

Table S1. Comparison of intervention and control continuous renal replacement protocols between and among study sites

Site Number		1		2		3	
Number of subjects randomised		119		37		3	
Number of circuits randomised		496		175		4	
		Citrate	Heparin / Protamine	Citrate	Heparin / Protamine	Citrate	Heparin / Protamine
<i>Equipment</i>	Machine(s) Used	Prismaflex	Prismaflex	Prismaflex & Infomed	Prismaflex & Infomed	Prismaflex	Prismaflex
<i>Description of settings</i>	Mode	CVVHDF	CVVHDF	CVVH	CVVH	CVVHDF	CVVHDF
	Pre- or post-dilution	Pre-	Pre-	Pre- (but 30% post with Infomed)	50% Pre-dilution, 50% post-dilution	Pre-	Pre-
<i>Fluids: Pre-Filter or Pre-Blood Pump (PBP)</i>	Manufacturer	Gambro/Hospal	Gambro/Hospal	Baxter	Gambro/Hospal	Gambro	Gambro
	Trade name (volume)	Prismocitrate 10/2 (5L)	Hemosol B0 (5L)	Citrate Replacement Fluid	Hemosol	Prismocitrate 10/2 (5L)	Hemosol B0 (5L)
	Usual additives	nil	nil	potassium 4 mmol/L	potassium 4 mmol/L	KCl 4mmol/L (if K<5.5)	KCl 4mmol/L (if K<5.5)
	Default starting flow rate	2250ml/h (=1/4 x blood flow (set automatically by Prismaflex))	2000 ml/h	Infomed 1400 ml/h, Prismaflex 2000 ml/h	1000 ml/hr	Controlled by Prismaflex software	800ml/hr
<i>Fluids: dialysate</i>	Manufacturer	Gambro/Hospal	Gambro/Hospal	N/A	N/A	Gambro	Gambro
	Trade name (volume)	Prismocal (5L)	Hemosol B0 (5L)			Prismocal	Hemosol B0(5L)
	Usual additives	potassium 4 mmol/L	potassium 4 mmol/L			KCl 4mmol/L (if K<5.5)	KCl 4mmol/L (if K<5.5)
	Default starting flow rate	500 ml/h	500 ml/h			1000ml/hr	25 ml/kg (min 50kg and max 100kg)
<i>Fluids: Post-Filter or Replacement</i>	Manufacturer	Gambro/Hospal	Gambro/Hospal	For infomed only Baxter	For infomed only Gambro/Hospal	Gambro	Gambro
	Trade name (volume)	Hemosol B0 (5L)	Hemosol B0 (5L)	Citrate Replacement Fluid	Hemosol B0	Prismocal	Hemosol B0 (5L)
	Usual additives	potassium 4 mmol/L	potassium 4 mmol/L	potassium 4 mmol/L	potassium 4 mmol/L	Nil	Nil
	Default starting flow rate	200 ml/h	200 ml/h	Infomed 600 ml/hr	1000 ml/hr	200ml/hr	200ml/hr
<i>Blood Flow Rate</i>	Starting default (ml/min)	150	150	150	200	150ml/min	200ml/min
<i>Anticoagulation Details</i>	Starting dose default	citrate 3mmol/L in filter blood	heparin 1500 units/h pre-filter + protamine 15 mg/h post-filter	approx 3.3 mmol/L in filter blood	1500 IU heparin pre-filter and 15 mg of protamine post filter	Citrate 3mmol/L Calcium compensation 85% using Prismaflex software	Heparin 1000 units/hr and Protamine 10mg/hr
	Route of administration	separate syringe driver into dedicated CVC lumen	Heparin: Prismaflex syringe driver into pre-filter blood. Protamine: external syringe driver into high-flow 3-way connector on return limb	within replacement fluid	Delivered by volumetric pumps as part of a diluted prepared infusion	CaCl via Prismaflex syringe driver using Gambro Calcium line into dedicated CVC lumen	Heparin via IV pump running via high-flow three-way tap at access lumen of vascath. Protamine via IV pump running via high-flow three-way tap onto return lumen of vascath
	Monitoring targets	normal ionised calcium (1.0-1.2 mmol/l) in patient, via use of algorithm	normal APTT in patient	ionized calcium 1-1.2 mmol/L	APTT not targeted	Patient ionised calcium 0.91-1.1	APTT patient < 40 and circuit APTT between 50-80 using table
	Comments	Magnesium replacement as needed		Mg and Calcium delivered in a Baxter pre-mixed infusion by volumetric pumps			

