

Organisation
Albert Schweitzer Hospital

Sponsor details
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Sponsor type
Hospital/treatment centre

Website
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ROR
https://ror.org/028xtgx62

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

Publication and dissemination plan
Abstracts, posters in the Netherlands, Europa and USA. Article in international journal.

Intention to publish date

01/01/2022

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study will be stored in a non-publically available repository. The raw data are currently stored in the network of the hospital. After the last analysis and publication they will be stored in the general scientific repository of the research department of the hospital.

IPD sharing plan summary

Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet			08/07/2021	No	Yes
Protocol file	version v3		08/07/2021	No	No