Anticoagulation in severely ill patients treated with continuous hemofiltration

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Continuous renal replacement therapies are increasingly used to treat acute renal failure (ARF) in the ICU setting. The slow and steady removal of plasma water and/or uremic toxins in an inherent advantage for both continuous hemofiltration and hemodialysis (CAVH, CAVHD) over intermittent dialysis. However, as in other extracorporeal circuits, anticoagulation is essential to provent activation of the clotting mechanisms within the circuit[1]. The adequacy of anticoagulation plays a key role in the efficacy of the filter in fluid and solute removall, overall filter longevith and optimum patient management. If anticoagulation is insufficient, filtration performance deteriorates and the filter may eventually clot[2], contributing to blood loss. Excessive anticoagulation, on the other hand, may result in bleeding complications reported to occur in 5 to 26 % of treatment[1,3].

This review presents the currently available methods of anticoagulation for continuous renal replacement therapy and discusses factors influencing selection of an appropriate anticoagulant. The oldest and most frequently used anticoagulant in continuous dialysis procedures is heparin. However, alternatives have recently emerged, including variable heparin dosing, low molecular weight heparin (LMWH), regional heparinization and neutralization with protamine, regional citrate anticoagulation (RCA) with trisodium citrate, nafomostat mesilate and prostaglandin analogue infusion. The efficacy of these techniques and their relative advantages and disadvantages will be discussed.

Factors affecting anticoagulation in continuous renal replacement

Technical aspects

a) *Access:* A key determinant of anticoagulation in continuous renal replacement is the access utilized. When a pump is used delivery of blood as in continuous veno-venous hemofiltration (CVVH) or dialysis (CVVHD), the method of anticoagulation is essentially similar to that utilized in conventional hemodialysis. Most centers have used systemic heparin in doses of 5-10 u/kg/hr preceded by a bolus dose of 10-20 u/kg[4,5]. Similarly, prostacyclin infusion of LMWH have been used in doses similar to that in hemodialysis[6,7]. Regional citrate anticoagulation has not been utilized in this setting but should be possible for CVVHD provided a calcium and alkali free dialysate is used and ionized calcium is monitored[8]. This method might be difficult for CVVH since convective clearance alone may be insufficient to remove the citrate load[9], but this needs further assessment.

The driving force in continuous arteriovenous hemofiltration (CAVH) or dialysis (CAVHD) is the patient's own mean arterial pressure (MAP). The blood flow rates in CAVH are as low as one sixth those in machine dialysis (50-100 ml/min : 300 ml/min). The slower blood flow rates are more conducive to activation of clotting mechanisms. Good arteriovenous access with minimal resistance (short blood lines) is thus essential for optimal blood flow and filter patency.

The choice of arterial and venous catheters can significantly influence blood flow rates. Jenkins et al.[10] assessed the effect of catheter dimensions on blood flow in CAVH. They found that the internal diameter (I.D.) of the catheter was a major factor but catheter length had less effect on blood flow rates (Qb). Catheters with I.D. of less than 1.0 mm do not provide adequate blood flow and most adult systems require 2.0-3.0 I.D. catheters. Ideally, an 8 French catheter should be used for both arterial and venous access; however we have also used a 14F double lumen catheter for femoral venous access without compromising blood flow. Additionally, the MAP should be maintained above 70 mmHg and interruption in blood flow through the circuit avoided, particularly if the patient is moved.

b) *Membrane factors:* Membranes for continuous therapies can be broadly classified into hemofilters such as the Amicon polysulphone and the Gambro polyamide membrane versus hemodialyzers, e.g. the Hospal polyacrylonitrile membrane. There appear to be no significant differences in the effect of these membranes on complement activation or on the clotting cascade[11]. The

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geometry of the hemofilter may, however, affect filtration characteristics with a parallel plate configuration giving better convective and diffuse clearances[12] and a long filter patency.