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Site Number		4		5		6	
Number of subjects randomised		13		17		1	
Number of circuits randomised		45		49		4	
		Citrate	Heparin / Protamine	Citrate	Heparin / Protamine	Citrate	Heparin / Protamine
<i>Equipment</i>	Machine(s) Used	Aquarius	Aquarius	Prismaflex	Prismaflex	Prismaflex	Prismaflex
<i>Description of settings</i>	Mode	CVVH/CVVHDF	CVVH/CVVHDF	CVVHDF	CVVHDF	CVVHDF	CVVHDF
	Pre- or post-dilution	Pre	Pre	Pre-	Pre-	Pre-	Pre
<i>Fluids: Pre-Filter or Pre-Blood Pump (PBP)</i>	Manufacturer	Gambro/Hospal	Gambro/Hospal	Gambro/Hospal	Gambro/Hospal	Gambro/Hospal	Gambro/Hospal
	Trade name (volume)	Hemosol B0 (5L)	Hemosol B0 (5L)	Prismocitrate 10/2 (5 L)	Prismocitrate 10/2 (5 L)	Lactosol B0 (5L)	Lactosol B0 (5L)
	Usual additives	KCL (4mmol/L)	KCL (4mmol/L)	nil	nil	potassium 4 mmol/L	potassium 4 mmol/L
	Default starting flow rate	1500ml/hr	1500ml/hr	2250ml/hr	2250ml/hr	800ml/hr	800ml/hr
<i>Fluids: dialysate</i>	Manufacturer	Gambro/Hospal	Gambro/Hospal	Gambro/Hospal	Gambro/Hospal	Gambro/Hospal	Gambro/Hospal
	Trade name (volume)	Hemosol B0 (5L)	Hemosol B0 (5L)	Prismocal (5L)	Hemosol B0 (5L)	Prismocal (5L)	Lactosol B0 (5L)
	Usual additives	KCL (4mmol/L)	KCL (4mmol/L)	potassium 4 mmol/L	potassium 4 mmol/L	potassium 4 mmol/L	potassium 4 mmol/L
	Default starting flow rate	1500ml/hr	1500ml/hr	1000ml/hr	20ml/kg/hr	1000ml/hr	1000ml
<i>Fluids: Post-Filter or Replacement</i>	Manufacturer	nil	nil	Gambro/Hospal	Gambro/Hospal	Gambro/Hospal	Gambro/Hospal
	Trade name (volume)			Hemosol B0 (5L)	Hemosol B0 (5L)	Hemosol B0 (5L)	Hemosol B0 (5L)
	Usual additives			opt: potassium 4 mmol/L	opt: potassium 4 mmol/L	opt: potassium 4 mmol/L	opt: potassium 4 mmol/L
	Default starting flow rate			200ml/hr	15ml/kg/hr	200ml/hr	200ml/hr
<i>Blood Flow Rate</i>	Starting default (ml/min)	200	200	150	150	150	150
<i>Anticoagulation Details</i>	Starting dose default	citrate 3mmol/L	heparin 1500 units/h pre-filter + protamine 15 mg/h post-filter	citrate 3mmol/L	heparin 1000 units/h pre-filter + protamine 10 mg/h post-filter	citrate 3mmol/L	heparin 1000 units/h pre-filter + protamine 10 mg/h post-filter
	Route of administration	pre-filter into dedicated access port	hep: syringe driver onboard Prismaflex into pre-filter. Prot: syringe driver into hi-flow Y connector on return limb	separate syringe driver into dedicated CVC lumen	Heparin: Prismaflex syringe driver into pre-filter blood. Protamine: external syringe driver into high-flow 3-way connector on return limb	separate syringe driver into dedicated CVC lumen	Heparin: Prismaflex syringe driver into pre-filter blood. Protamine: external syringe driver into high-flow 3-way connector on return limb
	Monitoring targets	normal ionised calcium (1.0-1.2 mmol/l) in patient, via use of algorithm	normal APTT in patient	normal ionised calcium (1.0-1.2 mmol/l) in patient, via use of algorithm	normal APTT in patient	normal ionised calcium (1.0-1.2 mmol/l) in patient, via use of algorithm	normal APTT in patient
	Comments	post-filter ionised Ca ⁺⁺ will be monitored					

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Site Number		7	
Number of subjects randomised		22	
Number of circuits randomised		84	
		Citrate	Heparin / Protamine
<i>Equipment</i>	Machine(s) Used	Aquarius	Aquarius
<i>Description of settings</i>	Mode	CVVH	CVVH
	Pre- or post-dilution	Pre	Pre
	<i>Fluids: Pre-Filter or Pre-Blood Pump (PBP)</i>		
	Manufacturer	Baxter	Baxter
	Trade name (volume)	14mmol/ml citrate (made to order)	Accusol
	Usual additives	KCL KPO4	KCL KPO4
	Default starting flow rate	30 ml/kg/hr (in 10 kg weight brackets dependent on pt weight)	30 ml/kg/hr (in 10 kg weight brackets dependent on pt weight)
<i>Fluids: dialysate</i>	Manufacturer	N/A	N/A
	Trade name (volume)		
	Usual additives		
	Default starting flow rate		
<i>Fluids: Post-Filter or Replacement</i>	Manufacturer	N/A	N/A
	Trade name (volume)		
	Usual additives		
	Default starting flow rate		
<i>Blood Flow Rate</i>	Starting default (ml/min)	150 - 250 depending on weight	250
<i>Anticoagulation Details</i>	Starting dose default	Fixed with Ca and Mg infusion titrated to iCa	Baseline ACT done. If ACT<120, an IV bolus of 40 u/kg may be given via the pre- filter port
	Route of administration	Approx. 2.5-3mmol/L citrate in filter blood	Start infusion at 10 u/kg/hr (=2.5 ml/hr)
	Monitoring targets	ionised calcium	ACT 140-160 secs
	<i>Comments</i>		