

A Novel Regional Citrate Anticoagulation Protocol for CRRT Using Only Commercially Available Solutions

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Purpose: To describe a citrate regional anticoagulation (CRA) protocol for patients with acute renal failure and contraindications to heparin who require continuous renal replacement therapy (CRRT), using only commercially available solutions, for units that do not want or cannot prepare extemporaneously made solutions.

Materials and Methods: Case report and series from a medical/surgical intensive care unit of a university teaching hospital. A CRA protocol was developed by using only commercially available solutions. Five dialysis-specific clinical parameters were

identified to allow simplified measurement and control.

Results: There was a dramatic improvement of dialysis filter survival in the index patient that was seen in the subsequent patients receiving CRA. This was accompanied by excellent control of the clinical and biochemical parameters as well as nursing acceptance and ownership of the protocol.

Conclusion: It is possible to provide safe and effective CRA with only commercially available solutions. The protocol is applicable to most patients requiring CRRT. © 2003 Elsevier Inc. All rights reserved.

CITRATE REGIONAL anticoagulation (CRA) has the potential to maintain or extend circuit life during continuous renal replacement therapy (CRRT) without a systemic anticoagulant effect or the need for heparin exposure.^{1,2} It also has been shown to prevent blood filter membrane interactions maintaining fiber bundle function.³ The use of citrate has been limited previously by the requirement for pharmacy-produced designer solutions and extemporaneous mixing as well as the lack of standardized protocols. In this report we describe our experience with a new method for providing CRA for CRRT by using only commercially available solutions in an algorithm-driven protocol that allows each of the parameters of dialysis to be adjusted individually.

In March of 1999, a patient with cryptogenic cirrhosis and multiorgan system failure caused by sepsis developed acute renal failure with hemodynamic instability requiring inotropic support to maintain an adequate blood pressure. Dialysis was initiated for volume and solute management with CRRT by using a systemic heparin protocol using the Prisma HF system (COBE, Lakewood, CO) continuous dialysis machine, set in continuous veno-venous hemodialysis (CVVHD) mode with an M100 filter (AN-69 hollow fiber; Cobe, Lakewood, CO). Filter life over the first 3 days was under 24 hours. On day 4 the platelet count, which was normal at the start of dialysis, had decreased critically and heparin was withdrawn. An assay for heparin-induced thrombocytopenia (HIT) was positive. Without systemic heparin, filter life was less than 12 hours even with saline flushes, 100 mL/hr, then every half hour. Over the next 3 days the platelet count returned to normal.

Systemic anticoagulation with danaparoid sodium (Organon, Toronto, Canada) led to hemoptysis into the endotracheal tube and no further danaparoid was given. A CRA protocol as described in the literature was contemplated but required the preparation of extemporaneously made solutions that the pharmacy at this center could not provide.^{1,2} A method was devised to provide a CRA protocol using only commercially available solutions. In addition, this protocol sought to individually control each of the dialysis parameters (clearance, anticoagulation, calcium and electrolytes, volume and acid base balance). By using this protocol the first filter lasted 72 hours and was replaced at that time as recommended by the filter manufacturer. The patient remained on CRRT with the CRA protocol for 3 further weeks. She eventually recovered renal function and was able to be discharged from the intensive care unit. The CRA protocol was refined into a set of standardized orders (M.B.) by the critical care Nurse Educator and was evaluated in the next 15 CRRT patients who had contraindications to heparin. After this it became the default method of CRRT in the institution.

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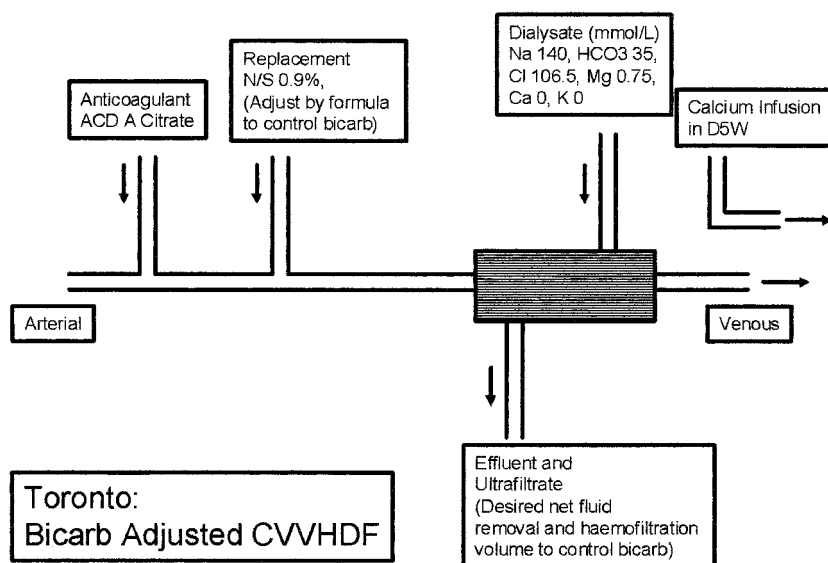


