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CONTINUOUS VENO-VENOUS HAEMODIALYSIS USING THE FRESENIUS MULTIFILTRATE

A USER GUIDE

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Criteria

- Citrate (Ci-Ca) anticoagulation is the first line treatment in patients requiring continuous renal replacement therapy (CRRT). However, some patients **may not** tolerate citrate (Ci-Ca) including those with:
    - **acute severe liver failure**
    - **patients with severe global hypoperfusion**
    - **metformin, severe paracetamol or ethylene glycol overdose**
- In these patients discuss with a Consultant Intensivist/Renal Physician whether a trial of citrate (Ci-Ca) with close monitoring is appropriate.
- If you suspect that the patient maybe developing a citrate accumulation, follow the flow chart on page 10.

Preparation for commencement of treatment

- Machine used for Citrate (Ci-Ca) anticoagulation is the Fresenius multiFiltrate®.
- A senior critical care clinician must be informed before commencing CRRT.
- The prescription must be written under the supervision of an experienced clinician.
- Select prescription chart for citrate (Ci-Ca) anticoagulation.
- Prescribe the following on the drug chart
    - Calcium Chloride 50mmols in 500mL Sodium Chloride 0.9% (as per protocol).
    - 1000mL Sodium Citrate 4% (as per protocol).
- Documentation required:
    - Ci-Ca observation chart
    - Ci-Ca prescription chart
- The Fresenius MultiFiltrate® machine should only be set up by a member of the team who has had relevant training. The lined and primed machine should always be checked by a second nurse who has undergone relevant training before commencing.

Setting Up

Fluids
Calcium Chloride 50mmols in 500mL of Sodium Chloride 0.9%
1000mL Sodium Citrate 4%
5L Citrate (Ci-Ca) K4 Dialysate Solution (yellow label) x4 Bags
1 X 1000mL Sodium Chloride 0.9% for priming and wash back

Equipment
Citrate (Ci-Ca) CVVHD 1000 MultiFiltrate® Circuit (Yellow label)
Wash back equipment - 1000mL Sodium Chloride 0.9%, dressing pack, priming spike adapter, yellow bag and pressure transducer line.
Red & blue Y connectors and 2 into 4 connector.

To Start

1. Switch on the machine
2. Wait for functional test to be completed
3. Select Ci-Ca anticoagulation
4. Select a new treatment
5. Choose CVVHD
6. Check all the starting conditions have been fulfilled:
Citrate solution concentration – 136 mmol/L (4%)
Citrate volume 1000ml
Calcium solution concentration – 100 mmol/L
Calcium volume 500ml
Calcium free HF solution used
7. Confirm conditions are fulfilled
8. Follow the step by step guide to line the machine
9. **Measure post-filter iCa^{2+} 5 minutes after starting to confirm there is adequate anticoagulation.**

PLEASE NOTE:

The citrate and calcium line clamps should be moved to the bag connection end of the lines and need to be clamped.

Always read the instructions and do not skip a section.

Remember the access chamber and return drip chamber needs to be primed manually.

The citrate and calcium lines are primed first.

Ensure the filter is turned upside down during the ultrafiltration (UF) rinse phase to ensure the outer compartment of the filter has had all of the air removed.

Dialysis Flow Rate

The default dialysis flow rate is 25mL/kg/hour.

Only consider increasing dialysis flow rate up to 35mL/kg/hour in the following circumstances:

- Severe metabolic acidosis
- Hyperkalaemia (Potassium > 6.5mmol/L)
- Inadequate response to default dialysis flow rate
- Poisoning (e.g. ethylene glycol, lithium)

Start-up flow rates (based on dialysate flow rate 25mL/kg/hour)

The ratio of Dialysis Flow Rate: Blood Flow Rate should be 20:1 at the start of CVVHD, and can then be adjusted according to the acid base balance of the patient. These are the standard start up rates. Remember your patients systemic ionised calcium may need to be pre-treated prior to commencement (page 4)

TABLE 1

Ideal Body Weight	<60kg	60 – 90kg	>90kg
Dialysis Flow Rate	1600 mL/h	2000 mL/h	2400 mL/h
Blood Flow Rate	80 mL/min	100 mL/min	120 mL/min
Citrate Dose	4.0 mmol/L	4.0 mmol/L	4.0 mmol/L
Calcium Dose	1.7 mmol/L	1.7 mmol/L	1.7 mmol/L