Another consideration is membrane permeability to the anticoagulant used. Heparin removed across the filter results in a reduced systemic affect with minor increases in systemic partial thromboplastin time (PTT)[2]. These studies have predominantly been done in CAVH and the impact of diffusive forces in this clearance is not known but is likely to be additive. When citrate is used as an anticoagulant dialysate administration is required, so that adequate quantities of free citrate and citrate-calcium chelate can be removed across the filter; convective clearance alone is not sufficient[9].

c) *Operational characteristics:* A major difference between conventional hemodialysis and continuous therapies is the latter's considerably longer duration of treatment. As a result, the cumulative dose of anticoagulants is much larger and has a greater potential for systemic side effects. Since solute clearances in continuous therapies are dependent on both convective and diffusive transport, factors influencing these impact on anticoagulant need. Convective clearance is dependant on the UFR which is largely determined by the BFR. Thus, reduction in BFR to less than 50 ml/min, will reduce UFR and solute clearance[13]. This is particularly important for citrate anticoagulation as citrate doses are based on the BFR, and a decrease in BFR usually requires a reduction in citrate flow rates. Attempts to enhance UFR are important as initial UFR of less than 200 ml/hr was seen in 60 % of filters that clotted early[14]. Enhancement of UFR by pre-dilution as advocated by Kaplan[15] is also very effective in CAVH-D[8] for enhancing filter longevity. Conversely, suction alone to improvide UFR may also increase the tendency for clotting by increasing the viscosity of blood in the filter. Enhancement of solute clearance by modification in dialysate flow rates has not been systematically studied for its impact on anticoagulation requirements in heparin anticoagulation. In citrate anticoagulation, convective clearance appears to influence removal of citrate calcium chelate across the filter more than diffusive clearance at dialysate flow rates of 1 L/hr, however, higher dialysate flow rates have not been studied.

Patients

Continuous renal replacement requires extensive monitoring and is particularly suitable for patients in the intensive care setting. Most of these patients have acute renal failure and/or overhudration following trauma or multiple organ failure and are generally hemodynamically unstable. The patients are often septic with hypotension and are at high risk for bleeding from primary or secondary insults (e.g. disseminated intravascular coagulation). Additionally, the necessity for surgical intervention affects risk for bleeding, while low mean arterial pressure increases the risk of filter clotting. It is thus necessary to minimize the risk for bleeding from anticoagulation while maintaining the circuit free of clots.

Several factors may influence the choice of an anticoagulant. Insufficient anticoagulation leads to deterioration of filter performance and eventual clotting[1,2], contributing to blood loss. Excessive anticoagulation may cause bleeding complications. In general, the antithrombotic and anticoagulative (i.e. hemorrhagic) effects of an anticoagulant must be distinguished. It's antithrombotic effects should be high, with a low risk of hemorrhaging. Drug action should be brief and ideally limited to the blood in the filter. Drug monitoring should be easy and suited for bedside use in the intensive care unit. Long-term treatment should not be associated with severe systemic side effects. An antagonistic drug should be available in case of overdose. Table I summarizes the advantages and drawbacks of current anticoagulation methods in continuous therapies.

Heparin

The oldest and most frequently used anticoagulant in continuous dialysis procedures is heparin[16]. Its effects in CAVH are relatively localized to the circuit in contrast to its use in conventional machine dialysis, where anticoagulation occurs in the systemic circulation and the extracorporeal circuit[2]. These differences may be due to the lower blood flow rate in CAVH; also, heparin is more likely to be removed across the filter's more permeable membrane as compared to conventional dialysis. Heparin doses depend on the presence or absence of coagulation abnormalities secondary to the underlying illness[16].

The standard technique for CAVH has been to prime the filter with two liters of saline with 5,000-10,000 units of heparin, and to give the patient an initial loading dose of heparin intravenously followed by a continuous infusion pre-filter at the minimum rate which maintains adequate anticoagulation in the circuit[16]. Three different levels of heparinization have been proposed based on the hemorrhagic risk of the patients (Table II)[2]. Group 1 patients are those with thromboembolic complications or signs of disseminated intravascular coagulation, with an intact vascular system and no visible risk of bleeding. Group 2 patients have an intact vascular system or have potential or manageable sources of bleeding. Group 3 patients are those with a high risk of bleeding, for example after multiple trauma or surgery.

