REGIONAL CITRATE ANTICOAGULATION PROTOCOL FOR CONTINUOUS VENO-VENOUS HEMOFILTRATION (CVVH) USING REGIOCIT 18/0 IN COMBINATION WITH BIPHOZYL 22

CKRT MONITOR

Monitor: **PRISMAX**. Modality: **CVVH**

SOLUTIONS ADOPTED

1. Citrate solution as pre-dilution replacement fluid: Baxter **Regiocit 18/0** (citrate 18 mmol/l)
2. Phosphate and bicarbonate containing solution as post-dilution replacement fluid: Baxter **Biphozyl** (HCO_3^- 22 mmol/l, K^+ 4 mmol/l, Ca^{2+} 0 mmol/l, Mg^{2+} 0.75 mmol/l, HPO_4^{--} 1 mmol/l)
3. $CaCl_2$ solution f. 10 ml 10 % (Ca^{2+} 272 mg or 0.68 mmol/ml) infused in a central venous line separated from other infusions

1. INITIAL RCA-CVVH SETTING

- **Regiocit 18/0** solution must be infused as pre-dilution replacement fluid using the **white scale (PBP**), remembering to keep all the clamps along the white line open. **Biphozyl** solution (the solution containing phosphate and bicarbonate) must be infused as post-dilution replacement fluid.
- Different flows rates must be set up according to blood flow rate (Qb) as shown in **Table I**.

Table I *– Setting of pre-dilution replacement fluid (Regiocit 18/0) in relation to Qb and post-dilution replacement fluid (Biphozyl) corresponding to a prescribed dialysis dose, not corrected for pre-dilution, of 35 ml/Kg/h for a 70 Kg male patient*

	Qb (ml/min)	**Q Regiocit (ml/h)**	**Q Biphozyl post-dilution replacement fluid (ml/h)**
A	130	1300	1200
B	**140**	**1400**	**1100**
C	150	1500	1000

The recommended setting is the one marked with B.

ACID–BASE STATUS: in relation to the citrate load (1 mmol of citrate is converted to 3 mmol of bicarbonate) and to the patient's status, the control of acid-base balance may require some adjustments:

- In case of **metabolic acidosis** (HCO_3^- < 18 mmol/l), after the exclusion of citrate accumulation related to inadequate citrate metabolism, the citrate dose has to be increased by increasing Qb and also by modifying Biphozyl flow rate, according to the indications reported in Table I (Example: shift from B to C).
- In case of **metabolic alkalosis** (HCO_3^- > 30 mmol/l), Regiocit 18/0 flow rate has to be decreased (by decreasing Qb), and by Biphozyl flow rate modified, according to the indications reported in Table I (Example: shift from B to A).

2. CALCIUM CHLORIDE ($CaCl_2$) FLOW SETTING

Prepare **a 50 mL syringe pump with 5 fl of $CaCl_2$ 10 mL 10%** and set up the infusion rate according to the **patient's s-Ca^{2+}** (remember to perform a blood gas analysis immediately before starting dialysis) and the **total effluent volume** (pre- and post-dilution replacement fluid flow rates and ultrafiltration rate) as shown in **Table II**.

Table II *– Setting of $CaCl_2$ infusion rate*

Patient's s Ca^{2+} before CVVH start	**Selected option with relative flow rates (Qb: ml/min) (others: ml/h)**	A Qb 130 PBP 1300 Post-dil 1200 Ultraf 100	**B (standard)** **Qb 140** **PBP 1400** **Post dil 1100** **Ultraf 100**	C Qb 150 PBP 1500 Post-dil 1000 Ultraf 100
	≤1.1 mmol/l	*5.2*	***5.3***	*5.4*
	1.1 < Ca^{2+} < 1.3 mmol/l	*5.6*	***5.7***	*5.8*
	≥1.3 mmol/l	*6.1*	***6.2***	*6.3*

If significant changes of ultrafiltration rate are needed (> 500 ml/h compared to the indications reported in Table II), variations of $CaCl_2$ infusion rate may be recommended, according to blood gas analysis controls.