Fig 1. CRA protocol for CRRT schematic.

The following report describes in detail the protocol, the first 15 patients receiving the CRA protocol, and a comparison of filter life and metabolic parameters of all patients who received CRRT with heparin or the CRA protocol during the 18-month period after the index case. The index case was not included in the analysis because this patient received heparin, saline flushes, and a nonstandardized version of the CRA protocol.

METHODS

Heparin Protocol

The patients described for both heparin and citrate protocols all received CRRT with the Prisma HF system (COBE) continuous dialysis machine with an M100 filter (AN-69 hollow fiber). For heparin anticoagulation, heparin was administered by syringe pump on the Prisma CRRT machine to achieve a partial thromboplastin time of 60 to 90 seconds. The partial thromboplastin time was measured according to protocol every 6 hours during the first day and every 12 hours thereafter. The blood pump was run at a minimum of 100 mL/min and faster if clinically indicated to reduce filter clotting. The dialysate used was Normocarb (Dialysis Solutions, Inc., Richmond Hill, Canada) at a rate of 20 mL/kg/hr. Normocarb was prepared by the addition of 240 mL of sterile concentrate to 3 L of sterile water for irrigation (C2B7117; Baxter, Chicago, IL) before use to make 3,240 mL of

sterile bicarbonate dialysate (Na 140, K 0, Ca 0, Mg 0.75, HCO₃ 35, Cl 106.5 all in mmol/L). No hemofiltration was performed. Calcium was replaced centrally with 40 g of calcium chloride (AstraZeneca, Mississauga, Canada; each calcium chloride ampule contained 7 mmol calcium chloride in 10 mL, 10 g/10 mL) in 1 L D5W at 50 cc/hr (1.4 mmol/hr). Calcium boluses were given as clinically indicated according to ICU protocol.

Citrate Protocol

The blood pump speed was set at 100 mL/min. This CRA protocol primarily is diffusive but includes a convective component for bicarbonate modulation and therefore requires a CRRT system that can be set up in hemodiafiltration mode.

The protocol can be broken down into 5 steps, each addressing the dialysis parameters. A schematic can be found in Figure 1.

The clearance needs of the patient were calculated at 20 mL/kg/hr according to Garred et al.⁴ Normocarb (Dialysis Solutions, Inc), a commercially available Food and Drug Administration–approved bicarbonate-based calcium-free CRRT solution, was used for the dialysate. Normocarb was prepared by the addition of 240 mL of sterile concentrate to 3 L of sterile water before use to make 3,240 mL of sterile bicarbonate dialysate (final concentration: Na 140, K 0, Ca 0, Mg 0.75, HCO₃ 35, Cl 106.5 all in mmol/L).

Table 1. Citrate Infusion Protocol

| Post-filter Ionized Calcium mmol/L | Citrate Infusion Adjustment |
|------------------------------------|-------------------------------------|
| <0.25 | Reduce rate by 10 mL/hr |
| 0.25–0.35 | No adjustment or 150 mL/hr at start |
| 0.36–0.45 | Increase rate by 10 mL/hr |
| >0.46 | Increase rate by 20 mL/hr |

Modified from Kutsogiannis et al.⁵

Anticoagulant Citrate Dextrose Solution, Formula A (ACD-A; Baxter Fenwall, Chicago, IL) is used for anticoagulant and is infused by IMED Gemini PC1 (Alaris, San Diego, CA) pump by Y connectors into the venous line at the connection with the dual lumen dialysis catheter at 2.5% of the blood flow rate (eg, blood flow is typically 6,000 mL/hr [100 mL/min] and ACD-A is run at 150 mL/hr). The ACD-A Solution contains trisodium citrate 74.8 mmol/L, citric acid 38 mmol/L, and dextrose 123.6 mmol/L.