Other recommendations for heparinization have, of course, been offered; Swann & Paganini have suggested an initial administration of 500-2,000 IU followed by continuous infusion of 500 IU/h[17]. We modified Geronemus & Schneider's protocol for heparin dosing[18] in CAVH-D and use the circuit shown in Fig. 1a. The filter is primed

Table I*. Anticoagulation modalities for continuous renal replacement

Method	Filter Prime	Initial Dose	Maintenance Dose	Monitoring	Advantages	Disadvantages
Saline solution	2L saline	150-250 ml pre-filter	100-250 ml/hr pre-filter	Visual check	No anticoagulant used	Poor filter patency
Heparin	2L saline 2,500-10,000 U	5-10 U/kg	3-12 U/kg/hr	ACT 200-250; PTT 1.5-2 times normal	Standard method; easy to use; inexpensive	Bleeding risk; thrombocytopenia
LMW heparin	2L saline	40 mg	10-40 mg/ 6 hr	Factor Xa levels; maintained between 0.1-0.41 U/ml	Decreased risk of bleeding	Special monitoring; not available everywhere; expensive
Regional heparin	2,500 U/2L saline	5-10 U/kg	3-12 U/kg/hr; + protamine post-filter	PTT; post-filter ACT 200-250	Reduced bleeding risk	Complex; risk of thrombocytopenia; protamine effects; hypotension
Regional citrate	2L saline	4 % trisodium citrate 150-180 ml/hr	100-180 ml/hr 3-7 % of BFR, Ca replaced by central line	ACT: 200-250 maintain ionized calcium .96-1.2 mmol/L	No bleeding; no thrombocytopenia; improved filter efficacy, longevity	Complex; needs Ca monitoring; alkalosis
Prostacyclin	2L saline + heparin	Heparin 2-4 U/kg 4-8 ng/kg/min	4-8 ng/kg/min	ACT, PTT, platelet aggregation	Reduced heparinization	Needs heparin addition; hypotension
Nafomostat mesilate	2L saline	–	0.1 mg/kg/hr	ACT	No heparin	New procedure? filter efficacy

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with 2 L of saline containing 2.400 U heparin. After a bolus of 5-10 U/kg, heparin is infused pre-filter at 3-12 U/kg/hr to maintain activated clotting times (ACT) between 200-250 seconds (normal 150-170 secs) post-filter. This results in minimal changes in systemic PTT with no apparent reduction in filter longevity[6]. In neonates Ronco et al.[19] used a loading dose of 100 u/kg and maintained a continuous infusion at 5-7 u/kg/hr. Post-filter ACT's simplify monitoring and correlate with PTT determinations. We found that reduced BFRs were more often associated with filter clotting if post-filter ACT's were much below 200 seconds.

Major side effects of heparin are excessive bleeding (up to 30 %)[20], thrombocytopenia and allergic reactions. In our series of over 1,000 hours of heparin anticoagulated CAVHD in 11 patients, serious bleeding occurred in 3[21]. If complications occur, heparin can sometimes be continued in markedly reduced doses. Usually, however, non-heparin anticoagulation must be considered especially when thrombocytopenia develops[22]. An important sign of heparin associated antibodies is progressively increasing doses of heparin required to maintain adequate PTT associated with decreased platelet counts.

Table II*. Recommended heparin dose in CAVH-D patients with different bleeding risks

Group	Initial dose (IU/kg)	Continuous dose (IU/kg)/h)	Time (PTT)
I: Low risk	50	10-20	2x norm
II: Moderate risk	15-25	10	10-15 sec > normal
III: High risk	10	5-8	< upper norm

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Low molecular weight (LMW) heparin

The usual preparations of heparin have several fractions with different molecular weights ranging from 4,000-50,000. Heparin's inhibiting effect on thrombin (measur-