Subsequent modifications of $CaCl_2$ infusion rate must be realized on the basis of **patient's s-Ca^{2+}**: blood gas analysis must be performed **every 2 hours** for the first 6 hours and then every 4 hours, with the aim of keeping the patient's s-Ca^{2+} within the normal range (1.1-1.25 mmol/L), according to the indications in **Table III**. Moreover, control of post-filter circuit Ca^{2+} will be done after 2 hours from the dialysis start.

Table III *– Modifications of $CaCl_2$ infusion rate in relation to patient's systemic Ca^{++} (mmol/L)*

if s-Ca^{2+} ≥ 1.50 decrease 40%
if s-Ca^{2+} ≥ 1.25 decrease 20%
if s-Ca^{2+} > 1.1 and < 1.25: no change needed
if s-Ca^{2+} ≤ 1.1: increase 20%
if s-Ca^{2+} ≤ 1.0: increase 40%
if s-Ca^{2+} ≤ 0.90: increase 50%
if s-Ca^{2+} ≤ 0.8: contact on-call physician

In case of persistence of inadequate s-Ca^{2+} values, check the syringe pump and increase the frequency of s-Ca^{2+} controls: if needed, perform further modifications of infusion rate. Remember that s-Ca^{2+} controls must be effectuated only using the blood gas syringe.

Remember to stop the $CaCl_2$ infusion if dialysis treatment with regional citrate anticoagulation is interrupted.

Finally, **lactic acid controls** should be performed before the start of dialysis and after 2 hours from the beginning.

OTHER SUPPLEMENTATIONS:

- **Magnesium**: In the ionized form, magnesium is a divalent cation (Mg^{2+}) and during Regional Citrate Anticoagulation (RCA) is chelated by citrate exactly like ionized calcium (Ca^{2+}); thus, given the high diffusive/convective clearance of Mg-citrate complexes, a significant amount of magnesium is lost in the effluent fluid. Therefore, daily magnesium controls are needed and, in case of depletion, the infusion of variable amount of magnesium sulfate ($MgSO_4$ 2-5 g/24h) may be recommended.

- **Phosphate** and **Potassium**: the use of Biphozyl ($HPO4^{-}$ 1 mmol/l and K^{+} 4 mmol/l) allows a better control of phosphate and potassium levels, compared to other available dialysis solutions, strongly reducing the need of supplementations. However, potassium levels should be monitored by blood gas analysis and phosphorus with daily scheduled laboratory test. In case of depletion, adequate supplementations should be provided according to the serum concentrations.

REGIONAL CITRATE ANTICOAGULATION PROTOCOL FOR CONTINUOUS VENO-VENOUS HEMODIAFILTRATION (CVVHDF) USING REGIOCIT 18/0 IN COMBINATION WITH BIPHOZYL 22

CKRT MONITOR

Monitor: **PRISMAX**. Modality: **CVVHDF**

SOLUTIONS ADOPTED

1. Citrate solution as pre-dilution replacement fluid: Baxter **Regiocit 18/0** (citrate 18 mmol/l)
2. Phosphate and bicarbonate containing solution as dialysate and post-dilution replacement fluid: Baxter **Biphozyl** (HCO_3^- 22 mmol/l, K^+ 4 mmol/l, Ca^{2+} 0 mmol/l, Mg^{2+} 0.75 mmol/l, HPO_4^{--} 1 mmol/l)
3. $CaCl_2$ solution f. 10 ml 10 % (Ca^{2+} 272 mg or 0.68 mmol/ml) infused in a central venous line separated from other infusions

1. INITIAL RCA-CVVHDF SETTING

- **Regiocit 18/0** solution must be infused as pre-dilution replacement fluid using the **white scale (PBP**), remembering to keep all the clamps along the white line open. **Biphozyl** solution (the solution containing phosphate and bicarbonate) must be infused as dialysate and post-dilution replacement fluid.
- Different flows rates must be set up according to blood flow rate (Qb) as shown in **Table I**.