Citrate flow was then adjusted according to the algorithm developed by Kutsogiannis et al,⁵ found in Table 1. This algorithm is based on lowering the ionized calcium levels in the blood in the venous limb of the extracorporeal circuit (after flowing through the filter) to a range of 0.25 to 0.35 mmol/L. The post-filter ionized calcium is therefore the measure of anticoagulation efficacy. Anticoagulation safety is measured every 6 hours as well with systemic levels of ionized calcium. Systemic ionized calcium levels are maintained at a level greater than 0.8 mmol/L. The goal is for the total corrected calcium level to be between 2.2 and 2.6 mmol/L.

Decreasing systemic ionized calcium levels with a stable total calcium level and an increasing anion gap indicates that systemic citrate levels are increasing. When the systemic ionized calcium level decreases below 0.8 mmol/L, the ACD-A citrate is turned off for 3 hours and the levels are repeated. If the systemic ionized calcium increases above 0.8 mmol/L, the citrate is turned back on but at a reduced rate (20 mL/hr lower). If the ionized calcium level has not recovered, ACD-A citrate remains off and an investigation for liver failure is initiated. Although Kutsogiannis et al's⁵ protocol was developed for 4% trisodium citrate, it was adapted for use with ACD-A citrate with no modifications.

Calcium replacement external to the dialysis circuit balances the calcium removed by the calcium-

free dialysis solution. To balance the hypernatremic ACD-A citrate solution (Na 224 mmol/L) running at approximately 150 mL/hr, the calcium solution was formulated to run at 50 cc/hr in D5W. Calcium chloride 40 g prepared in 1 L D5W was infused centrally at 50 cc/hour (1.4 mmol/hr).

Volume adjustment was set so that the total hourly patient fluid removal rate by the dialysis machine included the desired patient fluid removal (net ultrafiltration) as well as the volume of the ACD-A citrate infusion and the calcium replacement solution. The determination of the net ultrafiltration was a medical decision made by the team at least twice daily based in large part on the nondialysis intravenous fluids administered to the patient as well as oral feeds and nondialysis fluid losses during the day.

Bicarbonate removal for metabolic alkalosis was initiated if serum bicarbonate levels increased above normal (25 mmol/L). Excess bicarbonate was removed by hemofiltration (convection) and fluid removed was replaced with normal saline.

The Prisma HF system (COBE) continuous dialysis machine automatically replaces fluid removed by hemofiltration with the solution hanging on the hemofiltration scale. As the use of replacement solution increases the total clearance above that calculated the dialysate rate was reduced by a similar amount. This has a number of effects. One is to conserve the dialysate used. The second is to reduce exposure of the blood to bicarbonate from the dialysate. Finally, bicarbonate removed by convection treats the metabolic alkalosis. Normal saline replacement typically is started at 300 mL/hr for bicarbonate levels that increase by 1 mmol/L over 6 hours. The replacement rate is adjusted iteratively every 6 hours by 150 to 300 cc/hr if serum measured bicarbonate levels continued to increase or be reduced by the same amount if the bicarbonate levels were decreasing below the normal range. Each change in replacement rate with normal saline was mirrored by an adjustment in the dialysate rate.

Monitoring of parameters was performed 2 hours after starting therapy, then every 6 hours during dialysis. Anticoagulation efficacy was determined by the post-filter ionized calcium level as per Kutsogiannis et al⁵ (Table 1). Systemic total and ionized calcium levels drawn from an arterial catheter or peripheral vein were used to assess safety.

Table 2. Baseline Parameters of the First 15 Patients Receiving the CRA Protocol

| Parameter | Mean | ± SD |
|--------------------------------|-------|-------|
| Age | 64.6 | 11.6 |
| pH | 7.31 | 0.07 |
| Bicarbonate mmol/L | 16.8 | 2.8 |
| Urea | 23 | 11.9 |
| Creatinine μ mol/L | 384.8 | 156.4 |
| Glucose mmol/L | 9.1 | 4 |
| Hemoglobin gm/L | 87.1 | 13.2 |
| International Normalized Ratio | 1.35 | 0.32 |
| Albumin | 20.8 | 5.6 |
| Bilirubin μ mol/L | 71.3 | 111.9 |
| Lactate mmol/L | 2.9 | 2.3 |

For hypokalemia potassium chloride, 3 to 4 mmol/L was added to either or both of the dialysate and replacement solution. The collection of data on these patients was approved by the Human Subjects Review Committee.