Start-up flow rates (based on dialysate flow rate 35mL/kg/hour)

TABLE 2

Ideal Body Weight	<60kg	60 – 90kg	>90kg
Dialysis Flow Rate	2000 mL/h	2600 mL/h	3200 mL/h
Blood Flow Rate	100 mL/min	130 mL/min	160 mL/min
Citrate Dose	4.0 mmol/L	4.0 mmol/L	4.0 mmol/L
Calcium Dose	1.7 mmol/L	1.7 mmol/L	1.7 mmol/L

Note:

Ci-Ca CVVHD mode uses blood flow rates at least half those used with conventional anticoagulation. As a result, there may be less wear and tear on the blood pump segment of the circuit and therefore a reduced risk that this part of the device may split. Because of this Ci-Ca CVVHD circuits in South Tees will be running for a maximum of 120 hours rather than 72 hours recommended by the manufacturer. If using multiBic CVVHD, then the circuits will need to be changed every 72 hours due to the higher pump speeds being used.

After the blood pump has been running for 72hr a pop-up message will alert you the recommended time has been reached. After this, a red warning stays on in the bottom right hand corner of the screen to indicate that the maximum delivery volume on the blood lines has been exceeded. This can be ignored, but you must document the time that the 5 days will be reached and the time that the elective wash back must be done.

If you restart Ci-Ca CVVHD following wash back (see page 11), or connect a new circuit within four hours of interruption, you can set the dialysate/blood flow rates, citrate and calcium doses as they were before, except when the patient's clinical condition has changed. If concerned about a change in condition, discuss with someone experienced.

If it is greater than 4 hours after disconnection, restart CVVHD according to the protocol.

Management of patient's systemic ionised calcium: pre-treatment

To enable the safe management of the patient's systemic iCa^{2+} you must ensure that the patient's systemic iCa^{2+} is within safe levels. To do this check the patient's systemic ionised calcium (iCa^{2+}) via a blood gas at least one hour prior to starting the treatment. You must then use the below guide (table 4) to help you maintain the patient's systemic iCa^{2+}.

TABLE 4

Systemic iCa^{2+} (mmol/L)	< 1.01	1.01 - 1.11	1.12 - 1.20	1.21 - 1.45	> 1.45
Pre-treatment with calcium Chloride **	Yes	Yes	No	No	No
Starting dose Calcium Chloride (mmol/L)	2.0	1.9	1.7	1.5	1.4
Check first systemic iCa^{2+} and review calcium dose after	2 hours	6 hours	6 hours	6 hours	6 hours

**** Infuse 10mmol calcium chloride in 50mL sodium chloride 0.9% over 30 minutes**

Please note: you will see a drop in the patient's systemic iCa^{2+} on commencement of treatment. This is not an indication of citrate accumulation as an isolated figure. See the algorithm for citrate accumulation (page 10) for management of this.

First Post filter ionised Calcium check

Measure the post filter iCa^{2+} five minutes after starting and adjust the citrate dosage according to Table 3. This check ensures the circuit is adequately anti-coagulated. The optimum range is between 0.25 – 0.34. Subsequent post filter iCa^{2+} should be confirmed and the citrate dose reviewed once every six hours.

Monitoring post Filter Ionised Calcium levels

If there is suspected citrate accumulation refer to Page 10.

TABLE 3

Post- filter ionised calcium (mmol/L)	Change of the citrate dose (Citrate/blood)	Check Post- filter ionised calcium and review citrate dose after
> 0.45	Increase by 0.3 mmol/L ***Inform senior doctor***	6 hours
0.41 - 0.45	Increase by 0.2 mmol/L	6 hours
0.35 - 0.40	Increase by 0.1 mmol/L	6 hours
0.25 - 0.34	**No Change**	6 hours
0.20 - 0.24	Reduce by 0.1 mmol/L	6 hours
↓↓↓↓	Reduce by 0.1 mmol/L	6 hours

Monitoring Systemic Ionised Calcium

TABLE 5

Systemic ionised calcium (mmol/L)	Change of the calcium dose (Calcium/filtrate)	Check systemic ionised calcium and review dose after
> 1.45	Reduce by 0.6 mmol/L ***Inform senior doctor***	6 hours
1.31 - 1.45	Reduce by 0.4 mmol/L	6 hours
1.21 - 1.30	Reduce by 0.2 mmol/L	6 hours
1.12 - 1.20	**No Change**	6 hours
1.05 - 1.11	Increase by 0.2 mmol/L	6 hours
0.95 - 1.04	Increase by 0.4 mmol/L	2 hours
< 0.95	Increase by 0.6 mmol/L ***Inform senior doctor***	2 hours

Important note:

If the systemic ionised calcium rises to the point where the protocol indicates you to turn off the Calcium, you must change to multiBic or assess whether or not CVVHD is required. Under no circumstances should you run the Citrate without the Calcium running too.