Table I *– Setting of pre-dilution replacement fluid (Regiocit 18/0) in relation to Qb and post-dilution replacement fluid (Biphozyl) corresponding to a prescribed dialysis dose, not corrected for pre-dilution, of 35 ml/Kg/h for a 70 Kg male patient*

	Qb (ml/min)	Q Regiocit (ml/h)	Q Biphozyl dialysate (ml/h)	Q Biphozyl post-dilution replacement fluid (ml/h)
A	130	1300	500	700
B	**140**	**1400**	**500**	**600**
C	150	1500	500	500

The recommended setting is the one marked with B.

ACID–BASE STATUS: in relation to the citrate load (1 mmol of citrate is converted to 3 mmoles of bicarbonate) and to the patient's status, the control of acid-base equilibrium may require some adjustments:

- In case of **metabolic acidosis** (HCO_3^- < 18 mmol/l), after the exclusion of citrate accumulation related to inadequate citrate metabolism, the citrate dose has to be increased by increasing Qb and also by modifying post-dilution flow rate, according to the indications reported in Table I (Example: shift from B to C).
- In case of **metabolic alkalosis** (HCO_3^- > 30 mmol/l), Regiocit 18/0 flow rate has to be decreased (by decreasing Qb), and by post-dilution flow rate modified, according to the indications reported in Table I (Example: shift from B to A).

2. CALCIUM CHLORIDE ($CaCl_2$) FLOW SETTING

Prepare **a 50 mL syringe pump with 5 fl of $CaCl_2$ 10 mL 10%** and set up the infusion rate according to the **patient's Ca^{++}** (remember to perform a blood gas analysis immediately before starting dialysis) and the **total effluent volume** (pre- and post-dilution replacement fluid flow rates, dialysate flow rate and ultrafiltration rate) as per **Table II**.

Table II *– Setting of $CaCl_2$ infusion rate*

Patient' s Ca^{++} before CVVHDF start	**Selected option with relative flow rates (Qb: ml/min) (others: ml/h)**	A Qb 130 PBP 1300 Dialysate 500 Post-dil 700 Ultraf 100	**B (standard)** **Qb 140** **PBP 1400** **Dialysate 500** **Post dil 600** **Ultraf 100**	C Qb 150 PBP 1500 Dialysate 500 Post-dil 500 Ultraf 100
	≤1.1 mmol/l	*5.2*	***5.3***	*5.4*
	1.1 < Ca^{++} < 1.3 mmol/l	*5.6*	***5.7***	*5.8*
	≥1.3 mmol/l	*6.1*	***6.2***	*6.3*

If significant changes of ultrafiltration rate are needed (> 500 ml/h compared to the indications reported in Table II), variations of $CaCl_2$ infusion rate may be recommended, according to blood gas analysis controls.

Subsequent modifications of $CaCl_2$ infusion rate must be realized on the basis of **patient's s-Ca^{2+}**: blood gas analysis must be performed **every 2 hours** for the first 6 hours and then every 4 hours, with the aim of keeping the patient's s-Ca^{2+} within the normal range (1.1-1.25 mmol/L), according to the indications in **Table III**. Moreover, control of post-filter circuit Ca^{2+} will be done after 2 hours from the dialysis start.

Table III *– Modifications of $CaCl_2$ infusion rate in relation to patient's systemic Ca^{2+} (mmol/l)*

if $Ca^{++} \geq 1.50$ decrease 40%
if $Ca^{++} \geq 1.25$ decrease 20%
if $Ca^{++} > 1.1$ and < 1.25: no change needed
if $Ca^{++} \leq 1.1$: increase 20%
if $Ca^{++} \leq 1.0$: increase 40%
if $Ca^{++} \leq 0.90$: increase 50%
if $Ca^{++} \leq 0.8$: contact on-call physician

In case of persistence of inadequate s-Ca^{2+} values, check the syringe pump and increase the frequency of s-Ca^{2+} controls: if needed, perform further modifications of infusion rate. Remember that s-Ca^{2+} controls must be effectuated only using the blood gas syringe.

Remember to stop the $CaCl_2$ infusion if dialysis treatment with regional citrate anticoagulation is interrupted.