Informed consent was obtained from each subject via a surrogate individual if necessary. Data was collected on all patients receiving CRRT from the index case for the following 18 months.

Baseline data only was collected on the first 15 patients receiving the CRA protocol. To compare filter life between the traditional heparin anticoagulation protocol and the CRA protocol that replaced it, those patients who received the heparin protocol after the index case were reviewed for filter life and metabolic control (sodium and bicarbonate levels) and compared with those who received the CRA protocol over the same time period. Eighteen months after the index case the CRA

protocol was made standard in the institution and data on the 49 patients treated during this time is presented as well to compare the filter life during CRA and systemic heparin anticoagulation. The data are presented as mean (\pm SD or SEM as indicated) and were analyzed by using the SAS program version 6.12 (Cary, NJ). The log rank test was used for the life table analysis. Filters that were discontinued for a reason other than clotting or completion of a maximum of 72 hours of continuous use were censored. Daily morning laboratory values were used to track metabolic control.

RESULTS

First Fifteen Patients Receiving CRA Protocol

During the pilot study period, 15 patients (11 men and 4 women) were treated with continuous veno-venous hemodiafiltration (CVVHDF) and regional citrate anticoagulation in the intensive care unit (see Tables 2 and 3). At that time, patients were selected for regional citrate anticoagulation owing to clinical contraindications to heparin. There were a total of 2,310 patient-hours of CVVHDF treatment by the regional citrate anticoagulation protocol in the 15 patients. The duration of CVVHDF was 153 ± 137 hours per patient. The CRRT was performed with a mean blood flow rate of 101.6 ± 4.3 mL/min, dialysate flow rate $1,211.6 \pm 253$ mL/hr, replacement with normal saline 310 ± 281 mL/hr, ACD-A citrate rate 156.9 ± 16.2 mL/hr, calcium replacement 51.73 mL/hr.

Table 3. Etiology of Acute Renal Failure and Clinical Results for the First 15 Patients Receiving the CRA Protocol

| Age | Sex | Clinical Condition | ARF Etiology | Outcome |
|-----|-----|---------------------------------|--------------|----------|
| 82 | M | Postop AAA repair | ATN | Died |
| 66 | M | Postop CABG | ATN | Died |
| 62 | M | Postthoracic aneurysm repair | ATN | Died |
| 65 | M | Postop AAA repair | ATN | Died |
| 77 | M | Postop AAA repair | ATN | Died |
| 65 | F | Thermal burn-38% of BSA | ATN | Died |
| 66 | M | Sepsis post-cancer chemotherapy | ATN | Died |
| 68 | F | Postop CABG | ATN | Survived |
| 79 | M | Postop AAA repair | ATN | Died |
| 64 | M | Postop CABG | ATN | Survived |
| 49 | M | Sepsis and cirrhosis | ATN | Died |
| 37 | F | Sepsis post-cancer chemotherapy | ATN | Survived |
| 73 | M | Postop CABG | ATN | Survived |
| 67 | M | Postop CABG | ATN | Survived |
| 37 | F | Thermal burn - 55% of BSA | ATN | Died |

ARF, acute renal failure; M, male; postop, postoperative; AAA, abdominal aortic aneurysm; ATN, acute tubular necrosis; CABG, coronary artery bypass graft; F, female; BSA, body surface area.

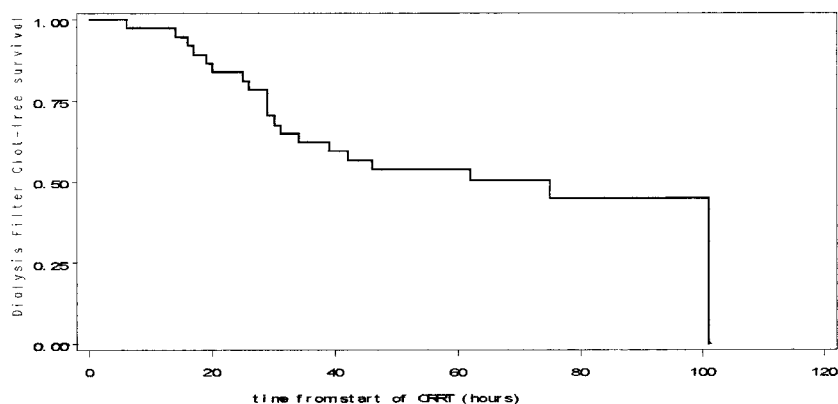


Fig 2. Clot-free filter survival for first 15 patients on CRRT.

