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Using citrate as anticoagulation for haemodlalysis

Submission date	Recruitment status	[_] Prospectively registered
04/11/2017	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
08/11/2017	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
10/07/2018	Urological and Genital Diseases	

Plain English summary of protocol

Background and study aims
Haemodialysis is a method where blood is diverted to a machine to remove waste products and extra fluid that build up when the kidneys are not functioning properly. The drug heparin is normally used to stop haemodialysis circuits from clotting. When heparin cannot be used, the standard practice is to flush the circuit regularly with saline (salt water). This method is not well proven to stop circuit clotting. Clotted circuits mean unnecessary blood loss. Citrate has been used to stop circuit clotting (anticoagulation) for prolonged dialysis methods in Intensive Care. The aim of this study is to find out whether using citrate for short haemodialysis treatments is better than saline flushes at stopping clots in the circuit while also being safe.

Who can participate?
Hospital in-patients scheduled for at least two heparin-free hemodialysis sessions

What does the study involve?
Participants are randomly allocated to receive either citrate anticoagulation or standard heparin-free haemodialysis. At their next haemodialysis session they switch over to the alternate method. Blood tests are performed during and at the end of the citrate treatment sessions.

What are the possible benefits and risks of participating?
Citrate is known to be effective and works by lowering blood calcium so that clotting cannot take place. Low calcium levels can however be life threatening (e.g. heart arrhythmias). Citrate is infused into the blood only when it is outside the body to stop it from clotting when it goes through the dialysis circuit. Calcium is then infused back into this blood just before it re-enters the body so that the calcium levels remain normal. The risks are if not enough calcium is infused back into the body calcium levels become too low, but calcium levels are checked regularly to prevent this from happening.

Where is the study run from?
Khoo Teck Puat Hospital (Singapore)

When is the study starting and how long is it expected to run for?
April 2014 to July 2016

Who is funding the study?
Alexandra Health National Medical Research Centre (Singapore)

Who is the main contact?
Dr Terina Seow

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Study information

Scientific Title
Simple citrate anticoagulation protocol for low flux haemodialysis

Study objectives
For patients unable to receive heparin anticoagulation during haemodialysis, saline flushes to reduce circuit clotting are often the norm. Regional citrate anticoagulation (RCA) although effective is not used by many centres including in Singapore. The aim of this study is to demonstrate the superiority and safety of a simple regional citrate anticoagulation regime, compared to saline flushes, for heparin-free low flux haemodialysis.

Ethics approval required
Old ethics approval format

Ethics approval(s)
National Health Group Domain Specific Research Board, 02/04/2015, ref: 2014/01037

Primary study design
Interventional

Study design
Prospective open-label cross-over study

Study type(s)

Treatment

Health condition(s) or problem(s) studied
Haemodialysis

Interventions
Patients were allocated either to regional citrate anticoagulation or standard heparin free haemodialysis and subsequently cross over to the alternate method. The same cohort underwent both treatment arms (citrate and saline flushes) in consecutive haemodialysis sessions which would have been 48-72 hours apart. Citrate is 60-80% dialysed out immediately as it passes through the dialyser and the rest is metabolized by the body within minutes so no washout period is required. Blood tests were performed during and at the end of the citrate treatment sessions

Trisodium Citrate 13% or 500mM (Dirinco BV, Netherland) was infused at a fixed rate pre-filter (into the "heparin" line) according to blood flow (QB) as shown.

Trisodium Citrate 13% Infusion:
Blood flow Trisodium citrate 13%
150 ml/min 60ml/hour
200 ml/min 80ml/hour
250 ml/min 100ml/hour

Calcium Gluconate 10% (2.2 mmol Ca2+ in 10ml vial) was infused post filter (using a 3-way connector into the "venous" return line). Infusion rate was started at 70ml/hour. Calcium infusion rate is then adjusted to pre-filter iCa2+ level.

Calcium Gluconate 10% Infusion:
iCa2+ Level Calcium Gluconate Infusion
<0.65 mM Notify doctor. Terminate citrate infusion and change to heparin free dialysis. Give 40 ml bolus over 30 mins
0.65-0.74 mM Give 20ml bolus over 30 mins and increase infusion by 20 ml/hr
0.75 – 0.9 mM Increase infusion by 20 ml/hr
0.91 – 1.2 mM Infuse at 70ml/hr
>1.2 mM Hold infusion for 30 mins and recheck

For the control arm, 100ml saline flushes were given per 30 minutes, extra flushes were allowed as per nurses's discretion according to standard practice of monitoring for clots in the circuit.

Intervention Type
Procedure/Surgery

Primary outcome(s)
1. Thrombosis and circuit loss: at the end of the dialysis session, arterial and venous drip chambers and the filter were inspected by the nurse for visible signs of coagulation. A score of 1 (no clots), 2 (small clots), 3 (large clots) and 4 (complete clotting of circuit) was applied.
2. Anticoagulation achieved in citrate dialysis arm: post-filter iCa2+ (V) was tested at time 30, 60, 120 and 240 (just before ending) minutes.

Key secondary outcome(s)

Electrolytes and calcium levels for citrate dialysis arm: pre-filter iCa2+ levels (A) were measured at 0, 30, 60, 120 and 240 minutes. Electrolytes were sent to the lab at time 0 and 240 minutes.

Completion date
31/07/2016

Eligibility

Key inclusion criteria
1. Hospital in-patients scheduled for at least 2 heparin-free hemodialysis sessions between August 2015-Jul 2016 at Khoo Teck Puat Hospital, Singapore
2. Haemoglobin >7.0g/dL
3. Haemodynamically stable
4. Reasonably functioning vascular access
5. Chronic haemodialysis patients and acute kidney injury patients

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Decompensated liver disease
2. Received blood products within last 24 hours/required blood products during the dialysis session
3. Haemostatic disorders or deranged clotting
4. Known allergy to citrate products

Date of first enrolment
01/08/2015

Date of final enrolment
31/07/2016

Locations

Countries of recruitment
Singapore

Study participating centre

Khoo Teck Puat Hospital
Singapore
768828

Sponsor information

Organisation
Alexandra Health National Medical Research Centre

Funder(s)

Funder type
Research council

Funder Name
Alexandra Health National Medical Research Centre

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Dr Terina Seow once the study has been published. Consent from patient was obtained to permit data collected from the study to be allowed for use in future related studies. Data is anonymised. Research data and subject identifiers were stored separately.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	19/01/2018		Yes	No