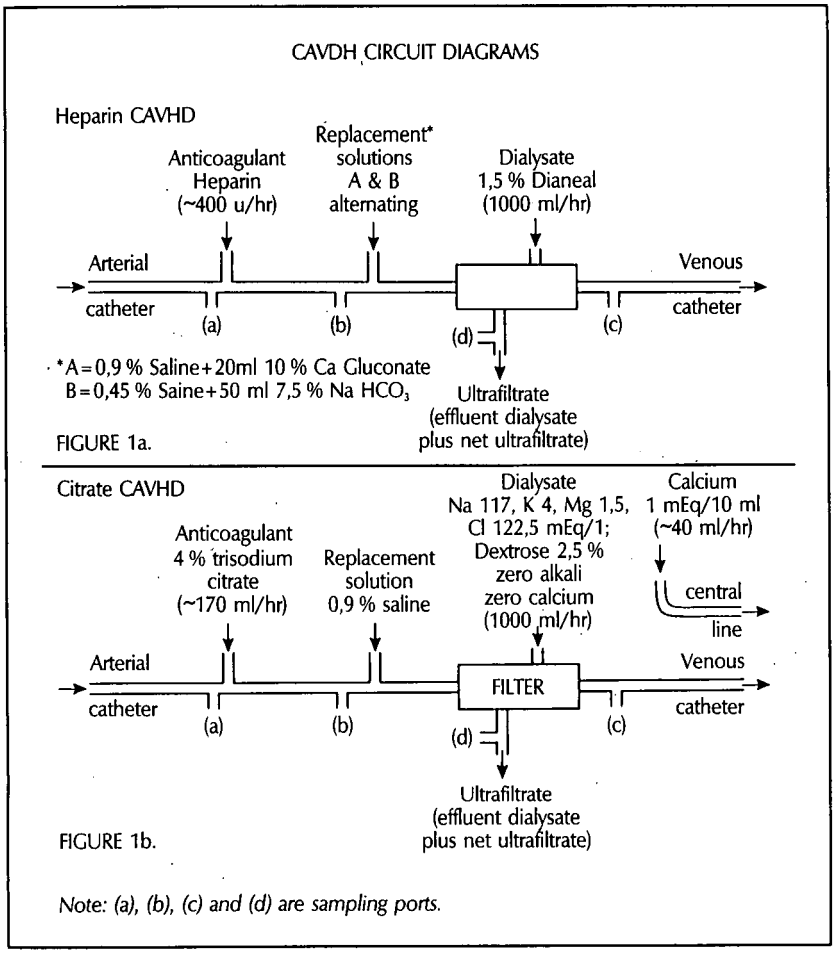

Fig. 1.—CAVH-D circuit diagrams. Comparison of circuit diagrams for heparin CAVH-D (a) and citrate CAVD-D (b). Sampling ports are marked (a) peripheral, (b) pre-filter, (c) post-filter, and (d) ultrafiltrate. (Reprinted with permission of Springer-Verlag, Kidney Int, *38:976-981, 1990.)*

ed by PTT) decreases with decreasing molecular weight, while Factor Xa (FXa) inhibition increases. Heparin's antithrombotic activity depends on FXa inhibition while it is the anti-thrombin effect (increased PTT) that is associated with enhanced bleeding risk; low molecular weight heparin should improve the ratio between desirable antithrombotic effects and undesirable bleeding risk. This supposition led to separation by fractionation of low molecular weight (LMW) heparin (4,000 to 7,000 daltons).

When LMW heparin was tested in conventional dialysis patients, it decreased complication rates[23-25] but experiences with LMWH as an anticoagulant in continuous therapy are few to date. Hory et al.[26] treated two ARF patients with CAVH and LMW heparin (Fraxiparin®). The resulting anti-FXa activity indicated a sucessful antithrombotic effect.

Wynckel et al.[27] used enoxaparin in seven ARF patients treated with slow continuous hemodialysis (pump driven) for 26-120 hours. A 40 mg initial dose was followed by intermittent infusions of 10-40 mg every 4-6 hours. There were no bleeding episodes of thrombocytopenia; one episode of thrombosis occurred due to technical reasons. Recently Lorenzini et al.[28] reported two cases treated with CAVH utilizing enoxaparin and found that a continuous infusion of 0.4-0.6 mg/kg/day was required to prevent filter clotting however, found a minimal correlation between FXa levels and anticoagulation efficiency.

The half-life of LMW heparin is approximately twice that of unfractionated heparin. Effectiveness is monitored by a chromogenic test to measure anti-FXa activity. The anti-FXa level should lie between 0.2 and 0.3 (or 0.4) IU/ml for patients with bleeding risk, and between 0.5 and 1.0 IU/ml for patients without bleeding risk[25]. Neutralization of LMW heparin by protamine is reduced. Since PTT and thrombin times are not elevated, the PTT test is not useful. More recently Swars et al.[29] have described the utility of measuring PMN-elastase as an indicator of anticoagulation status and found that it correlates better to inhibition of thrombin than FXa levels in acute dialysis.