| Time | Clot-free Survival, % |
|-------|-----------------------|
| 24 hr | 81 |
| 48 hr | 53 |
| 72 hr | 19 |

The results of the filter performance on the regional citrate anticoagulation protocol from the first 15 patients showed that 48 dialysis filters were used during 2,276 patient-hours of CVVHDF. The mean dialysis filter life was 54 ± 22 hours. Eleven (23%) of the filters clotted spontaneously, 15 (31%) filters lasted 72 hours and were changed according to the manufacturer's instructions. Twenty-two (46%) filters were discarded when treatment was interrupted for diagnostic or surgical procedures or for termination of CRRT.

The citrate anticoagulation was titrated to a post-filter ionized calcium target of 0.25 to 0.35 mmol/L measured every 6 hours. The citrate sliding scale mean infusion rate was 156 ± 19 mL/hr (17.9 mmol/hr). During 337 post-filter ionized calcium 6-hour measurement periods, the mean ionized calcium was 0.32 ± 0.10 mmol/L during the 6-hour periods without filter clotting and 0.40 ± 0.15 mmol/L during the five 6-hour measurement periods that filters clotted. There was no difference ($P = .45$) between mean ionized calcium for clotting events. A life table of the filter survival from the first 15 patients receiving the CRA can be found in Figure 2.

After analysis of these 15 patients, a decision was made to adopt the CRA protocol for all pa-

tients requiring CRRT. If a patient was found to have fulminant hepatic failure and could not metabolize citrate, CRRT was continued as per protocol without the citrate owing to the inherent coagulopathy. Patients requiring systemic heparin also were put on the CRA protocol and the heparin was monitored according to intensive care unit protocol independent of the dialysis. This had the unexpected effect of eliminating the occasions when systemic heparin had been interrupted, when given as part of the CRRT procedure, if the CRRT was stopped for a clotted filter or the need to be transported for a diagnostic test. There was an overwhelming positive response from the nursing staff after adoption of the CRA protocol stemming in large part from the reduced filter clotting. The most frequent question asked in the first months after adoption of the CRA protocol was whether filters had to be changed at 72 hours as recommended by the manufacturer. This policy was maintained.

The following results are from the 49 patients who received CRRT during the 18-month period and include the first 15 patients receiving CRA. Thirty received CRA and 19 received heparin. After the first 15 patients and the index case, any patient requiring CRRT could receive the CRA.

Table 4. Results Comparing Patients Receiving CRA Protocol With Heparin Protocol (Mean \pm SEM)

| Parameter | CRA Protocol | Heparin Protocol |
|------------------------------------|---------------------|---------------------|
| N | 30 | 19 |
| Hours of dialysis | 132.7 \pm 108.25 | 144.32 \pm 115.89 |
| Filters used | 2.56 \pm 1.87 | 4.36 \pm 4.29 |
| Mean hours per filter | 51.8 \pm 57.9 | 33.1 \pm 27.0 |
| Blood flow mL/min | 101.68 \pm 5.88 | 117.19 \pm 19.25 |
| Dialysate flow mL/hr | 1360.7 \pm 374.17 | 1359.4 \pm 376.78 |
| Replacement flow mL/hr | 397.9 \pm 500.24 | 137.16 \pm 467.38 |
| Citrate rate mL/hr | 151.43 \pm 17.47 | N/A |
| Calcium replacement rate mL/hr | 51.73 \pm 6.0 | N/A |
| Systemic ionized calcium mmol/L | 0.95 \pm 0.14 | N/A |
| Total corrected calcium mmol/L | 1.71 \pm 0.08 | N/A |
| Post filter ionized calcium mmol/L | 0.32 \pm 0.043 | N/A |
| Bicarbonate mmol/L | 23.08 \pm 3.2 | 18 \pm 4.2 |
| Sodium mmol/L | 137.9 \pm 2.3 | 135 \pm 1.4 |

N/A, not available.