Finally, **lactic acid controls** have to be done before the start of dialysis and after 2 hours.

OTHER SUPPLEMENTATIONS:

- **Magnesium**: In the ionized form, magnesium is a divalent cation (Mg^{2+}) and during Regional Citrate Anticoagulation (RCA) is chelated by citrate exactly like ionized calcium (Ca^{2+}); thus, given the high diffusive/convective clearance of Mg-citrate complexes, a significant amount of magnesium is lost in the effluent fluid. Therefore, daily magnesium controls are needed and, in case of depletion, the infusion of variable amount of magnesium sulfate ($MgSO_4$ 2-5 g/24h) may be recommended.

- **Phosphate** and **Potassium**: the use of Biphozyl ($HPO4^{-}$ 1 mmol/l and K^{+} 4 mmol/l) allows a better control of phosphate and potassium levels, compared to other available dialysis solutions, strongly reducing the need of supplementations. However, potassium levels should be monitored by blood gas analysis and phosphorus with daily scheduled laboratory test. In case of depletion, adequate supplementations should be provided according to the serum concentrations.

REGIONAL CITRATE ANTICOAGULATION PROTOCOL FOR SUSTAINED LOW-EFFICIENCY DIALYSIS (SLED-f) USING REGIOCIT 18/0 IN COMBINATION WITH BIPHOZYL 22

CKRT MONITOR

Monitor: **PRISMAX**. Modality: **SLED-f** (on Prismax monitor select CVVHDF option)

SOLUTIONS ADOPTED

1. Citrate solution as pre-dilution replacement fluid: Baxter **Regiocit 18/0** (citrate 18 mmol/l)
2. Phosphate and bicarbonate containing solution as dialysate: Baxter **Biphozyl** (HCO_3^- 22 mmol/l, K^+ 4 mmol/l, Ca^{2+} 0 mmol/l, Mg^{2+} 0.75 mmol/l, HPO_4^- 1 mmol/l)
3. Bicarbonate containing solution as post-dilution replacement fluid: Baxter **Prismasol 4** (HCO_3^- 32 mmol/l, K^+ 4 mmol/l, Ca^{2+} 1.75 mmol/l, Mg^{2+} 0.5 mmol/l)
4. $CaCl_2$ solution f. 10 ml 10 % (Ca^{2+} 272 mg or 0.68 mmol/ml) infused in a central venous line separated from other infusions

1. INITIAL RCA-SLED SETTING

- **Regiocit 18/0** solution must be infused as pre-dilution replacement fluid using the **white scale (PBP)**, remembering to keep all the clamps along the white line open. **Biphozyl** solution (the solution containing phosphate and bicarbonate) must be infused as dialysate while **Prismasol 4** (the solution containing bicarbonate without phosphate) must be infused as post-dilution replacement fluid.
- Different flows rates must be set up according to blood flow rate (Qb) as shown in **Table I**.

Table I *– Setting of pre-dilution replacement fluid (Regiocit 18/0) in relation to Qb, dialysate (Biphozyl) and post-dilution replacement fluid (Prismasol 4) for a total effluent volume of 100 ml/min*

	Qb (ml/min)	Q Regiocit (ml/h)	Q Biphozyl dialysate (ml/h)	Q Prismasol 4 post-dilution replacement fluid (ml/h)
A	180	1800	3000	1200
B	**200**	**2000**	**3000**	**1000**
C	220	2200	3000	800

The recommended setting is the one marked with B.

ACID–BASE STATUS: in relation to the citrate load (1 mmol of citrate is converted to 3 mmol of bicarbonate) and to the patient's status, the control of acid-base equilibrium may require some adjustments:

- In case of **metabolic acidosis** (HCO_3^- < 18 mmol/l), after the exclusion of citrate accumulation related to inadequate citrate metabolism, the citrate dose has to be increased by increasing Qb and also by modifying Biphozyl flow rate, according to the indications reported in Table I (Example: shift from B to C).
- In case of **metabolic alkalosis** (HCO_3^- > 30 mmol/l), Regiocit 18/0 flow rate has to be decreased (by decreasing Qb), and by post-dilution flow rate modified, according to the indications reported in Table I (Example: shift from B to A).