Acid-Base Balance Management

Fifty per cent of the calcium citrate complexes are dialysed out into the waste and 50% is re-infused into the patient along with some unbound citrate. Citrate is typically metabolised to bicarbonate, and the bound calcium is released as free ionised calcium. Management of the acid-base balance is therefore an important factor of citrate anticoagulation.

If the acid-base balance is within normal ranges and you are changing the blood flow rate due to vascular access issues then dialysate flow rate also needs to be changed to maintain the 20:1 ratio.

If an acid-base derangement occurs it is important to distinguish if this is due to a primary metabolic process in the patient or the accumulation of citrate. If a primary metabolic process is considered likely this should be treated first.

Metabolic acidosis potential causes:

- Patient's underlying condition.
- Continuous renal replacement therapy has not been running long enough.
- Inadequate dialysis dose.
- Dialysate flow rate too high in relation to the blood flow rate (insufficient citrate is being supplied to the patient).
- Citrate accumulation due to impaired metabolism (e.g. acute severe liver failure, severe lactic acidosis). This is indicated by a T:I calcium ratio >2.5.

Metabolic acidosis potential action:

- Consider increasing dialysate rate to 35ml/kg/hour - See Table 2 for recommended settings.
- Increase blood flow rate by 20mL/min. This will not be effective if citrate accumulation is the cause.
- If no improvement after 4 hours, refer to the Consultant Intensivist / Renal Physician.

Metabolic alkalosis potential causes:

- Patient's underlying condition.
- Dialysate flow rate too low in relation to blood flow rate.
- Medication that may cause alkalosis (e.g. sodium bicarbonate, acetazolamide).
- Patient has been receiving treatment for 3 days with improving biochemistry. Watch for a rising bicarbonate and base excess.

Metabolic alkalosis potential actions:

- First action is to decrease blood flow rate by 20mL/min. If not effective ….
- Increase dialysate flow rate by 500mL/hour.
- If no improvement after 4 hours, refer to the Consultant Intensivist / Renal Physician.

Alteration of blood or dialysate rates is a change in prescription. This must be documented on the chart.

Management of Potassium, Magnesium and Phosphate

Potassium

Ci-Ca K4 Dialysate contains 4.0 mmol/L of potassium.
Ci-Ca K2 Dialysate contains 2.0 mmol/L of potassium.

Serum potassium levels should be checked at least every 3 to 4 hours unless indicated.
If hyper/hypokalaemia occurs checking should be increased to 1 to 2 hourly.

If severe hyperkalaemia (potassium >6.5 mmol/L) is present at the commencement of treatment or during treatment prescribe a dialysis flow rate at 35mL/kg/hr. See Table 2 for recommended settings. If Ci-Ca K4 is being used consider changing to Ci-Ca K2 (if available).

If severe hyperkalaemia persists refer to the consultant intensivist/renal physician

Hypokalaemia can be corrected by giving Potassium Chloride supplementation according to ICU guidelines.

Phosphate

Ci-Ca K2/K4 Dialysate does not contain phosphate.

Daily checks of phosphate levels should take place and should be substituted as clinically required.

Magnesium

Magnesium forms complexes with citrate which can be dialysed out.

Ci-Ca K2/K4 dialysate contains 0.75 mmol/L of magnesium which should help maintain good levels of systemic magnesium.

Daily checks of magnesium levels should take place and should be substituted as clinically required.

Citrate Accumulation

Detection of citrate accumulation

Problems may occur if the patient is unable to adequately metabolise citrate in the presence of acute severe liver failure and/or severe lactic acidosis. Therefore, there will be a rise in the patient's systemic citrate-calcium complex levels, leading to a higher total systemic calcium relative to the ionised systemic calcium – this will lead to a higher T:I (Total:Ionised) ratio. Signs associated with impairment of citrate metabolism and citrate accumulation include:

- T:I ratio > 2.5 (see below)
- Marked drop in systemic ionised calcium
- Elevated adjusted (laboratory) calcium > 3mmol/L
- Metabolic acidosis - due to failure to metabolise citrate to bicarbonate and the accumulation of citrate ions producing an elevated anion gap acidosis.