Results comparing dialysis parameters can be found in Table 4. Calcium levels were monitored in all the patients. The predialysis total corrected calcium was 1.7 ± 0.2 mmol/L (corrected by albumin level). During CRRT with CRA, the mean systemic ionized calcium was 1.0 ± 0.2 mmol/L and the post-filter ionized calcium was 0.32 ± 0.008 mmol/L. Over more than 400 measurement periods there were 10 systemic ionized calcium events less than 0.80 mmol/L in 6 patients. No adverse events were reported during these times. All responded to stopping the citrate infusion for 3 hours then restarting the citrate 20 mL/hr slower as well as correcting systemic hypocalcemia if present with bolus calcium by a separate central line according to ICU protocol.

The mean bicarbonate level for all the patients predialysis was 16.8 mmol/L (immediately before dialysis) and the mean bicarbonate level during treatment was 24.4 ± 3.5 mmol/L. All patients who required CRRT for greater than 72 hours required bicarbonate modulation with saline replacement (mean saline replacement rate 310 mL/hr).

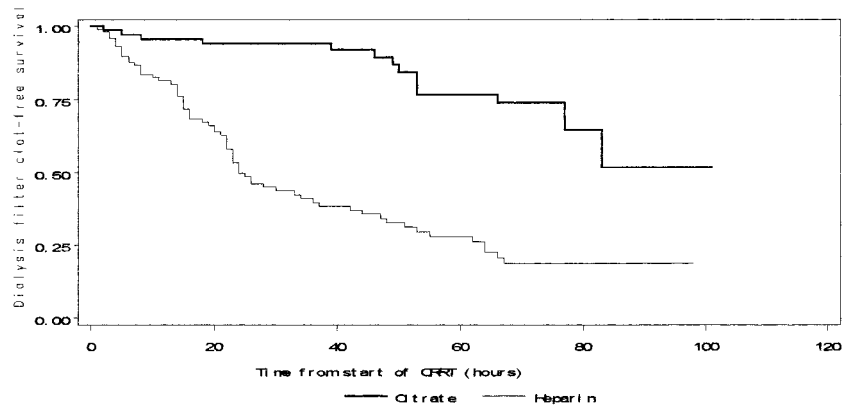
A life table analysis was performed for filter life for the heparin and citrate protocol (see Fig 3). Filter survival with the CRA was significantly greater than with heparin ($P < .001$ by log rank test). The median filter life was 24 hours for the heparin protocol compared with over 60 hours for

the CRA protocol. At 48 hours 90% of CRA filters were running compared with 35% of heparin filters.

DISCUSSION

Since Mehta et al^{1,7} reported a method of performing citrate CRRT in 1990, popularity of the technique continues to increase.^{5,15} The benefits of avoiding heparin during CRRT are primarily the ability to provide dialysis without the need for systemic anticoagulation and the associated potential for bleeding complications or heparin-induced thrombocytopenia. There is also an improvement in extracorporeal circuit and filter life and function. Extended filter life with many filters lasting to the mandatory 72-hour cut off was the most noticeable change. Using Kutsogiannis et al's⁵ protocol for adjusting citrate by the prefilter ionized calcium eliminated the need to monitor activated clotting times.

Regional citrate anticoagulation was introduced as an alternative to the risks of systemic heparinization by Mehta et al¹ in 1990. Although there are other methods of anticoagulation, each has unique problems. For example, saline flushes alone are associated with a high degree of filter clotting.¹ Protamine regional anticoagulation is very time and resource consuming and may itself cause coagulopathies or hemodynamic instability. Other newer anticoagulants such as danaparoid and argatroban (a thrombin inhibitor) have no specific antidotes to reverse excessive anticoagulation if it occurs.¹⁶ ACD-A was used as the anticoagulant in this protocol. This solution has some advantages for this protocol over trisodium citrate. ACD-A is approved for use in plasmapheresis and is available in most centers. Also, because one third of the citrate in the formulation is in the form of citric acid there is less total bicarbonate production. The solution also has a lower sodium concentration than 4% trisodium citrate (224.4 vs 408 mmol/L). The citrate solution is potentially the most toxic part of the therapy. Only dilute citrate solutions are appropriate and very concentrated citrate solutions have been removed from the marketplace. Regular monitoring for efficacy (post-filter ionized calcium or potentially activated clotting times) and for safety (systemic ionized calcium levels) is necessary. Citrate affects anticoagulation by chelating calcium, required for the calcium-dependent steps in the clotting cascade.¹⁷ Citrate lowers the level of ionized calcium in the extracorporeal circuit, anti-



