CRRT Clinical Goal Prescribing With Web Application Translation Into CRRT Settings

Balazs I. Szamosfalvi and Lenar T. Yessayan

Department of Internal Medicine, University of Michigan

Purpose

In the era of sophisticated CRRT machines with integrated citrate- and Ca-pumps and bicarbonate (Bic)-based Ca-free CRRT fluids, the next challenges of early start extracorporeal Multi-Organ Support Therapy include the ability to provide CRRT with regional citrate anticoagulation (RCA) safely to all patients without contraindication. Furthermore, CRRT-RCA use must be feasible in a broad variety of settings e.g. the emergency room and smaller ICU programs with limited expertise. To address this we:

1. Present the complexity of CRRT circuit and intra-patient solute kinetic phenomena during CRRT-RCA as a major reason for the lack of a standardized best practice of RCA
2. We propose a new conceptual approach where providers can focus on prescribing the clinical goals of CRRT-RCA and use a Progressive Web Application (PWA) to translate these into specific CRRT machine settings and fluid compositions based on the novel paradigm of Fixed Flow Ratio (FFR)-CRRT-RCA which optimizes the prescription's initial (at 24 hours) as well as sustained (at ≥72 hours) fidelity to small solute control goals.

Methods

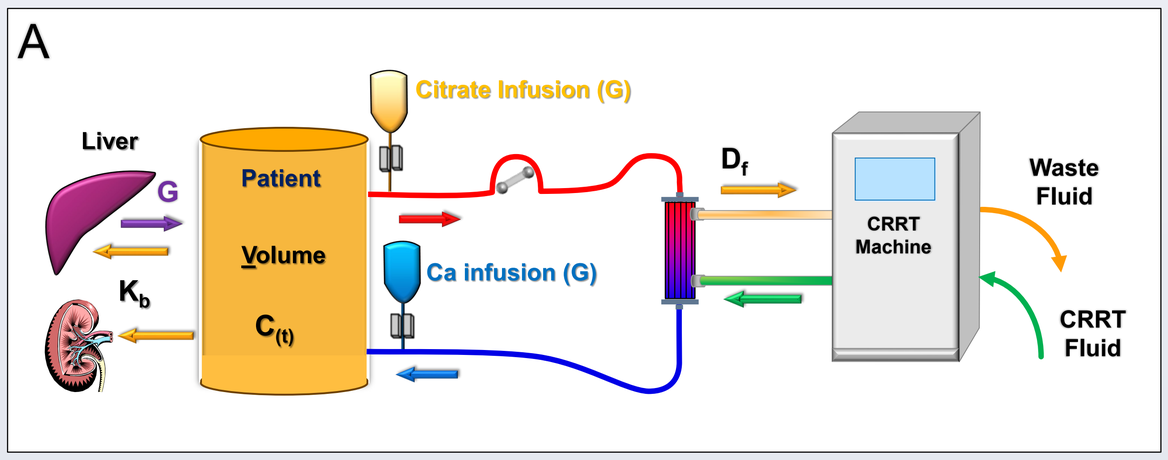

Figure 1: The complexity of targeting optimal systemic solute levels with CRRT-RCA

Every time a patient is started on CRRT-RCA a very complex solute kinetic "experiment" is initialized as shown in Figure 1, Panel A with multiple factors contributing in a variable and unpredictable manner, e.g. liver metabolism of citrate. The level of any specific solute as a function of time, C(t) can be described using a kinetic equation, Panel B. The kinetic parameters V, G, D_f, and K_b, Panel C are different for Na, HCO3, citrate, total Ca, etc. Un-coordinated changes to citrate infusion, blood flow, CRRT fluid flow and Ca-infusion rates can lead to "runaway" solute kinetics in terms of systemic Na, HCO3, citrate and ionized calcium (iCa) levels. In summary, the complexity of the system greatly hinders consistently optimized bedside prescribing even by an expert provider.

We propose that humans should prescribe a set of clinical goals instead (Table 2). A PWA used on a smartphone would then generate a computationally optimized initial FFR-CVVHD(F)-RCA prescription based on the provider-defined clinical goals and the patient's current laboratory values and anthropometric data. The PWA would incorporate the local CRRT program specific CRRT machine's operational characteristics and the compositions of the ACDA solution, HCO3-based CRRT fluids and $CaCl_2$ solution.

Smartphone Progressive Web Application Features

- **CONNECTIVITY INDEPENDENT** - Enhanced with service workers to work offline
- **APP LIKE** - Feels like an app to the user with app-style interactions and navigation.
- **FRESH** - Always up-to-date thanks to the service worker update process.
- **INSTALLABLE** - Allows users to "keep" apps they find most useful on their home screen without the hassle of an app store middleman.
- **LINKABLE** - Easily shareable via URLs.

Results

The new method of FFR-CRRT-RCA is necessary to use PWA-based RCA in all patients without contraindications and without frequent individual prescription adjustments. We present this method (Poster, 2020 CRRT Conference) and presented its *ex vivo* validation at ASN 2019 Kidney Week (Szamosfalvi and Yessayan, et al). In summary, prescribing 75-95% single pass citrate removal on the filter eliminates clinically significant variability in systemic citrate levels and bicarbonate generation from citrate metabolism. Keeping the ratio of ACDA flow, dialysate (QD) + replacement (QRF) flows and Ca-rate (QCa) all fixed to circuit blood flow allows flexible adjustment of the total effluent flow in as little as 45 ml/hour increments while ensuring consistent steady state systemic Na 140 and HCO3 20-25 with the default CRRT fluid Na 140 and HCO3 35. The use of Combinatorial CRRT Fluid Personalization (Poster, 2020 CRRT Conference Szamosfalvi & Yessayan) allows the PWA to generate a final CRRT fluid with any permutation of K = 0, 1, 2, 3, 4 mM x HCO3 = 25, 30, 35, 40, 45 mM using only 4-types of stock CRRT fluids (0K/25Bic, 0K/45Bic, 4K/25Bic and 4K/45Bic) without spiking. Rarely, D5W or 3% saline at a calculated rate with a fixed ratio to QB would be used to target unusual systemic Na levels 125-155 mM range.