LMW heparin may have a role in continuous renal replacement therapy, but so far the reported experience in continuous dialysis is insufficient. The reduced neutraliza-

tion by protamine may present problems. In addition, few facilities able to monitor anti-Xa levels. Also, dose recommendations of LMW heparin vary, depending on the manufacturer; their products are not interchangeable[23,24].

Regional heparinization and neutralization with protamine

Protamine is an antithromboplastin with an anticoagulative effect in high doses[30]. Heparin's anticoagulative effect can be neutralized by the basic protein protamine (protamine sulfate) with 90-114 USP units of heparin inactivated by 1 mg protamine (Lilly). In regional heparinization, heparin is infused pre-filter and neutralized by protamine administered post-filter to limit anticoagulation to the extracorporeal circuit.

Kaplan and Petrillo treated ten ARF patients with CAVH and regional heparin neutralization with protamine[31]. Seven patients had preexisting coagulopathies (PTT > 43 or platelets < 50,000). After heparinization, the blood in the filter displayed an elevated PTT (>150 seconds) but systemic values did not differ significantly from pre-treatment values. Nevertheless, hemorrhaging was reported in two patients. While Kaplan[31] found regional heparinization to be a simple and easily monitored method it has not been extensively used because of potential side effects and the requirement for meticulous dosage adjustment. Kim et al.[32] have described a unique method of immobilizing protamine in a cellulosic hollow fiber filter thereby reducing the hemodynamic and thrombocytopenic effects of protamine while effectively removing heparin from the circuit. This method will still require further development but seems promising. Regional heparinization is an alternative means of anticoagulation but one that requires careful monitoring.

No anticoagulation

Intermittent hemodialysis without anticoagulants using saline flushes has been successfully used with dialyzer patency maintained for the duration of therapy[33,34]. Experience with anticoagulant-free non-pumped continuous therapy has been controversial. Kaplan et al.[3] dispensed with heparinization completely in CAVH patients with preexisting platelet counts of <100,000 platelets/mm^3 and elevated PTT. With predilution, filter function could be maintained for up to 58 hours without anticoagulation. Geronemus et al.[18] found that filters clot within 24 hours, and we reported similar results a median filter life of 16 hours for filters maintained with saline flushes[8]. Smith et al.[35] studied the characteristics of 15 patients treated with no anticoagulation over a period of one year. Sixty-eight percent of these patients had platelet counts less than 80,000, or a prothrombin time >18 secs. Mean time to filter clotting was 17.6 hr for SCUF while patients with CAVH averaged 70.1 hr. Fluid replacement, infusion of packed cells, plasma platelets, or pressor therapy did not have any impacto of clotting. Twenty-eight percent of all filters clotted in the first 24 hours; 26 % within 48 hours; 22 % after 48 hours; and 24 % did not clot at all. It is difficult to establish from this data whether decreased filter efficacy was taken as a parameter for clotting, as this can occur prior to actual clotting of the circuit. Recently Bellomo et al.* carried out a randomized trial of no anticoagulation versus low dose heparin (500 IU/hr) in CAVHD in patients utilizing femoral catheters with evidence of endogenous coagulopathies or at high risk of bleeding, and found no significant differences in filter longevity which were more than 48 hours in each group. It is difficult to attribute the improved filter longevity to variations in the patient population as Smith[35] and Bellomo* did not find any significant differences in the prior anticoagulation status of these patients. These data needs to be confirmed at other centers. Given the results obtained by these investigators, it is probably worthwhile to attempt saline flush as sole anticoagulant in patients who are actively bleeding, or with coagulopathy if alternate methods to heparin are not available. However, in this setting, saline flush of 50-100 ml/hr administered pre-filter are required and need to be considered in the volume load. Saline flushes are best used with CAVHD at a dialysate flow rate of 2 liters/hour to maximize solute clearance during filter patency.

Regional citrate

Citrate is an anticoagulant by virtue of its ability to chelate calcium. The anticoagulant effect is overwhelmed and neutralized when citrated blood from the extracorporeal circuit returns and mixes with central venous blood. Citrate has been used for conventional hemodialysis[36,37], but not previously for CAVHD.