Note - exclude other causes of metabolic acidosis as this may not necessarily be secondary to citrate accumulation.

If Calcium Chloride (CaCl2) infusion dose is >2.1 mmol/L, the machine will prompt you to consider citrate accumulation.

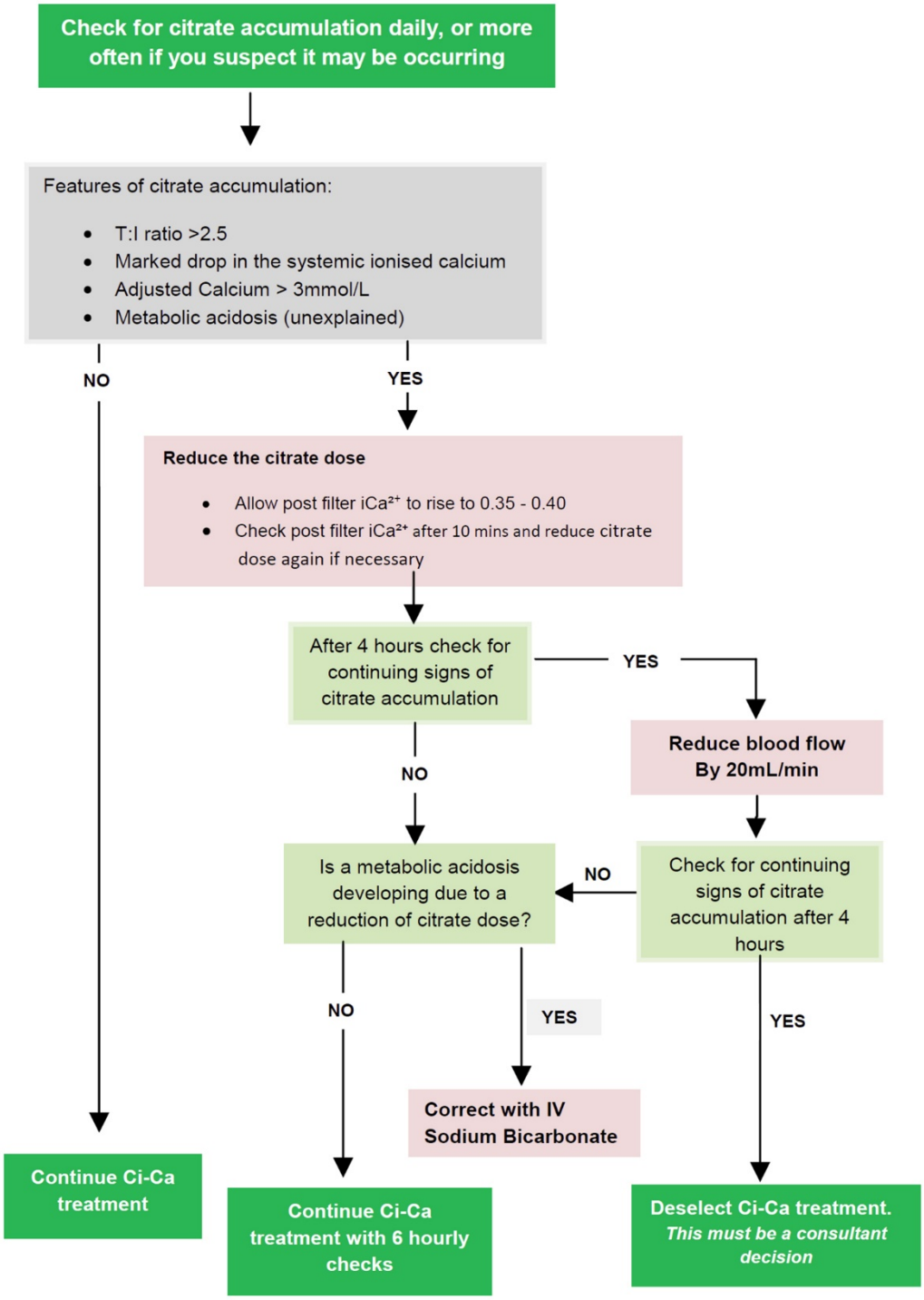
It is important to monitor the total calcium: systemic ionised calcium (T: I) ratio at least once each day to ensure it does not rise >2.5 as this correlates with citrate accumulation. **In high risk patients, this can be done up to 4 times a day**. Refer to the Consultant Intensivist / Renal Physician if this occurs.