2. CALCIUM CHLORIDE ($CaCl_2$) FLOW SETTING

Prepare **a 50 mL syringe pump with 5 fl of $CaCl_2$ 10 ml 10%** and set up the infusion rate according to the **patient's Ca^{++}** (remember to perform the blood gas analysis immediately before starting dialysis) and the **total effluent volume** (pre- and post-dilution replacement fluid flow rates, dialysate flow rate and ultrafiltration rate) as per **Table II**.

Table II *– Setting of $CaCl_2$ infusion rate*

Patient's Ca^{++} before SLED start	**Selected option with relative flow rates (Qb: ml/min) (others: ml/h)**	A Qb 180 PBP 1800 Dialysate 3000 Post-dil 1200 Ultraf 200	**B (standard)** **Qb 200** **PBP 2000** **Dialysate 3000** **Post dil 1000** **Ultraf 200**	C Qb 220 PBP 2200 Dialysate 3000 Post-dil 1200 Ultraf 200
	≤1.1 mmol/l	*9.6*	***10.1***	*10.7*
	1.1 < Ca^{++} < 1.3 mmol/l	*10.8*	***11.3***	*11.8*
	≥1.3 mmol/l	*12.0*	***12.5***	*12.9*

If significant changes of ultrafiltration rate are needed (> 500 ml/h compared to the indications reported in Table II), variations of $CaCl_2$ infusion rate may be recommended, according to blood gas analysis controls.

Subsequent modifications of $CaCl_2$ infusion rate must be realized on the basis of **patient's s-Ca^{2+}**: blood gas analysis must be performed **every 2 hours** for the first 4 hours and then every 4 hours, with the aim of keeping the patient's s-Ca^{2+} within the normal range (1.1-1.25 mmol/L), according to the indications in **Table III**. Moreover, control of post-filter circuit Ca^{2+} will be done after 2 hours from the dialysis start.

Table III *– Modifications of $CaCl_2$ infusion rate in relation to patient's systemic Ca^{2+} (mmol/L)*

if $Ca^{++} \geq 1.50$ decrease 40%
if $Ca^{++} \geq 1.25$ decrease 20%
if $Ca^{++} > 1.1$ and < 1.25: no change needed
if $Ca^{++} \leq 1.1$: increase 20%
if $Ca^{++} \leq 1.0$: increase 40%
if $Ca^{++} \leq 0.90$: increase 50%
if $Ca^{++} \leq 0.8$: contact on-call physician

In case of persistence of inadequate s-Ca^{2+} values, check the syringe pump and increase the frequency of s-Ca^{2+} controls: if needed, perform further modifications of infusion rate. Remember that s-Ca^{2+} controls must be effectuated only using the blood gas syringe.

Remember to stop the $CaCl_2$ infusion if dialysis treatment with regional citrate anticoagulation is interrupted.

Finally, **lactic acid controls** have to be done before the start of dialysis and after 2 hours.

OTHER SUPPLEMENTATIONS:

- **Magnesium**: In the ionized form, magnesium is a divalent cation (Mg^{2+}) and during Regional Citrate Anticoagulation (RCA) is chelated by citrate exactly like ionized calcium (Ca^{2+}); thus, given the high diffusive/convective clearance of Mg-citrate complexes, a significant amount of magnesium is lost in the effluent fluid. Therefore, daily magnesium controls are needed and, in case of depletion, the infusion of variable amount of magnesium sulfate ($MgSO_4$ 2-5 g/24h) may be recommended.

- **Phosphate** and **Potassium**: the use of Biphozyl ($HPO4^{-}$ 1 mmol/l and K^{+} 4 mmol/l) allows a better control of phosphate and potassium levels, compared to other available dialysis solutions, strongly reducing the need of supplementations. However, potassium levels should be monitored by blood gas analysis and phosphorus with daily scheduled laboratory test. In case of depletion, adequate supplementations should be provided according to the serum concentrations.