Our method for using citrate anticoagulation in CAVHD[8] is depicted in Figure 1b. Four percent trisodium citrate solution is infused pre-filter at approximately 3-7 % of blood flow rate, initially 170 ml/hr (range 100-200 ml/hr). Citrate flow rate is adjusted to maintain post-filter ACT at 200-250 seconds. Ten percent $CaCl_2$ is given in a separate line to replace chelated, dialyzed calcium. The dialysis solution has a sodium concentration of 117/meq/L, and is calcium, and alkali-free; it is infused at a flow rate of 1 L/hr. The hyponatremic dialysate allows removal of the sodium load imposed by the trisodium citrate. Effective removal of both free and complex citrate occurs across the filter[9]. Hourly ultrafiltration rates (UFR) are maintained between 400-800 ml/hr with the desired fluid balance attained by infusing 0,9 % saline as replacement fluid pre-filter.

* Personal communication from R. Bellomo, 1991.

Table III. CAVHD at UCSD (December 88-December 90)

Group	Anticoagulant method and filter patency			
	Number of patients	Total hours of CAVHD	Total numbers of filters used	Average life of filters, hours (mean SEM)*
All	45	6,445	114*	56.5 ± 4.7
Heparin	14	1,152	29	39.7 ± 5.4
Citrate	31	5,293	86	61.5 ± 4.9

* ANOVA heparin vs. citrate: p = 0.03.
* 1 filter used with heparin anticoagulation and then converted to citrate anticoagulation.

In our comparison of citrate (31 patients) versus heparin (14 patients) anticoagulation in CAVH-D for more than 6,000 hours of continuous theraphy (Table III), we found citrate group had significantly higher UFRs and urea clearances than the heparin group (mean 19.9 ml/min vs. 22.7 ml/min for urea clearance). Both groups had adequate anticoagulation as evidenced by ACT and PTT determinations. The mean filter life for the citrate group (61.5 hrs) was superior to that with heparin (39.7 hrs, p = 0.03). When all filters were considered, 72 hr patency was 40 % for citrate vs. 25 % for heparin filters.

Three (30 %) heparinized patients had serious bleeding and one developed heparin-induced thrombocytopenia. No bleeding or thrombocytopenia occurred with citrate. The major problems with citrate were transient metabolic alkalosis which developed in six patients (26 %) four of whom had hepatic insufficiency. This was easily corrected by infusion of 0.2 M HCl through a central vein. Peripheral ionized calcium levels ranged between 0.84 to 1.24 mmol/L (normal 1.1-1.32 mmol/L) in most patients and no patient developed symptomatic hypocalcemia or evidence of ECG changes or myocardial depression. Citrate allows adequate anticoagulation for CAVH-D and the procedure is well tolerated by most patients, including those with hepatic insufficiency who metabolize citrate despite significant deterioration in liver function. The trade-offs of citrate vs. heparin are increased complexity of the citrate procedure and higher risk of metabolic alkalosis in patients. This citrate anticoagulation protocol should also be applicable to pumped sustems, such as CWHD.

Prostacyclin (PGI_2) analogues

A metabolite of arachidonic acid, PGI_2 inhibits aggregation and adhesion of platelets by increasing platelet cyclic-AMP levels via an increase in adenylate cyclase activity[38]. Thus, contact with non-endothelial surfaces (e.g. dialysismembranes) does not result in degranulation and subsequent platelet aggregation. PGI_2 has a relaxing effect on the vascular musculature, it's half-life is 2 minutes, however, it's antiaggregating effect lasts for 2 hours[1,38].

PGI_2 has been used as an anticoagulant in chronic hemodialysis patients[38,39], but information on prostacyclin and its analogues in continuous therapy is limited. Zobel et al.[40] treated 6 children with high bleeding risk with CAVH, and combined low dose heparin (2.5-5 IU/kg/hr) and heparin (4-8 ng/kg/min) for anticoagulation. Urea clearance after 24 hours was higher and filter life was longer than in patients treated with heparin alone. Bleeding, thrombosis or hypotension did not occur. Stevens et al.[41] similarly used a combination of heparin and prostacyclin for anticoagulation in CAVHD.