Filter clot free survival at fixed time intervals according to method of anticoagulation

| Hours | Citrate | Heparin |
|--------|---------|---------|
| 24 hrs | 93.8 | 54.0 |
| 48 hrs | 89.7 | 34.4 |
| 72 hrs | 72.1 | 19.0 |

Fig 3. Life table of citrate versus heparin.

coagulating blood as it passes through the dialysis filter. The anticoagulant effect is regional as citrated blood from the circuit (usually 100 mL/min) is diluted as it enters the high flow of the central circulation ($>1,000$ mL/min) and citrate then is metabolized rapidly by the liver. All citrate protocols published to date require calcium-free solutions and additional calcium is delivered by a separate central line.^{10,14} A calcium-containing dialysis solution¹⁸ would increase the requirements for citrate, leading to a higher risk for unmetabolized citrate chelating calcium in the blood. This has been called and can be resolved by stopping the citrate infusion for 2 to 4 hours before restarting at a lower rate.¹⁹

Metabolic acidosis is almost universal at presentation of acute renal failure and during continuous dialysis tends to resolve over the first 96 hours.²⁰ The protocols of both Palsson and Niles¹⁰ and Mehta¹⁴ used citrate alone for buffering and required additional parenteral bicarbonate to be given if metabolic acidosis persisted. A protocol that used both a regional citrate anticoagulant system as well as a bicarbonate-buffered dialysate has less need for the addition of bicarbonate boluses. In the protocol described, the use of saline replacement to modulate metabolic alkalosis provided

very tight control of bicarbonate levels. An additional difference from the protocols described by Mehta¹⁴ and Palsson and Niles¹⁰ was that these earlier protocols relied on citrate infusion for provision of bicarbonate as well as for regional anticoagulation. Alteration of citrate rate for anticoagulation purposes will also have effects on acid/base control. The protocol described allows these parameters to be controlled independently. During the typical course of CRRT the patient has profound metabolic acidosis for the first 24 to 48 hours. If CRRT is required beyond this point bicarbonate levels usually have returned to normal and may increase further, causing a metabolic alkalosis. At this point the bicarbonate modulation with normal saline replacement is required. In our experience, the protocol described works best if the dialysate rate is at least equal to or greater than the normal saline replacement rate. Lactate-buffered solutions should be avoided owing to less-effective metabolic control and greater hemodynamic instability.²⁰⁻²³

The evolution of CRRT has been iterative with local innovations and developments of which the most significant recently is the development of regional citrate anticoagulation strategies.^{6,7} Ashton et al⁶ reported an increase in filter life from

12 hours with saline flushes to 30 hours with systemic heparin and 48 hours with a CRA. There is great interest in citrate CRRT but many units are prevented from adopting the protocols described previously because of the need for extemporaneous mixing on a large scale. Because organ replacement therapies should not induce further derangements, and to avoid immunomodulation in these critically ill patients, all solutions used in CRRT must be as sterile and pyrogen free as possible.⁸ In the absence of commercially available solutions suitable for CRA, physicians have had to rely on local hospital pharmacies to prepare prescribed solutions extemporaneously. Most protocols published today require specialized solutions produced by the hospital pharmacy⁹⁻¹² or by the dialysis unit technicians.¹³ Despite best intentions, most hospital pharmacies cannot match the quality control of regulated commercial pharmaceutical manufacturers. Normocarb has been found to save time and to potentially reduce pharmacy liability.¹⁹

The longer filter life realized with the CRA protocol with fewer clotting events reduces the

nursing time required to manage the CRRT process. Also, this protocol results in superior metabolic control (acid/base and sodium levels) than the previous heparin protocol, which may also lead to fewer changes in therapy and therefore more time to be devoted to caring for these critically ill patients. An interesting question that came up with the improved filter life was whether the filter set had to be changed at 72 hours. Because the manufacturer recommends this timing, it was adhered to. With the dramatic reduction of clotted filters during the CRA protocol, it was found that when a filter set did clot, the cause could almost always be traced back to the access catheter.

Published reports of CRA for CRRT all rely on extemporaneous mixing of fluids, which may amount to tens of thousands of liters annually.^{2,5,14} This article describes a regional citrate protocol for CRRT using only commercially available solutions and allows control of the individual parameters of dialysis including bicarbonate modulation. In an uncontrolled comparison the filter life on the CRA was significantly greater than that with systemic heparinization.

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