The T: I ratio is calculated using the 6.00 am routine bloods and an arterial blood gas sample taken within 1 hour of this time for your systemic ionised calcium (iCa^{2+}).

Use the <u>uncorrected calcium</u> level from the laboratory blood results as your total calcium level.

Please follow the algorithm on the next page to manage a suspected citrate accumulation.

For Management of Citrate Accumulation



Frequently asked questions

1. *How to convert from Citrate to Heparin / no anticoagulation without changing the circuit*

- Use if citrate is accumulating, circuits keep clotting, or the patient requires systemic heparin for another indication. Changing to heparin from citrate must be a consultant (ICU or renal) decision.

- Select anticoagulant to be used: (Refer to non-citrate protocol for details)
- if using heparin, use a 50mL syringe on the Fresenius machine.
- if using epoprostenol, a separate syringe driver is needed.

- ***A different dialysis fluid (multiBic K2/K4) is required.***

Step by Step Guide on how to change the circuit

1. When using heparin, go to **'Treatment'** screen, then **'Syringe Change'.**
2. Attach the heparin syringe and manually prime the line.
3. Fit in the carrier and start as per the non-citrate protocol.
4. When using epoprostenol attach syringe to the line and prime manually. Use the separate syringe driver and commence after doing the following steps.
5. On the **'Treatment'** screen select **'Deselect Ci-Ca anticoagulation'.**
6. Confirm decision by selecting **'Yes'** on the next screen.
7. Confirm all conditions for change are fulfilled.
8. All pumps will stop except the blood pump. You will be asked to change the bags, which you will change to **multiBic K2/K4**. Once change made and accepted, the pumps will recommence.

The blood flow rate needs to be changed when you are not using citrate due to the size of the filter. Increase to a minimum of 250mL/min – if this is not possible due to poor flow rates from the dialysis catheter, then the maximum achievable flow rate is selected. If extra clearance is necessary you can then increase the dialysis flow rate to maximum rate of 4.8 litres/hour. Because these flow rates are higher the circuit must only be used for a maximum of 72 hours.

2. *What happens if you use the wrong dialysis solution during Ci-Ca?*

- Ci-Ca K2/K4 is a specific solution made for Ci-Ca anticoagulation. If you use multiBic fluid instead, you may encounter:
    - systemic bicarbonate increasing
    - systemic iCa^{2+} increasing
    - high post-filter iCa^{2+} (due to migration of calcium from the multiBic across the membrane), increasing citrate requirements (due to the increased post-filter iCa^{2+}) and an increasing systemic Na^{+} (due to the increased trisodium citrate)

- **If you use Ci-Ca fluid when you are treating the patient with CVVHD without calcium, you can potentially cause a fatal drop in the patient's systemic ionised calcium.**

If you notice any of the above, check that you are using the correct dialysis fluid.

3. *How to save a circuit when a patient needs to be temporarily disconnected*

- This is an aseptic procedure.
- Providing there has been no changes in their clinical state, and it is not more than 4 hours since the circuit was disconnected, patients can be re-connected using the previous rates for dialysate and blood flows, and citrate and calcium doses. If you are concerned about a change in condition discuss this with an experience practitioner.
- Circuits disconnected greater than 4hours must be replaced. The new circuit must be set up using the protocol settings for dialysate and blood flows, and citrate and calcium doses.

There are two methods of temporary disconnection.

METHOD 1 – Wash back and re-circulate – e.g. transfer to radiology.

The maximum disconnection time with this method is **4 hours**.

Step by Step Guide on how to recirculate

Requirements :- 1 litre bag of sodium chloride 0.9%, three way tap or Y connector and single spike adapter, dressing pack, and equipment to flush catheter.