Journois et al.[42] combined PGI_2 and LMW heparin in 42 CWH treatments and found that the combinated enhanced filter longevity by 55 % compared to that with standard heparin. Brierely and Hutchinson[43] have successfully used the prostacyclin anallogue Iloprost to prolong filter life in patients on heparin anticoagulated CAVHD. Ponikvar[44] used prostacyclin as a sole anticoagulant in 7 patients for 630 hours of CWH at a dose of 5 ng/kg/min and observed no alteration in hemodynamic stability however, lifespan of hemofilters was 30 % shorter.

Prostacyclin appears to be a possible alternative to heparin in pumped systems, but is likely to be more expensive. For CAVH and CAVHD, most centers have used prostacyclin in combination with heparin. Prostacyclin administration can be monitored by measuring the ADP-stimulated platelet aggregation. The procedure must be calibrated individually for each patient, complicating the monitoring for intensive care patients. Limitations for this method are the potential risk of hypotension and lack of a specific antagonist. If preliminary results from Ota et al.[45] regarding a prostacyclin derivative without hypotensive side effects are confirmed, the major argument against routine application of PGI_2 in CAVH procedures would be eliminated.

Nafomostat mesilate

Serine proteinase inhibitors such as gabexate mesilate have been used to reduce the risk of bleeding in hemodialysis patients[46]. This agent was found to reduced trans-

fusion requirements in high risk patients as compared to heparin. Nafomostat mesilate is a similar proteinase inhibitor with a molecular weight of 540 which has anticoagulative properties by virtue of its inhibition of thrombin, factor Xa and factor XIIa. Ohtake et al.[47] described its use in CAVH and CAVHD. They administered it in a dose of 0.1 mg/kg/hr and found a good correlation between this dose and elevation of the ACT levels. They reported a bleeding incidence as high as 67 % in heparin anticoagulation, 29 % for low molecular weight heparin and 5 % for nafomostat mesilate. Although it appears that there is a reduction in bleeding, filter patency duration and filter efficacy parameters were not described. At the present time this method has limited utility, because of the limited availability, cost and lack of data.

Monitoring of anticoagulation in continuous renal replacement

Adequacy of anticoagulation should be monitored by continuous evaluation of the circuit and filter patency. Some signs of clotting include: 1) a sustained (>3 hr) reduction in the volume of ultrafiltrate to less than 150-200 ml/hr not attributable to changes in hemodynamic status; 2) an alteration in the ratio of fluid urea nitrogen (FUN) to blood urea nitrogen (BUN) of <0.6 (under optimal operating conditions this should equal 1)[13]; and 3) coolness and darkening of the arterial and venous lines; d) separation of serum from cells in the blood lines.

Periodic monitoring of the post-filter ACT or PTT is necessary to assess anticoagulation efficacy. We routinely use the post-filter ACT's to adjust anticoagulation dosing and also check the FUN/BUN ratio every 12 hours, changing the filter if this ratio is below 0.6. In this setting it is possible to use the filter for a few more hours but efficacy is markedly reduced. Early recognition of filter dysfunction is thus an important consideration. Data regarding filter patency and longevity are not uniformly available. This is largely due to lack of a standard approach to assess filter patency. Filters are usually changed for one of the following reasons: a) clotted filter with evidence of line clotting; b) decreased filter efficacy; c) change of access; d) elective change; and e) discontinuation due to patients death. We usually change electively after 96 hours particularly to allow rotation of femoral arterial access when possible. This minimizes risk of infection and vascular damage. If access sites are limited it is prudent to maintain filters as long as possible provided efficacy is not impaired. Ideally filters should remain patent for more than 96 hours and there should be no decrease in efficiency during this period.

Future directions

Although there are several methods currently available for anticoagulation in continuous therapies no single method is as yet ideal. Current areas of active research are in the development of non-thrombogenic surface[48-50] with different methods of membrane preparation. Recently Arakawa et al.[51] have described a method using a polyacrylonitrile-polyethyleneoxide membrane interfaced with an ionically heparin bound catheter, tubing and module header. They have termed this system antithrombogenic continuous ultrafiltration system (ACUS). Initial results in 2 patients allowed hemofiltration without systemic heparinization for 44 hours however, further trial in seven patients with multiple organ failure had a mean filter duration of 19.2 hours[52]. Whether this technique will prove beneficial will need to be determined in clinical trials, however it is a step in the right direction wherein the goal is to have non-thrombogenic membranes which are also biocompatible and eliminated the need for any anticoagulation.

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