Nipro Elisio 1.5 m^2 / Effluent Flow	Blood Flow QB ml/min	ACDA Flow ml/hour	Dialysate Flow QD mL/hour	Post-Dilution Flow QRF mL/hour	$CaCl_2$ Flow mL/hour	Patient Net UF Flow mL/hour	Total Net UF Flow ml/hour
45 ml/h	1	3	30	10	1	1	5
2250 ml/h	50	150	1500	500	50	50	250

Table 1: Example of FFR-CVVHD(F)-RCA prescription. If the systemic Hb≥ 11 g/dL the QRF can be set to zero and the QD increased proportionally to keep QD+QRF unchanged.

Parameter	(ADJUST) Default Goals in 24h:		INPUT NEW Rx Anthropometric Data		INPUT NEW Rx Systemic Solutes at CRRT Start		INPUT ONCE CRRT Program Specifics
Systemic iCa	1.05-1.25	mM	Est. Dry Weight	kg	Hemoglobin	g/dL	CVVHDF or CVVHD
Circuit iCa	≤0.25(-0.4)	mM	Current Weight	kg	Albumin	g/dL	$CaCl_2$ Composition
Systemic Citrate	0.5(-2.5)	mM	Height	cm	Sodium	mM	ACDA Composition
Systemic Na	138-142	mM	Age	ears	HCO3	mM	CRRT Fluids (x4)
Systemic HCO3	20-25	mM	Sex	M/F	L-Lactate	mM	QB steps ml/min
Systemic Phosphate	0.7-2	mM	Calculated TBW	L	Potassium	mM	QD/QRF steps ml/h
Effluent dose Weight	30(-90)	ml/kg/h	Calculated ECF	L			Net UF steps ml/h
Effluent dose BSA	2.3-6L/1.72 m^2		Calculated BSA	m^2			Dose: Weight or BSA
Patient Net UF	0(-500)	ml/h	Calculated FO	%			

Table 2: Information the PWA will need to generate a FFR-CRRT-RCA Rx. Goals can default to most common (safe) values to lessen data input burden. Data fields can be input as dropdown lists and value sliders to provide a range of acceptable data and eliminate free-typing and can eventually be pulled from the EHR by the PWA. Data entered into- or generated by the PWA can be collected in a cloud-based database instantaneously.

CRRT Parameter	OUTPUT Initial Settings	OUTPUT CRRT Fluid/ Other
Blood Flow	5-150 ml/min	*Suggested* K: 0-4 mM
ACDA Flow	15-300 ml/h	*Suggested* Bic: 25-45 mM
Dialysate Flow	150-6000 ml/h	
Replacement Flow	0-1500 ml/h	Machine Net UF ml/h
Ca-infusion	5-170 ml/h	Filtration Fraction %
(Rare) 3% NaCl IVF	0-150 ml/h	
(Rare) D5W IVF	0-400 ml/h	

Table 3: The PWA will display the calculated CRRT system settings that are most likely to approximate the selected 24-h clinical goals. The 3% saline or D5W infusions are only needed if unusual systemic Na levels are targeted in the 125-155 range.

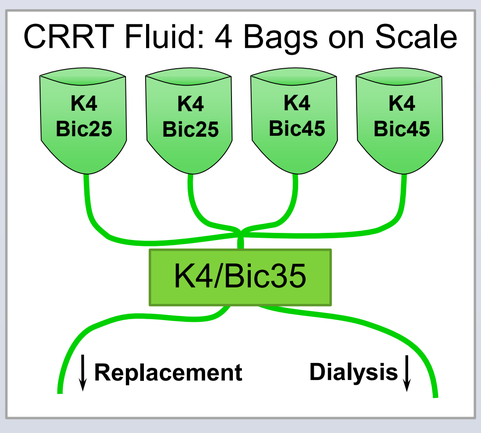

Figure 2: The provider adjusts-approves the PWA-suggested K/Bic CRRT fluid before the PWA screen helps select the 4 types of 5-L CRRT fluid stock bags that mix by gravity.

Discussion

PWA-based FFR-CRRT-RCA in fact increases the ability of the provider to personalize WHAT small solute level/clearance goals to target while categorically standardizing and restricting HOW these goals are achieved in terms of CRRT-RCA prescribing. We feel that in the interest of safely expanding CRRT-RCA use this is a compromise worth considering.

The fidelity of achieving the same set of clinical small solute goals at 24/72 hours with PWA-based FFR-CRRT-RCA versus human prescribing of a traditional CRRT-RCA protocol could be studied.

Conclusions

1. We demonstrated the solute kinetic complexity of CRRT-RCA which has hindered and will continue to limit broad RCA use relying on traditional prescribing and protocols.
2. We proposed a PWA to incorporate FFR-CRRT-RCA and Combinatorial CRRT Fluid Personalization into a consistent process of translating clinical goals into CRRT machine settings and CRRT fluid composition prescriptions regardless of provider expertise.