1. Press **STOP.**
2. Disconnect the access line **(red)** and connect to the three way tap or Y connector attached to the sodium chloride 0.9% bag.
3. Press **START/RESET -** this will restart the blood pump and wash back blood to the patient.
4. The optical detector will detect sodium chloride 0.9% solution. The blood pump will stop. A yellow warning will then be displayed informing you that the above change has been detected.
5. Press **START/RESET -** the machine will then ask you to confirm if you have interrupted the treatment. Press **YES.** The blood pump will now restart**.**
6. Decide how much more blood you want to be returned to the patient. Press **STOP** when you have reached the amount you wish to be returned.
7. Disconnect the return line **(blue)** from the patient and connect to the three way tap or Y connector attached to the sodium chloride 0.9% bag.
8. Press **START/RESET** and the machine will then be recirculating. (Balancing will automatically switch off).
9. Turn ultrafiltration (UF) to 0.

Step by step guide on how to reconnect the patient

1. Press **STOP.**
2. Disconnect the access **(red)** and return **(blue)** lines from the sodium chloride 0.9% bag and connect to the patient access as per protocol.
3. Press **START/RESET** and the blood pump will restart.
4. A yellow warning will be displayed when the optical detector has detected blood.
5. Press **START/RESET -** this will restart the blood pump (Balancing will automatically switch on).
6. Turn ultrafiltration (UF) to the desired removal rate.

METHOD 2 – Re-circulate with whole blood – e.g. when transferring bed space.

This method can be used for disconnections lasting up to 30 minutes.

Step by step guide on how to recirculate

Requirements: Blue adapter from kit (or three way tap or Y connector). Equipment to manage catheter

1. Press **STOP -** this will stop the blood pump.
2. Disconnect the access **(red)** line and connect it to the blue adapter.
3. Disconnect the return **(blue)** line and connect it to the other side of the blue adapter.
4. Press **START/RESET -** this will restart the blood pump.
5. Turn ultrafiltration (UF) to 0.

Step by step guide on how to reconnect the patient

1. Press **STOP** this will stop the blood pump.
2. Connect both access **(red)** and return **(blue)** lines to patient.
3. Press **START/RESET -** this will restart the blood pump.
4. Turn ultrafiltration to desired removal rate.

4. How to flush the dialysis catheter if not using it for 4 hours or more to prevent clotting

- This is an aseptic technique.
- Equipment: Dressing pack, alcohol swabs, 2 x 10mLs sterile 0.9% Saline, 5mLs TauroLock-Hep500, appropriate drawing up needles and syringes, 2 x obturators.
- Draw up the 0.9% saline into 2 x 10mL syringes and divide the TauroLock-Hep500 into 2 x 2.5mL.
- Clamp off the two dialysis catheter lumens and the access and return lumens of the circuit.
- Disconnect one lumen of the dialysis catheter, clean the hub, connect the 10 mLs 0.9% Saline syringe and release the clamp. Using a pulsatile method involving the repeated rapid injections of 2mL, inject the whole 10mL of 0.9% saline. Clamp off the dialysis catheter and remove the 10 mL syringe. Slowly inject enough TauroLock-Hep500 such that it only just fills the lumen (this is usually indicated on the catheter – if not, inject the whole 2.5 mLs). Re-apply the clamp and seal with a new obturator.
- Repeat with the other lumen.

Note: TauroLock-Hep500 contains (cyclo)-taurolidine as an antimicrobial agent, 500 units heparin per mL and citrate (4%). It's use is contra-indicated if the patient has a known adverse reaction to any of its components – this includes Heparin Induced Thrombocytopaenia (HIT). If HIT is suspected, use the heparin-free TauroLock instead. TauroLock-U25.000 may be used to salvage a partially thrombosed catheter – it is constituted from heparin-free TauroLock and 25,000 IU urokinase and left in the catheter until it is next used.

5. Using Heparin for other indications while on Ci-Ca CVVHD

- VTE prophylaxis should still be given according to Trust guidelines when a patient is on Ci-Ca CVVHD.
- Continuous unfractionated heparin (UFH) infusions for systemic anticoagulation can be given whilst on C-Ca CVVHD according to Trust protocol. There is no need to adjust the Ci-Ca settings under such circumstances.

Further resources:

1. **Ci-Ca Regional Anticoagulation.** Clinical implementation of Ci-Ca therapy protocols. ***Fresenius Medical Care (UK) Ltd. UK/ABT/MFT/0116/0001. January 2016.***
2. **Troubleshooting Guide for the multiFiltrate.** ***Fresenius Medical Care (UK) Ltd. 2008.***
3. **EMiC®2.** Enhanced Middle Molecule Clearance. ***Fresenius Medical Care (UK) Ltd. UK/ABT/MFT/0118/0001. January 2018.***

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